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**Title:** Assessment Of Pain Point Density On Physically Unimpaired People With A View To Clinical Application

**Poster Number** PTH001

**Authors**
Y. Takemura, K. Shiraki, T. Daikoku, T. Fukui, M. Yamazaki

University of Toyama, Toyama, Japan

**Aim of Investigation**
Since pain recognized in patients is subjective and so difficult to be evaluated objectively, there are many difficulties, including the evaluation of the strength and range of pain in some medical fields. Moreover, in the 'Herpes Zoster Model' mice, it has been confirmed that, with progression of the skin lesion, a number of peripheral nerve endings increased in the lesion penumbra, meanwhile decreasing within the lesion itself. It was predicted that there would be some changes concerning the pain point density on the skin lesions. However, the systematic pain point distribution of Homo sapiens is not yet known. Therefore, we tried to get basic data of pain point density on physically unimpaired people using the pain point density assay; which is widely and frequently performed on students using an algometer for neurological medical examinations in Japan. And, based on the distribution, we analyzed features of the pain concerning anesthesia and pain clinic fields.

**Results**
As a result of having checked the distribution of pain points in the thoracic and lumbar spinal cord domains, we recognized that there was a difference in the pitch of the pain point density among parts. The pain point density in the paramedian area of the spinous process line was significantly higher than in the median area (p<0.001). In addition, we classified the run of the intercostal nerve area into three parts: the front domain, the side domain and the back domain. The pain point density in both the front
and side domains were significantly higher than in the back domain (p<0.001). Our findings suggest that the best area for injecting local anesthetics in spinal or epidural anesthesia with the minimum amount of discomfort for patients is the median area. These findings can also provide useful information for evaluating the strength and range of acute and chronic pains such as the Herpes Zoster.

**Conclusion**
In this study, we analyzed the distribution of pain points in the thoracic and lumbar spinal cord domains of physically unimpaired people. This data concerning pain point density can become useful information when used in anesthesia and pain clinic fields.
Title: Validation Of Physiological Parameters For Pain Assessment In Nonverbal Adults With Intensive Care

Poster Number PTH003

Authors
N. Hsiung

Tzu Chi University of Science and Technology, Hualien, Taiwan

Aim of Investigation
This paper is to examine the discriminant validity of physiological parameters to document pain presence for critically ill adults unable to self-report. Recommendations and guidelines of pain management suggested that the pain assessment routine should always begin with an attempt from the health caregiver to obtain the patient’s self-report for pain intensity (Prkachin et al. 2007, Barr et al. 2013). Despite this, pain assessment still remains challenge for most patients due to the difficulty for precisely assessing the pain. Valid assessment tools are required for effective pain assessment in nonverbal communicated patients (NVCPs), such as infants and preverbal toddlers, or critically ill/unconscious patients (Cade 2008). Because the autonomic nervous system may be active during an acute painful event, physiological parameters could be considered as cue of the presence of discomfort (Kehlet 2006). Studies found that physiological parameters in critically ill patients and health subjects are either not consistent with patient’s self-report of pain (Payen et al. 2001, Young et al. 2006, Gélinas and Johnston 2007, Arbour and Gélinas 2010, Arbour et al. 2014). Given that little research has supported the validity of physiological parameters for assessment, research is urgently needed to extend and refine the validation of physiological parameters for the purpose of detecting pain in this specific ICU group.

Results
A total of 237 NVCPs from 9 ICUs of 5 hospitals participated in this study. The majority of NVCPs (n=164, 69.2%) were male and had a mean age of 66 years old (SD=15.9) ranged from 25 to 95 years. NVCPs were receiving infusions of analgesic and sedative medications as part of standardized ICU management protocols. For the three testing periods, all or most every patients were on a fentanyl infusion. These physiological parameters’ fluctuations were found to be significant in all three testing points for MAP, SBP, DBP, HR, and RR. Overall, when NVCPs were at rest pre-procedure, they had lower baseline values for MAP, SBP, DBP, HR, and RR compared with then they received non-painful and painful procedures.
Post hoc paired t-tests allowed identification of when their physiological parameters changed significantly over time. Over all, MAP, SBP, DBP, HR, and RR significantly increased during the painful procedure. A pair-samples t-test determined that the increase of mean MAP, SBP, DBP, HR, and RR similar during assessment periods at rest and the non-painful procedures' points at p≥ 0.01. Statistically significant fluctuations in MAP (t=10.48; p< 0.01), SBP (t=11.59; p< 0.01), DBP (t=13.49; p< 0.01) HR (t=13.10; p< 0.01), and RR (t=6.26; p< 0.01) were found across assessments between at rest and the painful procedure.

**Conclusion**

Our study findings support discriminant validation of the use of MAP, SBP, DBP, HR, and RR for pain assessment in NVCPs with critically illness. Results from this study seem to reverse the clinical recommendations of the ASPMN (Herr et al. 2011), Gélinas and Johnston (2007), Arbour and Gélinas (2010), and Arbour et al. (2014) studies in which vital signs are not considered as valid indicators for pain assessment. However, these previous little studies had only been completed with a small and homogeneous patient group. This study was conducted in different ICUs adult groups and with large sample size. The results from this study should be more powerful to address the study question. However, this study only examined the discriminant validation of physiological parameters for assessing NVCPs’ pain intensity. To date, the capillary saturation (SpO2) and the end-tidal CO2 have been examined in two studies with critically ill adults (Arbour & Gélinas 2010, Arbour et al. 2014). Future research is needed to further explore the validation of more physiological parameters for documenting pain presence. Also, the changes in vital signs seem to be associated with the self-report of pain in critically ill adults (Gélinas & Johnston 2007, Arbour & Gélinas 2010, and Arbour et al. 2014). Considering the lack of criterion validation of vital signs for pain detection, further research is warranted to support its validity in ICU patients with their self-report. Knowing this, the nurse should use physiological parameters with caution when evaluating a patient’s pain even if those indicators are easily accessible by monitoring in the ICU. So far, according to available evidence-based knowledge in pain assessment, the nurse should rely on valid behavioral pain scales developed for critically ill adults when they can no longer self-report to detect the presence of pain.
Title: Image-Guided Epidural Blood Patch Done In Patients With Post-Dural Puncture Headache After Labor Epidural Analgesia: Case Series Of Three Patients

Poster Number PTH004

Authors
S. Khan, S. ElMasry, U. Alzoraigi, A. alshoaiby

King Fahad Medical City, Riyadh, Saudi Arabia, KING FAHAD MEDICAL CITY, RIYADH, Saudi Arabia

Aim of Investigation
To summarize the benefit of use of image guidance in performing Epidural blood patch (EBP) in patients who complained of severe headache due to accidental dural puncture sustained while receiving epidural analgesia for labor.

Results
All three patients had uneventful EBP course under image guidance. All three patients had immediate relief of headache within few hours and were discharged home in ambulatory condition the following day without any residual symptoms of headache.

Conclusion
Image guidance has added benefit of confirming needle location and preventing further dural puncture in performing epidural blood patch in patients with post dural puncture headache who had accidental dural puncture sustained while having labor epidural analgesia.
Title: Benchmarking And Improvement Of Postoperative Pain Assessment And Management At The University College Hospital, Ibadan Nigeria: Report Of A Pilot Iasp/Pain-Out Study

Poster Number PTH005

Authors
O. Olawoye, S. Ademola, O. Iyun, A. Michael, O. Oluwatosin, O. Soyanwo, R. Zaslansky

University College Hospital, Ibadan, Ibadann, Nigeria, University College Hospital, Ibadan, Ibadan, Nigeria, University College Hospital, Ibadan, Ibadan, Nigeria, University College Hospital, Ibadan, Nigeria, Hospice and Palliative Care Unit, Ibadan, Nigeria, Jena University Hospital, Berlin, Germany

Aim of Investigation
The aim of the research was to test the feasibility of using a Plan-Do-Study-Act cycle to improve management of post-surgical pain at the University College Hospital, Ibadan Nigeria. The project was carried out in the context of pilot lead by International Association for the Study of Pain's post-operative pain management improvement project: The project was led by the International Pain Registry and Developing Countries Working Groups assessing feasibility of using methods of quality improvement in Low Resource countries to improve management of pain.

Results
Data was collected from a total of 56 patients, 18 patients for Baseline phase and 38 patients for post-intervention phase. Analyses of the data indicated a minimal reduction in the mean worst pain intensity from 6.33 (SD 2.24) in the baseline data to 6.29 (SD 2.32) in the post intervention data. Similarly, there was a marginal reduction in the mean least pain score from 3.55 (SD 2.05) in the baseline data to 3.42 (SD 2.07) in the post intervention data. These differences were however not statistically significant. The Mann-Whitney test of the PROs showed no change in the patient’s perception of care between the pre and post intervention phases. Regarding the non-pharmacological methods of pain relief, prayer was the most commonly employed method by 93.3% and 94.7% of the respondents pre and post intervention respectively

Conclusion
This pilot study provides some insights to the modality for post-operative pain management at a tertiary health institution in a developing country. The information provides opportunities to discuss options for
change. However, there was limited data at this point to carry out extensive analysis so a larger study involving more wards will be useful.
**Title:** Estimating Risk Of Chronic Pain: A Clinical Prediction Model ("Pickup Tool") For Patients With Acute Low-Back Pain

**Poster Number** PTH006

**Authors**
A. Traeger, N. Henschke, M. Huebscher, C. Williams, S. Kamper, C. Maher, L. Moseley, J. McAuley

Neuroscience Research Australia, Sydney, Australia, Prince of Wales Clinical School, University of New South Wales, Sydney, Australia, Institute of Public Health, University of Heidelberg, Heidelberg, Germany, Hunter Medical Research Institute, Newcastle, Australia, School of Medicine and Public Health, University of Newcastle, Newcastle, Australia, The George Institute for Global Health, Sydney, Australia, University of South Australia, Adelaide, Australia

**Aim of Investigation**
Most patients with acute low back pain (LBP) recover quickly with minimal or no intervention. Around 25% develop chronic LBP (pain for 3 months), which has a poor prognosis and is costly to manage. 'Treat all' approaches to prevent chronic LBP expose high numbers of low-risk patients to unnecessary intervention. A more efficient approach to preventing chronic LBP would be to stratify treatments and advice according to risk profile. The aim of this investigation was to develop and validate a prediction model that could help clinicians make an early estimate of a patient's risk of chronic LBP.

**Results**
Five questions were included in the final prognostic model: Q1 = How much low back pain have you had during the past week? (1-6 scale); Q2 = Do you have leg pain? (y/n); Q3 = Is your back pain compensable e.g. worker’s compensation or third party insurance? (y/n); Q4: How much have you been bothered by feeling depressed in the past week? (0-10 scale); Q5: In your view, how large is the risk that your current pain may become persistent? (0-10 scale). The 5-question model could discriminate between those who developed chronic LBP and those who did not with acceptable accuracy in the development sample (area under the receiver operator curve [AUC] 0.67 (95% confidence interval [CI], 0.64 to 0.70)). When tested in the external validation sample, the model had similar predictive performance (AUC 0.66 [95%CI 0.63 to 0.69]; positive likelihood ratio 2.99 [95%CI 2.81 to 3.18]), indicating acceptable generalisability. Although model calibration was acceptable in the external validation sample (intercept = -0.55, slope =0.89), some miscalibration was observed for higher risk groups. Using a decision curve
analysis, we estimated that if clinicians were to only treat patients with a 30% or greater risk of chronic LBP, this would lead to a net reduction of 40 unnecessary interventions per 100 patients without missing any patient who developed chronic LBP.

**Conclusion**
The 5-item PICKUP Tool can provide informative predictions of risk for chronic pain in patients with acute LBP presenting to primary care. Using the tool in clinical practice could reduce the number of unnecessary interventions provided to low-risk patients.
Aim of Investigation
Neuropeptide Tyrosine (NPY) is a 36-amino acid peptide which is widely distributed in the central and peripheral nervous system. It contributes to transmission of neuropathic pain in rodents. However, its role in the transmission of postoperative pain is not known. Management of postoperative pain in the clinics is suboptimal. Consequently, the present study correlated the expression of NPY in the dorsal root ganglia (DRG) and spinal cord of rats with postincisional pain.

Results
There was higher expression of NPY in small-sized neurons of the DRG and the spinal cord following plantar incision. In the spinal cord, maximum increase was observed in neurons of the Rexed's laminae I-II. Some increase was also noted in the ventral horn neurons.

Conclusion
The results show that NPY is associated with nociception in the hind paw incision model.
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Title: Review Of Peri-Operative Pain Management In Two Rwandan Teaching Hospitals

Poster Number PTH008

Authors
G. NYIRIGIRA, E. VanDenKerkhof, R. Wilson, D. Goldstein, T. Twagirumugabe, R. Mahaffey, J. Parlow, A. Johnson

Butare University Teaching Hospital, Butare, Rwanda, Queen's University, Kingston, ON, University of Rwanda, Butare, Rwanda

Aim of Investigation
Most studies examining postoperative pain care have been conducted in high resource countries, but there is a paucity of data from developing countries. The current study reviewed postoperative pain management practices, and barriers and facilitators to care among healthcare providers in Rwanda, with the aim to develop strategies to improve the provision of acute pain therapy.

Results
131 (93%) questionnaires were completed. The majority of participants were unit nurses (24%) and AT/NA (28%). 46% had training in acute pain and most training occurred during health professional education programs or in-services. 74% always or often used validated pain scales, and unit nurses (77%) used them most often, followed by PACU/ICU nurses (62%), AT/NA (50%) and physicians (50%). The majority reported that tramadol (78%), morphine (79%) and paracetamol (75%) were used most often to treat pain. 65% reported that morphine was the preferred drug. 56% always or often used a pain protocol, and unit nurses (71%) used them most often, followed by PACU/ICU nurses (54%), AT/NA (53%), and physicians (35%). Availability of drugs was the most frequently cited barrier to treating pain. There were statistically significant differences across disciplines in the preferred drugs to treat uncontrolled pain and in the limitations to providing acute pain care. Overall, intent to treat postoperative pain was high (5.7/7.0). After controlling for specialty/discipline only attitudes about assessing postoperative pain and perceived control (self efficacy) were associated with the intent to treat pain.

Conclusion
All disciplines reported high intent to treat postoperative pain; however further validation of the TPB is required to address potential cultural and language factors specific to the Rwandan context. Several
systemic and knowledge barriers exist, including availability of certain medications, use of practice protocols, and adopting evidence-based approaches to assessing and treating pain. Interventions to address barriers and facilitators may lead to improved postoperative pain care.
Title: Psychophysical Analyses Approach To A Pain Behavioral Scale

Poster Number PTH009

Authors
J. de Jesus, R. Tristão

Area of Medicine for Children and Adolescent, University of Brasília, Brazil, Brasilia, Brazil

Aim of Investigation
The Neonatal Facial Coding System (NFCS) is a one-dimensional pain assessment tool developed to evaluate the response to painful event in term newborns. It's composed by 10 subscores based on the presence of the following responses: brow bulge, eye squeeze, naso-labial furrow, open lips, vertical mouth stretch, horizontal mouth, taught tongue, tongue protrusion, chin quiver and lip purse. Increase of its score during painful event is related to activation of the central nervous system and denotes pain.

The aim of this study was to evaluate whether the psychophysical parameters of intensity, reactivity and regulation are achieved in pain assessment on newborns using the NFCS total score and its subscores.

Results
Overall NFCS and all its subscores of facial action met the psychophysical parameters of intensity and reactivity (p < 0.01). Overall NFCS and the majority of its subscores of facial action met the psychophysical parameter of regulation after 1 minute of the heel prick, except tongue protrusion and chin quiver (p >0.05). The heart rate variation indicator did not meet any parameter (all p > 0.05). Two minutes after heel prick, only the tongue protrusion of all subscores and overall NFCS don't meet the regulation parameter (p > 0.05).

Conclusion
It was concluded that the overall NFCS and the majority of its subscores meet the assumptions of the psychophysical parameters of a physiological measurement, being the tongue protrusion and the chin quiver those which less fit to this model.
Title: Multi-Modal Pain Management For Ophthalmic Cataract Surgeries

Poster Number PTH010

Authors
p. doctor, T. DOCTOR

Akshi Eye Hospital, Gandhinagar, GUJARAT, B.J.MEDICAL COLLEGE, AHMEDABAD, GUJARAT, INDIA, Gandhinagar, Gujarat, GUJARAT

Aim of Investigation
To evaluate the need of analgesic in the post ophthalmic surgeries To evaluate the efficacy of Topical analgesia

Results
Out of 50 patients, anxiety related issues were noted in only 5% of patient, normally believed that 'It happens' for the eye pain. Hemodynamics were stable in most of the patients. Intra operative only 5%-6% required the supplementation of local block to prevent eye movement and relieve anxiety with increasing the comfort level and counseling. All the patients were advocated analgesics on first day in form of NSAIDs or simple analgesics. Counseling had effect on requirement of analgesics. It was found to be more consumed in such patients (5-6%). Total 44 patients required pain medication for mild to moderate pain control post surgery. 15/50 patients required analgesic on first 24hrs twice for pain control. 20/50 required only analgesic once in 24hrs and rest required analgesic

Conclusion
Topical anaesthesia is best for ophthalmic surgery considering the associated general co existing conditions. Pre operative counseling helps in reducing the requirement of analgesic in intra and post operative period since patient gives the best possible co operation. Local blocks in very fussy/anxious patients helps in reducing the analgesic requirement. limitations ; Eye movements can not be controlled completely. Patient may under or over rate the pain. Difficult judgement; interpretation problems. advantages: reduces the cost of hospitalization; less drugs required; early pain free period; early discharge; early ambulation; effective communication reduces the anxiety and affects the doses/requirement of pain medication especially in elderly patient.
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Title: Harpagophytum (Devil'S Claw Root) Decreases Postoperative Pain And Opioids Requirements In Patients Undergoing Inguinal Hernia Surgery

Poster Number PTH011

Authors
S. Golzari, D. Aghamohammadi

Tabriz University of Medical Sciences, Tabriz, Iran

Aim of Investigation
Since it's difficult to control pain after operations and lack of other studies in this field, we determined to study the effects of Harpagophytom on reducing pain in inguinal hernia surgeries and the effects of it on the rate if using opioids and non-opioid drugs. In this study we studied on 60 candidate patients in two groups of A and B.

Results
Group B: No pills used for this group but all the patients were physically resembled. After complete soberness pain rate recorded by VAS and dose of anti-pain drug. All the patients were male and their age medium were 19.39+-49.54. youngest patient was 18 and the eldest one was 89. 75% of patients used opioid drugs in the first 8 hours after surgery and 16.7% of them used non-opioid drugs. In both groups VAS rate was recorded between 2 and 8 hours after operation.

Conclusion
It seems to be the effects of Telotenal480mg in decreasing pain and reducing the rate of using opioids in patients of inguinal hernia surgery is effective. Also this drug is herbal and less side effects of herbal drugs are proven.
Aim of Investigation
Multidisciplinary treatment for chronic low back pain (LBP) is recommended. However, it has been difficult to confirm the efficacy, because chronic LBP is complex, heterogeneous medical conditions that include wide variety of social environment. The aim of present study was to identify the predictors achieving good outcome in patients with chronic LBP by analyzing the associations between pretreatment parameters and one-year outcome with multidisciplinary treatment.

Results
Pretreatment scores of VAS, PDAS, and affective subscale of SF-MPQ, and the number of nonorganic pain-drawings, male, pain to just touching in the good outcome group were tendency to be lower than those in the poor outcome group. Binary logistic regression analysis showed that pretreatment lower score of PDAS was the only independent factor for identifying patients in the good outcome group.

Conclusion
Pretreatment scores of PDAS is an effective predictor resulting in better condition for the patients with chronic LBP through one-year multidisciplinary treatment.
Title: A New Method For Objective Evaluation Of Nociceptive And Tactile Disorders In Patients With Chronic Kidney Disease Using Focused Ultrasound

Poster Number PTH013

Authors
D. Belinskaya, N. Shestakova, E. Shchekanov, N. Vanchakova, E. Tsirulnikov

Sechenov Institute of Evolutionary Physiology and Biochemistry, Saint Petersburg, Russian, Pavlov First Saint Petersburg State Medical University, Saint Petersburg, Russian

Aim of Investigation
More than half of patients with chronic kidney disease suffer from chronic pain and pruritus of unknown etiology after 2 years of treatment with hemodialysis. Complex pharmacological and psychological correction is prescribed to such patients, the result of which is evaluated subjectively by visual analog scales for pain and itching. Previously, we showed that the patients with chronic kidney disease suffering from chronic pain and itching have increased thresholds of tactile and pain sensitivity compared to healthy patients. The aim of the presented study is to develop a method of the objective evaluation of patients status and treatment monitoring system.

Results
Latency of near threshold ultrasound stimuli for EEG deflection and tops of nystagmoid eye movements in healthy volunteers was about 500 ms. The patients under hemodialysis have higher thresholds of sensations, a longer latency and lesser amplitude of electrical activity and eye movements. The duration of pain around the threshold level correlated with the time of return of EEG and eye movement oscillations to the isoelectric level. For all patients and healthy volunteers, ECG, heart rate, respiration and blood oxygen saturation did not correlate with pain and tactile sensations triggered by FUS. The value of the thresholds and latency of tactile sensations and pain depend on neither the duration of hemodialysis treatment nor sex nor age of the examined patients.

Conclusion
The developed polygraphic method can be used for the objective evaluation of patients status and treatment monitoring system.
Title: The Proposed Classification Of Chronic Primary Pain For Icd-11

Poster Number PTH014

Authors
M. Nicholas, J. Vlaeyen, A. Barke, I. Task Force

Pain Management Research Institute, Sydney, NSW, Health Psychology, Leuven, Belgium, Philipps University Marburg, Marburg, Germany, IASP, Marburg, Germany

Aim of Investigation
Currently chronic pain syndromes are not represented in the International Classification of Diseases (ICD) in a systematic manner. Especially pain syndromes with multi- or unclear etiologies are not represented well. The International Association for the Study of Pain (IASP) has long campaigned for improvements in the classification system and an international Task Force of pain experts has developed a proposal for a systematic and pragmatic classification of chronic pain for the inclusion as a virtual chapter into the upcoming 11th revision of the ICD.

Results
In the proposed classification chronic pain has been pragmatically defined as pain that persists or recurs for more than 3 months. Chronic primary pain is chronic pain in one or more anatomical regions that is characterized by significant emotional distress and functional disability. Chronic primary pain is multi-: biological, psychological and social factors contribute to the pain syndrome. The diagnosis is appropriate independently of identified biological or psychological contributors unless another diagnosis would better account for the presenting symptoms. It is further subdivided into chronic widespread pain / fibromyalgia and more localized chronic pain syndromes. The term 'primary pain' was chosen in close liaison with the ICD-11 revision committee. 'Primary' also indicates the epidemiological relevance of this group of pain syndromes, and that pain is a primary problem by itself.

Conclusion
In the context of the overall classification proposal, several improvements can be expected. For the first time, the most frequent chronic pain syndromes will be represented as chronic primary pain in their own, phenomenological defined category in the ICD. The diagnosis overcomes the dichotomy between somatic and psychological aspects since it is appropriate independently of identified biological or psychological contributors unless another diagnosis would better account for the presenting symptoms.
Moreover, the definition takes into account distress and disability associated with the pain. Despite having been widely recognized and described, this association had so far not found its way into the classification. It is hoped that the better representation in the ICD will translate into improved pain relief and access to multimodal pain treatments for patients with chronic primary pain.
Title: Factors That Predict Treatment Efficacy In Neuropathic Pain Patients Undergoing Low-Dose Ketamine Infusion


Krembil Research Institute, Toronto, Ontario, Canada, University of Toronto, Toronto, Ontario, Canada, Toronto Western Hospital, Toronto, Ontario, Canada

Aim of Investigation
Neuropathic pain (NP) has a prevalence of ~7% (Bouhassira, et al., 2008) and is associated with many diseases and injuries that affect the nervous system. Conventional treatments for NP are often ineffective and many patients undergo an exhaustive trial-and-error approach to pain management. Recent evidence suggests that low dose infusions of ketamine can result in significant NP relief and is also an effective treatment for depression (Schoevers, et al., 2016). However, the adverse side effects associated with ketamine may negate the benefits of this treatment. We have recently developed a regimen for individualized titration of low dose infusions of ketamine to reduce these side effects. Nonetheless, approximately 50% of NP patients treated do not obtain significant pain relief. The factors that contribute to the analgesic effectiveness in some, but not in other patients, are unknown. Ketamine is an NMDA receptor antagonist that can reduce pain facilitation/temporal summation (TSP) (Graven-Nielsen, et al., 2000), and enhance pain inhibition/conditioned pain modulation (CPM) (Nieters, et al., 2013). Therefore, the aim of this study was to identify factors that predict ketamine treatment efficacy for NP patients. We hypothesized that ketamine treatment would be more efficacious for patients with high pre-treatment pain facilitation and/or low pain inhibition.

Results
The patients had pre-treatment pain ranging from 5-8/10 and most had clinical levels of depression and anxiety. Ketamine treatment resulted in: 1) clinically significant pain relief for more than half the patients, 2) reduced depression and PCS scores, and improved mental health scores in most patients, 3) reduced anxiety scores in half the patients, 4) little or no change in resilience scores. Furthermore, patient's pre and post-treatment TSP and CPM scores were within the range of healthy control scores (Patients pre: TSP range 0 to 20, CPM range -40 to 20; Patients post: TSP range 0 to 40, CPM range -40 to
15, Controls: TSP range -5 to 20 and CPM range -80 to 25). Pain relief following ketamine treatment was not predicted by pre-treatment depression, anxiety, PCS or resilience scores, or by TSP or CPM scores on their own. However, there was a statistical trend in predicting pain relief based on the pre-treatment balance between TSP and CPM.

**Conclusion**
Our initial findings suggest that the balance between pain facilitation and pain inhibition may predict ketamine treatment efficacy. This ongoing study is a first step in identifying features that predict pain relief following a slow infusion of ketamine in patients with NP.
Title: Limitations Of Self-Report In Chronic Pain: Validation Of A Measure Of Chronic Pain Resilience

Poster Number PTH016

Authors
J. Sturgeon, K. Cook, B. Darnall, A. Zautra, S. Mackey

Stanford University, Palo Alto, CA, Northwestern University, Chicago, IL, Arizona State University, Tempe, AZ

Aim of Investigation
The concept of resilient functioning in chronic pain has been defined in several ways, but typically involves examination of at least one of three processes: sustained positive functioning despite pain, effective recovery from pain and pain-related difficulties, and long-term growth or learning due to pain. The current study proposed to validate a measure of resilience in chronic pain using this theoretical model.

Results
Item responses had high internal consistency and convergent validity estimates. However, in several rounds of factor analyses and item response theory modeling, significant misfit was identified, regardless of how the underlying factor structure was specified. Of note, model fit appeared consistently worse for items related to long-term personal growth or learning related to one's chronic pain condition, compared to more immediate indices of current positive function despite pain. Similarly, there appeared to be significant differences in model fit between those participants who appeared resilient according to other measures (i.e., those participants reporting high pain intensity but low levels of depressive or anxious symptoms) and those that reported high degrees of both pain intensity and emotional distress.

Conclusion
Given the rigorous nature of the validation approach and subsequent statistical analysis, our results highlight the challenge of measuring resilience to chronic pain via self-report across a diverse population of individuals with chronic pain. Future research in this area should evaluate different approaches for quantifying resiliency. Alternative forms of assessment may yield more valid and reliable measures of chronic pain resilience. Candidate approaches include construction of resilient profiles of function from
more general aspects of self-report, observations by knowledgeable others, and use of differing time frames of assessment.
Title: Descriptive Characteristics Of Patients Prescribed Opioids For The Treatment Of Chronic Pain

Poster Number PTH017

Authors
J. Goesling, S. Moser, A. Hassett, C. Brummett

Department of Anesthesiology, University of Michigan, Ann Arbor, MI

Aim of Investigation
There is little empirical evidence supporting the use of long-term opioid therapy for chronic pain. Pain reduction, improved functioning, and quality of life are typically considered broad markers of therapeutic benefit; however studies continue to demonstrate that opioid users are worse off in all domains. In clinic settings, physicians must address the growing concerns about the role of opioid therapy for patients with chronic pain, while taking into account both the risks and benefits of opioids. One of the challenges faced by physicians is determining what to do with patients who were started on opioids for therapeutic use (i.e. pain relief) but who continue to use opioids even when benefit is not apparent. Few studies have considered opioid use from the perspective of the patient prescribed opioids for pain management. The primary aim of this study was to solicit information regarding opioid use from current opioid users with chronic pain.

Results
Of the 150 patients, 55.26% (N=84) reported current opioid use. Current opioid use was associated with a worse clinical phenotype, including higher pain severity (t(137) = -3.75, p < 0.001), worse physical functioning (t(131) = 3.13, p = 0.002), and more symptoms of depression (t(136) = 1.98, p = 0.050) compared to patients not taking opioids. For patients taking opioids, the majority reported taking Hydrocodone/Norco (41%) and 62% reported their opioids were prescribed by a primary care physician. Additionally, 78% of patients reported opioid use for 3 months or longer. With regards to helpfulness, 39% of patients reported an hour or less of pain relief after taking an opioid, the average pain relief was 4.98 (SD=2.41), improvement in functioning was 4.41 (SD=2.88) and the average helpfulness rating of opioids in the past month was 2.32 (SD=1.12). Patients also reported low confidence in their ability to manage pain without opioids (M=3.52, SD=3.57) but report interest in learning alternative coping strategies for managing pain without opioids (M=8.56, SD=2.61).
Conclusion
These data question the benefits of long term opioid use. The data from this study also highlight important target areas for helping patients not benefiting from opioids taper off opioids. For instance, patients report low confidence in their ability to manage pain without opioids. Importantly, the majority of patients report interest in learning alternative strategies for managing their pain. Our long-term goal is to use patient centered data to inform the development of an intervention to help patients not benefiting from opioids taper off this medication and provide non-opioid interventions for pain management.
Title: Real-World Evidence Of Multimodal Spinal Cord Stimulation Clinical Outcomes: A Prospective Global Registry Study

Poster Number PTH018

Authors

Boston Scientific Corporation, Valencia, CA, Piedmont Comprehensive Pain Management Group, Anderson, SC, Spine Team Texas, Rockwall, TX, The Center for Clinical Research, Winston-Salem, NC, Northwestern University Medical Center, Chicago, IL, Ohio State University Wexner Medical Center, Columbus, OH, Carolinas Pain Institute, Winston-Salem, NC

Aim of Investigation
Different treatment modalities in Spinal Cord Stimulation (SCS) are now available including standard rate stimulation, 1 khz, 10 khz, burst, anode intensification, Multiple Independent Current Control (MICC), etc. On the other hand, identification and analysis of clinically-relevant patient sub-populations using these different modalities, via mining large datasets ('Big Data') of real word evidence (RWE) and implementation of advanced analytics, have not yet been conducted. We report here the largest SCS study of its kind designed to investigate real-world, 'multimodal' SCS which collects data consisting of a variety of measures of pain control, quality of life, and patient satisfaction from different cohorts utilizing a range of waveforms and paradigms.

Results
Analyzed subjects used a large number of programs/waveforms from 0-30 days post-implant (10-11 programs) but stabilize by 6 months post-implant (2-3 programs). Most subjects utilized the standard SCS waveform (62.6%) compared to others (1k, anode intensification, burst). Seventy-two percent of subjects utilized multimodal SCS versus single mode (28%). Of these, approximately 90% of subjects use at least 2 modes (~10% use 3 or more) with most using a combination of 1 kilohertz and standard rate programs (29%).

Conclusion
This study collects and analyzes a large dataset of RWE. Subjects have so far been found to use multiple...
modalities/waveforms long-term, using a variety of options at different times each day. This initial observation underscores the clinical-relevance of a single device capable of multimodal SCS.
Title: Whisper: A Prospective Multicenter Trial Evaluating The Use Of Subperception Scs At ≤ 1.2 Khz

Poster Number PTH019

Authors
J. North, D. Campbell, N. Mekel-Bobrov
Carolinas Pain Institute, Winston-Salem, NC, Boston Scientific Corporation, Valencia, CA

Aim of Investigation
Spinal Cord Stimulation (SCS) has relied on understanding that dorsal column stimulation-induced paresthesia must be generated around an area of pain to achieve pain relief. However, studies suggest that effective pain relief may be obtained by employing stimulation without paresthesia (1). These studies have focused on high rate (~10kHz) and burst stimulation programs. However, concerns have been voiced regarding potential for significant charging burden and decreased time before IPG replacement due to frequent recharging (2, 3). Exploratory research on subperception SCS (SPSCS) at ≤1.2kHz suggests that effective pain relief can be achieved at lower rates with appropriate patient selection.

Results
The accompanying report provides details of the study design, demographics, and other preliminary data from the study. The study is currently ongoing.

Conclusion
This study will report the outcomes in subjects with chronic pain of the trunk and/or limbs when using a spinal cord stimulator (SCS) system at subperception amplitude with commercially available parameters. This is particularly relevant in those who prefer no paresthesia with use of their SCS system while receiving effective pain control.
Title: New Procedure To Evaluate The Pain Behavior In Experimental Model With Neuropathic Pain: Validation Of 3D Kinematic Analysis As A Measure Of Neuropathic Pain In Rats

Poster Number PTH020

Authors
T. Seto, T. Kanchiku, H. Suzuki, T. Taguchi

yamaguchi university, Ube city, Japan, Dept of Orthopedics Surgery, Yamaguchi Univ., Graduate school of medicine, Ube, Japan, Dept of Orthopedics Surg., Yamaguchi Univ. Graduate school of medicine, Ube city, Japan

Aim of Investigation
The Kinema-tracer system (Kissei Comtec, Nagano, Japan) is a three dimensional kinematic analysis tool for detecting alterations in gait. It may also be capable of detecting minor changes in neurological function. Here, we evaluated neurological outcomes following sciatic nerve injury using the Kinema-tracer system. We used this system to detect neurological changes between spinal nerve ligation (SNL) and sham treated animals, as well as differences in various parameters within these groups.

Results
Significant differences in step length and foot lifting time were observed in the SNL group at 7 and 14 days compared to sham. There were also significant differences in the amount of height shift in the knee and hip joints.

Conclusion
Neurological alterations were detected using the Kinema-tracer system analysis regardless of flexion reflex. This system could be a useful tool for monitoring changes in neuropathic pain and reflect pain behavior.
Title: Long-Term Opioid Use In Chronic Pain Patients In Sweden: An Observational Study Of Quality Of Life And Adverse Effects

Poster Number PTH021

Authors
H. Bergendahl, J. Persson
Karolinska University Hospital, Stockholm, Sverige

Aim of Investigation
The aim of this study was to collect long-term data on pain relief, treatment satisfaction, quality of life and adverse effects in patients treated with opioids according to standard practice by their physician, reflecting clinical practice in Sweden.

Results
The patients exhibiting low pain had an opioid dose of 179 mg/day (mean oral morphine equivalents). The medium pain patients a dose of 139 mg/day, and the high pain patients a dose of 121 mg/day. The most common adverse effects were fatigue (46%, 80%, 45%, low pain / medium pain / high pain groups respectively), dry mouth (41%/ 70%/ 35%), sexual dysfunction 13%/ 65%/ 50%), constipation (45%/ 58%/ 25%). A significant negative correlation with QoL ratings was observed for sexual dysfunction, pain intensity, fatigue and dizziness. A positive correlation with QoL was found for daily activity, physical activity and pain treatment satisfaction. Sexual dysfunction was the side effect most closely linked to QoL.

Conclusion
There was an inverse relationship between opioid dose and pain. The higher the opioid dose the patients had, the lower the VAS pain score. This might suggest that the patients in the two higher pain groups were under-treated. Somewhat surprisingly patients with medium pain scores had more symptoms indicative of opioid adverse effects than patients with low or high pain scores. Contrary to common perceptions, fatigue, dry mouth and sexual dysfunction were the most common adverse effects, in addition to constipation. Quality of life was most negatively affected by sexual dysfunction, followed by pain intensity, fatigue and dizziness. It was positively affected by daily activity, physical activity and pain treatment satisfaction.
Title: Ptsd In A Chronic Pain Sample: Prevalence, Clinical Characteristics, And Measurement With The Posttraumatic Diagnostic Scale (PDS)

Poster Number PTH022

Authors
S. Åkerblom, S. Perrin, M. Rivano-Fischer, L. McCracken

Lund University, Lund, Sweden, Skåne University Hospital, Lund, Sweden, King's College London, London, United Kingdom

Aim of Investigation
To validate a Swedish version of the Posttraumatic Diagnostic Scale (PDS); to examine the prevalence of traumatic experiences, trauma types and posttraumatic stress disorder (PTSD) in a sample of people with chronic pain seeking treatment from a specialist pain center in Southern Sweden; to examine how indices of pain-related functioning vary with a history of traumatic exposure and current PTSD.

Results
The translated version of the PDS showed high levels of internal consistency and a factor structure similar to that reported in previous validation studies. The majority of the study participants (71.8%) reported one or more traumatic events with 28.2 % fulfilling criteria for a current PTSD diagnosis. A wide range of traumatic events were reported. Significant mean differences were found between the three investigated groups using a MANOVA. A series of succeeding ANOVAs showed that the participants fulfilling criteria for PTSD reported significantly higher levels of anxiety, depression, pain interference and kinesiophobia as well as significantly lower levels of life control and pain-related acceptance compared to others who were traumatically exposed without fulfilling the criteria for PTSD and those with no trauma history.

Conclusion
In a large sample of people seeking treatment for chronic pain, a significant proportion was found to have a history of traumatic exposure as well as fulfilling criteria for PTSD prior to commencing treatment for pain. The presence of PTSD was associated with greater levels of interference from pain and lower levels of pain acceptance and other factors that have been previously shown to influence the effectiveness of treatments for chronic pain. The present results support routine screening for PTSD in chronic pain services and self-report measures like the PDS may be used for that purpose.
Title: Brachial Plexus Catheter Analgesia For Rehabilitation Of Upper Extremity In Patients With Spinal Cord Injury: Case Series Of Four Patients

Poster Number PTH023

Authors
S. Khan, U. ALZORAIGI, S. ELMASRY, T. ALZAHRANI

King Fahad Medical City, Riyadh, Saudi Arabia, KING FAHAD MEDICAL CITY, RIYADH, Saudi Arabia, KING SAUD UNIVERSITY, RIYADH, Saudi Arabia

Aim of Investigation
Spinal cord injury patients usually have weakness/paraplegia below the level of lesion. These patients have a long hospital course with rehabilitation directed towards functional restoration of upper extremity. The therapists work towards achieving this goal by different techniques. The ultimate goal is to help perform daily activities and self-care. Pain is most important hindrance in achieving this goal. We report this summarize the effectiveness of brachial plexus nerve catheter in reducing pain and aid in rehabilitation of upper extremity in patients with spinal cord injury.

Results
All four patients showed reduction of pain at two weeks of therapy. The therapist could attain good range of motion in the clenched fingers passively attaining full extension in all joints of the hand in all three patients. The patient with stiff elbow was able to allow passive movement with full range of motion in elbow joint without pain. All four patients had pain scores on Numeric Rating Scale (NRS) of less than 3/10.

Conclusion
Brachial plexus catheter can be used in providing analgesia in reducing pain while providing therapy to patients needing rehabilitation after spinal cord injury.
Title: Pain Scoring: What Is New In The 21St Century?

Poster Number PTH024

Authors
M. Ahmad Sabry, A. Desoky

Alexandria University., Alexandria, Egypt, The Claflin University, Department of Computer Science, Orangeburg, SC

Aim of Investigation
Pain scoring is still deficient even in the 21st century. As we still need better scoring system, I am proposing a new pain scoring system (SAT/Function pain score) that may be an addition for the evaluation of amount of pain and can make us evaluate our treatment effect on patient pain.

Results
The pain score, area and time is multiplied and number is used with the letter for the function attached to it. Minimum is 0/A (No pain patient work full time) and worse 24000/F (Pain all over the patient can’t care for himself) An electronic version that the patient can download to his phone or computer is under processing. The SAT/Function score is still patient dependent, needs patient educations more complex than other pain scoring systems and still in the validation process.

Conclusion
SAT/Function score with its electronic version is an addition to pain scoring systems that is available for use. Further studies are needed for better evaluation of its potentials.
Title: Nociceptive Reflex Receptive Fields Are Enlarged In Patients With Knee Osteoarthritis: Preliminary Results

Poster Number PTH025

Authors

Aalborg University, Aalborg, Denmark, Aalborg University Hospital, Aalborg, Danmark

Aim of Investigation
Chronic pain conditions are often associated with pain hypersensitivity, but the underlying mechanisms are not fully understood. A number of recent studies have identified enlarged reflex receptive fields (RRF) in patients with endometriosis, chronic low back pain and chronic neck pain patients, most likely associated with widespread central sensitization. The assessment of the RRF thus provides a new tool in the identification of possible mechanisms behind hypersensitivity states in pain patients. In line with this, the aim of the present study was to determine if patients suffering from severe knee osteoarthritis (OA) present enlarged RRF.

Results
Data from 6 patients and 3 healthy controls were discarded because reflexes could not be detected following any of the stimulations. RRF sensitivity areas were significantly enlarged in knee OA patients (median = 0.42, IQR = 0.43) compared to healthy controls (median = 0.16, IQR = 0.28; U = 107, p = 0.006). Additionally, RRF average probability was significantly higher in knee OA (mean = 0.51, SD = 0.25) compared to healthy controls (mean = 0.32, SD = 0.26; t40 = 2.310, p = 0.026).

Conclusion
These results provide evidence for expansion of RRF in knee OA patients compared to age- and gender-matched healthy controls, most likely as a result of widespread central sensitization.
Title: Demographic Characteristics And Clinical Practices Of Family Physicians Attended The Chronic Non-Cancer Pain (Cncp) Educational Workshop In Urban Area Of Pakistan

Poster Number PTH026

Authors
S. Lakha, P. Pennefather, F. Safdar, S. Zafar Siddiqui, M. Iqbal, A. Ahmad, S. Haider

University of Toronto, Toronto, ON, Foundation University Medical College, Karachi, Pakistan, Civil Hospital Karachi, Karachi, Pakistan, The Indus Hospital, Karachi, Pakistan, NAYS, Islamabad, Pakistan, Indus Hospital Karachi, Karachi, Pakistan

Aim of Investigation
To describe the demographic characteristics and clinical practices of family physicians, attended one of 5 educational workshop on CNCP in the province of Punjab, Pakistan over a 6 month period starting in September of 2013.

Results
In our study, the ratio of female to male family physicians was 0.8:1. More than half (54%) of participants and 80% of female participants were between 20 and 30 years of age. All were under 50 years of age. Of the 93 participants who reported their years of practice, only 2 women and 3 men reported practicing more than 10 years and 12 reported having no practice at the time. Only 93/145 participants (63%) reported receiving formal pain education. In terms of years of experience 16/40 (40%) female practitioners who reported having practiced for less than 5 years and 7/42 (16%) had no practice. While 22/58 (38%) of male practitioners participants had practiced for less than 5 years and only 5/58 (9%) had no practice. One third of all participants (32%) stated that they see more than 30 CNCP patients per week. In all cases, practitioners reported that women made up most of the CNCP patients treated.

Conclusion
This study represents an initial step in representing attributes describing the nature of clinical practices offered for CNCP management in the Punjab province of Pakistan. These preliminary results can guide development of a more comprehensive study conducted using randomly selected samples of family physicians throughout Punjab and other Pakistan provinces to determine capacity and need for CNCP management services. Opportunistic studies during educational workshops combined with regular
surveys of practitioners can help develop a better understanding of needs and opportunities for reducing burden of CNCP at the primary care level in Pakistan and other developing health systems.
Title: Psychosocial Predictors In The Transition From Acute To Chronic Pain: A Systematic Review

Poster Number PTH027

Authors
V. Hruschak

University of Pittsburgh, Pittsburgh, PA

Aim of Investigation
Chronic pain is a major health problem given its high prevalence rate, impact on individuals' quality of life, and economic costs within utilization of health care and social resources. There is growing evidence that suggest psychosocial factors play a vital role in chronicity. Given that there are limited studies which have thoroughly examined this subject, this systematic review investigated if psychosocial factors are predictors in the transition from acute to chronic pain.

Results
A total of 1389 studies were identified and 22 of which met inclusion criteria. Of these studies, 19 (86%) detected some effect of psychosocial prediction of chronicity with three (13%) studies failing to identify a causal relationship. Seven of the studies (32%) demonstrated that depression was predictive of the transition from acute to chronic pain, with five of the 14 (36%) studies examining depression in acute to subacute back pain. Fear avoidance was found to be predictive by six of the studies (27%) and five of which were examined again, in acute to subacute low back pain (36%).

Conclusion
This systematic review provides moderate support that psychosocial factors are predictive in the transition from acute to chronic pain. Further research is needed to determine what psychosocial predictors are most influential in which pain conditions. Implications of this review prove value in eliciting more aggressive prevention strategies in clinical practice and research.
**Title:** Family Function Is Associated With The Physical And Psychological Function Of Patients With Chronic Pain

**Poster Number** PTH028

**Authors**
K. Anno, M. Shibata, R. Iwaki, C. Hayaki, H. Kawata, N. Sudo, M. Hosoi

Kyushu University Hospital, Fukuoka, Japan, Kyushu University, Fukuoka, Japan

**Aim of Investigation**
Previous studies have reported that spouse responses to pain behaviors are associated with the pain-related outcomes of patients with chronic pain. However, the relationship between family function and chronic pain has been much less studied. We examined the relation of family function to the physical and psychological dysfunction of patients with chronic pain.

**Results**
For men, 'Communication' was significantly associated with pain disability and 'Affective Involvement' was significantly associated with depression. After controlling for pain catastrophizing, significance remained only in the former association. For women, 'Affective Involvement' was significantly associated with pain disability and depression. After controlling for pain catastrophizing, these associations were no longer significant.

**Conclusion**
The results demonstrate an association between the physical and psychological function of patients with chronic pain and some aspects of family function.
Title: Relationship Between Fear Of Movement And Health-Related Quality Of Life In Patients With Chronic Pain

Poster Number PTH029

Authors
P. Koho, H. Kautiainen, H. Hurri

Orton, Helsinki, Finland, University of Helsinki, Helsinki, Finland

Aim of Investigation
Chronic musculoskeletal pain relates to impaired health related quality of life (HRQoL), pain and disability. Patients with chronic pain report lower scores on several factors related to HRQoL compared to controls. Patients with chronic low back pain and patients with multiple pain localizations have reported decreased health related quality of life. Variables related to fear avoidance model (FAM) have demonstrated association to HRQoL. Depressive symptoms and pain catastrophizing have shown even stronger association with quality of life than pain intensity. High levels of fear avoidance beliefs relate to increased levels of disability. In particular, fear of movement is significantly associated with disability in chronic low back pain. However, there is lack of studies regarding relationship between HRQoL and fear of movement. Aim of the cross-sectional study was evaluate association between (HRQoL) and fear of movement among patients with chronic musculoskeletal pain.

Results
Sample consists altogether 637 (54% were women) chronic pain patients (pain over 3 months), mean (SD) age was 47.7 (7.7) yrs. Mean (SD) pain intensity was 68.9 (21.6). Men had higher (p<0.001) scores [mean (SD) 40.8 (8.0)] in the TSK-FIN compared to women [mean (SD) 36.2 (8.4)]. Cronbach's alpha for TSK-FIN was 0.82 (95% CI: 0.80 to 0.84). Mean (SD) Oswestry index was 34.5 (14.2). Only 2.7 % of the patients did not have any sick leave and 3.3% were retired. Age and sex adjusted correlations between TSK-FIN and all RAND36 scales were significant (p<0.001) after Sidak multiple adjustment. Role physical –scale had lowest correlation [-0.32 (95% CI -0.39 to -0.26)] and General health –scale had highest correlation [-0.47 (95% CI -0.53 to -0.40)]. Correlation between the TSK-FIN and physical component score (PCS) was [-0.36 (95% CI -0.30 to -0.43)] and with mental component score (MCS) [-0.39 (95% CI - 0.32 to -0.45)], respectively. Age and sex adjusted correlation between TSK-FIN and OSW was 0.49 (0.43 to 0.55) and correlation between TSK-FIN and VAS was 0.26 (0.18 to 0.34). Using best subsets variable
selection with Akaike’s information criterion the TSK-FIN items 1, 3 and 4 explained 16% of variance of the PCS. Respectively, items 3, 5, 6 and 15 explained 19% of variance of the MCS.

**Conclusion**
Among this sample of chronic musculoskeletal pain patients with high levels of pain and disability, fear of movement showed significant inverse association to all scales of HRQoL measured by RAND36. Further studies assessing relationship between fear of movement and HRQoL and the clinical significance of observation are warranted with larger set of FAM related variables.
Title: Pain Vision Apparatus Can Measure The Chronic Pain Objectively And May Assess The Correlation Between Environmental Parameters And Chronic Pain

Poster Number PTH030

Authors
K. Terayama, K. MIURA, M. Tsuchiya, T. Watanabe, H. Mitsuhata

Koto Hospital, Koto, Japan, Koto Hospital, Koto-Ku, Tokyo, Teikyo University, Tokyo, Itabashi-ku, Juntendo University Juntendo Tokyo Koto Geriatric Medical, Tokyo, JAPAN

Aim of Investigation
In clinical studies and clinical situation, pain assessment scale are most commonly used as the numerical rating scale (NRS) and the visual analogue scale (VAS) based on the subjective complaint by patients, however, it had a clinical problems because NRS and VAS are absence of objectivity. A newly developed device, Pain Vision PS-2100 has been used to measure the quantitatively determination of pain intensity. Pain vision calculated as the 'degree of pain' calculated from the current production of electrical threshold perception and the current production of a comparable pain sensation. In this study, we investigated to evaluate the efficacy of Pain Vision for the assessment of meteorological elements in chronic pain.

Results
We assessed 5 patients with chronic pain patient. There were not statistically correlation between weather parameters and the degree of pain (atmospheric pressure:$R^2 = -0.017$, $p= 0.47$, air humidity :$R^2 = -0.034,p=0.76$, temperature: $R^2 = -0.038,p<0.03$) nor NRS (atmospheric pressure:$R^2 = -0.002$, $p=0.34$, air humidity:$R^2 =0.146,p< 0.03$, temperature: $R^2 =0.062,p= 0.11$). In secondary outcomes, the degree of pain could not be showed a correlation with NRS at each time point ($R^2 = 0.288$, $p< 0.002$). Pain Vision was safe and did not produce significant complications. We could not find the correlations between the degree of pain and weather parameters.

Conclusion
It is reported that the atmospheric pressure participates in blood pressure and the pulse, and the possibility that a pain is reinforced is thereby guessed. This is the first report evaluating the influence of meteorological elements for a chronic pain using Pain Vision. However, there was no any statistically significant correlation between weather parameters and the degree of pain calculated using Pain Vision.
Further studies with larger sample sizes need to be conducted to confirm the results.

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Aim of Investigation
The strong association between joint hypermobility and comorbid conditions, particularly chronic pain and panic/anxiety disorders, has implications for illness progression and overall patient outcomes. This study aims to raise the need for awareness of the presence of comorbid conditions with joint hypermobility syndrome and the subsequent implications for diagnosis and intervention. Practitioners' awareness of hypermobility syndrome and comorbid medical and psychiatric conditions with patients presenting with chronic pain problems, the most common complaint of patients presenting with joint hypermobility, are surveyed to highlight the current awareness of comorbidities in joint hypermobility. The implications of this awareness for diagnosis and intervention are discussed.

Results
Results will be qualitatively analysed in terms of our null hypothesis: Clinicians are familiar with the association of joint laxity and associated conditions, particularly anxiety, and routinely screen for these and make considerations for these within their treatment recommendations.

Conclusion
Although the association between joint hypermobility and anxiety disorders is strong, and has been well described within the literature, awareness of this association within research and clinical practice appears limited. We conclude that there is a need for a greater awareness of the association between joint laxity and associated conditions, particularly anxiety disorders and chronic pain, as this has implications for assessment and intervention. This awareness needs to occur within both musculoskeletal/physiatry and orthopaedic settings, as well first points of patient contact including general practice and mental health settings. This study aims to raise the need for awareness of the presence of comorbid conditions with joint hypermobility syndrome and the subsequent implications for
diagnosis and intervention, including the need for a multidisciplinary team approach to assessment and intervention.
Title: Sensitivity Of The Dn4 In Screening For Neuropathic Pain Syndromes

Poster Number PTH032

Authors

Queen’s University, Kingston, ON, Western University, London, ON, LW Stitt Statistical Services, London, Canada, Dalhousie University, Halifax, NS, Wasser Pain Management Centre, Toronto, ON, University of Ottawa, Ottawa, Ontario, University of Ottawa, Manotick, ON, Burnaby Hospital, Burnaby, BC, McGill University, Montreal, QC

Aim of Investigation
The sensitivity of the Douleur Neuropathique en 4 Questions (DN4) for screening for neuropathic pain in clinical populations ranges from 62%-100%. Sensitivity varies by underlying condition, but reports have been based on relatively small sample sizes. This study examined the sensitivity of the DN4 in a large clinic sample of individuals diagnosed with various forms of neuropathic pain. The specific objectives were to assess the sensitivity of the DN4; i) for specific neuropathic pain conditions, ii) in the presence and absence of demographic, psychological, clinical, and pain characteristics, and iii) for broad categories of neuropathic pain conditions while controlling for patient characteristics.

Results
The mean age of study participants was 53.5 years, 45.3% were male and 66.8% were married/common-law. The average pain intensity scale score of the four Brief Pain Inventory (BPI) pain intensity measures was 5.9 (SD=1.9) and the average BPI pain interference score (7 measures) was 6.0 (SD=2.4). The median duration of pain was 36 months. Eighty-three percent (n=652/789) screened positive on the DN4 (≥4/10). The sensitivity was highest for central neuropathic pain (92.5%, n=74/80) and symmetric polyneuropathies (92.1%, n=139/151), and lowest for trigeminal neuralgia (69.2%, n=36/52). After controlling for pain catastrophizing magnification, disability and age, the sensitivity of the DN4 remained significantly higher for individuals with symmetric polyneuropathies (RR=4.35 (95% CI 2.15, 8.81)) and central neuropathic pain (RR=3.76 (95% CI 1.56, 9.07)) compared to mononeuropathies (overall p value <0.001). Several pain-related and patient characteristics were associated with a positive screen on the DN4. Pain Catastrophizing Scale (PCS) scores were significantly higher in patients who screened positive compared to those who screened negative (mean (SD) of 25.3 (12.6) and 20.3 (11.9), respectively,
Disability was also higher with mean (SD) pain disability scale scores of 39.0 (16.2) for those who screened positive versus 32.1 (16.7) for those who screened negative (p<0.001). Similarly, significantly poorer health-related quality of life (SF12) physical and mental component scores were reported in those who screened positive compared to those who screened negative. Younger age was also associated with a positive screen (mean (SD) of 52.8y (13.9) vs. 56.8y (15.1), p=0.002).

**Conclusion**
The DN4 performed well overall, with a sensitivity of 82.6%. However, sensitivity varied by neuropathic pain syndrome. Clinical and demographic characteristics also affected the sensitivity of the DN4. Findings that a positive DN4 was associated with greater pain catastrophizing, disability and anxiety/depression are clinically relevant. This may be due to these patients having more severe disease, but a possible explanation may also be that these scales reflect magnification of sensory symptoms and findings. These results reaffirm the value of DN4 as a valid screening tool for most patients with central and peripheral neuropathic pain. Future research could examine how the DN4 could be further refined to improve its sensitivity for specific neuropathic pain conditions, such as trigeminal neuralgia.
Title: Improvement Of Body Image In Chronic Pain Patients After Multidisciplinary Group Treatment Program

Poster Number PTH033

Authors
Tokoha University, Hamamatsu, Japan, Multidisciplinary Pain Center Aichi Medical University, Nagakute, Japan, CARE, Nagoya University, Nagoya, Japan

Aim of Investigation
Complicated pathological conditions such as somatognosia and psychological factors are generally underlying in development and maintenance of chronic pain. We have confirmed the therapeutic effect of multidisciplinary group program based on cognitive behavioral therapy such for chronic pain patients. The aim of the present study was to investigate the factors associated in the outcome of chronic pain state from physical faculties.

Results
The range of motion of the lower trunk was not much change after the program. The range of displacement from midline was significantly smaller after the program (2.4 ± 1.7 °) than that of before the program (6.8 ± 2.1 °). In addition, the degree of pain perception change and the degree of displacement change from midline showed significant correlation.

Conclusion
These results showed that body image distortion in chronic low back pain patients was improved in correlation with the pain perception improvement after multidisciplinary group treatment program. It is suggested that assessment of body image may be one of the important factor to understanding chronic pain statement.
Aim of Investigation
There is a high prevalence of Chronic Pain within studied populations; coupled with more liberal prescribing attitudes towards opioids, there has been an increase in prescription opioid abuse. This is well documented in the United States where the use of prescription opioids exceeds street narcotics, however little data exists with regards to the chronic pain population in the United Kingdom. The authors sought to i) identify risk factors for opioid misuse in this study population ii) evaluate the role of the Prescription Opioid Misuse Index (POMI) alongside 'clinician intuition' when identifying patients at risk of opioid misuse.

Results
Uptake of tool 477 patients were seen over the 3-month period. 277 questionnaires were excluded. Of those with incomplete information (n = 144), 30.3% of patients were unaware that one of their medications contained a morphine preparation, and 12.5% of patients chose not to disclose any information. Clinician compliance with the project was 61%. Demographics and risk factors The study population was normally distributed with a mean age of 51.8 years (range of 18 - 88 years). The median ages for those identified as 'at risk of misuse' was 43 years with both the POMI and clinician tools. This was statistically significant. 65.5% of group seen by the chronic pain outpatient service were female (p < 0.05), however males scored consistently higher with both scoring systems (RR ≥ 1.45). 72.3% of 18 - 64 years age group were unemployed with increased incidences seen in both POMI opioid misuse group and the clinician red flag group (RR ≥ 2.11). 38.1% of study population were single (RR ≥ 1.49), 9.3% admitted to recreational drug use (RR ≥ 1.24) and 66.1% had a recognised mental health condition (RR ≥ 1.70). Study tools for recognition of opioid misuse 13.0% of the study population were identified by the clinician as having a concerning 'red flag'. These included suicidal ideation, multiple opioid prescriptions, escalating or high doses and illicit drug abuse. In comparison, 18.5% of patients had a POMI ≥ 2 presumed to correspond with opioid misuse. The positive POMI scores and 'clinician intuition'
correlated in 16.1% of patients, however 51.3% of those with a POMI ≥ 2 did not have a corresponding completed clinician tool.

**Conclusion**
The authors found significant increased risk associated with lower age, male sex, single marital status, unemployment, associated mental health conditions and the use of recreational drugs. This is consistent with other published material. There are many tools that have been developed to identify opioid misuse, but few have been validated in clinical practice. The POMI is short and user friendly with a patient uptake of 87.5%. It is reliant on patient responses, and the nature of the questions may allow those abusing medication to deliberately underscore. This may skew the results in favour of those misusing their medication due to poor pain control. By comparison, our 'clinician intuition' tool was only completed in 48.7% of the study population and had a wide variety of perceived 'red flags'. We would recommend the POMI for use in a Pain Clinic setting but that it should be combined with an additional tool to allow for more complete assessment of benefits and risks associated with the use of prescription opioids.
Title: Can The Sensory And Affective Dimensions Of Pain Be Selectively Modulated? A Systematic Review

Poster Number PTH035

Authors
K. Talbot, V. Madden, S. Jones, L. Moseley

University of South Australia, Adelaide, Australia, University of South Australia, Adelaide, South Australia, University of South Australia, Adelaide, SA

Aim of Investigation
Over the last century pain has been recognized to consist of not just a sensory dimension but an affective dimension as well. Studies suggest differential influences of the sensory (termed herein as pain's 'intensity') and affective (termed herein as pain's 'unpleasantness') dimensions on pain. This differential influence has prompted investigation into whether each dimension can modulated selectively. Some studies report a selective modulation, but others argue that the modulation observed is merely bias. The aim of this systematic review was to identify and critically evaluate the available literature in order to determine the current state of evidence as to whether the sensory and affective dimensions of pain can be selectively modulated using cognitive manipulations.

Results
Of the initial 4270 articles (following duplicate removal) identified, we found 12 articles that met the inclusion criteria. The risk of bias revealed that all studies performed poorly in selection, performance and detection bias, or failed to provide sufficient data for risk of bias to be assessed. The main concerns in ROB for all studies were the selective recruitment, convenience sampling and failure to blind participants and/or researchers. From the included 12 studies, four cognitive manipulations were identified; hypnotic suggestion, suggestion alone, valence modulation using exteroceptive stimuli and mediation. Full subject-by-subject data were obtained for three studies. The mean difference (MD) and standard error (SE) for the four different modulatory directions are: [1] Increase pain intensity; suggestion alone- phasic pain (8.26 MD; 3.25 SE), suggestion alone- tonic pain (14.5 MD; 4.74 SE), hypnotic suggestion- high susceptible group (-0.05 MD, 0.28 SE), hypnotic suggestion- low susceptible group (0.67 MD; 0.46 SE); [2] Decrease pain intensity; hypnotic suggestion - high susceptible group (-0.45 MD, 0.29), hypnotic suggestion- low susceptible group (0.025 MD, 0.19 SE); [3] Increase pain unpleasantness; suggestion alone- phasic pain (11.80 MD, 4.61 SE), suggestion alone- tonic pain (14.36 MD, 3.57 SE), negative imagery-disaster (2.90 MD, 1.12 SE), negative imagery- model pain (1.35 MD,
1.20 SE), hypnotic suggestion- high susceptible group (-1.11 MD, 0.49 SE), hypnotic suggestion- low susceptible group (0.05 MD, 0.19 SE) [4] Decrease pain unpleasantness; hypnotic suggestion – high susceptible group (-0.45 MD, 0.29 SE), hypnotic suggestion- low susceptible group (0.02 MD, 0.19 SE).

**Conclusion**
The evidence strongly suggests that pain unpleasantness can probably be selectively modulated using cognitive manipulations, but pain intensity probably cannot. This finding highlights that despite apparent widespread support, several important questions regarding the separation of the unpleasantness and intensity of pain remain unanswered.
**Title:** The Effect Of Verbascoside In Neuropathic Pain Induced By Chronic Constriction Injury In Rats  

**Authors**  
B. Amin  
Department of Physiology and Pharmacology, Sabzevar University of Medical Sciences, sabzevar, Iran

**Aim of Investigation**  
We aimed to examined the potential effects of verbascoside in the chronic constriction injury (CCI) model of neuropathic pain in rats.

**Results**  
CCI rats exhibited a marked mechanical allodynia, cold allodynia, and thermal hyperalgesia on days 3, 5, 7, 10, and 14 post-CCI. A significant increase in the levels of Iba (a marker of microglia activation) and Bax (a proapoptotic factor) was observed on day 3. Iba remained high on day 7. In contrast, there were no differences in glial fibrillary acidic protein contents between sham and CCI animals. Malondialdehyde increased and reduced glutathione decreased on day 14. Verbascoside significantly attenuated behavioral changes associated with neuropathy. Bax decreased, while Bcl-2 was increased by verbascoside on day 3. Verbascoside also reduced Iba protein on days 3 and 7.

**Conclusion**  
The results support evidence that microglial activation, apoptotic factors, and oxidative stress may have a pivotal role in the neuropathic pain pathogenesis. It is suggested that antinociceptive effects elicited by verbascoside might be through the inhibition of microglia activation, apoptotic pathways, and antioxidant properties.
Title: Suppression Of Offset Analgesia As A Tool To Diagnose Chronic Pain

Poster Number PTH037

Authors
H. Kobinata, E. Ikeda, S. Zhang, T. Li, K. Makita, J. Kurata

Department of Anesthesiology, Tokyo Medical and Dental University Graduate School of Medical and Dental Sciences, Tokyo, Japan, Department of Anesthesiology and Pain Clinic, Tokyo Medical and Dental University Hospital of Medicine, Tokyo, Japan

Aim of Investigation
Offset analgesia (OA), a disproportionately large decrease of pain sensation on the slight decrement of thermal pain stimulus, is considered mediated by the descending pain inhibitory system, and was reported to be absent in patients with neuropathic pain. Here we examined whether such suppression of OA depends on the magnitude of pain sensitization; and whether it distinguishes chronic pain patients and healthy controls.

Results
The patients showed a significantly smaller ΔOA than the controls at T2 = 5 s (35.3 ± 5.1 vs. 61.8 ± 4.4; patients vs. controls; p = 0.001) and at T2 = 10 s (52.8 ± 6.4 vs. 70.5 ± 4.6; p = 0.04), but not at T2 = 15 s (62.5 ± 6.5 vs. 72.3 ± 4.0; p = 0.52). The patients showed a significantly longer maxVAS latency than the controls (16.4 ± 1.5 vs. 11.5 ± 0.6; p=0.004) but a comparable maxVAS (63.9 ± 4.6 vs. 59.3 ± 3.7; p = 0.56). The maxVAS latency was negatively correlated with ΔOA in the patients (R = 0.45). The OA index, at T2 = 5 s, showed a considerable diagnostic potency between the patients and controls at a cut-off point of 261.3 (sensitivity, 0.87; specificity, 0.75) with an area under the receiver operating characteristic curve being 0.892.

Conclusion
Chronic pain patients developed OA as well as healthy controls after a longer duration (T2 = 15 s) of pain sensitization. A slower build-up of thermal pain sensation was associated with a smaller OA, which implies that an attenuation of temporal sharpening in sensory perception might play a role in reduction of OA magnitude and a possible dysfunction of the descending inhibitory system in chronic pain patients. We propose that the OA index could be used as a diagnostic tool for chronic pain.
Title: The Proposed Classification Of Chronic Headache And Chronic Orofacial Pain For ICD-11

Poster Number: PTH038

Authors:
P. Svensson, R. Benoliel, S. Evers, S. Wang, A. Barke, I. Task Force

Orofacial Pain and Jaw Function, Aarhus University, Aarhus, Denmark, Rutgers School of Dental Medicine, Rutgers, The State University of NJ, Newark, NJ, N/A, Muenster, GERMANY, Taipei Veterans General Hospital, Taipei, Taiwan, Philipps University Marburg, Marburg, Germany, IASP, Marburg, Germany

Aim of Investigation
Currently chronic pain syndromes are not represented in the International Classification of Diseases (ICD) in a systematic manner. Owing to the work of the International Headache Society (IHS), a comprehensive list of headaches, and to a lesser extent of orofacial pain, is included in the neurology chapter of the ICD, but this is not part of a general strategy and rationale of classifying chronic pain. The International Association for the Study of Pain (IASP) has long campaigned for improvements in the classification system of chronic pain in general, and aimed to develop a proposal for a systematic and pragmatic classification of chronic pain for the inclusion as a virtual chapter into the upcoming 11th revision of the ICD.

Results
In the proposed classification chronic pain has been pragmatically defined as pain that persists or recurs for more than 3 months. Chronic headache and orofacial pain is defined as headaches or orofacial pains that occur on at least 50% of the days during at least 3 months. The chapter on chronic headache as well as on chronic orofacial pain will be subdivided into primary and secondary headache/orofacial pain. The former will be cross-referenced to the diagnoses of chronic primary pain.

Conclusion
In the context of the overall classification proposal, the classification proposed by the IHS will be recognized and preserved, but better integrated in a general chronic pain classification approach of ICD-11. The classification of chronic orofacial pain conditions will be much improved and be more detailed, which is expected to facilitate the provision of better treatments.
Title: The Relation Between Activities That Aggravate Symptoms Of Low-Back Pain With Structural Abnormality Of The Spine

Poster Number PTH039

Authors
D. Emril, N. Astini, E. Rahayuningsih, N. Lestari, A. Bakri
Neurology Department, Medical Faculty of Syiah Kuala University, Banda Aceh, Aceh, Neurology Department, Medical Faculty Syiah Kuala University, Banda Aceh, Aceh, Indonesia, Neurology Department, Medical Faculty Syiah Kuala University, Banda Aceh, Aceh, Indonesia

Aim of Investigation
The aim of this study was to determine the relationship between activities that aggravate the symptoms of low back pain with the structural abnormality of the spine.

Results
The results analysis found that the dominant symptoms of the patients with LBP is pain when standing (93.8%), sitting (70.1%), squats (93.8%), bending (57.7%), walking (92.8%), waking up (80.4%), sit to stand (83.5%), back extension (47.4%), and rotation (33.0%). There are significant relations between facet joint arthropathy with walking (p = 0.021), sit to stand (p = 0.039), extension (p = 0.011), as well as disc degeneration with walking (p = 0.007), spinal stenosis with bending (p = 0.014) and back extension (p = 0.024). In addition, there is no significant relationship between other activities with structural abnormality of the spine.

Conclusion
There is significant relationship between activities that aggravate the symptoms of low back pain with the structural abnormality of the spine.
Title: Beliefs, Opinions, And Attitudes Towards The Use Of Opioids: A Nationwide Study In The Spanish General Population

Poster Number PTH040

Authors
I. Failde, H. de Sola, A. Salazar, M. Dueñas, B. Ojeda, I. Sanchez-Magro

Prev. Med. and Public Health Area. Observatory of Pain, Grünenthal Fundation-University of Cadiz, Spain, Salus Infirorum Faculty of Nursing, University of Cadiz, Spain, Medical Department-Grünental Fundation, Spain

Aim of Investigation
Taking opioids is sometimes perceived by the general population as a sign of being in an extreme situation in their state of health. This has led to the concept of 'opiophobia'. The factors influencing this behaviour may differ across the countries. In this study, we were aiming to evaluate beliefs, opinions, and attitudes towards the use of opioids in the Spanish general population.

Results
50.7% of the sample were women, the average age was 50.4 (DT=15.9) years old and the majority had completed secondary education (45.9%) or university studies (28.1%). 8.9% of the subjects had been under a treatment with opioids in the past and 3.8% were under treatment at the moment of the interview. The term 'opioids' were associated mainly with terms like 'medicine', 'pain' and 'illegal drugs'. Morphine was the most recognized opioid (64.7%) followed by tramadol (14.2%). 72.9% of the subjects reported that opioids can produce somnolence and sedation, nausea (55.7%), nervousness (40.3%), and constipation (33.5%). Those interviewed agreed with the opinions that the opioids produce tolerance (62.9%), their prescription is associated with serious disease (42.6%), and it is used as the last treatment option (55.5%). However, only 30.3% reported that opioids are only for the terminally ill. In addition they fear the side effects (47.6%), addiction (35.6%) and death (27.1%) caused by these drugs. The majority would accept taking opioids if prescribed by a physician (86.3%), mainly due to the confidence transmitted by these professionals (64.4%) and the absence of other alternatives to treat pain (43.1%). The subjects who were moderately (OR=0.679), quite or very afraid (OR=0.359) of the side effects, and those who related the opioids with severe illness (OR=0.570), were more likely to reject a treatment with these drugs. Conversely, a greater knowledge of opioids (OR=1.384) was associated with a greater
acceptance to take opioids. Finally, neither the level of studies nor the level of contact with these drugs were associated with the acceptance of treatment.

**Conclusion**
This study revealed that some worries exist in the Spanish population regarding the acceptance of treatment with opioids, even in the case of severe pain. However, the study also demonstrated a greater acceptance of these drugs when the physicians conveyed appropriate drug-information and instilled confidence in the patients. As a result, a greater implication of the physicians regarding patient's education in relation to opioids acceptance seems necessary.
Title: Post-Herpetic Neuralgia: A Reflection From Pain Clinic, Hospital Kuala Lumpur

Poster Number PTH041

Authors
S. Kiung, E. Lim
Hospital Kuala Lumpur, Kuala Lumpur, Malaysia, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia

Aim of Investigation
Post herpetic neuralgia (PHN) is the commonest complications of herpes zoster. The characteristics of PHN in the Malaysian population is unknown.

Results
There were 17 patients with the mean age of 62.7 years, of which 71% were females. Presence of both diabetes and hypertension were seen in 35.3% and immunosuppression in 29.4%. Majority (70%) were referred from neuromedical and dermatology departments. The mean time to referral was 4.3 months. Thoracic dermatome (47.1%) was the commonest site affected followed by the fifth cranial nerve (35.3%). The mean pain score on presentation in pain clinic was 7.4 based on visual analogue scale of 0 to 10. Hyperalgesia and dysaesthesia were seen in 35%. Gabapentinoids and tramadol was the most prescribed analgesics. The mean pain score improved significantly from 7.4 pre-treatment to 3.8 (p<0.001) after an average treatment follow up of 12.3 months. At the end of follow up, 53% of them achieved a pain score of less than 3. The pain score at presentation was not affected by age, gender, presence of diabetes and dermatome affected (p>0.05). Use of non-pharmacological methods (physiotherapy and occupational therapy) did not contribute to significant pain score reduction (p = 0.83).

Conclusion
PHN is a very painful condition but can be effectively treated in specialized pain centre. At our institution, we conclude that age, gender, comorbidities and dermatomal distribution do not influence the pain severity.
Date: 09/29/2016 09:30:00 AM

Title: Aberrant Drug Behavior For Long-Term Opioid Therapy In Germany: Prevalence, Risk Factors, And Socioeconomic Consequences

Poster Number PTH042

Authors
T. Tölle, I. Gralow, K. Kern, N. Scherbaum, K. Weckbecker, W. Haeuser

Klinikum rechts der Isar, Munich, Germany, Klinik Und Poliklinik Fuer, Muenster, GERMANY, Institute of Pain Medicine, Wiesbaden, Hessen, University Medical Center Friedrich-Wilhelms-University, Bonn, Germany, University of Duisburg, Essen, Germany, Klinikum Saarbrücken, Saarbruecken, Germany

Aim of Investigation
On a nation-wide level, data on the prevalence and risk factors of aberrant drug behavior of long-term opioid therapy for non-cancer pain (LTOT) are largely unknown. Here, we present for the first time analysis representative for a general population of a country. This study investigates the prevalence of LTOT and risk indicators of abuse/addiction of prescribed opioids and compares patient characteristics as well as socioeconomic parameters of LTOT patients with and without a profile of prescription abuse risk

Results
The prevalence of LTOT for CNCP was 0.8% of all insureds. 25.9% of LTOT patients showed an increased risk for opioid abuse/addiction (defined by fulfillment of minimum one named risk indicator). The most common indicator was a high-dose therapy regimen (9.9%), followed by parallel prescription of tranquilizers (8.5%), doctor hopping (6.5%) and abuse/addiction-specific diagnoses (5.8%). Fulfilling one of these risk indicator was associated with younger age (in mean 69.9 years vs. 72.7 years), male gender (31.9% vs. 28.2%, Odds Ratio [OR]: 1.19), diagnoses of unspecific pain (63.0% vs. 49.6%, OR: 1.73), depression (45.3% vs. 32.5%, OR: 1.72), somatoform pain disorder (36.1% vs. 24.8%, OR: 1.71) and sleep disorder (27.0% vs. 16.3%, OR: 1.90). Patients with risk for opioid abuse/addiction also had a higher probability for hospitalization (44.6% vs. 38.3%, OR: 1.29) and higher annual overall costs for medical treatment (SHI perspective) with an average amount of 10,866.65€ (SD 9,223.15) vs. 7,851.28€ (11,930.17), especially resulting from higher expenses for pharmaceutical products.

Conclusion
This study is the first one which investigates the prevalence of LTOT in representative data sample of the
population. There was a strong association between increased risk for abuse/addiction of prescribed opioids with younger age and mental comorbidities. These observations will hopefully harmonize prescription behavior with risk factor adherence, and can serve as a decision maker to optimize prescription behavior in other countries, worldwide.
Title: Prevalence Of Chronic Pain In Dialysis, And Impact Of Pain On Sleep, Mood, And Activities Of Daily Living: A Point Prevalence Study Of 125 Patients On Dialysis From A Tertiary Institution In India

Poster Number PTH043

Authors
M. Menon, S. Tapiawala, A. Nair, J. Jith, N. Taha
Kokilaben Dhirubhai Ambani hospital and medical research centre, Mumbai, India

Aim of Investigation
To measure the prevalence of chronic pain in patients on dialysis To measure the impact quality of life in terms of insomnia, anxiety, depression, activities of daily living in these patients To measure associations between chronic pain and parameters like renal status, nutrition, comorbid illness etc

Results
Out of 125 patients, close to one third of the patients were in pain of scores greater than or equal to 4 on 10. Most of them were chronic pains, with the lower limbs being the most common site of pain. These patients were suffering from renal disease for longer and had been on dialysis for longer than the group with lower or no pain scores. As compared to the other patients, this group had a higher prevalence of insomnia, low mood and an adverse impact on activities of daily living. Preliminary data suggests an an association with renal parameters and poor nutritional status.

Conclusion
Chronic pain is an under-recognized problem in patients on dialysis. It appears to be myofascial, with a predominant lower limb distribution. It may be more in patients who have been suffering from renal disease or have been on dialysis longer. Morbidity in these patients extends to disturbed sleep, mood, anxiety and function. There may be an association between chronic pain and nutritional factors and renal parameters. More research is needed to treat this subgroup of renal patients.
Title: How Does Chronic Pain In Patients With Psychiatric Disorders Differ From Chronic Pain In A General Population Sample? A Pilot Study

Poster Number: PTH044

Authors
I. Løvås, S. Butler, A. Woodhouse, P. Borchgrevink

Tiller CMHC, St. Olav's University Hospital, Trondheim, Norway, Tiller, Norway, Uppsala University Hospital, Uppsala, Sweden, Norwegian University of Science and Technology (NTNU), Trondheim, NORWAY, National Competence Center for Complex Symptom Disorders, St. Olav’s University Hospital, Trondheim, Norway

Aim of Investigation
The co-existence of chronic pain in psychiatric disorders is known from clinical practice. However, classification and characteristics of these chronic pain problems are often less well described. The aim of this study was to perform clinical evaluations of outpatients at a Community Mental Health Centre (CMHC) with psychiatric disorders and chronic pain in order to classify the pain using ICD-10. A second aim was to assess if certain pain syndromes were more common in the psychiatric pain population. The reference population was a cohort of subjects with moderate to severe chronic pain assessed similarly in the HUNT Pain Examination Study – a general population survey of health and chronic pain in Mid-Norway. Since functional pain syndromes seemed overrepresented in the psychiatric population we compared the prevalence with the reference HUNT population. Functional pain syndromes assessed were chronic widespread pain (CWP) (ACR-1990 Criteria), fibromyalgia (FMS) (ACR-1990 Criteria), chronic headache and irritable bowel syndrome (IBS).

Results
Results from the structured clinical examinations are as follows: chronic widespread pain: 19/21 - 90.5% (30.6% in HUNT Pain Examination Study), fibromyalgia 12/21 - 57.1% (15.5% in HUNT Pain Examination Study), chronic headache: 17/21 - 81.0% (1.9% in HUNT Pain Examination Study). Irritable bowel syndrome: 11/21 - 52.4% (3.3% in HUNT Pain Examination Study). All 21 subjects reported 3 or more pain sites, 13 subjects reported pain intensity of their main pain problem as severe or very severe.

Conclusion
This pilot study was intended to identify pain characteristics in a population of patients attending an outpatient psychiatric clinic. Distinguishing features as compared to the reference cohort (the HUNT
Pain Examination Study) are the high prevalence of certain functional pain disorders. This is a unique finding. Resistance to treatment of psychiatric disease when comorbid pain exists is well known, identifying particular pain syndromes for concomitant treatment should improve psychiatric treatment outcomes. This study shows the importance of identifying specific pain syndromes, here being functional pain syndromes in populations with psychiatric disorders.
Title: Pain In France: Prevalence And Impact Across The Lifespan

Poster Number PTH045

Authors
Y. Hadjiat, J. Vietri

Laboratoire Mundipharma, Paris, France, Kantar Health, Horsham, PA

Aim of Investigation
To investigate the prevalence and impact of pain on adults in France according to age using patient reported outcomes in recent survey data.

Results
Pain was reported by 20.2% of the sample, and was more common in women than men (23.1 vs. 17.1%, p<0.01), with prevalence varying according to age (p<0.001). Pain was reported by 18% of those <35 years old, and increased to 23% and 24% among those aged 45-54 and 55-64, respectively, but reported by only 15% of those age 75 and older. PCS, MCS, and SF-6D scores were lower among those reporting pain across all age groups with the exception of MCS among those 75 and older (2.9 points, p=0.057). The magnitude of the decrement associated with pain varied with age, however, with mean PCS decrements 3.4 points among those <35 and as much as 8.1 among those 45-54, and then smaller among the elderly (5.4 points among those 75 and older). The magnitude of the associations between pain and MCS, SF-6D, and activity impairment followed a similar, although less dramatic pattern of smallest impact among those <35 years old, higher and fairly stable impairment in middle age, followed by a modest reduction in impact among those aged 75 and older. In contrast, this pattern was not observed in the number of healthcare visits.

Conclusion
Pain is commonly reported across adulthood, though may be most common during middle age, when it is associated with the largest impact on quality of life.
Title: Pain Is The Second Prevalent Reason To Seek Primary Medical Care In Israel: An Epidemiological Study

Poster Number PTH046

Authors
A. Mosek, S. Vinker

The Headache Clinic, Department of Neurology, Sourasky Medical Center, Tel Aviv, Israel, Dep. of Family Medicine, Sackler school of Medicine, Tel Aviv University, Tel Aviv, Israel, Tel Aviv, Israel

Aim of Investigation
To assess the prevalence of seeking pain consultation in primary care clinics.

Results
CHS insures more than 54% of the Israeli population. During 2014, 42,072,485 medical visits were documented. Of these, 36,056,911 visits were reported by primary care physicians and the rest were consultants. Most of other consultations were in the five specialties where direct consultations are allowed (ophthalmology, ENT, dermatology, gynecology and orthopedics). More than 17 million (48.8%) of primary care visits were administrative (prescriptions, laboratory referrals etc.); 18,445,954 records included a medical diagnosis, and the 100 most prevalent diagnoses (12,191,224 records, 66.1%) were analyzed. Upper respiratory infections were the most common reason for encounter (19.9%), followed by pain from various origins (14.6%); gastrointestinal causes (10.8%); infections (5.9%) and metabolic disorders (5.5%). The remaining records reflected various medical areas with <4% prevalence each. The pain records included 1,785,554 diagnoses, of which backache was far the most prevalent (49.4%). Headaches were diagnosed in 18.5%, pain in the limbs in 11.5%; cervicalgia in 8.7%; pain in the hip in 5.4%; pain in muscle in 3.8% and flank pain in 2.7%.

Conclusion
Pain was the second most common complaint for which patients were seeking primary medical care during 2014 in Israel. Back pain and headaches were the most prevalent complaints. Currently, there is a discrepancy between the high demand for pain consultations and insufficient trained pain physicians and training in pain management in primary care curriculum. With aging of the population the number of pain consultations is presumed to increase and these data show the necessity of a structural approach in preparing future medical services for dealing with pain.
Title: Association Of Comorbidity And Pain In Multiple Sclerosis Patients

Poster Number PTH047

Authors
A. Ivashynka, National Research and Clinical Center for Neurology & Neurosurgery, Minsk, Belarus, University of East Piedmont, Novara, Italy

Aim of Investigation
To examine the relationship between comorbidity and pain in multiple sclerosis (MS) patients. Comorbidities can affect the management of MS patients and reduce their quality of life. The increased prevalence of pain in MS patients is established; however little is known about how comorbidities influence these symptoms.

Results
Of 648 participants, most were female (69.2%), with a mean (SD) age of 44.6(9.4) years, and a relapsing-remitting course (69.3%). Most had ≥1 comorbidity (61.1%), 48.3% had pain and the mean (SD) DFIS score was 13.6(7.6). Pain that disrupts normal activities was more often reported by those with ≥1 comorbidity (64.1%) than by those without a comorbidity (25.4%; p< 0.05). Irritable bowel syndrome (odds ratio [OR] 1.93; 95%CI:1.11-3.12), rheumatoid arthritis (OR 2.92;95%CI:1.45-4.58), and fibromyalgia (OR 6.14;95%CI:2.21-14.32) were associated with more disruptive pain. Anxiety (regression coefficient: 3.27;95%CI:1.85-5.62), depression (3.95;95%CI:2.05-6.23), and fibromyalgia (4.22;95%CI:1.58-7.28), were associated, on average, with increased fatigue.

Conclusion
Pain are concerns for all persons with MS but more so for those with comorbidities. Closer examination of these associations may provide guidance for better management of these disabling symptoms in persons with MS.
Title: Changes In Work-Related Pain, Forward Head Posture, And Autonomic Nerve Activity Following Visual Display Terminal Work In Subjects With And Without Chronic Neck Pain

Poster Number PTH048

Authors

Tokai Memorial Hospital, Kasugai, Aichi, Japan, Nihon Fukushi University, Handa, Aichi, Japan, Nagoya Gakuin University, Seto, Aichi, Japan

Aim of Investigation
Chronic neck pain is a very common symptom in Japan. Chronic neck pain is regarded as a work-related pain because it can often be induced by improper head posture during desk job such as visual display terminal (VDT) work in office workers. It has been suggested that people complaining of chronic neck pain tend to move the head forward during VDT work. In our previous study, we reported the disturbance of sympathetic nerve activity that did not response to isometric exercises performed by subjects with chronic neck pain. However, the relationships among pain, forward head posture, and autonomic nervous system activity during VDT work are not clear. The aim of this study was to compare the changes in work-related pain, forward head posture, and sympathetic nerve activity following VDT work in healthy volunteers and subjects with chronic neck pain.

Results
There were no significant differences in age, height, and weight between the two groups. The VAS score significantly increased immediately after and 15 minutes after VDT work compared with that before work in the pain group. For postural alignment, flexion of the lower cervical and upper thoracic spine was observed during VDT work in both groups, and extension of the upper cervical spine was observed during and 15 minutes after work only in the pain group. The HF value significantly decreased during VDT work in both groups, and the LF/HF ratio increased in the control group during and immediately after work, but there were no changes in the LF/HF ratio in the pain group throughout the experiment.

Conclusion
This study showed that neck pain increased and continued following VDT work in people with chronic neck and shoulder pain. The results suggested that forward head posture, especially that which occurred
by extension of the upper cervical spine, and the disturbance of autonomic nervous system, particularly sympathetic nerve activity, help enhance and maintain dull pain and stiffness in the neck and shoulder.
Title: Chronic Pain Prevalence, Characteristics, And Disability: First Brazil Population-Based Nationwide Study

Poster Number PTH049

Authors

Hospital Universitário - Universidade Federal de Santa Catarina, Sao Paulo, Brazil, SBED - Sociedade Brasileira para o Estudo da Dor, Sao Paulo, Brazil, Aliviar-Medicina da Dor, Sao Paulo, Brasil, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil, CET Integrado da Faculdade de Medicina do ABC, Sao Paulo, Sao Paulo

Aim of Investigation
The prevalence and impact of chronic pain was a public health problem. In Brazil, a few studies reported prevalence of pain and none of those bring up a large profile of chronic pain throughout this continental country. Identify chronic pain prevalence among the 5 geographic regions of Brazil may help public and private organizations to develop and define some public health strategies. We aimed to assess the chronic pain prevalence in Brazil.

Results
Nine hundred and nineteen participants answer the interview, 42% report pain and 37% respondents live with pain more than 6 months long. We observed a trend of difference in the prevalence of chronic pain among Brazil (p = 0.05) with a prevalence of 24% in Midwest, 28% in Northeast, 36% North, 38% Southeast and 42% in South; and also a trend of difference between gender prevalence of chronic pain (p = 0.05) were North, Southeast and South had woman predominant prevalence, Midwest had half-half, in contras of Northeast had a man predominant prevalence. No difference on pain intensity assessed by VAS (6.6 +2.4; ANOVA p NS) neither pain descriptors. However, Southeast participants reported more frequently pain disability (ANOVA F = 4.96, p < 0.01) and highlight long periods with pain disability (ANOVA F = 6.01, p < 0.01) compared to other regions.

Conclusion
This was the first nationwide epidemiological study of pain in Brazil. We observed trends of higher prevalence of chronic pain in the South and the Southeast regions. Both regions that stand out in
population numbers and differ socioeconomically the North and Northeast regions. To better map the chronic pain in Brazil will need to increase the sample size to control its heterogeneity and geographical extent.
Title: Thirteen Thousand And Counting: Eppoc Data Is Not Just Numbers – It’S Real People And Real Pain: The Electronic Persistent Pain Outcome Collaboration Is Collecting Data At 37 Adult Pain Clinics In Australia And New Zealand, Providing Insights To Improve P

Poster Number PTH050

Authors
A. Daly, M. Blanchard, H. tardif

Austin Health, Heidelberg, VIC, Australia, The Health and Disability Strategy Group, The Transport Accident Commission and WorkSafe Victoria, Melbourne, VIC, Australia, Australian Pain Society, Sydney, NSW, Australia, Australian Health Services Research Institute, University of Wollongong, Wollongong, NSW

Aim of Investigation
ePPOC is a program which aims to improve services and outcomes for people experiencing chronic pain. It involves specialist pain services collecting a standard set of information to measure outcomes for their patients as a result of treatment. This poster aims to summarise the data collected in the first 30 months of ePPOC from July 2013 to December 2015, to provide a comprehensive view of Australians and New Zealanders presenting to pain services.

Results
By the end of the 30 months, 37 adult pain services had joined ePPOC and provided baseline data for 13446 clients. Females comprised 59%, with the average age of all clients 52 years. While around 75% were of working age, less than one in four identified themselves as currently working. The lumbar spine was the most common site of the main pain (43%) but the majority of clients (82%) recorded pain in more than one area, with the upper limb and shoulder (11%) and abdomen (9%) also common. While 22% reported an injury at work or school, 18% reported no obvious cause for their pain. Comorbidities were common, with only one in five clients not recording any. Depression and/or anxiety were the most common comorbidities (39%), followed by osteoarthritis (27%) and high blood pressure (23%). More than 50% of clients listed two or more comorbidities. The BMI of 37% of clients fell within the obese range. Around 50% of patients had experienced their pain for more than 5 years, rated it as severe and/or claimed it severely interfered with activities of daily living. 89% said their pain was always present. At the time of referral, a large proportion of patients were severely or very severely depressed (47%), anxious (41%) and stressed (39%). Pain-related cognition was impaired in many patients, with
one in two experiencing severe levels of pain catastrophising and low pain self-efficacy. Health service utilisation information revealed the equivalent of a weekly visit to a health care clinician in the three months prior to referral. On average, clients reported using 3 of the 6 major medication groups (paracetamol, NSAIDs, opioids, antidepressants, benzodiazepines, anticonvulsants) with 56% reporting they took opioids on more than 2 days per week. For these clients, the average morphine equivalent daily dose was 79 mg.

**Conclusion**
This rich data set, collected at referral or entry into a pain service, demonstrates the complexity, disability and distress of Australians and New Zealanders waiting in pain. ePPOC offers growing opportunities to observe, benchmark and improve the outcomes for Australians and New Zealanders who engage with pain services.
Title: The Relationship Between Ethnicity And Patient Participation Preferred Role In Analgesic Decision-Making: A Descriptive Study In Breast Cancer Patients In Malaysia

Poster Number PTH051

Authors
S. Japar, B. Gillespie, S. Kim Lam, L. Aitken

Universiti Putra Malaysia, Serdang, Malaysia, Griffith University, Gold Coast, Queensland, Universiti Putra Malaysia, Serdang, Selangor, Griffith University, Woolloongabba, Queensland

Aim of Investigation
This study aimed to determine the relationship between ethnicity and breast cancer patients' preferred role in analgesic decision-making.

Results
Characteristics of Participants Eighty women were recruited into this study. The majority of participants were Malay ethnicity (n = 56; 70%) followed by Chinese (n = 15; 19%) and Indian (n = 9; 11%). The predominant religion was Islam (n = 50; 71%) followed by Buddhist (n =12; 15%), Hinduism (n = 8; 10%) and Christianity (n =3; 4%). The age of participants ranged from 19 to 72 years old with a mean age of 53.0 years (SD =11.2 years). Nearly half of the participants (n =39; 49%) had upper secondary school education. More than 80% participants had family income less than RM4000 per month (n = 65). Patients' Participation in Analgesic Decision Making The results suggested that none of the participants preferred to use an 'active-active' role (Figure 1). The most preferred role selected by the participants was 'passive-passive' (n = 31; 39%) with more than half of the Chinese and Indian participants preferring the 'passive-passive' role (n = 9; 60% and n = 5; 56% respectively). Twenty-two participants (28%) preferred an 'active-collaborative' role. About 17% (n = 14) and 16% (n = 13) preferred the 'collaborative-passive' and 'passive-collaborative' roles, respectively. Relationship between Ethnicity and Patient Participation None of the participants chose an 'active-active' role, therefore the Chi-square analysis could not be performed in regard to that role. The Chi-square analysis revealed there was a significant relationship between Malays and the 'passive-passive' preferred role (p = .019). The result for the relationship between Chinese participants and the 'collaborative-passive' preferred role was p < .05; however, this result was not considered significant since the numbers were so small. There were no significant relationships between other Chinese and Indian participants and the CPS role. The details of these results are provided in Table 1.
Conclusion
Many participants in this study preferred the passive role in participating in analgesia decision-making. A significant relationship was found between Malay women and the passive role. However, no significant relationship was found between other ethnic groups and other preferred roles. The low level of education of many participants is likely to influence their preferred role of not being actively involved in analgesia decision-making. Education may promote a more active role among patients. As a routine component of clinical practice, adequate information on surgery, pain education, analgesia and pain management should be provided to patients. This information should be adapted to take into account the patients' level of understanding. An education process will promote two-way communication between patients and nurses, and encourage patients to raise questions, hence creating active involvement among patients. The information will encourage and empower patients to actively participate in their care management; so that effective post-operative pain management may be achieved.
**Title:** Teaching Nurses About Pain And Its Management Is A Fruitful Idea

**Poster Number** PTH052

**Authors**
N. Julien, A. Lacasse, J. Bernier

UQAT, Rouyn-Noranda, QC

**Aim of Investigation**
This study assessed whether a required undergraduate-level course on pain and its management improved knowledge about chronic non-cancer pain of registered nurses.

**Results**
A total of 64 students (26 in the experimental group and 38 in the control group) completed the pre- and post-test surveys. The participating students mean age was 32.02 ± 9.22 years (range: 20-54 years), they reported having 8.02 ± 7.82 years of clinical practice experience (range: 1-29 years), and they were almost all women (95.24%). These characteristics were similar between the two study groups (p>0.05). At the beginning of the semester, mean knowledge scores were comparable between groups (pain course group: 39.15 ± 4.84; control group: 36.97 ± 4.84, p>0.05). However, at the end of the semester, the pain course group knowledge scores improved significantly compared to the control group (average delta: 6.77 ± 7.34 vs. 2.53 ± 5.71, p=0.0118). In the pain course group, the most important improvements, expressed in %, were for the items regarding the relevance of antidepressant use in chronic pain patients (23.08%), the importance of early return to activities following recent onset back pain (30.78%), and the efficacy of cognitive behavioral therapy in chronic pain management (46.15%). It is noteworthy that the total post-test score of our experimental group is comparable to the one of pain specialists involved in the study for the development of the KnowPain-12 survey (45.92 ± 5.62 vs. 48 respectively).

**Conclusion**
The study described here, albeit small, supports the findings that registered nurses benefit from required instruction on pain and its management, bridging the gap between what they know and what we wish they should know.
Title: Using The Pain Self-Efficacy Questionnaire As Service Outcome Measure For A Community-Based Chronic Pain Service

Poster Number PTH054

Authors
J. Theron
Kent Community Health NHS Foundation Trust, Broadstairs, United Kingdom

Aim of Investigation
The NHS in East Kent serves a population of 750,000, managed by 5 different Clinical Commissioning Groups. Pain services consist of a comprehensive multidisciplinary service within primary care (offered by the Community Trust) and an interventional service within secondary care. They work collaboratively to support patients to develop self-management strategies. There is a single point of access for referral letters, where triage is done by senior clinicians. The Musculoskeletal Services Framework document published in 2006, lead to the remodeling of the pain services previously based solely in secondary care. The 'biopsychosocial' component with medicines management, non-pharmacological therapies and pain management programmes, takes place in the community across several regional sites. Regular yearly audits were being performed on the different treatment modalities and patient satisfaction. Key Performance Indices were published monthly but there was no measure in place to demonstrate the global improvement of a patient in their journey through the Community Service. Guidelines, like the IMMPACT criteria, exist for measuring changes in individual patients. It was less clear how global changes relating to a service should be measured. The chosen method also had to be fast, user-friendly and computer compatible. Local commissioners indicated that they wanted to see that patients became more self-sufficient when attending the service. It was thus decided to trial the Pain Self-efficacy Questionnaire (PSEQ) as a service outcome measure. This tool measures the confidence patients have to manage different areas of their lives, despite being in pain. The higher the score (out of a potential 60), the better a patient is coping. It was postulated that patients would score lower on entry into the service and would demonstrate higher scores on exit.

Results
1602 entry scores and 115 exit scores were captured. On entry into the service; 87% of patients score 30/60 or less, 64% score 20/60 or less, 30% score 10/60 or less, 3% scored zero. On exit from the service; none scored zero and 75% scored more than 30/60. These scores could be regarded as a
'snapshot' of entry and exit scores, as most were not of the same patients. There were 39 patients who had both an entry and exit score, with an average increase of 17 points (range minus 3 to +41). Only one patient scored less on exit. Records revealed he developed a large disc prolapse and was discharged to undergo spinal surgery. There were no scores captured for those who were discharged because of non-attendance, those who discharged themselves by phone or those discharged in the first appointment. This still left a gap between the number of patients with a planned discharge and those with a recorded exit score. Clinicians had to be reminded to always do the questionnaire.

**Conclusion**
First year data revealed a clear trend in increased levels of confidence and self-efficacy during a patient's time in the service and thereby potentially a higher likelihood to self-manage. Although numbers were still low, both commissioners and clinicians were satisfied that the PSEQ was a suitable way of measuring the outcome of the service itself.
Title: Reflection On A Multidisciplinary Pain Management Program From An Education Perspective By Content Analysis Of A Book Of Chronic Pain Patients' Stories

Poster Number PTH055

Authors
C. LAM, L. Luk

Department of Anaesthesiology, Alice Ho Miu Ling Nethersole Hospital and North District Hospital, Hong Kong, China, Nethersole Institute of Continuing Holistic Health Education, Hong Kong, China

Aim of Investigation
Pain management programmes based on cognitive behavioural principles have been recognized as an effective treatment for various chronic pain conditions (1). Other than understanding the programme from a psychological perspective, this study reflects on a multidisciplinary pain management programme from an education perspective.

Results
1. Perception about chronic pain patients (General public Vs COPE instructors) - patients are able In the story book, it was common to find that chronic pain patients were frustrated by their loss of physical function due to pain (p.35, 125) and loss of mental function due to the side effect of medication (p.26). The feelings of frustration were stronger when they were viewed as malingering by general public (p.118, 126). However, COPE instructors believed their feeling of pain (p.187) and believed they were able to overcome the pain and improve the physical capacities (p.189).
2. Patients are partners (Health care professional Vs COPE instructors) - patients are responsible Another source of frustration came from health care professionals who did not believe their pain (p.116) and even gave unhelpful comments leading to hopelessness (p. 117,124). COPE instructors educated the patients about pain pathophysiology, thought management, behavioural training with graded activities and exercises (2). Although patients were reluctant to increase physical effort initially, COPE instructors encouraged them to overcome the barrier with the concept of pacing. The confidence of patients improved when their physical function improved with the instructions (p. 127).
3. COPE instructors were described as coach who empowered the patients during the process (p. 172).
4. Patients took part in various activities including voluntary work (p.196) and regained their interests (p.100).
5. Hospital administrative and policies are supportive to the programme (p.198-200) while holistic health is the hospital culture (p.185).
Conclusion
Title: Pilot Survey For Assessing Awareness And Knowledge Of Basics Of Pain Management For The Purpose Of Developing Training Program Among Nursing Staff At Sassoon General Hospital, Pune, India

Poster Number PTH056

Authors
M. Lokapur, P. Patel, N. Page
B.J. Medical College & Sassoon General Hospital, Pune, India

Aim of Investigation
Sassoon General Hospital is a 1298 bedded, multi-specialty hospital affiliated to B.J. Medical College in Pune, India where we recently started Pain and palliative care unit. The aim of this survey was to: 1- To assess awareness of nurses towards pain patients and their needs 2- To gauge existing knowledge about basic pain management principles and medications. Accordingly a training program can be devised to address the deficiencies if any.

Results
Survey revealed significant lack of awareness about WHO analgesic ladder (p <0.000) and pain as fifth vital sign. Analysis of attitudes revealed majority (65%) believed that patient should endure as much pain as possible before giving narcotic medicine. Though 79% admitted to assess patients regularly, only 30% used VAS/NRS scales to measure pain. 34% of the nurses believed that pain relief demand by patient was due to anxiety, attention seeking or addiction. All 100% knew about side effects of NSAIDs. Regarding postoperative analgesia, majority 68% opted for round the clock schedule. However 21% felt that nurse should decide when to give the next dose and not on demand by the patient. Regarding opioid analgesic knowledge, only (52%) thought respiratory depression as a most important side effect in post op patients (p <0.000). Only 19% were aware that oral route is the most preferred route of administration of morphine in palliative care. Though 75% chose morphine as a drug of choice after treatment of pain in cancer patients, only 33% preferred to adjust the dose as per pain intensity (p<0.000). 40% felt that Morphine should be stopped or decreased after one month of therapy.

Conclusion
The pilot survey has shown that there is significant knowledge deficiency regarding basic pain management in our nursing staff. A significant number of the sample do not know how to assess the pain and respond effectively. The nurses are confident about NSAIDS use. However survey shows that
further training regarding opioid uses is needed. The attitude of majority of nurses who believed that patient should endure as much pain as possible before giving narcotic medicine will need to be addressed. As nurses are a very important part of the pain relief endeavor, training programs targeted to reduce the deficit in knowledge and inculcating proper attitudes is essential in our hospital.
Title: Pain As The Fifth Vital Sign: Evaluating The Teaching Program In An Undergraduate Nursing School Faculty

Poster Number PTH057

Authors
F. Romanek, M. Posso, V. Giaretta, R. Romanek, M. Koike

Faculdade Mario Schenberg`s, Sao Paulo, Brazil, FUNVIC Fundação Universitária Vida Cristã, Pindamonhangaba, Brazil, CET Integrado da Faculdade de Medicina do ABC, Sao Paulo, Brazil, Instituto de Assistência Médica ao Servidor Público Estadual, Sao Paulo, Brazil

Aim of Investigation
To identify the disciplines teaching the physiopathology and the treatment of pain, as well the introduction to pain as the 5th vital sign while a pedagogical proposal at a Nursing School Faculty.

Results
Totally, there were 15 disciplines as part of the pedagogical curriculum of the nursing school faculty. Of these, just four (26.6%) included subjects related to pain as a integral part of the teaching program. Nominally, these were: 'surgical nursing', 'postanesthesia care unit nursing', 'adult clinical care nursing', 'pediatric clinical care nursing' and 'intensive care unit nursing'.

Conclusion
In a local nursing school faculty, few disciplines included pain related themes as part of the graduation program. When it comes to pain, undergraduate education and information is mandatory, if nurse professionals are interested on better care for the pain patient.
Title: Impact On Hospital-Wide Program On Improving Pain Management

Poster Number PTH058

Authors
u. ungku ahmad, S. Ibrahim
Anaesthesiology, Hospital Sultan Ismail, Johor Bahru, Johor, Malaysia, Hospital Sultan Ismail, johor bahru, johor

Aim of Investigation
Prevalence of pain in hospital ranges from 43%-91%. These was shown by various study since 1987 eg. by Donovan until 2005 by Strohbuecker. Improving hospital pain management requires a special program which covers wide scopes and allows changes and improvement which can be implemented in all discipline. Pain free hospital (PFH) programs in Malaysia was introduce by Malaysia Ministry of Health in 2011. Three general hospitals was in the pilot project. In year 2012 another five hospital was in cooperated to implement the program. The 1st survey was conducted in 2014; the 1st three hospital was certified followed by another four hospital in 2014. PFH program has shown to give a big impact on improving the hospital pain management practiced and patients care tailored to the each hospital needs, capability and ability. PFH concept consists of maximizing anesthesia & analgesia, promoting minimal invasive surgery and incorporating other discipline such as pharmacy, rehabilitation team and traditional & complementary medicine (TC&M) to come together in managing pain. The objectives of PFH are pain free in surgery, pain free labour, pain free procedure,pain free rehabilitation and pain free discharge. Many changes in clinical hospital practiced such as expanding scope of pain service, improving acute pain services (APS), providing consistent training, changing drug usage, changing pain protocols, setting standard Key Performance indicator, providing new services such as Day care surgery, Labour analgesia, analgesia for wound dressing & fracture reduction, etc was done to meet the criteria and objective. The study aimed to see the effectiveness of the program in improving pain management in the hospital.

Results
Improvement in patient care was remarkably seen in following the implementation of the PFH program. All objectives was meet with impressive data indicating there was increases effort to improvement pain management in patients care. There we also new services provided such as Day Care Surgery, pain relief for procedure and labor analgesia was opened. All new services show gradual increments of statistic
data. All national Key Performance Index was meet successfully. There are changes in practice focusing towards adequate pain relief especially for procedural pain, rehabilitation and discharged. The multidisciplinary involvement was seen in the meeting session done, the statistic for patient receiving consultation from pharmacy, allied health team either in the ward or prior to discharged or pre-operative assessment clinic. Complimentary medicine technique was also utilized. The change of medication usage promotes reduction in pethidine usage as well as promotes multi-modal approach for treating pain. The patients satisfaction survey, the pain score data during procedures are among the important evidence indicating the success in the implementation of the program.

Conclusion
Pain Free Hospital projects helps to improves pain services of the hospital with the ability to create multidisciplinary involvement in providing good pain relief and recovery of patients.
Title: First-Year Residents' Knowledge And Practice Related To Postoperative Pain Management

Poster Number PTH059

Authors
S. Thienthong
Khon Kaen University, Khon Kaen, Khon Kaen

Aim of Investigation
The first year residents play an important role in post-surgical pain control. Assessing their knowledge and their practice is a key of success to improve their learning and patient service. We conducted this study to assess the first year residents' knowledge and practice of postoperative pain management.

Results
The response rate was 97.78%. The mean knowledge was 10.23 ± 2.02 and 68.2 percent from a total of 15 scores. The highest score was 14 and the lowest was 6. Their regular practice behaviors were about pain assessment (100%) and treatment of opioids side effect (66.36%). The areas that should encourage more practices were local infiltration at surgical field (43.19%) and using NSAIDs in combined with opioids (31.82%). Their knowledge that needs to be improved was about pharmacology of opioids and its common side effects such as nausea and vomiting.

Conclusion
The level of first year residents' knowledge and practice of postoperative pain management is an average that needs to be improved as well as some practice behaviors.
Title: Pharmacist Counseling For Patients With Persistent Pain: Patients’ And Pharmacists’ Perspectives

Poster Number PTH060

Authors
T. Hall, S. Tan, C. Noble, E. Lau, L. Nissen\(^3\)

Queensland University of Technology, Brisbane, Queensland, University of Queensland, Woolloongabba, Queensland, University of Queensland, Woolloongabba, Queensland, Australia

Aim of Investigation
The aim was to investigate the perceptions of pharmacists and persistent pain patients of pharmacist counseling for chronic pain.

Results
Pharmacists tend to focus on providing information on medications while chronic pain patients would like broader information, including information on other treatment modalities and general lifestyle advice. Chronic pain patients reported shorter interactions with pharmacists than that reported by pharmacists. Both pharmacists and patients identified that a lack of sufficient knowledge of persistent pain by pharmacists leads to a lack of confidence and understanding (empathy) when counseling persistent pain patients. Pharmacists and patients both identified time and lack of private counseling areas as some barriers to pharmacist counseling.

Conclusion
There are discrepancies between chronic pain patients' expectations and pharmacists' focus when counseling. This may be due to differences in the definition of counseling which for pharmacists has meant the provision of information about medication. Pharmacists' have shown a lack of empathy and confidence when working with chronic pain patients, which can be improved with further education and training. The current community pharmacy model needs to reviewed to provide a more patient-centred approach, including sufficient staffing to allow pharmacists to spend more quality time with persistent pain patients in a private counseling area.
**Title:** Exploration Of Pain Genes Expression-Pka, Pkc, Erk And Efficacy Of Pulsed Radiofrequency Application At Dorsal Root Ganglion And Pregabalin In Thoracic Postherpetic Neuralgia: A Randomized Controlled Study

**Poster Number** PTH061

**Authors**
a. saxena, A. Singh, T. Sharma, B. Banerjee, A. Singal

university college of medical sciences, Delhi, India, university college of medical sciences and GTB hospital, DELHI, INDIA, India, university college of medical sciences and GTB hospital, DELHI, INDIA,

**Aim of Investigation**
The aim of the investigation was to evaluate the modulation of Pain Genes expression (PKA (protein kinase A), PKC and ERK (extracellular related kinase)) and efficacy of combination of Pulsed Radiofrequency application at Dorsal root ganglion and Pregabalin for pain relief in thoracic Postherpetic Neuralgia.

**Results**
Both the groups of PHN patients were similar with respect to demographic profile. Statistically significant (p<0.05) downregulation of mRNA expressions of PKA and ERK genes was observed in study group PP at the end of 12th week. Also in the study group PP, statistically significant (p<0.001) reduction in VAS scores and NPSI scores for 'burning sensation' and 'alldynia' were observed on comparison with the control group. In addition, there was significant enhancement of quality of life in terms of significantly better SF-12 QOL scores (p<0.05) in the study Group PP on follow up. Side effects included giddiness, constipation and local bruising because of radiofrequency cannula insertion.

**Conclusion**
To conclude, this Integrated multimodal approach consisting of Pulsed Radio Frequency application at Dorsal Root Ganglion and Pregabalin led to significant downregulation of mRNA expressions of Pain Genes (PKA and ERK) and significant pain relief based on significant reduction in VAS and NPSI scores in thoracic Postherpetic Neuralgia patients. There was also significant enhancement of quality of life as based on SF-12 scores.
Title: Heat, Capsaicin Sensation, And Trpv1 Genome Snps In Human

Poster Number PTH063

Authors
N. Okamoto, M. Okumura, E. Ohki, O. Tadokoro, E. Kondo

Dept of Oral Anatomy, Matsumoto Dental University, Shiojiri, Nagano, Japan, Matsumoto Dental University Hospital, Shiojiri, Nagano, Japan

Aim of Investigation
TRPV1 is a receptor for both heat sensation and hot taste sensation, and the thresholds have been demonstrated as 43 degrees C and 0.6 µM capsaicin, respectively. However, awareness of these sensations obviously differs from person to person. The aim of this investigation is to elucidate the personal differences of heat and capsaicin sensations, and their relationships with TRPV1 genome sequences.

Results
The questionnaire showed that the subjects whose tongue is sensitive to heat do not like hot spicy food, and easily get chilblains. The mean of the withdrawal latency for the hot plate test was 7.23 sec ± 5.52 (min; 2.1 sec, max; 25 sec), and the mean of the capsaicin sensation test was 0.088 µg/ml ± 0.027 (min; 0.05 µg/ml, max; 0.15 µg/ml). Whereas almost of subjects had heat and capsaicin sensations that fell within a certain range (0.06 – 0.1 µg/ml for capsaicin sensation, 2.01 – 11.71 sec for heat sensation), a few subjects showed an especially high threshold for the heat sensation, for the capsaicin sensation, or for both. Genome analysis revealed many 63 SNPs in their TRPV1 gene, including novel 16 SNPs, and 6 SNPs were significantly related to the heat sensation. In particular, M315I (rs222747) is a missense SNP which showed a significant difference. Isoleucine type subjects were more sensitive to heat than Methionine type subjects.

Conclusion
Despite the fact that both heat and capsaicin are mediated by the same receptor, TRPV1, human heat sensation and capsaicin sensation did not show a clear correlation. Many SNPs were detected in the human TRPV1 gene, and some of them were significantly related to heat sensation but not to capsaicin sensation. Capsaicin sensation seems to be under a stronger influence by unknown epigenetic factors than does heat sensation.
**Title:** The Oprm1 A118G Polymorphism Modulates The Expressions Of Functional Connectivity Of The Pain Modulatory Systems In Women With Primary Dysmenorrhea

**Poster Number** PTH064

**Authors**
S. Wei, L. Chen, M. Lin, H. Chao, J. Hsieh

Institute of Brain Science, National Yang-Ming University, Changhua City, Changhua County, Taiwan, Institute of Brain Science, Institute of Biomedical Informatics, National Yang-Ming University, Taipei, Taiwan, Institute of Public Health, National Yang-Ming University, Taipei, Taiwan, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan, National Yang-Ming University, Institute of Brain Science, Taipei, Taiwan

**Aim of Investigation**
Opioids are common used drugs, which are mediated by the OPRM1 in central nervous system. The substitution of adenine (A) to guanine (G) at position 118 (A118G) is a common single nucleotide polymorphism within the OPRM1 gene. This change reduces the expression of OPRM1 gene, lowers threshold for pain perception, and require more analgesics after surgery. Nevertheless, few studies have addressed how OPRM1 A118G polymorphism modulates the neural processing of pain. We addressed this question with a spontaneous acute pain model (primary dysmenorrhea [PDM], menstrual pain without organic causes) and studied 3 types of pain experiences: the mnemonic overall menstrual pain (pain memory), the present menstrual pain (spontaneous pain), and the experimental induced heat pain (experimental pain). This imaging genetics study of PDM aimed to explore the effect of OPRM1 A118G polymorphisms on the functional expression of pain modulatory systems to shed light on individual differences of pain experience.

**Results**
The AA homozygotes, compared with the G allele carriers, rated their present pain experience lower than their recollective estimation. The AA homozygotes exhibited functional hyper-connectivity between the medial prefrontal cortex and the PAG that negatively correlated with the present menstrual pain experience. It is noteworthy that the G allele carriers exhibited no correlation between their pain rating index and PAG-seeded FC.
Conclusion
We present in this imaging genetics study the pain-genotype interplay related to descending pain modulatory systems in the context of PAG-seeded FC. As genetic testing may explain and predict many of the clinical responses seen with opioids, this study may provide a possible explanation for the differences in the pain perception of PDM patients in specific and of other clinical patients in general. Our data underpin the importance of individualizing analgesic therapy to optimize medical treatment.
Title: The Influence Of Rat Strain And Vendor When Backtranslating Pharmacological Response From A Typical Pain Patient

Poster Number PTH065

Authors
S. Hestehave, G. Munro, T. Brønnum-Pedersen, K. Abelson

Department of Experimental Medicine, University of Copenhagen, Frederiksberg, Denmark, Lundbeck A/S, Valby, Denmark, H. Lundbeck A/S, Valby, Denmark, University of Copenhagen, Copenhagen, Denmark

Aim of Investigation
The treatment of chronic pain remains a significant medical challenge for health professionals despite significant advances in our understanding of the pathophysiology involved, and major drug discovery efforts made by companies over the past two decades. Research efforts within the preclinical domain are increasingly adopting a number of backtranslational approaches that involve stricter design criteria and reporting standards to try to increase the chances of new drugs making it through early clinical development. Meanwhile, patient stratification and enrichment of clinical trials should help facilitate novel pain therapeutics making it to market (Demant et al., 2014, Pain, 155(11)). Whilst the concept of homogenizing a patient population in relation to pathophysiology is regarded as a hallmark of preclinical pain research via the use of well characterized inflammatory algogens and neuropathic animal models, the use of different species, strains and vendors for supplying animals likely mitigates any benefits accorded to research performed under controlled laboratory conditions. Moreover, the assumption that outbred rat strains such as Sprague-Dawley (SD) or Wistar represent the rat equivalent of a typical pain patient is largely untested. To address this fundamentally important issue, we have characterized three inbred rat strains (selected based on reported stress, depression, inflammatory and pain phenotypes) and SD rats supplied from two different vendors, in response to acute, inflammatory and neuropathic pain, as well as antinociceptive and analgesic response to morphine.

Results
F344 and SD were sensitive to morphine in hot-plate and CFA inflammatory hyperalgesia (Minimum Effective Dose (MED)=3.0mg/kg). WKY rats developed a far less robust mechanical hypersensitivity after CFA injection despite a similar level of inflammation to the other strains (mechanical threshold for WKY reduced to 71% of pre-CFA baseline, compared to LEW; 39%, F344; 42%, Crl:SD; 32%, Hsd:SD; 38%), and
were much less sensitive to morphine in both tests (MED=6.0mg/kg). LEW rats were completely insensitive to antinociceptive actions of morphine in hot plate, in contrast to the reversal of CFA induced hyperalgesia (MED=3.0mg/kg). Moreover, preliminary results indicate that neuropathic mechanical sensitivity develops with a later onset and less robustly in this strain (von Frey paw withdrawal thresholds at baseline and % paw withdrawal threshold compared to baseline at days 15/95 respectively: LEW 6.2±1.0 g, 129.8/50.3% vs Crl:SD 13.9±1.7 g, 20.6/22.1%; Hsd:SD 9.2±1.1 g, 21.0/19.1%; F344 7.7±1.3 g, 40.8/11.2%; WKY 8.7±1.0 g, 39.0/19.8%). The SNI-results further demonstrate that both SD-strains have fully developed mechanical allodynia at day 15, and do not decrease further in threshold, while the inbred strains require more time for full effect of the induced nerve injury. FIS develops the highest degree of mechanical alldynia compared to baseline (11.2%), while LEW develops the least (50.3%). All strains overall develop mechanical alldynia, but with a varying degree of response.

**Conclusion**

Sensory phenotyping, degree of hypersensitivity in response to both acute, inflammatory and neuropathic induced pain, as well as sensitivity to morphine in various strains of inbred and outbred rats indicates that different pathophysiological mechanisms are engaged after injury. This could have profound implications for translating preclinical drug discovery efforts into pain patients, and choice of strain for a given model should demand more attention.
A Genome-Wide Association Study Of Sleep Complaints In Chronic Pain Patients: A Potential Mechanism Of Action

Title: A Genome-Wide Association Study Of Sleep Complaints In Chronic Pain Patients: A Potential Mechanism Of Action

Poster Number PTH066

Authors
S. Khoury, G. Slade, S. Smith, R. Fillingim, R. Ohrbach, J. Greenspan, W. Maixner, L. Diatchenko

McGill University, Montreal, QC, Center for Pain Research and Innovation, University of North Carolina at Chapel Hill, Chapel Hill, NC, Center for Translational Pain Medicine, Department of Anesthesiology, Duke University Medical Center, Durham, NC, University of Florida, Gainesville, FL, University at Buffalo, Buffalo, NY, University of Maryland, School of Dentistry, Baltimore, MD, Duke University, Durham, NC, McGill University, Montral, Canada

Aim of Investigation
Between 50 and 70% of chronic pain patients complain about poor sleep quality and report insomnia as well as daytime sleepiness. In turn, disrupted sleep is a predisposing factor for development of chronic pain. The aim of this study is to identify underlying genetic pathophysiology linking sleep disturbances and pain.

Results
We identified three genome-wide significant loci associated with PSQI global scores in the OPPERA cohort. The top two hits were rs11976703; (p=4.08E-08) and rs73284230; (p=5.1E-08) on chromosome 7 and were situated upstream to NPY (neuropeptide Y) gene. The third SNP, rs60869707; (p=5.37E-08) was located on chromosome 2 downstream of the ATOH8 (atohal bHLH transcription factor8) gene. In all these three SNPs, minor alleles were risk factors for sleep disturbances. Both SNPs on chromosome 7 were also associated with increased anxiety, stress and a count of 20 comorbid pain conditions. Pathway analysis results suggested that sleep disturbances act through the NALP1 inflammasome complex (p=4.6E-05). This pathway is involved in the activation of immune response by converting pro-interleukin-1ß into mature interleukin-1 ß in irritable bowel syndrome, rheumatoid arthritis and neuropathic pain.

Conclusion
This study finding suggested that there is a genetic contribution to the deleterious interaction between poor sleep and pain. We identified two genetic loci located on chromosomes 2 and 7 associated with
poor sleep. Furthermore, SNPs on chromosome 7, located in close proximity with NPY, were also associated with stress, anxiety and pain. NALP1 inflammasome complex pathway identified by gene enrichment analysis provided potential molecular mechanism for this interaction. These findings need to be replicated and the role of NPY needs to be further investigated.
Date: 09/29/2016 03:15:00 PM

Title: A Role For Telomeres In The Modulation Of Pain

Poster Number PTH067

Authors
A. Muralidharan, N. Akkurt, S. Sotocinal, J. Austin, B. Ham, J. Mogil

Department of Psychology and The Alan Edwards Centre for Research on Pain, McGill University, Montreal, Quebec, Canada, Department of Psychology, McGill University, Montreal, Quebec, Canada

Aim of Investigation
Telomeres are repetitive nucleotide sequences that cap the ends of eukaryotic chromosomes. Recent findings in patients with fibromyalgia and migraine suggest a role for telomere integrity in the modulation of pain sensitivity (see Sibille et al., Pain, 2012). However, the findings from these studies are correlational and fail to shed light on the underlying pathobiological mechanisms. Hence, the aim of the present study was to use mice lacking telomerase RNA component (Terc) to investigate the impact of telomere shortening on pain sensitivity.

Results
Assessment of aTL in naïve Terc mice showed reduced aTL for both Terc+/- (P<0.05) and Terc-/- mice (P<0.01) compared to Terc WT mice. Agarose gel electrophoresis confirmed amplification of specific PCR products. Assessment of mechanical allodynia (von Frey test) in groups of naïve Terc mice showed no significant differences in the average hind paw mean (±SEM) PWT values for Terc WT, Terc+/- and Terc-/-.

In contrast, naïve Terc-/- mice, but not Terc+/- mice, showed significant thermal hyperalgesia (Hargreaves' test) and mechanical hyperalgesia (tail-clip test) relative to Terc WT mice. Intraplantar injection of formalin, but not saline, induced licking/biting behaviors in Terc WT and Terc+/- mice. Interestingly, Terc-/- mice did not display increased licking/biting behaviors following intraplantar injection of formalin compared to saline. In support of our behavioral formalin data, paw edema values for Terc-/- mice were significant lower than that for Terc WT or Terc+/- mice.

Conclusion
For the first time, our findings herein demonstrating thermal and mechanical hyperalgesia in Terc-/- mice with significantly reduced aTL, suggests a role for telomeres in the modulation of pain sensitivity. The absence of nocifensive behaviors and reduced paw edema in Terc-/- mice after formalin is intriguing. Although this may be explained, at least in part, by the absence of telomerase in these mice,
which previously has been reported to be required for inflammation (Ghosh et al., Nat. Cell Biol., 2012), the exact molecular mechanisms underlying this phenomenon remains unknown. Future studies to investigate different cell populations involved in the telomere-pain interface are warranted.
Title: Breast Cancer Patients With Treatment-Emergent Chronic Pain Display Brain Characteristics Of Centralized Pain

Poster Number PTH068

Authors
E. Ichesco, N. Henry, S. Harte, D. Clauw, R. Harris
University of Michigan, Ann Arbor, MI

Aim of Investigation
Patients with chronic centralized pain such as fibromyalgia (FM) exhibit increased resting state functional connectivity (rs-fc) between pro-nociceptive brain regions and the default mode network (DMN) both at rest and following painful stimulation. Here, we hypothesized that similar pain stimulus evoked increases in brain rs-fc would be identified in breast cancer patients with treatment-emergent chronic pain. We also investigated the rs-fc signature of pain after-sensations (PAS), i.e. pain sensations persisting beyond the cessation of an evoked stimulus in this patient population. We reasoned that brain rs-fc results similar to those seen in FM may suggest that some breast cancer patients display aspects of centralized pain.

Results
Cases (n=16; mean age = 54.8 ± 8.3 yrs) and age-matched controls (n=15; mean age = 55.7 ± 8.3 yrs) were enrolled. Cases had significantly greater pre-fMRI and post-fMRI clinical pain (VAS), and PAS scores compared to controls (all P < 0.05). NRS values did not differ following evoked pain scans between groups since evoked stimuli were titrated to similar levels of pain in all participants. At baseline cases had greater right mid IC to right inferior parietal lobule (IPL) rs-fc compared to controls (PFDR = 0.017). Following the evoked pain scans the cases were found to have increased perigenual ACC to left IPL connectivity compared to controls (PFWE = 0.043). Compared to baseline, cases had increased rs-fc between the left posterior IC and the left IPL (PFDR = 0.037) and increased intrinsic rs-fc between the DMN and the precuneus (PFDR = 0.018) following the two evoked pain scans. Also within cases, PAS were highly correlated with post-evoked pain rs-fc between the subgenual ACC and the precuneus (r = -0.839, PFDR = 0.001), the salience network and the primary somatosensory cortex (r = 0.917, PFDR = 0.003), and the salience network and the IPL (r = 0.911, PFWE = 0.030). Within controls PAS was correlated with post-evoked pain rs-fc between the perigenual ACC and the IC (r = 0.846, PFDR = 0.014).
Conclusion
These findings are consistent with the theory that similar brain mechanisms may be present in treatment-emergent pain in breast cancer patients as in FM, a centralized pain disorder. If true, treatments that normalize these brain patterns may be effective in these individuals with cancer pain. Additional research is required to determine if similar findings would be obtained in other non-breast malignancies.
Title: Disruption Of Placebo Neural Networks By Centrally Acting Analgesics In Neuropathic Pain Patients

Poster Number PTH069

Authors

University of Oxford, Oxford, United Kingdom, Botnar Research Centre, Oxford, UNITED KINGDOM, Pfizer Ltd., Cambridge, CB21 6GS, UK, Cambridge, United Kingdom, Neuroscience and Pain Research U, Pfizer Worldwide Research and Development, Cambridge, United Kingdom, Pfizer Ltd., Cambridge, CB21 6GS, UK, Cambridge, United Kingdom, Pfizer Inc, Groton, CT, USA, Groton, CT, United States, 4 Portsmouth Hospital, Queen Alexandra Hospital, Portsmouth, Hampshire, PO6 3LY, UK, Portsmouth, United Kingdom, Queen Alexandra Hospital, Portsmouth, United Kingdom

Aim of Investigation
Many promising new analgesic compounds fail to demonstrate behavioural analgesic effects in early proof-of-concept studies in drug development. These studies typically use a double-blind, randomised, placebo-controlled trial design, with subjective pain reports as outcome measures. To prove analgesic efficacy of a study compound, subjective pain reports during active treatment when compared with placebo must be significantly less. However, expectation of treatment outcome in these studies can result in behavioural pain relief during placebo treatment, which can be large, and confound potentially valuable, mechanistic and pharmacodynamically produced analgesic effects of the study drug. Placebo-analgesic responses have distinct neural mechanisms that can interact with CNS-acting drugs. Therefore, this 'additive' model, which assumes that expectation of treatment outcome-driven placebo analgesic effects are non-specific and therefore equal in both the drug and the placebo arm, is now being questioned. We hypothesised that the placebo-induced brain activity in a network implicated in placebo analgesia as measured by functional magnetic resonance imaging (fMRI) would be measurable during placebo treatment (to date not shown in a patient study with chronic dosing) but disrupted by centrally acting analgesics in a group of neuropathic patients.

Results
Mean age (± standard deviation) of the 16 patients was 45.8 ± 9.2 years. Mean duration (± standard deviation) of posttraumatic neuropathic pain was 3.9 ± 2.6 years. When compared with baseline, placebo significantly reduced DMA (P = 0.04; one-tailed). Brainstem-rACC Fc during placebo treatment
was significantly higher (P=0.002) than that during the baseline session while there was no significant difference between the two active treatments and baseline. The standardised effect size and 95% CI when compared to baseline is 1.04 (CI, 0.27 to 1.75) for placebo, 0.59 (CI, -0.13 to 1.28) for tramadol, and 0.64 (CI, -0.09 to 1.33) for pregabalin.

**Conclusion**
From a cohort of 16 patients with post-traumatic neuropathic pain, we present preliminary evidence that the placebo network is active in patients during a chronic placebo treatment arm, and that this may be disrupted by CNS-active drugs. This finding contributes to the growing body of evidence that challenges the validity of the 'additive' model in randomised placebo-controlled trials.
Title: Resting State Functional Connectivity Patterns Of Cognitive/Emotional And Sensorimotor Networks Differ In Opposite Ways In Chronic Pain

Poster Number PTH070

Authors
I. Timmers, L. Romanovska, V. van de Ven, R. Smeets, J. de Jong, A. Kaas

Maastricht University, Maastricht, Netherlands, Maastricht University Medical Center, Maastricht, Netherlands

Aim of Investigation
Recent studies have suggested that chronic pain patients show a shift away from the neural processing of sensory/nociceptive aspects of pain towards processing of cognitive and emotional aspects. One way to explore such a shift is to examine brain connectivity patterns at rest using functional connectivity (rs-FC) measures. Previous research has demonstrated abnormalities in resting-state networks, mostly described as increased rs-FC compared to pain-free controls. These increases have been found in several rs-networks including the default-mode network (DMN) and the salience (or cingulate-insular) network. However, alterations have been found in the sensorimotor network as well. The current study will investigate both cognitive-emotional rs-networks (e.g., DMN or salience network) and the sensorimotor rs-network, and their interaction, in two types of chronic pain: chronic low back pain (cLBP) and complex regional pain syndrome type I (CRPS-I). The exploration of connectivity patterns in cortical networks will allow for the investigation of the commonalities and differences between cLBP and CRPS-I, and further our understanding of the role of altered neural processing in chronic pain.

Results
Data analysis is ongoing. However, preliminary analyses showed several rs-networks identified using an ICA approach, among which the DMN and the sensorimotor network. Preliminary group contrasts indicate abnormalities in the DMN network, with patients showing increased functional connectivity of the mPFC within the network. Contrasting cLBP and CRPS-I patients appears to show a difference in connectivity patterns in the posterior part of the DMN (increased connectivity in CRPS-I compared to cLBP). In addition, within the sensorimotor network, patients show opposite patterns compared to controls: decreased functional connectivity of S1 and posterior insula/S2. Compared to cLBP patients, CRPS-I patients present with increased connectivity of posterior insula/S2 within the sensorimotor network.
Conclusion
Exploring rs-networks in chronic pain patients reveals interesting and specific connectivity patterns, further corroborating the disparity between cognitive-emotional and sensorimotor networks in chronic pain. Further analyses will be performed to investigate more subtle differences by using specific seed-regions, and to correlate findings with behavioral and psychophysical data to establish a link between such alterations and daily functioning. Ultimately, we will also address the malleability of these networks through rehabilitation treatment strategies aimed at cognitive-emotional aspects of pain.
Title: Altered Neural Functioning In Different Phases In Migraineurs

Poster Number PTH071

Authors
N. Meylakh, K. Marciszewski, L. Henderson

University of Sydney, Sydney, NSW

Aim of Investigation
Migraine is a neurological disorder that has been regarded as the third most prevalent disease in the world. It is widely believed that hyperexcitability along the spinal and trigeminal nociceptive pathways can lead to the migraine attack. Furthermore, it has been reported that central neural differences also exist between migraine attacks (interictal phase), as well as 24 hours before (prodrome phase) and 72 hours after (postdrome phase) an attack. We have recently shown that another orofacial neuropathic pain condition, trigeminal neuropathy, is associated with altered resting activity (increased infra-slow frequency oscillations) within trigeminal nociceptive pathways and within parts of the thalamocortical circuitry which we hypothesise is related to glial activation. It is possible that a similar situation also occurs in individuals with migraine and that this predisposes an individual to a migraine event. Given this, we hypothesise that migraineurs will present with altered resting activity, characterized by increased infra-slow oscillatory power in the period between migraine attacks and in particular during the 24 hours before a migraine attack.

Results
Significant increases in infra-slow oscillatory power occurred in migraineurs during their interictal phase in a number of brain regions, including the contralateral (to side of most frequent pain during attack) somatosensory cortex, motor cortex, medial thalamus and anterior cingulate cortex. Furthermore, a paired t-test was performed on four subjects who were scanned both in interictal and prodrome phases. This preliminary comparison shows significantly different alterations in infra-slow frequency oscillations in the brainstem including in the spinal trigeminal nucleus, the region of the nucleus raphe magnus and in the dorsolateral pons.

Conclusion
These findings provide evidence that migraineurs, even between attacks, have altered regional resting oscillatory activity. Further, the preliminary prodrome data suggests that differences are specific to the
phase of the migraine with increased oscillatory activity occurring within the brainstem immediately prior to an individual experiencing a migraine attack. It is possible that increased infra-slow oscillatory power represent changes in underlying astrocytic modulation of synaptic function since activated astrocytes display similar infra-slow oscillatory activities. These on-going activity changes may result in the precipitation of a migraine attack or the build-up to the migraine attack as measured in the prodrome phase. Alternatively, it may represent the consequence of aberrant activity that occurs during the attack itself.
Title: Spatio-Temporal Dipolar Source Analysis Of Somatosensory- And Laser-Evoked Potentials: A Combined Eeg And Meg Study

Poster Number PTH072

Authors
M. Mahmutoglu, U. Baumgaertner, A. Rupp

Section of Biomagnetism, Dept. of Neurology, Medical Faculty Heidelberg, Heidelberg University, Heidelberg, Germany, Centre for Biomedicine and Medical Technology Mannheim, Medical Faculty Mannheim, Mannheim, Germany

Aim of Investigation
Electrophysiological and neuroimaging studies indicate that nociceptive stimuli elicit activity in a wide network of cortical areas including operculo-insular cortex, prefrontal cortex, the cingulate gyrus as well as the primary and secondary somatosensory cortices which are also activated through non-nociceptive tactile stimulation. This 'pain network' has already been studied using dipolar modeling by means of electroencephalography (EEG) or magnetoencephalography (MEG), but rarely using both techniques simultaneously. The aim of this study is to investigate the temporal evolution of cortical activity in response to nociceptive (laser) and non-nociceptive (tactile) stimuli, recorded simultaneously with EEG and MEG.

Results
Dipolar source analysis of both noxious and non-noxious stimuli showed activation of primary (S1) and secondary (S2) somatosensory cortices. Furthermore, noxious laser stimuli other than tactile activated generators in anterior and posterior cingulate cortex as well as posterior insular cortex (PI). In the latest part of the LEP (300-500 ms), an additional contribution of S1 to the overall cortical response was seen in EEG only. Posterior insular activity interacting with the posterior cingulate cortex (PCC) activity at an overlapping time range of positive components between 300-500 ms (P2/P3) was shown by source strength analysis. Intensity coding within S2 and PCC sources was different compared with anterior cingulate, S1 and posterior insula. Anterior cingulate sources modeled in EEG data following laser radiant heat stimuli showed different temporal activity patterns than PCC. Additionally, MEG could detect later S2 activities of LEPs (300-600 ms) with different waveform patterns than EEG. EEG was more sensitive to the latest part of LEP responses in a time range of second major peak of global field power (GFP), whereas the most prominent response detected by MEG was the earliest overall cortical response.
represented by the first major peak of GFP. In contrast to that, tactile SEPs showed in both EEG and MEG data similar and overlapping GFP patterns.

**Conclusion**

These data show non-nociceptive tactile and nociceptive laser stimuli activating primary (S1) and secondary (S2) somatosensory cortices in common, whereas insular cortex and cingulate cortex are predominantly activated by laser stimuli. Methodically, EEG is more sensitive to the radially oriented deep cortical nociceptive related activity compared to MEG. MEG detects activity from superficial cortical regions such as S1 and S2, while showing different LEP waveform patterns than EEG, presumably due to its higher sensitivity to the tangentially oriented components. Supported by Deutsche Forschungsgemeinschaft; DFG SFB1158-B05.
**Title:** Diffusivity Changes Of The Trigeminal Sensory Pathway In Trigeminal Neuralgia Secondary To Multiple Sclerosis

**Poster Number** PTH073

**Authors**
D. Chen, J. Zhong, K. Liang, M. Hodaie

Krembil Research Institute, Division of Brain, Imaging and Behaviour, University Health Network, Toronto, Ontario, Krembil Research Institute, Mississauga, Ontario, Krembil Research Institute, Toronto, Canada, Toronto Western Research Institute, University Health Network & Division of Neurosurgery, Toronto, Canada

**Aim of Investigation**
Trigeminal neuralgia secondary to multiple sclerosis (TN-MS) is a facial neuropathic pain disorder similar to classic trigeminal neuralgia, with sudden, shock-like, paroxysmal pain in the trigeminal distribution. We have previously performed diffusivity study of the trigeminal nerve (CN V) in classic TN and TN-MS patients, and demonstrated that diffusivity changes of CN V occurred in the brainstem segment in TN-MS patients, whereas TN patients showed altered diffusivities in the cistern and root-entry-zone. In this study we aim to 1) analyze changes in the CN V after Gamma Knife (GK) radiosurgery in TN-MS patients; 2) examine the associated trigeminothalamic and thalamocortical diffusivities in these patients.

**Results**
Along the CN V, significantly lowered FA, and increased RD and AD were observed in the root entry zone (REZ) in TN-MS patients when comparing to controls. As CN V entered the brainstem, the right (affected) CN V FA was significantly lower, RD was significantly increased compared with controls, while the left (unaffected) CN V FA did not demonstrate significant differences. Post-GK CN V showed decreased FA in the REZ in both sides when comparing to pre-GK. FA was decreased in the GK target, together with increase in metric variability between subjects. The TGT decussations showed little significant differences between groups. The right TGT pathway however showed significantly lowered FA and increase in RD in the transition zone between the pontine TGT and the regions of the medial lemniscus. Along the S1 projections, there were significantly increased FA closer to the thalamus for TN-MS patients when comparing to controls. FA lowered as the cortex was approached. RD and AD were significantly higher in patients in the mid-regions of the projections. The pattern of changes in left and right S1 projections were similar.
Conclusion
This study is the first along-the-tract analysis of the trigeminal sensory pathway. The new analysis technique is able to pinpoint the exact location along the pathway where TN-MS diffusivity disruptions occurs. CN V changes suggest that the key segments of diffusivity disruption were at the REZ and its surrounding brainstem areas in MS-TN. The post GK decrease in FA was seen in the REZ, which agreed with our previous findings. Analysis of the TGT and S1 pathways suggest that MS negatively affects the trigeminal pathways in these individuals at all levels of the trigeminal sensory projections, noting that the changes may be related to the inherent pathophysiological and neuroanatomical changes in MS.

References
Date: 09/29/2016 09:30:00 AM

**Title:** Segregation Of Fractions In The Peripheral Nerve From Diffusion Weighted Magnetic Resonance Imaging Data Utilizing Two Multivariate Analyses

**Poster Number** PTH074

**Authors**
A. Suda, H. Matsuzawa, K. Suzuki, K. Seo, M. Terumitsu

Division of Dental Anesthesiology, Department of Tissue Regeneration and Reconstruction, Niigata Uni, Niigata, Japan, Center for Integrated Human Brain Science, Brain Research Institute, University of Niigata, Niigata, Japan

**Aim of Investigation**
Water diffusion in biological tissue is known to provide valuable information on its structural and functional characters and can be quantitatively assessed based on apparent diffusion coefficient (ADC). ADC is estimated from a set of diffusion weighted magnetic resonance imaging (DWI) data, usually by assuming a signal model as a function of the diffusion weighting factor, referred to as b-value. As an application of ADC, it has been utilized to evaluate pathological conditions of the peripheral nerve. ADC of a peripheral nerve is, however, considered to reflect a complex mixture of diffusion and perfusion components, and hence its signal model is unclear. In this study, we examined two types of multivariate analysis, cluster analysis and independent component analysis (ICA), with respect to their exploratory decomposition performance as applied to multi-b-value DWI of the trigeminal nerve.

**Results**
Among the three clusters, one cluster showed significantly higher ADCf than the other two, which were significantly different in f. No significant differences were observed for ADCs. Three ICs with similar map pattern to the clusters' were successfully extracted from each of the eight subjects. There were no significant differences in ADCf, ADCs and f among the ICs, while only one IC indicated significantly higher ADCs, comparing the clusters and ICs.

**Conclusion**
We suggest that one cluster included a significant perfusion component derived from microcirculation, and the abundance of diffusion and perfusion segregated the other two clusters indicating lower ADC. ICs did not necessarily depend on the double exponential model. The current two multivariate analyses
can potentially provide smaller segmented fractions than the exponential model. This may underpin the noninvasive novel method of evaluating the peripheral nerve.
Date: 09/29/2016 03:15:00 PM

**Title:** Does Size Matter? Systematic Review With Ale Meta-Analysis Of Brain Structure In Low-Back Pain

**Poster Number** PTH075

**Authors**
M. Bagg, S. Gustin, M. Hübscher, B. Wand, L. Moseley, M. Lotze, S. Eickhoff, J. McAuley

Neuroscience Research Australia, Sydney, New South Wales, Australia, Prince of Wales Clinical School, University of New South Wales, Sydney, New South Wales, Australia, School of Psychology, University of New South Wales, Sydney, New South Wales, Australia, School of Physiotherapy, University of Notre Dame Australia, Fremantle, Western Australia, Australia, Sansom Institute for Health Research, University of South Australia, Adelaide, South Australia, Australia, Functioning Imaging Unit, University of Greifswald, Greifswald, Germany, Institute of Clinical Neuroscience and Medical Psychology, Heinrich Heine University, Düsseldorf, Germany, Institute of Neuroscience and Medicine (INM-1), Research Centre Jülich, Jülich, Germany

**Aim of Investigation**
A number of studies have reported differences in brain structure between people with low back pain (LBP) and pain-free controls. However, variability exists regarding the nature of these differences and the specific brain regions involved. The aims of this systematic review and anatomic likelihood estimation (ALE) meta-analysis were to determine whether LBP is associated with structural differences in specific regions of the brain and to investigate whether clinical or methodological characteristics are correlated with the observed differences.

**Results**
Nineteen studies comprising 55 analyses were included in this review. All studies reported on people with chronic LBP and one study also reported on sub-acute LBP. These studies identified 51 regions across the brain that appear to exhibit structural differences between people with LBP and controls. Eleven studies reported regions of less gray matter in people with LBP than in controls. Four studies reported regions of more gray matter in people with LBP than in controls. Two studies reported regions of less white matter in people with LBP than in controls. The two studies reporting cortical thickness had inconsistent findings. Ten studies comprising 14 analyses of gray matter and two studies of white matter were eligible for ALE meta-analyses. ALE meta-analyses, as specified a priori, were not possible due to an insufficient number of studies for each analysis. We decided, post hoc, to pool all eligible gray matter.
studies in a single ALE meta-analysis. There were no significant findings with cluster-level FWE correction (p=0.634). We made a second post hoc decision to pool total gray/white matter volumes using random-effects models. Meta-analysis of published data revealed no significant difference for either gray matter (SMD -0.19 [95% Confidence Interval (CI) -0.45, 0.06], p = 0.14) or white matter (SMD -0.25 [95% CI -0.96, 0.45], p = 0.48). There were insufficient data to pool correlations with the clinical and methodological characteristics we had specified a priori. We made a third post hoc decision to pool correlations between age and total gray matter volume. Meta-analysis identified a weighted mean correlation of 0.435 [95% CI 0.183, 0.687] (p = 0.0007).

**Conclusion**

This ALE meta-analysis identified nil results with cluster-level FWE correction. Pooled total gray or white matter volumes did not differ between people with LBP and controls. We identified a moderate positive correlation between total gray matter volume and age. These findings suggest that, contrary to the commonly held view, the structural brain imaging literature is not conclusive about whether there are structural brain differences between those with and without LBP.
Title: Cortical Influences On Brainstem Circuitry Responsible For Conditioned Pain Modulation In Humans

Poster Number PTH076

Authors
A. Youssef, V. Macefield, L. Henderson

University of Sydney, Sydney, NSW, University of Western Sydney, Sydney, NSW

Aim of Investigation
Conditioned pain modulation (CPM) is a phenomenon whereby an initial painful stimulus is reduced by the application of a second painful stimulus, i.e. pain inhibits pain. The variability of an individual's CPM capacity is important clinically, as reduced CPM ability is associated with increased postoperative pain, the presence of persistent pain conditions and the efficacy of analgesic medications. Experimental animal investigations and human lesion studies suggest that the brainstem is critical for CPM expression, in particular the subnucleus reticularis dorsalis (SRD). Furthermore, we have recently shown that CPM expression is associated with activity changes within the SRD in pain-free individuals. While the brainstem is critical for CPM expression, the cortex can significantly modulate CPM, likely via the brainstem circuitry critical for CPM; although evidence for this does not exist. The aim of this investigation was to employ functional magnetic resonance imaging (fMRI) to extend our previous analysis of brainstem sites responsible for CPM by exploring cortical influences on brainstem circuitry associated CPM responsiveness.

Results
In all subjects, during the first fMRI scan, significant signal intensity increases were observed in the somatosensory cortices, primary motor cortices, insula, cingulate cortices and dorsolateral prefrontal cortex (FWE, p<0.05). During the second fMRI scan, 23 subjects displayed CPM analgesia (CPM subjects; mean ±SEM change in pain intensity: -29.0±2.9%) and 31 subjects did not (noCPM subjects; 3.7±3.2%), where a lack of CPM analgesia was associated with signal increases in the cingulate and dorsolateral prefrontal cortices (FDR, p<0.05). Signal intensity changes in these regions were also significantly positively correlated with CPM analgesia (small volume corrected, p<0.05). Finally, a lack of CPM analgesia was associated with increased connectivity strengths with the brainstem circuitry responsible for CPM. In contrast, those exhibiting significant CPM analgesia, showed no signal intensity or connectivity strength changes in these cortical regions.


**Conclusion**
These data suggest that during multiple or widespread painful stimuli, engagement of the prefrontal and cingulate cortices prevents the generation of CPM analgesia, raising the possibility altered responsiveness in these cortical regions underlie the reduced CPM observed in individuals with chronic pain.
Title: Rating The Intensity Of Nociceptive Laser Stimuli Modifies The Amplitude Of Laser-Evoked Potentials

Poster Number PTH077

Authors
D. Torta, M. Ninghetto, V. Legrain

Université catholique de Louvain, Brussels, Belgium, Department of Psychology, University of Turin, Turin, Italy

Aim of Investigation
Neuroimaging studies have shown that the magnitude and the spatial pattern of cortical responses to a tonic nociceptive stimulus can be modulated by paying attention selectively to specific features of the stimulus such as its intensity or location (Lobanov et al., 2013) or by rating its intensity (Schoedel et al., 2008). Due to their high temporal resolution, laser evoked potentials (LEPs) are considered the most suitable tool to investigate the integrity of nociceptive pathways. However, considering that paying attention selectively to some stimulus features such as during intensity could also affect cortical responses, we sought to characterize the effects of selective attention to location vs. intensity of brief nociceptive laser stimuli, whose intensity was or was not rated. Importantly, rating the intensity of a nociceptive stimulus while paying attention to its location constitutes a dual task, whose effect has never been formally investigated.

Results
The analysis of accuracy showed that detecting changes in the spatial location of the stimulus was easier than detecting changes in its intensity. Ratings did not affect the performance and did not differ significantly in the 'L+R' and 'I+R' conditions. The magnitude of the N2 and P2 peaks measured at Cz did not differ across conditions. Instead, the point-by-point analysis revealed significant larger LEPs magnitude at central-parietal electrodes in the 'I' than in the 'I+R' condition in the time window between 400 and 500 ms. No major differences were detected in the comparison 'L' vs. 'L+R'.

Conclusion
Our data point to the evidence that the magnitude of the LEP response is affected by providing a rating of intensity. This aspect should be considered in the clinical domain when using LEPs to assess the
Title: Transcranial Focused Ultrasonic Brain Stimulation: An Alternative Non-Invasive Technique To Modulate Or Study Pain In Humans?

Poster Number PTH078

Authors
J. Lambert, C. Craeye, A. Mouraux

Université catholique de Louvain, Brussels, Belgium, Université Catholique de Louvain, Louvain - la - neuve, Belgium

Aim of Investigation
Non-invasive techniques such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (TDCS) are increasingly used as treatments to reduce pain in patients with chronic pain. Furthermore, the transient and focal neuromodulatory effects of these procedures can provide insight on the cortical processes underlying pain perception in humans. The aim of this preliminary study was to examine whether transcranial focused ultrasonic stimulation (TFUS) could be used as an alternative non-invasive technique to modulate and/or study pain in humans. In animals, it was shown that TFUS of the primary motor cortex (M1) can generate motor responses in the contralateral limb. The effect of TFUS on neuronal excitability could result from an influence on voltage-gated sodium and calcium channels. Very recently, two studies have shown that TFUS delivered over the primary somatosensory cortex (S1) can modulate tactile processing and even generate tactile sensations Lee et al.(Nature Scientific Reports 2015). As compared to TMS and TDCS, TFUS has several advantages. First, the effect can be restricted to a more localized area of the cortex. Second, using transducers having a large focal distance, TFUS could be used to selectively modulate deep structures such as the operculo-insular cortex. Third, TFUS does not generate any unwanted auditory or tactile sensations. Finally, TFUS does not generate any electromagnetic artifact and can thus be combined with EEG to study its effects on brain function.

Results
Using fundamental frequencies between 250-500 kHz, the focal point of our transducer was located 31 mm in front of the transducer. The size of the focus varied between 6 and 10 mm in diameter and between 72 and 42 mm in length at full width half maximum, depending on the fundamental frequencies used. Interposing the cranial bone led to a marked reduction of Isppa, Ispta and MI, and the spatial acoustic profile was less spread.
Conclusion
We propose a simple device that could be used to modulate non-invasively and in a focal fashion the excitability of cortical structures currently targeted by TMS or TDCS to reduce pain in patients and/or study the cortical mechanisms underlying pain perception in humans. Different transducer designs (e.g. focused transducers with a greater focal point or phased-array transducers) could be used to target deeper structures such as the operculo-insular cortex.
Date: 09/29/2016 03:15:00 PM

**Title:** The Impact Of Trait Mindfulness On Sensory, Biological, And Cognitive Aspects Of Pain

**Poster Number** PTH079

**Authors**
R. Harrison, M. Moayedi, G. Kitsaras, L. Mattos Feijo, T. Salomons

University of Reading, Reading, United Kingdom, University College London, London, United Kingdom

**Aim of Investigation**
Mindfulness training leads to reduced pain and improved pain coping (including lower pain catastrophizing, decreased negative affect and better cognitive performance) in both clinical and non-clinical populations (Mrazek et al., 2013; Schutze et al. 2010; Zeidan et al., 2012). While the effects of mindfulness training on pain outcomes are well known, the degree to which trait mindfulness is associated with sensory, biological and cognitive aspects of pain remains poorly understood. We aimed to examine the behavioural and biological association between trait mindfulness and sensory and cognitive aspects of pain in individuals with no previous mindfulness training. To elucidate the underlying neural mechanisms, we examined resting state connectivity of the periaqueductal grey (PAG), a key region involved in descending modulation (Gebhart, 2004).

**Results**
There was a strong negative correlation between mindfulness and pain-catastrophizing, $r(67) = -0.49$, $p<.001$, as well as a negative correlation between pain-catastrophizing and threshold, $r(67) = -0.28$, $p<.05$. We found a positive correlation between trait mindfulness and pain threshold, $r(68) = .31$, $p<.05$. To elucidate the overlapping mechanisms underlying this association we conducted separate regression analyses to examine associations between resting state PAG connectivity and both threshold and trait mindfulness. We then conducted a conjunction analysis to examine overlapping mechanisms. We found that both threshold and mindfulness were associated with functional connectivity between PAG and left dlPFC (superior and middle frontal gyri, BA 6/9).

**Conclusion**
Consistent with previous research (Petter et al., 2013), individuals with higher trait mindfulness had lower pain catastrophizing scores. Importantly, we also found a positive association between trait mindfulness and pain threshold. Individual differences in this relationship were associated with resting state connectivity of PAG and left dlPFC. These findings indicate that trait mindfulness is associated with
both sensory and emotional aspects of pain and may therefore be a useful measure for examining pain sensitivity in clinical settings. Furthermore, connectivity between modulatory brain regions and cortical regions associated with cognitive and premotor processing may underlie these associations.
Title: The Impact Of Neonatal Tissue Injury On Brain Changes Following Adult Surgical Injury: A Structural MRI Study

Poster Number: PTH080

Authors
S. Beggs, S. Walker, M. Salter, J. Lerch

The Hospital for Sick Children, Toronto, Toronto, ON, UCL Institute of Child Health, London WC1N 1EH, United Kingdom, Hospital for Sick Children/University of Toronto, Toronto, Ontario, The Hospital for Sick Children, Toronto, Ontario

Aim of Investigation
Increased nociceptive activity following neonatal surgical injury produces long-term changes in the sensitivity of nociceptive circuitry and this aberrant activity, through neuroimmune interactions, drives long-term changes in brain structure that persists into adulthood. We have identified regions of the brain that are structurally altered by neonatal and adult surgery. Pre-clinical and clinical research has shown that there are long-term consequences as a result of neonatal painful events and here we suggest that those changes are a direct result of structural changes in brain areas associated with nociceptive processing. We aimed to map and quantify the anatomical extent of injury-induced expansion/contraction of specific brain regions by MRI and determine the influence of neonatal injury and whether these changes were sex-dependent.

Results
Hindpaw incision resulted in expansion and contraction of brain regions when performed in both neonatal and adult animals. Regions affected include those associated with nociceptive and pain processing: Thalamus, PAG, somatosensory cortex, and regions associated with cognitive processing including the hippocampal formation, amygdala, cerebellum. Statistical significance was confirmed using a 10% False Discovery Rate. Neonatal incision influenced brain changes following adult incision and significant interactions were seen in the cerebellar vermis, amygdala, dentate gyrus and corpus callosum (2 way ANOVA). Three way interaction of neonatal incision x adult incision x sex revealed significant changes in volume of the PAG.

Conclusion
Plantar hindpaw incision in both the neonate and adult leads to structural changes in the adult brain.
Neonatal incision interacts with the adult incision to change the direction of that change in some structures. Sex differences were also demonstrated in the PAG. These results show that tissue injury during the immediate postnatal period causes long-lasting structural changes to the CNS and influences the effects of further injury in later life. Changes were not restricted to brain structures associated with pain and nociceptive processing, but also included cognitive structures. Further understanding of the significance of these changes will better inform the long-term consequences of neonatal pain.
Title: Primary Dysmenorrhea May Be Associated With Reduced GABA Concentration In Menstrual Pain-Related Brain Area: An MRS Study

Poster Number PTH081

Authors
C. Tu, W. Li, D. Niddam, J. Hsieh, H. Chao

Graduate Institute of Acupuncture Science, China Medical University, Taichang, Taiwan, Integrated Brain Research Unit, Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan, Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan, Brain Research Center, National Yang-Ming University, Taipei, TAIWAN, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan, Department of Obstetrics and Gynecology, School of Medicine, National Yang-Ming University, Taipei, Taiwan

Aim of Investigation
Primary dysmenorrhea (PDM) is the most encountered gynecological problem for women in the reproductive age. We previously demonstrated that PDM is associated with functional and structural changes in the brain. Since the abnormal concentration of neurochemical substances have been reported in various chronic pain conditions (e.g., low back pain, neuropathic pain, migraine, and irritable bowel syndrome), we hypothesized that subject with primary dysmenorrhea may associated with altered concentration of neurochemical substances in menstrual pain-related brain regions.

Results
Due to incidental finding in the brain or fail of return, 21 PDMs and 17 controls were excluded from the analysis. The MRS signal in bilateral dorsolateral prefrontal cortex and orbitofrontal cortex in remained subjects were unable to analysis since the signal have been contaminated with large molecules. Among the remained regions, no significant interaction effect has been found for each neurochemical substance in each region. The test for main effect of group revealed significant hypo-concentration of GABA in PDMs than in controls in left thalamus and bilateral dorsal anterior cingulate cortex. The test for main effect of period further revealed significant hypo-concentration of GABA during menstruation period than during pre- and post-menstruation period in left hippocampus. No significant main effect of group and period has been found on the concentration of other neurochemical substances in menstrual pain-related brain regions. For psychological assessments, no significant interaction effect has been found...
on anxiety and depression level. The main effect analysis revealed significantly increased state-anxiety and depression level in PDMs than in controls, while no significant difference on trait-anxiety level. No significant main effect of period has been found.

**Conclusion**

In the present study, we found that GABA but not other neurochemical substances revealed hypo-concentration in the regions related to pain transmission and pain attention in PDM. The normal concentration of creatine, myo-inositol and NAA in PDM among all regions suggested that the regional gray matter volume changes in PDM may no due to the neuronal loss. Combining the hypo-concentration of inhibitory GABA and normal concentration of excitatory glutamate and glutamine in pain transmission and pain attention area, the central sensitization of pain perception in PDM may underpinned by the decreased inhibitory mechanisms but not increased excitatory mechanisms.
Title: Functional Brain Activity Associated With Noxious Stimulation In A Patient With Congenital Insensitivity To Pain

Poster Number PTH082

Authors
R. Staud, J. Boissoneault, J. Craggs

University of Florida, Gainesville, FL, University of Missouri, Columbia, MO

Aim of Investigation
Rare loss-of-function mutations in the SCN9A gene (which encodes the Nav1.7 sodium ion channel) have been shown to result in congenital insensitivity to pain. We have previously reported results of psychophysical testing of a then 9-year-old girl with two novel mutations in SCN9A, revealing a lack of pain sensation from thermal stimuli in the noxious range. In this report, we present results regarding brain activation measured using BOLD fMRI associated with heat stimulation in the same patient, who is now 16 years old.

Results
An abnormal pattern of stimulus-locked activity was noted, including a large cluster of deactivation (76488 mm3) encompassing lingual gyrus, fusiform gyrus, pre- and post-central gyri, and precuneus. Another large cluster of deactivation (16416 mm3) included anterior cingulate cortex. Relatively smaller clusters of activation in temporal and frontal regions (56-2632 mm3) were also detected. Thermal stimulation in the noxious range is typically associated with activation of particular brain structures, including anterior cingulate cortex, insula, and primary/secondary somatosensory cortices. In contrast, the current patient demonstrated a pattern of deactivations in these and other regions, suggesting profound alterations in neural processing associated with these stimuli.

Conclusion
These data provide preliminary evidence for the neural correlates of non-noxious and noxious heat stimulation in a participant with congenital insensitivity to pain due to SCN-9A mutations. Predominant deactivation of brain areas was observed in brain areas that generally become activated during noxious stimulation in healthy controls. These findings suggest a possible role of central nervous system mechanisms in the profound analgesia of individuals with SCN-9A mutations.
Title: Influence Of Acute Tonic Pain On Intracerebral Source Generators Using Spontaneous Eeg: An Eloreta Study

Poster Number: PTH083

Authors
E. Mark, T. Hansen, S. Olesen, M. Gram, J. Frøkjær, A. Drewes

Aalborg University Hospital, Nørresundby, Denmark, Mech-Sense, Department of Radiology, Aalborg, Denmark, Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg University Hospital, Aalborg, Aalborg, Germany, Aalborg University Hospital, Aalborg, Denmark, Mech-Sense, Department of Radiology, Aalborg, -- SELECT --, Aalborg University Hospital, Aalborg, -- SELECT --

Aim of Investigation
To investigate tonic pain source generators and test-retest reliability of brain activation during acute tonic pain and resting state electroencephalography (EEG).

Results
The eLORETA analysis revealed no significant differences in global cortical activities between days (resting state P>0.81 and cold pressor EEG P>0.27) and cingulate activity (resting state ICC: 0.65-0.80, cold pressor EEG ICC: 0.63-0.70) and insula activity (resting state ICC: 0.58-0.83, cold pressor EEG ICC: 0.47-0.66). Compared to resting state EEG, cold pressor EEG revealed increased cortical activities in the delta (P=0.002), theta (P=0.011), beta 1 (P=0.0004), beta 2 (P=0.0008), beta 3 (P=0.002) and gamma (P=0.0004) bands and decreased cortical activities in the alpha 2 band (P=0.007). No changes was seen in alpha 1 (P=0.06). Correlations between the pain response and the beta 2, beta 3 and gamma bands were seen for the cingulate cortex (P<0.04).

Conclusion
Source localization of EEG during cold pressor pain is a reliable method to estimate brain activation in distinct frequency bands and might be useful to identify abnormal pain processing.
Aim of Investigation
We have previously investigated how integrative brain connectivity patterns contribute to placebo analgesia (Hashmi et al., 2014). We used a combination of verbal suggestions and physical conditioning to induce positive expectations towards acupuncture treatment in participants with chronic pain caused by osteoarthritis of the knee. The positive expectations resulting from the conditioning induced significant placebo analgesia in both active and sham acupuncture treated patients; however the level of placebo analgesia showed significant variance. This variance could be predicted by individual differences in fine-tuning or mean local efficiency (Meanloc) in the pattern of organization of brain connections observed with graph analysis on resting state functional MRI (rsfMRI). Simply put, a connectivity pattern is said to be 'locally efficient', when it is able to share information between members of local networks through the fewest number of connections and through alternative paths. Here we tested if Meanloc predicts pain modulation reproducibly in different clinical and healthy populations, with different experimental models of pain modulation and also in a randomized controlled clinical trial (RCT) for acupuncture treatment.

Results
Meanloc measured in rsfMRI networks a prori to experimental manipulation or treatment significantly predicted pain modulation at a range of network sparsities. Hence for a network threshold of 25%, the relation between Meanloc and pain modulation was as follows: group 1: R= -0.42, p=0.006, group 2: R= -0.35, p=0.021, group 3: R= -0.52, p=0.02), group 4 (R= -0.31, p=0.036) and group 5 (R= -0.40, p=0.031). The prediction was significant (p<0.05) irrespective of the type of treatment and after FDR
correction for multiple comparisons. The SVM algorithm was able to classify 60-80% of responders correctly and was highest for the RCT trial.

**Conclusion**
Greater local efficiency (Meanloc) in brain networks is an a priori predictor of placebo analgesia regardless of the type of experimental model used for modulating pain. The predictive relation was significant for healthy subjects and chronic pain patients (OA and CBP). This finding was strikingly reproducible in all experimental studies tested and also in a clinical trial that contained no experimental manipulation of expectations. This investigation further confirms that fine-tuning within a connected cluster or group of brain regions proffered by Meanloc is conducive for the brain processes that generate intrinsic analgesic responses during the process of treatment. This brain property may serve as a biomarker for predicting those aspects of treatment response that are neurobiologically generated. This finding adds to our understanding of the neural origin of variability in treatment outcomes for chronic pain (Hashmi et al., 2012, Hashmi et al., 2014, Kong et al., 2006, Tetreault et al., 2014, Enck et al., 2013, Colloca et al., 2012, Wager et al., 2011) and may lead to new treatment targets, evidence-based tools for personalizing chronic pain management and new strategies for improving RCT assay.
Title: Effects Of A Cognitive Task On Static And Dynamic Functional Connectivity In Patients With Chronic Fatigue Using Arterial Spin Labeling Fmri

Poster Number PTH085

Authors
R. Staud, J. Boissoneault, J. Letzen, S. Lai, D. Price, M. Robinson

University of Florida, Gainesville, FL, University of Florida, Gainesville, FL, University of Florida, Glen Allen, VA

Aim of Investigation
Studies using arterial spin labeling (ASL) have shown that individuals with myalgic encephalitis/chronic fatigue syndrome (ME/CFS) have decreased regional cerebral blood flow, which may result in changes in functional neural networks. Indeed, recent studies indicate disruptions in functional connectivity, or correlated activity between brain regions, in ME/CFS patients between fatigue and pain-related regions during wakeful rest. We have demonstrated perturbations in static FC (i.e., average FC over a time course) during resting-state in ME/CFS patients between several brain regions subserving neurocognitive, motor, and affective-related networks. Although static FC provides useful information functional network reorganization that may contribute to ME/CFS symptomatology, measuring the temporal dynamics of these networks should improve our understanding of the cerebral mechanisms of fatigue over time.

Results
We found that ME/CFS participants had fewer changes in cognitive task associated static FC between brain regions associated with working memory, fatigue, and attention than HC. In addition, ME/CFS participants showed lower dynamic FC between the hippocampus and right superior parietal lobule, which correlated with a greater degree of fatigue induction.

Conclusion
These data provide the first indication that lower dynamic FC between memory and attention-related regions may underlie ME/CFS patients' report of task-induced fatigue. Further research is needed to determine whether behavioral and pharmacological treatments for ME/CFS may help normalize static and dynamic FC metrics for this population.
Title: Pain, Dopamine, And The Resting Brain In Parkinson’S Disease: An Fmri Study

Poster Number PTH086

Authors
G. Engels, B. McCoy, H. Weinstein, E. Scherder, A. Vlaar

VU University, Amsterdam, NL, Netherlands, VU University, Amsterdam, Netherlands, OLVG West Hospital, Amsterdam, Netherlands

Aim of Investigation
Parkinson’s disease (PD) is a severe neurodegenerative disease, characterized by the degeneration of dopaminergic (DA) midbrain neurons. Among many other symptoms, pain is an important part of the non-motor symptoms of PD, yet its underlying pathophysiological mechanism is not fully understood. Studying the brain at rest (resting state, RS) has given insight into the temporal and spatial co-activation between brain areas. This co-activation provides the basis for RS functional connectivity. The functionally connected networks that emerge during the RS have shown behavioral and clinical relevance in several disorders, including chronic pain states. In this study, we hypothesize that the RS functional connectivity of PD is disrupted, specifically in the neural networks that process pain (e.g. the medial and lateral pain systems), and that this altered connectivity is related to characteristics of pain. Moreover, we aim to investigate the effect that DA has on pain perception and RS connectivity.

Results
We are currently including patients, so this is ongoing research. We hope the board will accept that we present our results at the time of the World Congress of Pain. Our aim is to include 20 patients and 20 controls by the time of the conference.

Conclusion
Uncovering the underlying pathophysiological mechanism for pain in PD, as well as knowledge on the influence of DA on this mechanism, will aid in optimizing analgesic treatment in PD. Conclusions will be drawn based on the analyzed data.
Title: Dynamic Functional Connectivity Correlates Of Pain Interference During A Cognitive Interference Task

Poster Number PTH087

Authors
J. Cheng, R. Bosma, K. Hemington, A. Kucyi, M. Lindquist, K. Davis

Krembil Research Institute, Toronto, Ontario, Canada, Toronto Western Hospital, Toronto, Ontario, Canada, University of Toronto, Toronto, Ontario, Canada, Department of Psychiatry, Harvard Medical School, Boston, MA, Johns Hopkins University, Baltimore, MD

Aim of Investigation
Individuals performing a cognitive interference task (CIT) during concurrent painful stimuli prioritize task performance (A-type; attention dominates), or pain (P-type; pain dominates) (Seminowicz et al., 2004; Erpelding and Davis, 2013). Whereas the salience of pain may draw attentional resources necessary for effective task performance towards pain perception for P-type individuals, the inverse may occur for A-type individuals. Indeed, compared to A-type individuals, P-type individuals have greater grey matter in regions involved with pain and salience, and greater static functional connectivity (FC) within the salience network (SN) (Erpelding and Davis, 2013). Balancing pain and cognitive performance likely also involves dynamic cross-network communication between the SN and executive control network (ECN) [both implicated in CITs (Botvinick et al., 2004)], and between the SN and pain-related regions.

Therefore, we tested the hypothesis that individual differences in pain interference during a CIT are related to intrinsic, cross-network dynamic functional connectivity (dFC). We predicted that subjects with greater dFC between regions of the SN and ECN, and reduced dFC between the SN and regions involved with pain perception exhibit more A- than P-type behaviour.

Results
There was a wide range of individual RTdiff across our subjects (SD = 111 ms). A significant negative correlation was observed between RTdiff and the MCC-DLPFC dFC (\(\rho = -0.37, p = 0.01\)) across subjects, but not with MCC-S1 dFC (\(p =0.53\)) nor MCC-dplns dFC (\(p = 0.15\)). However, the ratios of dFC of 1) MCC-DLPFC/MCC-S1, and 2) MCC-DLPFC/MCC-dplns were significantly negatively correlated with RTdiff.
Conclusion
Our data suggests that individuals with more dynamic FC between their salience and executive control hubs than between their salience and pain hubs are better able to prioritize task performance in the face of pain.
Title: Does Brain Glial Activation Have A Role In Fibromyalgia? A $^{[11]C}Pbr28$ Pet Study

Poster Number PTH088

Authors

MIT/MGH/HST Martinos Center, Charlestown, MA, MGH/HST Gordon Center for Medical Imaging, Boston, MA, Division of Rheumatology, Immunology and Allergy, Brigham and Women’s Hospital, Boston, USA, Boston, MA, Brigham & Women's Hospital, Needham, MA, Massachusetts General Hospital, Boston, MA

Aim of Investigation
Fibromyalgia (FM) is a debilitating disorder, characterized by chronic pain, fatigue and other symptoms. While FM pathophysiology is poorly understood, the central nervous system (CNS) has been strongly implicated, with putative evidence of pathological neuroinflammation. FM patients exhibit increased CSF concentrations of pro-inflammatory cytokines produced in the brain by microglia and astrocytes$^{1-3}$. Furthermore, FM benefits from treatments thought to inhibit glial activation – e.g., low-dose naltrexone$^{4,5}$. Recently, emergent evidence from our laboratory suggests that CNS glial activation might play an important role in the pathophysiology of human chronic pain disorders$^{6}$, as predicted by the animal literature$^{7,8}$. In order to investigate the hypothesis that FM is associated with brain glial activation, we conducted a study using integrated Positron Emission Tomography / Magnetic Resonance (PET/MR) imaging and the recently developed radioligand $^{[C]}PBR28$. This ligand binds to the 18 kDa translocator protein (TSPO), which is a marker of glial activation.

Results
In FM patients, SUVR was higher than controls in bilateral cerebellar cortex and medulla ($p < 0.05$, corrected). ROI analyses revealed that FM patients did not have elevated thalamic SUVR compared to controls ($p = 0.41$).

Conclusion
The current data are in line with previous evidence of elevated glial activation in chronic pain patients. However, as opposed to chronic low back pain, FM patients demonstrate elevation of the glial marker...
Title: The Financial Aspect Of Pain Management In The Community: Is Setting Up A Pain Management Service In The Community Cost-Effective?

Poster Number PTH089

Authors
L. SCHACHTER
Maccabi Healthcare Services, Israel, Israel

Aim of Investigation
AIM - To assess the cost effectiveness of setting up a community pain service: 'Maccabi healthcare Services' is the second largest Health Insurance company in Israel - providing health services to over 3 million people. Some of the services are provided in the community and others – in Hospital outpatient clinics. Pain management is a relatively new service in the Organization. The service is currently provided in a limited number of community based clinics as well as in Hospital outpatient clinics. The referral to a community clinic or Hospital outpatient clinic is done by clerks solely according to availability with no consideration of the patients medical condition. Before deciding on developing a community based pain service, which, we believe, is a better option medically, we set out to examine the financial aspect of pain management in the community in comparison to outpatient hospital services. The aim of the study was to examine if there was a financial advantage to either of the two.

Results
A total of 46626 Patients were referred to pain clinics during the above mentioned years. 16579 Of them were seen primarily in the community and 30047 had the first encounter in the Hospital outpatient clinics. 50% of hospital treated patients underwent invasive under fluoroscopy treatments in comparison with 22% of patients treated in the community that were referred for invasive-under fluoroscopy treatments in the hospital. The average cost of pain management for patients having their first encounter in the community was 35% less than those seen and followed in the Hospital setting.

Conclusion
It is well accepted that Pain Management should be community based maintaining a good Doctor-Patient relationship with special attention to mind-body factors and providing an holistic multidisciplinary pain care service. This study proves that Community based pain clinics is financially also a better alternative.
Title: Hospitalization Time And Total Costs Due To Migraine In Patients From The Brazilian Public Health System In São Paulo

Poster Number PTH090

Authors
F. Romanek, R. Romanek, M. Posso, I. Posso, V. Giaretta, M. Koike

Faculdade Mario Schenberg’s, Sao Paulo, Brazil, CET Integrado da Faculdade de Medicina do ABC, Sao Paulo, Brazil, FUNVIC Fundação Universitária Vida Cristã, Pindamonhangaba, Brazil, Instituto de Assistência Médica ao Servidor Público Estadual, Sao Paulo, Brazil

Aim of Investigation
To analyze the hospitalization time and total costs due to migraine in São Paulo Brazil, funded by the Brazilian Public Health System (SUS), during 2013-2014.

Results
A total amount of 4,710,370 hospitalizations occurred during the time range of the study, with 319 cases due to migraine (0.007%). Of these, 69% were women, aged 7-89 years-old. Age distribution showed that 20% were less than 18 years-old, 7% were older than 65 years, and 73% were 18-65 years-old. Considering this last group, 71% had a mean age of 32±11 years. Among those under 18 years, migraine affected mainly girls (62%), with a mean age of 11±4 years. The interquartile range and mean for the period of hospitalization was 1-4 and 2 days, respectively. This led to an individual cost of US$52.00-132.00 to the public health system, with a mean cost of US$ 95.11 per person. The total sum related to hospitalizations of these patients during the studied period was of US$ 22,222.00.

Conclusion
The total cost associated with these hospitalizations imposes a heavy burden on an already low budget health system, especially considering that most of the cases occur during a socially productive period of life.
Title: Responsibility And Precautionary Principles On The Possibility Of Fetal Pain

Poster Number PTH091

Authors
M. FLORES
UNIVERSIDAD NACIONAL AUTONOMA DE MEXICO, CIUDAD DE MÉXICO, Mexico

Aim of Investigation
Even though there has been physiological and behavioral evidence that suggests that the fetus can feel pain since 20-23 weeks, it is still denied by many and therefore has resulted in mistreatment of fetuses. The classic principles put forth by Beauchamp and Childress are not sufficient, resulting in the requirement of other approaches to this problem.

Results
Results: Hans Jonas presents a principle of responsibility, understanding this as 'Responsibility is the care, recognized as a duty, of another being. This care, given the threat to his vulnerability, becomes concern.' The principle of responsibility is aimed at the protection and conservation of what has intrinsic value and is also vulnerable, those who may be affected by our technological power. The objects of responsibility are human beings, sentient living beings, the natural species, the ecosystems and nature as a whole. Without a doubt, the fetus is a sentient living being and is a part of nature. When there is the possibility of increased risks the Principle of responsibility is linked to the Precautionary Principle, prudence and even refraining from action to incur greater risk. In the case of the fetus, it is more prudent to use anesthesia due to the lack of certainty of the presence of pain. Precautionary Principle: The Precautionary Principle originated in the Rio De Janeiro declaration in the context of environmental dangers, but has been used in health care decision making. It is defined as: A set of measures that tend to modify, suspend or remove a system or action techno-scientific, when this is implied the plausibility of unacceptable damage to the environment or society, although there is not sufficient scientific certainty and convincing evidence of this, and if the potential damage is irreversible, expandable to large-scale or possibly incalculable benefit greater than projected. Basically, the precautionary principle applies where scientific evidence is insufficient, inconclusive or uncertain and preliminary scientific evaluation indicates that there are reasonable grounds for concern that the potentially dangerous effects on the environment, human, animal or plant health. The elements of the Precautionary Principle: 1) The application context is characterized by a situation of uncertainty, of the probability, the
magnitude and the causes of possible damage. 2) It is essential to have a prior scientific analysis of the plausibility of risks; supposition or unfounded suspicion is not sufficient to trigger the Precautionary Principle. 3) Caution is distinguished from prevention when it applies if the probability of damage is known. 4) The application of precautionary measures implies the need for more research and monitoring to collect further evidence of the risks. The problem of possible fetal pain in relation to the elements of the precautionary principle are 1) It is a situation of uncertainty. 2) There is a scientific analysis that supports the likelihood that the fetus suffers pain from 20-23 weeks. 3) It implies the need for more research and monitoring to collect further evidence of the risks.

**Conclusion**

Defending an academic stance of denying the pain in the fetus before providing the maximum assistance to avoid the probable suffering is NOT justified from an ethical point of view.
Aim of Investigation
Tramadol, an opioid analgesic, is classified as 'D: dangerous drug' by Food and Drug Administration (FDA) of Thailand which can be dispensed by a first grade pharmacist in community pharmacy. According to tramadol abuse and dependence, especially among teenagers, Thai-FDA announced a policy for controlling of tramadol dispensary since September 2013 [prohibit to dispense to children age under 17 years old, dispense to the patients with medical necessity not more than 20 tablets per case, record daily purchases and sale amount and limit monthly order quantity not more than 1,000 tablets per drugstore]. Our study was conducted to investigate the dispensing practice of tramadol, the current situation of tramadol abuse and the opinion on tramadol controlling policy by community pharmacist in Bangkok, Thailand.

Results
Base on the data collected from 130 pharmacists, tramadol were available in 75 drugstores (57.7%) as tramadol alone (14.7%), tramadol/paracetamol combination product (48.0%) or both (37.3%). The major reason for tramadol unavailable was to avoid tramadol abuse. Tramadol alone and combined tablet were dispensed to 4.3 and 1.7 patients/week with average amount of 13.08 and 9.33 tablets/patient, respectively. Generally, pharmacists made decision for prescribing tramadol in cases of refill medication (66.7%), moderate to severe pain (61.3%), ineffective with other analgesic drugs (52.0%) and allergy to other analgesic drugs (42.7%). The major indications of tramadol were for relieving bone pain (66.7%), backache (50.7%), cancer pain (42.7%) and muscle pain (24%). Most of pharmacists (85.3%) explained side effects to patients as nausea/vomiting (62.5%), drowsiness (51.6%), dizziness (40.6%) and constipation (34.4%). Special precautions were informed to the patients to use this drug only as required for pain (42.9%), to be aware of drug addiction (26.2%) and to avoid long term use (11.9%). Concerning to current situation, all pharmacists knew about tramadol abuse from television media (55.4%), social media (42.3%), press media (41.5%), FDA (36.2%) and patients (18.5%). Tramadol was used in
combination with carbonate beverage as well as cough and cold remedies (also known as 4 x 100 cocktail) to produce euphoria effect. Our results revealed that teenager (aged<17 year) frequently asked for tramadol about 7.4 cases/week/drugstore. Regarding to Thai-FDA controlling policy, most pharmacists (96.9%) knew about this policy and 80.8% of them thought that each rule was practical and easy to follow except rule of daily purchase and sale record and rule of limit sale amount not exceeding 20 tablets/patient. Concerning to the ability of the policy to decrease problems of tramadol misused, 42.3%, 37.7% and 20.0% of pharmacist disagreed, agreed and unassured, respectively. Moreover, 56.9% of them disagreed if tramadol will be prohibited to dispense in drugstore because this drug is still necessary for some patients in their community. They proposed that providing education to the people especially teenagers might be the better way to reduce the tramadol abuse problems.

**Conclusion**
In Bangkok, a first grade pharmacist precisely dispensed tramadol for relieving moderate to severe pain including bone pain, back pain and cancer pain. Some of them agreed that Thai-FDA tramadol restriction policy has been effective to diminish tramadol abuse. In their opinion, tramadol should be available in drugstore for some patients with medication necessary.
Title: The Impact Of Cognitive Impairment On The Pain Experience In Hospitalized And Community-Dwelling Older Adults

Authors
S. Gibson<sup>,2</sup>, J. Gracey, S. Savvas

National Ageing Research Institute, Melbourne, VIC, Caulfield Pain Management and Research Centre, Caulfield, Victoria, Australia, National Ageing Research Institute, Royal Melbourne Hospital, Australia

Aim of Investigation
Possible differences in pain frequency and severity in persons with cognitive impairment has been examined in a number of studies and results appear to differ dependent upon residential setting (community versus institutional care). However, differences in pain assessment methods, the country of origin and sample characteristics make it difficult to directly compare these findings. The aim of the current study was to examine pain prevalence, severity and impact in older persons with varying levels of cognitive impairment in a community sample and hospital sample using the same methods of pain assessment.

Results
Chi-square analysis revealed that individuals with cognitive impairment reported significantly less frequent pain (p=0.019) when compared to cognitively intact adults (47% prevalence M-SCI, 60% MCI versus 63% prevalence CI), but there was no difference in the severity nor in sites of pain in those who did self-report. Higher rates of current pain were found in the hospital sample regardless of cognitive status. MANOVA revealed that mood disturbance was increased in those with pain (p<0.006), those with cognitive impairment (p<0.008) and those in the hospital setting (p<0.001). There was a trend for more cognitively impaired participants with pain to report higher levels of depression and anxiety, but this finding failed to reach significance (p=0.141).

Conclusion
As might be expected, the presence of current pain was more frequent in the hospital setting and this occurred in both cognitively intact and impaired adults. However, cognitive impairment does appear to impact on the likelihood of reporting pain, regardless of setting, with overall pain prevalence being 16% lower in those with moderate-severe impairment. It remains unclear exactly why clinical pain should be
less prevalent in those with cognitive impairment, although future studies should undertake a more detailed analysis of pain aetiology, particularly within the hospital setting.
Title: Comparison Of Self-Reported Pain Scale With Observational Pain Scale For Post-Operative Pain Assessment Among Elderly Patients

Poster Number PTH094

Authors

C. Choy

Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Aim of Investigation

The aim of this study was to compare the observational pain scales with pain intensity measured by visual analogue scale pain score based on self-report by elderly patients without cognitive impairment.

Results

Pain scores from using these two scales showed moderate to mild correlation: 0.43 (recovery area), 0.45 (6 hr), 0.39 (12 hr) and 0.31 (24 hr) with statistical significance (p < 0.001).

Conclusion

The overall pain assessment postoperatively among elderly with observational pain scale as well as self-reported pain scale achieved moderate correlation for a period of 24 hours postoperatively.
Title: Pain-Related Cortex Function In Patients With Alzheimer Disease: Preliminary Results

Poster Number PTH095

Authors
G. Di Stefano, A. Pepe, S. La Cesa, C. Leone, F. D'Antonio, A. Trebbastoni, C. De Lena, G. Cruccu, A. Truini

'Sapienza' University, Rome, Italy

Aim of Investigation
Previous studies found that patients with Alzheimer's disease (AD) have increased pain threshold and pain tolerance. Nevertheless, it is still unclear whether these findings are explained by communication problems, or rather they are associated with degenerative processes affecting pain-related cortex. In this neurophysiological study, we aimed at assessing pain-related cortex function, by recording laser evoked potentials (LEPs) after hand stimulation in patients with AD.

Results
Whereas SEP variables and the N1-LEP component did not differ significantly between patients and healthy subjects, the LEP N2-P2 vertex complex was lower in patients than in controls.

Conclusion
Our findings suggest that in patients with AD the degenerative processes affect pain-related cortex. This damage predominantly involves the insular cortex and the anterior cingulate cortex.
Title: Using Simulation To Improve Pain Treatment Outcomes In Elderly Patients With Painful Diabetic Peripheral Neuropathy

Poster Number PTH096

Authors
J. Alexander, Jr, R. Edwards, A. Savoldelli, L. Manca, R. Grugni, E. Whalen, B. Emir, S. Dubrava, M. Brodsky, B. Parsons

Pfizer, New York, NY, Health Services Consulting Corporation, Boxborough, MA, Fair Dynamics Consulting, srl, 20154 - Milano MI, Italy, Pfizer, Groton, CT

Aim of Investigation
Age, obesity, low physical activity, and peripheral arterial disease are all risk factors for painful diabetic peripheral neuropathy (pDPN). Predicting pain treatment outcomes is especially important in the elderly population given the multiple interacting risk factors and comorbidities. We have created a first generation agent-based modeling and simulation (ABMS) application based on Java and Anylogic platforms. It integrates the numerous relevant variables at an individual patient level and combines them at a 'system-level' that can be utilized to predict therapeutic response to pregabalin in elderly patients with painful diabetic peripheral neuropathy. Simulation based on analytics can identify likely responders to specific therapies and can thus provide an improved tool for identifying optimal treatments for elderly with pDPN.

Results
Cluster analyses identified 4 clusters for the RCT and 6 clusters for the Observational study with clusters ranging in size from 68 to 180 for the RCT patients and 287 to 777 for the Observational Study patients. Multivariable analyses showed that different explanatory variables were significant in different clusters including different combinations of lagged pain and sleep interference. Age cohort was a predictor in 3 of 4 RCT clusters and 4 of 6 Observational Study clusters indicating the interaction of age in complex ways with other characteristics and time series data related to pain and sleep interference. Other covariates that were different in different ARMAX models included gender, BMI, taking insulin or not, medical history of depression and general feelings at baseline related to calm/relaxed, full of energy, or sad/discouraged. AUCs of the models for each individual cluster ranged from 0.8508 to 0.9692 for the 10 clusters. Simulations confirmed that a combination of week-to-week ARMAX models and weekly probability distribution functions (wPdf) could predict patient responses at week 6 from baseline with p-
values ranging from 0.20 to 0.74 for 4 of the 6 clusters. This was based on 226 (out of 1,759) patients in the observational study that were not matched with the RCT data and that the model considered eligible for simulation. (Observational study patients who matched with RCT data were used to calibrate the ARMAX models and could, therefore, not be used for assessing the predictive capability of the simulations.) Simulation included 1000 runs per each patient for a total of 22,600 simulations.

**Conclusion**

Age interacts in complex ways with covariates, pain levels, and sleep interference. Predicting treatment response requires identifying subgroups of patients that take into account time series information as well as patient characteristics.
**Title:** The Relationship Between Pain Threshold, Muscle Strength, And Qol In Elderly People

**Poster Number** PTH097

**Authors**
S. Shiozawa, T. Graven-Nielsen

Aalborg University, Aalborg, Denmark

**Aim of Investigation**
It is known that painful knee osteoarthritis patients have deep tissue hyperalgesia and low pressure pain threshold (PPT). Furthermore, knee extension strength is reduced under the condition of knee pain. However, the relationship between knee PPT, knee muscle strength and quality of life (QOL) in elderly people is still unclear. The aim of this study was to investigate the relationship between PPT, muscle strength, and QOL in elderly people.

**Results**
Averaged PPT and maximum knee extension strength were 197.2 kPa +/- 76.2 kPa and 121.0 N +/- 54.6 N (mean +/- SD). QOL was 24.6 +/- 18.3 (Physical Functioning), 33.4 +/- 16.4 (Role Physical), 43.0 +/- 12.1 (Bodily Pain), 42.2 +/- 13.8 (General Health), 47.1 +/- 12.5 (Vitality), 42.2 +/- 14.3 (Social Functioning), 36.5 +/- 16.7 (Role Emotional), 43.9 +/- 11.7 (Mental Health). Significant correlations were found between the knee strength and QOLs ($r > 0.38$, $p < 0.05$), whereas the PPT and QOLs were not correlated. A significant correlation was also indicated between averaged PPT and maximum extension strength ($r = 0.38$, $p < 0.05$)

**Conclusion**
The relationship between knee pain threshold, knee muscle strength, and QOL in elderly people was demonstrated. It seems that the functional effect of the painful condition is important for the reduced quality of life.
**Title:** Perceived Discrimination Is Related To Emotional Impact Scores Of The Patient-Reported Outcome Measure, The Adult Sickle Cell Quality-Of-Life Measurement (Ascq-Me)

**Poster Number** PTH098

**Authors**  

University of Florida, Gainesville, FL, University of Illinois at Chicago, Chicago, IL

**Aim of Investigation**  
Perceived discrimination has been associated with health outcomes in patients with sickle cell disease (SCD) including greater pain burden,1 but its association with ASCQ-Me, a sickle cell disease-specific patient-reported outcome, has not been studied. The purpose of this descriptive correlational study was to examine the relationship between perceived discrimination and ASCQ-Me subscales (emotional impact, social functioning impact, sleep impact, stiffness impact, pain impact, frequency of pain episode, and severity of pain episode)5 in adults with SCD.

**Results**  
The mean scores for the study variables were: Perceived discrimination (1.8±0.7); emotional impact (46.7 ± 6.1); social functioning impact (47.1 ± 8.1); sleep impact (48.1 ± 8.2); stiffness impact (46.7 ± 7.0); pain impact (45.9 ± 7.6); frequency of pain episode (47.5±9.6); and severity of pain episode (51.5 ± 9.8). Perceived discrimination was negatively correlated with emotional impact (rs =-.33, p=.03). Patients who reported greater perceived discrimination are significantly more likely to have lower scores on emotional impact, where lower scores mean unhealthy emotional status. There were no statistically significant differences between perceived discrimination, and social functioning impact (rs =-.23, p=.13), sleep impact (rs =-.15, p=.33), stiffness impact (rs =-.07, p=.66), pain impact (rs =-.04, p=.78), frequency of pain episode (rs =-.03, p=.85), or severity of pain episode (rs =-.03, p=.82).

**Conclusion**  
This is the first report of a statistically significant negative relationship between perceived discrimination and ASCQ-Me emotional impact. Findings are consistent with previous reports of the negative relationships between perceived discrimination and quality of life in many pain patient populations.4, 6-8 Results from future studies in this population will provide additional evidence to better understand
the non-significant relationship we found between perceived discrimination and other ASCQ-Me subscales in this vulnerable population whose lifelong disease trajectory poses myriad opportunity for perception of discrimination that could influence their quality of life.
Title: Service Availability Of Anti-Neuropathic Pain Medications, $\alpha_2\delta$ Ligands, For The Treatment Of Neuropathic Pain In Government Hospitals In Thailand

Poster Number: PTH099

Authors
T. Suansanee, T. Suebjakin, N. Poomkumarn

Department of Pharmacy, Faculty of Pharmacy, Mahidol University, Bangkok, --- please select a state ---

Aim of Investigation
The $\alpha_2\delta$ ligands which was gabapentin and pregabalin were the mainstay pharmacological choices for treatment of various neuropathic pain conditions. This type of pain generally can be treated by general practitioners if they have anti-neuropathic pain medications in their practice settings. Thus, the objective of this study was to assess the distribution of gabapentin and pregabalin in term of available brand name and formulation in government hospitals in Thailand.

Results
There were 653 hospitals responded to this survey which accounted for 73% of all government hospitals in Thailand. These participated hospitals were classified as 73%, 93%, 90% and 70% of all university/teaching hospitals, regional hospitals, general/province hospitals and community hospitals in Thailand, respectively. All university/teaching hospitals had both gabapentin and pregabalin. For regional hospitals and general/province hospitals, gabapentin was available in 96% and 97%, respectively. While, pregabalin was obtainable only 81% and 65% at regional hospitals and general/province hospitals, respectively. Focus on community hospitals, gabapentin and pregabalin were available in a small number (26% and 2%, serially).

Conclusion
In Thailand, the anti-neuropathic pain medications, $\alpha_2\delta$ ligands, was not widely distributed in all level of healthcare units. They were generally available in tertiary hospitals which were university/teaching hospitals, regional hospitals and general/province hospitals. Most of the community hospitals which were located in all small community were neither have gabapentin nor pregabalin. This may contribute a big impact on the quality of care for neuropathic pain management.
Title: Analysis Of Patients Presenting At Pain Clinic Of A Tertiary Care Government-Run Hospital In India: Changing Scenarios And Difficulties Faced

Poster Number PTH100

Authors
D. Khurana, S. Tuteja

DDU Hospital, New Delhi, IN

Aim of Investigation
1. To analyse the patients presenting to pain clinic of a tertiary care centre in a developing country. 2. To find problems faced by young pain physicians in starting a pain clinic.

Results
A total of 1109 patients visited pain clinic during the period from April 2012 to April 2014, out of which 612 were males and 497 females. Total number of visits was 1481. Pain type recorded was neuropathic in 12%, nociceptive in 21% and mixed in 67% patients. Oral management of pain was done in 502 patients, TENS+ oral treatment in 369 patients & 170 patients required interventional pain management for uncontrolled pain or upon unavailability of opioid for pain management. Strong opioid (oral morphine) for pain management is not available at our clinic. The patients were referred to pain clinic by colleagues from medicine, orthopaedics, surgery & ENT department; some patients came directly to the pain centre.

Conclusion
The biggest problem faced was to start the pain clinic & obtain referrals from other specialities. Sparing the anesthesiologist from other schedules was a challenge. Availability of opioids for pain management was another problem that has eased over the years due to policy changes by the government. Most patients come from far off areas and are lost to follow up hence performing blocks on first visit was considered more suitable by the pain physician.
Title: Admixture Mapping For Pain Sensitivity Differences Among Races

Poster Number PTH101

Authors
S. Khoury, M. Barakatt, G. Slade, S. Smith, R. Fillingim, R. Ohrbach, J. Greenspan, W. Maixner, S. Gravel, L. Diatchenko

McGill University, Montreal, QC, McGill University, Montreal, Quebec, Center for Pain Research and Innovation, University of North Carolina at Chapel Hill, Chapel Hill, NC, Center for Translational Pain Medicine, Department of Anesthesiology, Duke University Medical Center, Durham, NC, University of Florida, Gainesville, FL, University at Buffalo, Buffalo, NY, University of Maryland, School of Dentistry, Baltimore, MD, Duke University, Durham, NC, McGill University, Montral, Canada

Aim of Investigation
It is widely accepted that ethnic group differences exist in clinical pain perception, in pain-related disabilities and in the response to experimental pain testing. For instance, African Americans (AA) report more disability with regards to clinical pain and show greater sensitivity to experimental pain. In this study, we aimed to investigate the differences in sensitivities to noxious stimuli among races using admixture mapping. For this purpose, we used heat pain tolerance and average heat pain rating in order to elucidate genetic component of racial difference in pain sensitivity.

Results
Individuals with the lowest African ancestry proportion have lower heat pain ratings than individuals with highest African ancestry proportion at the three temperatures tested (at 46°C: y=-12.9; r²=0.02; p<0.0001; at 48°C:y=-14.9; r²=0.03; p<0.0001; at 50°C:y=-14.4; r²=0.04; p<0.0001). Heat pain tolerance was not associated with proportion of African ancestry. Next, using African ancestry proportion as a dependent variable, a linear regression model showed that heat pain ratings at 46°C, at 48°C, and at 50°C were associated with a locus mapping to chromosome 10q22 (at 46°C: r=0.1; p=3.3e-08; at 48°C:r=0.2; p=1.4E-15; at 50°C:r=0.2; p=2.1E-21). This region encodes the C10orf11 gene, a leucine-rich repeat protein which is thought to play in melanocyte differentiation.

Conclusion
Using admixture mapping, we were able to confirm that AA are more sensitive to experimental pain but also that this higher heat sensitivity is proportional to the percentage of African ancestry derived
genomic loci. C10orf11 gene locus was shown to be associated with sensitivity to heat pain, with this association being proportional to African ancestry. This is the first study identifying a gene contributing to racial differences in pain perception.
Title: Resilience Does Not Explain The Dissociation Between Chronic Pain And Physical Activity In HIV-Positive South Africans

Poster Number PTH102

Authors
A. Wadley, D. Mitchell, P. Kamerman

Brain Function Research Group, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, SOUTH AFRICA

Aim of Investigation
The burden of pain is high in HIV-positive individuals, but, at least in African populations, having pain does not correlate well with pain-related functional impairment. Resilience, the ability to cope with adversity, may promote adaptation to pain, so we hypothesised that higher resilience would correlate with less impairment of activity in the face of pain.

Results
Our patients indeed were highly resilient (all patients scored > 73% of maximum score). Greater resilience was positively correlated with better quality of life (Spearman's; r = 0.41, p < 0.0001), but was not associated with pain intensity (Spearman correlations; p > 0.05). There was no difference in the duration or intensity of activity between those with and without pain (Wilcoxon rank sums; p > 0.05), and although there was a significant negative correlation between resilience and the duration and intensity of activity, the association was very weak (Spearman's correlations; p < 0.05). A significantly greater proportion of patients in pain reported higher levels of worry for every stressor than those without pain. Worries about money were the most frequent for both cohorts, with 84% of patients in the pain cohort and 55% in the pain-free cohort worried about money 'nearly all the time'. Patients in pain indicated that one of their other greatest worries was being 'gossiped about', that is, their HIV status being revealed and discussed by others. Indeed, 44% (44/99) had not told their friends and 9% (9/99) had not told their families about their chronic pain for fear that it would reveal their HIV status.

Conclusion
Financial stresses and the fear of HIV stigma may have driven the patients to conceal pain and to suppress its expected impairment of activity. Despite the lack of associations between resilience and both pain and activity, resilience was a significant determinant of quality of life. HIV-related pain is
difficult to treat pharmacologically and strategies to improve resilience in those patients with low quality of life may be beneficial.
Title: The Pain Perception In The Experience Of Childhood Cancer

Poster Number PTH103

Authors
H. Moura-Siqueira, R. Falconi Gomez, T. Raminelli da Silva, S. Saltareli, O. Gomes Colhado, F. Faleiros Sousa

Universidade de São Paulo, RIBEIRAO PRETO, São Paulo, Universidade de São Paulo, Ribeirão Preto, São Paulo, Universidade Estadual de Maringá, Maringá, São Paulo

Aim of Investigation
The main aim of this study was to evaluate how children/adolescents with cancer (n=100) and their family caregivers could understand the pain.

Results
The results showed that the age distribution (05-07, 08-11, and 12-18 years), with prevalence rates for age group between 12 and 18 years (45%), female (53%), elementary education (95%), and Catholics (62%). In addition, it was identified the highest rates for chronic pain (51%) and leukemia (47%). For the FAS results, the most indicated was the F-I figure (71%) representing a pain negative effect. For EMADOR instrument, the results for age group showed that the descriptors characterized in acute pain were related with affective and cognitive dimensions. On the other hand, in relation to chronic pain, such dimensions were perceived as a procedural way, according to the cognitive development, varying from concrete thinking (sensory descriptors) to abstract (affective descriptors). For technical drawing, the child/adolescent with cancer indicated perception of pain ranging between the magical thinking to the mental representations with metaphors more elaborated. The reports revealed that the pain was associated to experience and subjectivity of children/adolescents with cancer through the physical, social, emotional, and spiritual dimensions. In relation to the relatives, especially by mothers, it was noticed that the childhood cancer painful experience was perceived in similar way to the ill child, i.e. bidirectionally linked to the context and the time in which the disease entered them. The pain was perceived by summing the qualitative (subjective) and quantitative (objective). Thus, it was concluded that the pain was thought multidimensionally. EMADOR was considered an easy and reliable tool to assess the pain in the development process; i.e., children with cancer from 05 years old were able to understand painful phenomenon as well as their mothers, after themselves.
Conclusion
This multidimensional complex interrelation of pain indicates the importance of using appropriate instruments in the public health, specifically, by means of the interdisciplinary team ('care-pain') for pain evaluation, in which it takes into account feelings, perceptions, and meanings possibly related with the pain experience ('pain-experience'). Therefore, this study brings opportunities to reflect on the improved management of the pediatric pain in the medical field, nursing, psychology, physiotherapy, among others.
Title: Pain Extent And Function In Youth With Physical Disabilities

Poster Number PTH104

Authors
J. Miró, R. de la Vega, C. Tomé-Pires, E. Sanchez-Rodriguez, E. Castarlenas, M. Jensen, J. Engel

Unit for the Study and Treatment of Pain – ALGOS, Universitat Rovira i Virgili, Tarragona, Spain, University of Washington. Department of Rehabilitation Medicine, Seattle, WA, Department of Occupational Science and Technology, University of Wisconsin-Milwaukee, USA, Milwaukee, WI

Aim of Investigation
There is a significant knowledge gap regarding the influence of pain extent (as reflected by the number of body areas with pain) as a contributing factor to the functioning in persons with physical disabilities and chronic pain. The aim of this study was to increase our understanding of the role that pain extent plays in function among young people with disabilities and chronic pain.

Results
There was a positive association between pain extent and intensity with pain interference, and a negative association with psychological functioning and disability in the study sample. Moreover, pain intensity at specific sites contributed to the prediction of pain interference (back pain), psychological functioning (shoulder pain) and disability (pain in the bottom/hips).

Conclusion
The findings support the importance of assessing pain intensity at specific locations as part of a thorough evaluation of young people with disabilities and chronic pain, as well as the importance of addressing pain at multiple sites, when managing pain in this group of young people.
Title: Parent Perceptions Of Injustice About Their Child’S Chronic Pain

Poster Number PTH105

Authors
M. Miller, E. Scott, Z. Trost, A. Hirsh

Indiana University-Purdue University in Indianapolis, Indianapolis, IN, University of Michigan, Ann Arbor, MI, University of Alabama, Birmingham, United States, Indiana University - Purdue University Indianapolis, Indianapolis, IN

Aim of Investigation
Perceiving one's pain as unjust has been identified as an important cognitive-emotional factor in the pain experience of adults and, more recently, in that of children. We recently found that injustice perceptions predicted pain intensity and emotional, social, and school functioning in a pediatric chronic pain sample. Parent-child relationships also play an important role in the pain experience of children. Research suggests that children often model parents' coping behaviors and other cognitive-emotional reactions to pain. For example, children and parents have been found to engage in similar levels of pain catastrophizing, which is associated with worse pain outcomes. The current study extended this literature by examining the concordance in injustice perceptions between children/adolescents with chronic pain and their parents. We also examined the association between child-parent concordance in injustice perceptions and clinical pain outcomes.

Results
Results indicated that parent injustice perceptions were significantly higher than child injustice perceptions (t(138) = 5.80, p < .001, d = .50). Intraclass correlation analysis indicated moderate concordance between parent- and child-reported injustice perceptions (r = .48). Difference scores and an IEQ clinical cutoff score of 18 were used to categorize parent-child dyads into one of four groups based on their concordance of injustice perceptions: (1) concordant high (within ±1 SD of the mean difference score, and child or parent IEQ score > 18), (2) concordant low (within ±1 SD of the mean difference score, and child or parent IEQ score ≤ 18), (3) discordant high parent (P) – low child (C) (< –1 SD of the mean difference score), and (4) discordant low parent (P) – high child (C) (> 1 SD of the mean difference score). One-way ANOVAs identified significant group differences in child-reported pain intensity (F(3,138) = 2.80, p < .05, η2 = .06) and QOL (F(3,138) = 15.11, p < .01, η2 = .25). For pain intensity, discordant low P – high C dyads reported the highest pain of the four groups, and significantly
higher pain than discordant high P – low C dyads (MD = 1.94, p < .05). Concordant high dyads reported the second highest pain, and significantly higher pain than discordant high P – low C dyads (MD = 1.68, p < .05). A similar pattern emerged for QOL. Discordant low P – high C dyads reported the worst QOL, and significantly worse QOL than concordant high dyads (MD = -10.22, p < .01), concordant low dyads (MD = -23.70, p < .01), and discordant high P – low C dyads (MD = -28.97, p < .01). Concordant high dyads reported the second worse QOL, and significantly worse QOL than concordant low dyads (MD = -13.48, p < .01) and discordant high P – low C dyads (MD = -18.75, p < .01).

**Conclusion**
Results from the current study suggest that children/adolescents with chronic pain have different perspectives about pain than do their parents, particularly on issues of fairness and justice. Children/adolescents with high injustice perceptions may be at increased risk for worse pain and poorer quality of life compared to children/adolescents with low injustice perceptions, regardless of their parents' perceptions. Interestingly, the worse outcomes appear to be experienced by children/adolescents with high injustice perceptions who have parents with low injustice perceptions. This discrepancy may engender feelings of invalidation in the child – that their parent is not taking their pain seriously – and lead to maladaptive pain behaviors intended to communicate the severity of their pain. Future research is needed to replicate these findings and to better characterize the nature and consequences of injustice perceptions in children with chronic pain and their parents.
Title: The Pain Perception In The Experience Of Childhood Cancer

Poster Number PTH106

Authors
H. Moura-Siqueira, R. Falconi Gomez, S. Saltareli, T. Raminelli da Silva, O. Colhado, F. Faleiros Sousa

Universidade de São Paulo, RIBEIRAO PRETO, São Paulo, Universidade de São Paulo, Ribeirão Preto, São Paulo, Universidade Estadual de Maringá, Maringá, Paraná

Aim of Investigation
The main aim of this study was to evaluate how children/adolescents with cancer (n=100) and their family caregivers could understand the pain.

Results
The results showed that the age distribution (05-07, 08-11, and 12-18 years), with prevalence rates for age group between 12 and 18 years (45%), female (53%), elementary education (95%), and Catholics (62%). In addition, it was identified the highest rates for chronic pain (51%) and leukemia (47%). For the FAS results, the most indicated was the F-I figure (71%) representing a pain negative effect. For EMADOR instrument, the results for age group showed that the descriptors characterized in acute pain were related with affective and cognitive dimensions. On the other hand, in relation to chronic pain, such dimensions were perceived as a procedural way, according to the cognitive development, varying from concrete thinking (sensory descriptors) to abstract (affective descriptors). For technical drawing, the child/adolescent with cancer indicated perception of pain ranging between the magical thinking to the mental representations with metaphors more elaborated. The reports revealed that the pain was associated to experience and subjectivity of children/adolescents with cancer through the physical, social, emotional, and spiritual dimensions. In relation to the relatives, especially by mothers, it was noticed that the childhood cancer painful experience was perceived in similar way to the ill child, i.e. bidirectionally linked to the context and the time in which the disease entered them. The pain was perceived by summing the qualitative (subjective) and quantitative (objective).

Conclusion
Thus, it was concluded that the pain was thought multidimensionally. EMADOR was considered an easy and reliable tool to assess the pain in the development process; i.e., children with cancer from 05 years old were able to understand painful phenomenon as well as their mothers, after themselves. This
multidimensional complex interrelation of pain indicates the importance of using appropriate instruments in the public health, specifically, by means of the interdisciplinary team ('care-pain') for pain evaluation, in which it takes into account feelings, perceptions, and meanings possibly related with the pain experience ('pain-experience'). Therefore, this study brings opportunities to reflect on the improved management of the pediatric pain in the medical field, nursing, psychology, physiotherapy, among others.
Title: Breast Feeding Is The Best Pain Control Method When Giving Routine Intramuscular Vitamin K Injection To Full Term Neonates

Poster Number PTH107

Authors
S. Bandara, A. Kariyawasam, K. Pethiyagoda, M. Ratnayake

Teaching Hospital Peradeniya, Kandy, Sri Lanka, Lady Ridgeway Hospital For Children, Colombo, Sri Lanka, Colombo, Sri Lanka, University of Peradeniya, Kandy, Sri Lanka, Hoptan Devisonal Hospital, Badulla, Sri Lanka

Aim of Investigation
Find out the best pain control method for the routine intramuscular vitamin K in full-term neonates. In Sri Lanka vitamin K is routinely given to all new born babies to prevent hemorrhagic disease of newborn because when vitamin K is administered orally there is a high incidence of late on set hemorrhagic disease of newborn. Within several hours of birth all term new born babies are given vitamin K 1mg intramuscularly and no repeated doses are necessary. Although the intramuscular vitamin K is very effective it is painful to the new born. But there are no studies available for the pain management during this routine intramuscular vitamin K injection. This is usually given in the very first hours after baby is born, that we call golden hours and it is very important to manage this pain. The neonates who get exposed to a severe pain while the routine intramuscular vitamin K injections can have short term problems such as increase in heart rate, drop of saturation and physiological studies indicate that very early pain or stress experiences have more than immediate consequences for infants. So neonates will have great benefits and mothers will be happy that their precious baby is getting an injection with less pain.

Results
Results: Using SPSS (ver. 22) for Windows Table 1: Pain Score during Vitamin K injection in interventional group and routine procedure group

<table>
<thead>
<tr>
<th>Score</th>
<th>SD</th>
<th>Median</th>
<th>Range</th>
<th>95% CI Interventional group</th>
<th>Mean Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.80</td>
<td>1.74</td>
<td>3</td>
<td>0 to 6</td>
<td>-3.22 to -1.86</td>
<td>-3.46</td>
</tr>
<tr>
<td>5.34</td>
<td>1.67</td>
<td>6</td>
<td>1 to 7</td>
<td>-3.22 to -1.86</td>
<td>-3.22</td>
</tr>
<tr>
<td>4.07</td>
<td>2.12</td>
<td>4</td>
<td>0 to 7</td>
<td>-7.44 df= 98 P&lt; 0.001</td>
<td>-7.44</td>
</tr>
</tbody>
</table>
Conclusion
It was found that the neonates who were breast fed while Vitamin K injection was administered suffered less pain when compared with neonates who were not breast fed while the injection was given. The difference was statistically significant (t= -7.44, df= 98, P< 0.001)
Title: A Systematic Review And Meta-Analysis Of Adjuvants To Caudal Analgesia In Children Undergoing Infra-Abdominal Surgeries

Poster Number PTH108

Authors
J. Shahani
KK Women's and Children's Hospital, Singapore, Singapore

Aim of Investigation
Caudal analgesia combined with general anaesthesia is a common procedure for providing postoperative pain relief in children undergoing infra-abdominal surgeries. There are many adjuvants added to the local anaesthetics to provide longer duration of pain relief in these patients. The aim of the study is to review and analyse the published papers on the topic and confirm the ideal adjuvant for this technique keeping in view the advantages and disadvantages of each adjuvant drug.

Results
The five adjuvants commonly used are fentanyl, ketamine, clonidine, dexamethasone and dexmedetomidine. The duration of analgesia was longer with clonidine, dexamethasone and dexmedetomidine. The adverse effects were more with fentanyl compared to the other adjuvants.

Conclusion
In the absence of any new longer acting local anaesthetic drug, the use of adjuvants is likely to continue. The systematic review and meta-analysis from the papers published in last 14 years favour the use of clonidine and dexmedetomidine for prolongation of duration of analgesia with least side effects.
Date: 09/29/2016 03:15:00 PM

Title: Pediatric Pain Pathway In Improving Post-Surgical Persistent Pain In The Pediatric Amputee Population

Poster Number PTH109

Authors
M. Parekh¹, R. Naidu

University of California, San Francisco, San Francisco, CA

Aim of Investigation
Persistent post-surgical pain (PPSP) is defined as pain that develops after a surgical procedure, lasts for at least 2 months, with other causes such as malignancy or chronic infection being excluded. The estimated incidence of PPSP following amputations in the UK & US populations is 50-85% with the number of operations approximately 145,000 in both the UK & US, combined. It clearly affects a large number of patients and has major implications on public health, economics and quality of life. An observational study evaluating the economic and humanistic burden of post-trauma and post-surgical persistent pain, found that this patient population had high pain scores and used a significant amount of health care resources. Risk factors for PPSP include demographic factors, genetic factors, psychosocial factors, intensity of acute postoperative pain, surgical factors, and anesthetic technique. The incidence of persistent post-surgical pain in the pediatric amputee population has not been reported separately. There are two reasons this is of concern: 1) The potential life expectancy is greater in the pediatric population compared to the adult population and 2) The risk for the development of PPSP is greater for ages 15-19 versus older age groups. Based on the above, one could infer that the incidence of pediatric PPSP would be high. In this retrospective case control series, we propose a pediatric pain pathway which includes multimodal therapies (regional and neuraxial techniques, gabapentin, ketamine) to decrease the incidence of persistent post-surgical pain in the pediatric amputee population.

Results
Pending.

Conclusion
The incidence of phantom limb pain in cancer-related amputation without multimodal therapy is reported as high as 90% and with the use of preamputation therapies (epidural, continuous nerve block, and gabapentin) decreased to 76%. This case series will show whether a pain pathway in order to
reduce PPSP is important. The limitations of this study include its retrospective nature and small sample size. Further studies in pediatric persistent post-surgical pain are needed. Conclusions are pending results and analysis.
Title: Associations Between Pain And Executive Function Impairments Among Emerging Adults: Is Poor Sleep To Blame?

Poster Number PTH110

Authors
A. Bohnert, C. Bates, K. Polnaszek, C. Murray, R. Silton

Loyola University Chicago, Chicago, IL

Aim of Investigation
Emerging adulthood is a distinct developmental period that is characterized by transitions across multiple domains as well as ongoing maturation of executive functions (EFs). EFs represent a collection of inter-related domains, including inhibition, shifting, and updating, that enable individuals to successfully navigate day-to-day experiences. These functions are essential to modification of thoughts and behaviors, which may be a key component of effective management of pain through redirection or shifting of attention and inhibition or suppression of ruminative thoughts about pain. In fact, research suggests that pain severity is associated with EF impairments. Further, sleep difficulties, which are more pronounced among emerging adults with pain, may also exacerbate EF impairments. Little is known about the combined effects of pain and sleep difficulties on EFs in emerging adults. The primary aim of this study are to examine whether relations between pain and EF impairments are moderated by sleep difficulties.

Results
Correlational analyses revealed significant positive relations between most pain and sleep difficulty variables, with correlations ranging from $r = .11$ to $r = .24$. Hierarchical multiple regression analyses were conducted to investigate the relation between pain and EFs and whether these relations were moderated by sleep difficulties. The main effects of pain variables were entered in the first step. The main effects of the sleep variables were entered in the second step, estimating the effect of sleep difficulties on EFs after accounting for the variance associated with pain. Pain x sleep interactions were entered in the third and final step. Separate regressions were conducted for each EF outcome (i.e., inhibition, shifting, and updating). Results revealed main effects of day dysfunction on all EF domains ($p < .05$), as well as a significant interaction between pain impairment and sleep disturbance predicting inhibition ($p < .05$) and updating impairments ($p < .05$).
Conclusion
Pain is associated with impairments in inhibition and updating EFs specifically under conditions of high sleep disturbance. These findings have relevant implications for psychosocial interventions for pain conditions that target sleep hygiene as an important pathway toward recovery and wellness.
Title: Do Attitudes About Pain Influence The Coping Strategies That Adolescents Use?

Poster Number PTH111

Authors
E. Sánchez-Rodríguez, E. Solé, C. Tomé-Pires, S. Galán, M. Racine, M. Jensen

Unit for the Study and Treatment of Pain - ALGOS, Universitat Rovira i Virgili, Tarragona, Spain, Research Center for Behavior Assessment (CRAMC), Department of Psychology, Universitat Rovira i Virgili, Tarragona, Spain, Institut d’Investigació Sanitària Pere Virgili; Universitat Rovira i Virgili, Tarragona, Spain, University of Western Ontario, London, Ontario, Canada, Department of Rehabilitation Medicine, University of Washington, Seattle, WA, Chair in Pediatric Pain Universitat Rovira i Virgili-Fudación Grünenthal, Tarragona, Spain

Aim of Investigation
The aim of this work was to determine the extent to which pain beliefs are associated with the coping strategies that adolescents use to manage their pain. Based on previous research, we hypothesized that adaptive beliefs about pain would show significant and independent associations with the use of adaptive pain coping strategies (i.e., approach and problem-focused avoidance strategies) whereas maladaptive beliefs about pain would be more strongly associated with maladaptive pain coping strategies (i.e., emotion-focused avoidance strategies). Furthermore, we anticipated that both maladaptive pain beliefs and maladaptive pain coping strategies would show significant and independent associations with disability.

Results
Predicting adaptive coping strategies: Beliefs that others should be solicitous in response to pain, that pain is something that one can control and that emotions can impact pain all evidenced significant, positive and independent associations with the use of 'Approach' coping strategies. Beliefs that exercise is beneficial for pain management demonstrated significant, positive and independent associations with the use of 'Problem-Focused Avoidance' coping strategies, and the belief that one is disabled by pain evidenced a significant, negative and independent association with the use of 'Problem-Focused Avoidance' strategies. Predicting maladaptive coping strategies: The beliefs that one is disabled by pain and that emotion can impact pain evidenced significant, positive and independent associations with the...
use of 'Emotion-Focused Avoidance' coping strategies, whereas the beliefs that pain is controllable and that medications are appropriate for pain management evidenced, negative and independent associations with the use of 'Emotion-Focused Avoidance' strategies. Predicting disability: Finally, the belief that one is necessarily disabled by pain and the pain coping strategies based in externalizing and internalizing/catastrophizing made significant contributions to the prediction of disability (positive associations) whereas the beliefs that exercise is beneficial for pain management and that a medical cure exists for pain made significant and negative contributions to the prediction of disability.

Conclusion

As predicted, significant adaptive beliefs about pain were positively related with the use of adaptive pain coping strategies and negatively related with the use of maladaptive coping strategies. Maladaptive beliefs about pain showed the opposite pattern. Moreover, the belief that emotion impacts pain were positively associated with both the use of adaptive and maladaptive coping strategies; that is, this belief predicted more coping in general. Also, and as predicted, maladaptive pain beliefs and maladaptive pain coping strategies were significantly and positive related with disability, while adaptive beliefs about pain were significantly and negative related with disability. The findings support the potential importance of pain treatments (such as CBT) that teach and encourage the use of adaptive beliefs and coping, and discourage the use of maladaptive beliefs and coping in children and adolescents.
Title: Effects Of Multidisciplinary Team Management In Pediatric Chronic Pain On Quality Of Life And Emotional Functioning: A Follow-Up Study

Poster Number PTH112

Authors
U. Caverius
Lund University, Lund, Sweden

Aim of Investigation
Evaluate the impact of multidisciplinary treatment in a CBT/ACT approach in an open clinic setting at discharge and three months follow-up on 1. Children's scores on QoL, physical functioning, emotional distress, Psychological flexibility 2. Parent's scores of the child's QoL, physical functioning and emotional distress 3. Parents psychological flexibility and emotional distress for their children's pain

Results
21 patients were included in the study. 8 were still in treatment at the end of the study period. 10 were included for follow up at end if the study and 8 three months after treatment. Significant improvements were found in quality of life, physical functioning, emotional distress and psychological flexibility at end of treatment and 3 months follow-up

Conclusion
This pilot study indicates that MDT in a CBT/ACT model improves quality of life, physical functioning and emotional distress for children and adolescents with chronic, non-malignant pain.
Title: Comparison Of Thoracic Epidural Fentanyl With Or Without Bupivacaine In Multimodal Analgesia For Fast Track Thoracic Surgery

Poster Number PTH113

Authors
J. SOOD, M. Baansal, M. Basnet, S. Sharma

Sir Ganga Ram Hospital, New Delhi, India, New Delhi, India, Institute of Medicine Maharajgunj Medical campus, Lalitpur, Nepal

Aim of Investigation
To compare thoracic epidural fentanyl, with or without bupivacaine, for fast track thoracic surgery with respect to analgesia, side effects and mobilization.

Results
Demographic data (age, sex, weight, height, BMI) and procedural data (type of surgery, surgical side, open/VATS approach, and epidural site) were similar. Three patients of group F were excluded due to incomplete data record. Mean VAS scores at 6,12,24,36 and 48 hours during rest and coughing were similar. Number of patients with satisfactory pain relief (VAS score <3) was similar in both groups, however more number of patients belonging to group F experienced pain (VAS>3) than those belonging to group B+F during 6-12 hours (2 vs. 9, p=0.018). However the difference was not significant during coughing. Rescue analgesic requirements were similar in both groups (8 vs. 11, p=0.45) Interruptions of epidural were considerably more in Group B+F (15 vs. 6, p=0.05). Hypotension was the most common side effect and was significantly more in Group B+F (15 vs 3, p=0.0025). Nausea/vomiting was more common in Group F (3 vs. 10, p=0.03). Other side effects such as bradycardia, pruritus, muscle weakness, desaturation, respiratory depression (SpO2<92%, respiratory rate <10/min) were absent. Sedation was experienced by patients in both groups which was not statistically significant (p=1.0).

Delays in mobilization were more common in Group B+F (10 vs 1, p=0.005). ICU stay, when needed, was slightly prolonged in Group B+F, although not statistically significant. (10 vs. 6, p=0.5)

Conclusion
Thoracic epidural analgesia in combination of bupivacaine and fentanyl provides more satisfactory analgesia for thoracic surgeries. For early mobilization and better hemodynamic stability, multimodal...
analgesia including thoracic epidural analgesia with fentanyl in normal saline may be more appropriate for fast track thoracic surgeries.
Title: Results From Using The Nausea Intensity Scale: The Severity Of Nausea Is Significantly Reduced By CL-108 Compared With A Standard Hydrocodone/Acetaminophen Analgesic When Used To Treat Moderate-To-Severe Pain

Poster Number PTH114

Authors
E. Schachtel, S. Daniels, K. Patrick, S. Richardson, S. Royall, M. Lorton, B. Zhang, S. Cho, B. Schachtel
Charleston Laboratories, Inc., Jupiter, FL, Optimal Research, Austin, TX, INC Research, Raleigh, NC, Jean Brown Research, Salt Lake City, UT, Jean Brown Research, St. George, UT, MacroStat, Inc., Wilmington, DE, Daiichi Sankyo, Inc., Parsippany, NJ

Aim of Investigation
Patients in clinical trials often voluntarily report nausea after using a medication and rate the severity of this adverse event on a categorical scale. As in the measurement of other symptoms, however, patients can use a spectrum of choices to express the severity of symptoms other than 'mild/moderate/severe.' In designing a controlled clinical trial on patients treated with an opioid, hydrocodone, which is known to induce nausea and vomiting, we took a different approach. By employing a 0–10 Nausea Intensity Scale (NIS; with 'no nausea' and 'severe nausea' as anchors) we enabled patients to convey how nauseated they felt. Here we report the results of this active surveillance for nausea severity before and after opioid administration for postoperative pain.

Results
CL-108 was demonstrated to be effective at reducing moderate-to-severe pain (p<0.001 compared to placebo). Over the 5-day trial, 134 (53.6%) of 250 patients who used HC/APAP reported moderate or severe nausea (ie, NIS ratings of 4–6 or 7–10) compared with 72 (28.6%) of 252 patients who used CL-108, most of whom had mild or no nausea (p <0.001). There was a significant difference between the mean peak severity of nausea for patients who used CL-108 (2.6) compared with patients who used HC/APAP (4.5), resulting in >40% reduction in the worst severity of nausea experienced by patients treated with CL-108 compared with HC/APAP (both p <0.001). Other patient-reported OINV outcomes such as reduced frequency of vomiting (8.3% for CL-108, 24.4% for HC/APAP) and less use of antiemetics (13.5% for CL-108, 46.0% for HC/APAP, both p<0.001) provided additional evidence of the efficacy of CL-108 for OINV, consistent with a reduced severity of nausea.
Conclusion
These results confirm the utility of the NIS as an instrument for measuring the severity of nausea. When patients used the NIS they reported a wide range of nausea severity, distinguishing CL-108 effects from HC/APAP. In addition to experiencing significantly less OINV than patients treated with standard HC/APAP, patients treated with CL-108 had significantly milder nausea (or none) compared with patients treated with standard HC/APAP. We recommend the use of NIS for other investigators who study opioids and OINV. Sponsored by Charleston Laboratories and Daiichi Sankyo Bruera E, <i>J Palliat Care</i>, 1991.
Aim of Investigation
Pain associated with acute flares of osteoarthritis (OA) can significantly limit a patient's ability to perform routine activities such as getting dressed and bathing, limitations which can impact the quality of life. The goal of OA treatment is to relieve joint pain and stiffness, and importantly, to improve physical function. In a previous randomized, double-blind, placebo- and active-controlled trial, CL-108 (hydrocodone 7.5 mg, acetaminophen 325 mg [HC/APAP] with rapid-release promethazine 12.5 mg) was demonstrated to be effective for moderate-to-severe pain and opioid-induced nausea and vomiting (OINV) in postoperative patients (both p <0.001). In an open-label actual-use study on patients with an acute flare of OA, CL-108 was shown to be safe and efficacious for the treatment of moderate-to-severe pain and stiffness, with a low incidence (2.2%) of OINV. Here we report the effects of CL-108 on the performance of activities of daily living (ADL) as indicators of physical function.

Results
One-hundred and seventy-four patients with a mean age of 61.2 ± 10.1 (SD) years used on average 2 doses/day of CL-108 to treat flares of OA in the knee or hip. Compared to their pre-treatment status, patients reported significant (>20%) improvement at the end of the study in all 10 ADLs (all p <0.001): vigorous activities (by 39% of the patients), moderate activities (39%), lifting or carrying groceries (36%), climbing one flight of stairs (47%), climbing several flights of stairs (42%), the ability to bend, kneel, or stoop (48%), bathing or dressing oneself (35%), and walking more than a mile (43%), several blocks
(45%), or one block (45%). No clinically relevant safety signals emerged; AEs were consistent with the known safety profiles of the components of CL-108.

**Conclusion**
Patients with acute flares of OA of the knee or hip taking CL-108 on a short-term basis under conditions of actual use reported consistent improvement in the performance of different activities of daily living.


Sponsored by Charleston Laboratories, Inc. and Daiichi Sankyo, Inc.
**Title**: The Crucial Role Of Nad+-Dependent Sirt1 Deacetylase During Acute Inflammatory Pain

**Poster Number** PTH116

**Authors**

**San Raffaele Roma S.r.l., Catanzaro, Italy, Department of Experimental Medicine, University of Rome “Sapienza”, Rome, Italy, Research Center, IRCCS San Raffaele Pisana, Rome, Italy, IBSA Foundation for scientific research, Lugano, Switzerland, IRC_FSH, Department Health Sciences, University of Catanzaro Magna Graecia, Catanzaro, Italy, Saint Louis University, Chesterfield, MO**

**Aim of Investigation**
Inflammatory pain represents an important unmet clinical need with important socioeconomic implications. In the last years, considerable evidence demonstrates the central role of reactive oxygen species and reactive nitrogen species (ROS and RNS) in inflammation and subsequent development of inflammatory pain. Superoxide is implicated in the development and maintenance of hyperalgesia; it stimulates the production of cytokines and contributes to the formation of the peroxynitrite (PN) and lipid peroxidation products. Sirtuins, the class III histone deacetylases (HDACs), are widely distributed and have been shown to regulate a variety of physiopathological processes, such as inflammation, metabolism, and cell cycle regulation. Sirtuins catalyze the deacetylation of the ε-amino group of lysine residues of histones and non-histone proteins and are involved in regulating transcriptional activity and protein function. The best characterized sirtuins is SIRT1, a nuclear protein reported to regulate critical metabolic and physiological processes. SIRT1 either directly or indirectly can influence the redox property of the cell and it is also regulated by oxidative stress. SIRT1 activation confers protection against myocardial infarction and ischemia/reperfusion injury in the heart.

**Results**
Our studies revealed that intraplantar injection of carrageenan leads to a time-dependent development of hyperalgesia and inflammation. We reported that inflammatory pain is associated to SIRT1 inactivation in the spinal cord of carrageenan treated rats and this event seems to be related to nuclear protein hyperacetylation and s-nitrosoylation. Removal of free radicals by antioxidant during acute inflammation exerts anti-hyperalgesic effect together with inhibition of hyperacetylation, nitrosylation, lipid peroxidation, PGE2 and cytokines release, and enhanced SIRT1 activity.
**Conclusion**
These findings are innovative since virtually nothing is known on the roles of post-translational modulation due to acetylation/deacetylation in pain. The development of new therapeutic scheme would allow the inhibition of free radicals post-translational modulation by regulation of intra-and intercellular signals transmission without directing blocking involved neurotransmitters action. The activation of SIRT1 by polyphenols would be a new target in therapeutic intervention for the management of pain. This work has been supported by funds from PON03PE_00078_2, PON03PE_00078_1/F1, PON03PE_00078_2/F1 and IBSA Foundation.
**Title:** Preemptive Analgesia To Alleviate Postoperative Pain In Patients Undergoing Hallux Valgus Correction Surgery: Compared The Regimens Of Peripheral Nerves Block With Peri-Incisional Administration

**Poster Number** PTH117

**Authors**
K. CHENG, Y. Shen, K. Tseng, P. Huang, S. Chau

department of anesthesiology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, Province Of China, department of anesthesiology, Kaohsiung Medical University Hospital, Kaohsiung, -- SELECT --, department of anesthesiology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, department of Orthopedic, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

**Aim of Investigation**
to investigate the preemptive analgesic technique either with peripheral nerve blocks (tibial and peroneal nerves) or peri-incisional administration provides adequate postoperative pain control in patients undergoing Hallux Valgus correction surgery

**Results**
patients’ demographic data were comparable in 3 groups. Group N patients decreased consumption of fentanyl dose significantly at each time interval with group C and at Poh6 and Poh12 time intervals with group P and decreased resting and moving (dorsiflexion 10 degree and plantar flexion 40 degree) pain at recovery room and Poh6 time interval as compared with group C and group P. Group P patients decreased consumption of fentanyl dose significantly at Poh6 but did not decrease pain scale as compares with group C. there is no significant differences among groups after Poh6 daily activities, sleep disturbance, and mood changes.

**Conclusion**
preemptive analgesia with peripheral nerve blocks decreased postoperative PCA fentanyl consumption and decreased resting and moving pain at least 6 hours. Peri-incisional local anesthetic single shot did not provide adequate postoperative pain relief.
Title: Setting Up Of An Acute Pain Service In A Medium-Sized Private Hospital In Malaysia

Poster Number: PTH118

Authors
R. Rasiah, R. Jabar, J. BAKAR, H. AZMI, W. ZAINAL ABIDIN

DEMC SPECIALIST HOSPITAL SHAH ALAM, MALAYSIA, PETALING JAYA, Malaysia, DEMC SPECIALIST HOSPITAL SHAH ALAM, SHAH ALAM, Malaysia, DEMC SPECIALIST HOSPITAL, SHAH ALAM, MALAYSIA, SHAH ALAM, Malaysia

Aim of Investigation
To assess the implementation of the acute pain service in DEMC Specialist Hospital, Shah Alam, Malaysia by way of an audit on the services provided by the acute pain service team.

Results
A total of 2472 cases was done from January 1st, 2015 to December 31, 2015. Of this number 20.95% (518) of cases received either one of the regional technique or I/V Patient Controlled Analgesia. About 72% of these patients received intrathecal morphine as the most common technique for management of postoperative pain. Nursing records on follow up of these patients are available in the ward. About 10% of nurses in the ward did not understand the role of Pain as the 5th vital sign.

Conclusion
The audit highlighted problems of organization and implementation of the Acute Pain Service. This will help us to make safer protocols to make the service more effective. It will also help us to make this service multidisciplinary with the final goal of patient satisfaction.
Aim of Investigation
The neural mechanisms for the generation of pain in knee OA are not fully understood. A proportion of patients have been found to have features of neuropathic pain, and previous work suggests that the underlying mechanism for this is through central sensitisation. This mechanism-based understanding of pain is important in order to aid targeted intervention. The aim of this study was to identify the neural correlates, with a particular focus on changes in the brainstem’s descending pain modulatory circuit - known to be involved in the establishment and maintenance of central sensitization - of neuropathic pain in patients with moderate to severe knee OA, using functional magnetic resonance imaging (fMRI). The hypothesis was that patients with features of neuropathic pain prior to surgery would also demonstrate increased activation in areas of the brainstem previously shown as involved in central sensitization, namely the nucleus cuneiformis, periaqueductal grey, and rostral ventromedial medulla.

Results
Patients with neuropathic pain (N=14/24) were found to have increased sensitivity to punctate and cold stimuli, as well as significantly higher levels of pain catastrophising prior to surgery. fMRI demonstrated significantly lower levels of activation in the rostral anterior cingulate cortex (rACC) and higher levels of activation in the rostral ventromedial medulla (RVM) and ipsilateral nucleus cuneiformis (NCF) in response to punctate stimulation prior to surgery, in patients with features of neuropathic pain compared to those without. The magnitude of rACC activation was significantly negatively correlated to the severity of neuropathic pain, represented by the modified painDETECT questionnaire (mPD-Q) score (r=-0.41, p=0.05). Similarly, RVM activation was significantly positively correlated to the mPD-Q score. (r=0.62, p=0.001).

Conclusion
The psychophysical and neuroimaging data suggest that neuropathic pain is associated with centrally
mediated pain sensitisation in patients with knee OA. Specifically this is likely due to both a reduction in
descending inhibitory pain modulation (evidenced by decreased rACC activation) and increased
supraspinal facilitation of nociceptive signaling in the dorsal horn (increased RVM activity). The
neurobiological confirmation of CS in patients with neuropathic pain, identified using the mPD-Q,
provides further support for the use of drug and behavioral treatments to target this mechanism, which
may in turn have a positive impact on outcome following knee replacement surgery. Data from two
larger cohort studies have shown that patients with neuropathic pain, identified using the modified
painDETECT questionnaire, prior to knee arthroplasty have a clinically significantly worse outcome post-
operatively.
Title: Therapeutic Benefits Of Targeting Cb2 Receptors In The Mia Model Of Osteoarthritis

Poster Number PTH120

Authors
M. Kostrzewa, N. Malek, A. Pajak, K. Starowicz
Pain Pathophysiology Lab Department of Pain Pharmacology Institute of Pharmacology PAS, Krakow, Poland

Aim of Investigation
Osteoarthritis (OA) is the most common joint pathology, as well as the most common cause of pain and disability in the elderly population of developed countries. OA therapy is limited to NSAIDs, which not always provide adequate pain relief. Therefore, there is a strong need to develop new strategies to control pain associated with OA. Compelling evidence suggests an active participation of the cannabinoid receptors (CB) in the pain modulation and perception. While ligands with agonist activity at the CB1 receptor cause the CNS unwanted effects, the attention now focuses on the functional role of CB2 receptor because of their peripheral distribution. In the preclinical studies CB2 selective agonists inhibit signs of acute and chronic pain. Our aim was to investigate CB2 receptors as a potential new therapeutic target in OA.

Results
OA progression in rats was accompanied by a biphasic pain behaviour with significant elevation in pain sensation at the advanced stages of the disease. Moreover the development of tactile allodynia assessed in von Frey’s test provided an evidence for the accompanying neuropathic pain component in osteoarthritis. Additionally the most significant changes of CB2 expression both in mRNA level in DRG and protein level in the rat osteoarthritic knee cartilage correlated with the chronic and most severe pain phase, which highlights its contribution to OA pain. Administration of JWH-133 (i.p.) resulted in reduction in joint hypersensitivity in PAM measurement and antiallodynic properties in von Frey’s test. Moreover the effect of JWH-133 was attenuated by the CB2 receptor antagonist, AM-630, suggesting that the analgesic effect was mediated by CB2 receptor.

Conclusion
Our results demonstrate antinociceptive action of JWH-133 and its therapeutic potential in animal model of OA pain. Moreover this effect was mediated through peripheral CB2 receptors. Thus, using
novel treatment regimen of peripherally restricted CB2 agonists may yield more successful treatments also in human OA. Supported by National Science Centre, Poland grants: OPUS UMO-2014/13/B/NZ7/02311, SONATA BIS/NCN/2012/07/E/NZ7/01269 and statutory funds.
Aim of Investigation
Patients with joint hypermobility syndrome/Ehlers-Danlos syndrome, hypermobility type (JHS/EDS-HT) commonly suffer from pain. How this hereditary connective tissue disorder causes pain remains unclear although previous studies suggested it shares similar mechanisms with neuropathic pain and fibromyalgia. In this prospective study seeking information on the mechanisms underlying pain in patients with JHS/EDS-HT, we enrolled 27 consecutive patients with this connective tissue disorder.

Results
Clinical examination and diagnostic tests disclosed no somatosensory nervous system damage. Conversely most patients suffered from widespread pain, the fibromyalgia rapid screening tool elicited positive findings and quantitative sensory testing showed lowered cold and heat-pain thresholds and an increased wind-up ratio.

Conclusion
While the lack of somatosensory nervous system damage is incompatible with neuropathic pain as the mechanism underlying pain in JHS/EDS-HT, the lowered cold and heat pain thresholds and increased wind-up ratio imply that pain in JHS/EDS-HT might arise through central sensitization. Hence, this connective tissue disorder and fibromyalgia share similar pain mechanisms.
Title: Extracellular Matrix Biomarker C1M And Pro-Inflammatory Cytokine IL6 In Relation To Synovitis And Pain In Osteoarthritic Patients

Poster Number PTH123

Authors
M. Radojčić, K. Henriksen, K. Tan, I. Chessell, A. Dudley, A. Guermazi, M. Crema, M. Karsdal, A. Bay-Jensen, C. Th

Nordic Bioscience Biomarkers & Research, Nordic Bioscience A/S, Herlev, Denmark, Department of Drug Design and Pharmacology, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark, Neuroscience Innovative Medicines, Medimmune, Cambridge, United Kingdom, Quantitative Imaging Center, Department of Radiology, Boston University School of Medicine, Boston, MA, Department of Radiology, Hôpital Saint-Antoine, University Paris VI, Paris, France

Aim of Investigation
Osteoarthritis (OA) affects all joint tissues including synovial membrane, and synovitis has been found to be associated with pain. Extracellular matrix turnover biomarkers, such as the neo-epitope of collagen I cleaved by matrix metalloproteinase (C1M), are good candidates for understanding the pathophysiological processes that lead to joint failure and pain in OA patients. Pro-inflammatory cytokines, such as interleukin 6 (IL-6), are inflammation markers and potential treatment targets. Thus, we aimed to investigate association between C1M and IL-6 with synovitis and pain in OA patients.

Results
We found that sf-IL6 is associated with MRI synovitis sum score (beta (B)=0.009; 95% confidence interval (CI):0.002, 0.016; p=0.018) and MRI synovitis in parapatellar subregion (B=0.006; 95% CI: 0.002, 0.009; p=0.003). No association was found between p-IL6 and synovitis. Additionally, a statistically significant association was observed between C1M and MRI synovitis in peri-ligamentous subregion (B=0.012; 95% CI: 0.002, 0.022; p=0.018). Further, we observed that sf-IL6 was significantly associated with pain, measured by both instruments: WOMAC (B=0.022; 95% CI: 0.004, 0.040; p=0.016) and NPQ (B=0.043; 95% CI: 0.005, 0.082; p=0.026); but p-IL6 was not associated with pain. We did not observe an association between C1M and pain measured by WOMAC, but did find an association between C1M and NPQ (B=0.229; 95% CI: 0.036, 0.422; p=0.020). Lastly, we tested whether associations between biomarkers and pain were confounded by MRI synovitis, and we found that synovitis explained the associations including NPQ, but not WOMAC pain.
Conclusion
This cross-sectional study showed that serum C1M and sf-IL6, but not p-IL6, are associated with MRI synovitis in peri-ligamentous and parapatellar subregions, respectively. Sf-IL6 is associated with OA pain measured by WOMAC, independently of synovitis. Additionally, C1M and sf-IL6 were also associated with neuropathic pain and these associations appear to be explained by MRI synovitis. The findings of this study may help in defining an inflammatory OA phenotype that may be sensitive to anti-IL6 treatment.
Title: Autoantibodies To Citrullinated Proteins Induce Joint Pain Independent Of Inflammation Via A Chemokine-Dependent Mechanism

Poster Number PTH124

Authors

Karolinska Institutet, Stockholm, Sweden, Department of Unidad Academica Multidisciplinaria Reynosa Aztlan, Reynosa, Mexico

Aim of Investigation
An interesting and so far unexplained feature of chronic pain in autoimmune disease is the frequent disconnect between pain and inflammation. This is illustrated well in rheumatoid arthritis (RA) where pain in joints (arthralgia) may precede joint inflammation and persist even after successful anti-inflammatory treatment. In the present study, we have addressed the possibility that autoantibodies against citrullinated proteins (ACPA), present in RA, may be directly responsible for the induction of pain, independent of inflammation.

Results
Mice injected with either human or murinized ACPA developed long-lasting pronounced pain-like behavior in the absence of inflammation, while non-ACPA IgG from RA patients or control monoclonal IgG were without pro-nociceptive effect. This effect was coupled to ACPA-mediated activation of osteoclasts in the bone marrow, and release of the nociceptive chemokine CXCL1 (analogue to human IL-8), which can directly stimulate sensory nerves. ACPA-induced pain-like behavior was reversed with the CXCR1/2-inhibitor reparixin.

Conclusion
The data suggest that CXCL1/IL-8, released from osteoclasts in the bone marrow, in an autoantibody-dependent manner, induces pain by activating sensory neurons. The identification of this new pain pathway may open new avenues for pain treatment not only in RA, but also in other painful diseases associated with autoantibody production and/or osteoclast activation.
Title: Self-Efficacy Mediates The Relationship Between Pain Catastrophizing And Adverse Outcomes Following Total Knee Arthroplasty

Poster Number PTH125

Authors

McGill University, Montreal, Canada, Dalhousie University, Halifax, Canada, University of Queensland, Herston, QLD

Aim of Investigation
Research evidence from cross-sectional and prospective studies indicates that pain catastrophizing is associated with pain severity and disability following total knee arthroplasty (TKA). Several models have been put forward to elucidate the pathways by which catastrophic thinking might impact on pain and disability in patients with severe osteoarthritis (OA). Catastrophic thinking has been shown to impact on pain severity and disability in patients with OA via reduced self-efficacy. Pain catastrophizing has also been discussed as a cognitive antecedent to fear of movement that in turn has a negative effect on pain and disability outcomes in patients with chronic pain. It remains unclear whether reduced self-efficacy or amplified fears of movement independently mediate the relationship between pain catastrophizing and adverse post-TKA outcomes. The primary aim of this study was to determine whether beliefs about self-efficacy and fear of movement simultaneously mediate the relationship between pain catastrophizing and pain severity and disability after TKA.

Results
Consistent with previous research, cross-sectional analyses revealed significant correlations between pain catastrophizing, fear of movement, self-efficacy and self-reported measures of pain severity and disability. Bootstrap mediation analyses revealed that the relationship between pain catastrophizing and pain severity was mediated by reduced self-efficacy. The relationship between pain catastrophizing and disability was partially mediated by reduced self-efficacy but remained significant.

Conclusion
The current findings suggest that pain catastrophizing exerts its negative impact on pain and disability after TKA via reduced perceptions of self-efficacy. Pain catastrophizing was also found to be associated with reduced disability independent of perceived self-efficacy, fear of movement and pre-surgical
ratings of disability, indicating the existence of another pathway by which catastrophic thinking about pain exerts its influence on disability. The results of the present study indicate that psychosocial interventions designed to target pain catastrophizing and bolster self-efficacy before and after total knee replacement surgery may be useful for reducing pain and disability in patients at risk.
Title: Exercise-Induced Hypoalgesia In People With Knee Osteoarthritis With High Versus Low Pressure Pain Sensitivity

Poster Number PTH126

Authors
C. Doody, C. Fingleton, K. Smart

University College Dublin, Dublin, Ireland, St Vincent’s University Hospital, Dublin, Ireland, Dublin, Ireland

Aim of Investigation
Normal function of exercise-induced hypoalgesia (EIH) has been demonstrated in response to isometric and dynamic resistance exercise in people with knee osteoarthritis. The aim of the current study was to investigate EIH in response to aerobic exercise, in addition to isometric exercise, in people with knee OA, and to compare EIH in knee OA patients with varying degrees of pain sensitization, as determined by high and low pressure pain sensitivity (PPS).

Results
No significant differences were demonstrated between knee OA and control groups, or between high PPS, low PSS and control groups, for changes in PPTs post-aerobic or isometric exercise (P > 0.05). A significant within-group increase in PPTs was demonstrated post-aerobic and isometric exercise in controls (and in the low PPS group post-isometric exercise) (P < 0.05), while no significant change in PPTs occurred in the full knee OA group (or high PPS group) (P > 0.05).

Conclusion
While no significant differences were demonstrated between groups for changes in pain sensitivity in response to exercise, results indicating attenuation of pain sensitivity in controls and the low PPS group, but not in the full knee OA group or high PPS group, are suggestive of a decreased EIH response in people with knee OA that may be related to baseline degree of pain sensitization.
Title: Using The Dc/TMD To Evaluate Tmj Involvement In Jia Patients

Poster Number: PTH127

Authors:
A. Michelotti, L. Ammendola, R. Rongo, M. Alessio, F. Fontana, P. Chiodini, V. D’Antò

University of Naples, Napoli, Seconda Università di Napoli, Napoli

Aim of Investigation
Juvenile Idiopathic Arthritis (JIA) is a rheumatic disease with a Temporomandibular joint (TMJ) involvement in up to 87% of the patients. The classical sign of inflammation are rubor, calor, dolor, tumor and function lesa; however these signs are rarely present in JIA patients with TMJ involvements; this is a very important problem for the early diagnosis in these patients. TMJ arthritis can be assessed by means of magnetic resonance (MRI) but it is very difficult to evaluate with a clinical examination. The diagnostic criteria for temporomandibular disorders (DC/TMD) are currently considered the gold standard of TMD classification and diagnosis and the analysis and summary of the complete DC/TMD procedure leads to a specific and unique TMD diagnosis, however no information are available in patients with JIA. Hence, the aim of this study was to assess the potential use of the DC/TMD exam to evaluate the TMJ involvement in patients affected by JIA.

Results
In this study, the clinical examination had medium sensibility and specificity in the identification of TMJ involvement in patients with JIA (Sensibility=0.6; 0.41-0.77; Specificity=0.5; 0.16-0.84, PPN=0.82; 0.6-0.95; NPV=0.25; 0.07-0.52). Among the variables analysed the highest sensibility was obtained by the Pain with masseter palpation (Sensibility=0.53; 0.34-0.72, Specificity=0.75; 0.35-0.97; PPV=0.89; 0.65-0.99; NPV=0.3; 0.12-0.54); while the highest specificity was reached by the Pain with temporal palpation (Sensibility=0.13; 0.04-0.31; Specificity=1; 0.63-1, PPV=1; 0.4-1; NPV=0.23; 0.11-0.41).

Conclusion
In this study performed in a small sample, the DC/TMD clinical examination did not show good diagnostic ability in the identification of the involvement of TMJs in patient with JIA. However, further researches with a larger samples are needed.
Title: Clinical Diagnosis Of Temporomandibular Joint Arthritis

Poster Number PTH128

Authors
P. Alstergren, O. Björnsson, M. Pigg, M. Nilsson

Malmö University, Malmö, Sweden, Skåne University Hospital, Malmö, Sverige, N/A, Malmö, SWEDEN, Karolinska Institutet, Stockholm, Sverige

Aim of Investigation
Arthritis in the temporomandibular joint (TMJ) is due to either local or systemic factors. Clinically, TMJ arthritis may present with articular pain and pain in adjacent structures, cartilage and bone tissue destruction, impaired function and, if present in children and adolescents, mandibular growth arrest that may lead to micrognathia. Inflammation is a complex, rapid, first-line and highly unspecific immune system response with the purpose to locate and eliminate pathogens and injured tissue as well as to promote tissue healing. This reaction has a clear and important biologic purpose in the acute phase but may transfer into a chronic state with very unclear, if any, biologic purpose. Traditionally, inflammation has clinically been described and diagnosed by the presence of the five cardinal signs swelling, redness, warmth, pain and impaired function. This is often adequate regarding acute inflammation, for example pericoronitis and skin cut wound. However, for chronic inflammation (and some acute inflammatory states) these cardinal signs are neither sufficient nor adequate to describe, diagnose or monitor inflammation. Although one or more of these clinical signs may be found in some sites with chronic inflammation at a certain time-point, in other sites they may be absent. For example, chronic periodontitis seldom displays any of the cardinal signs in spite of there being an ongoing inflammatory process, local immune system activation and disease progression. Signs and symptoms of arthritis therefore lie on a continuum from no sign or symptom to any combination of pain, swelling/exudate, tissue degradation or growth disturbance. There is also a temporal variation, the inflammatory activity in chronic arthritis varies over time and presentation of the signs and symptoms at any time-point may include may include none or one or more of these signs and symptoms. In rheumatology, the definition of 'definite synovitis' in a particular joint is a swollen or painful joint. The TMJ differs to some extent from other synovial joints since the TMJ is seldom swollen, seldom shows redness and pressure-pain threshold over the TMJ is only weakly, if at all, related to an inflammatory intra-articular milieu but rather to systemic inflammatory factors. The aims of this study were to find clinical variables with the highest sensitivity and specificity to diagnose temporomandibular joint (TMJ) arthritis using synovial
fluid levels of TNF, IL-1beta and serotonin as reference standard and to establish clinically useful variables to determine the degree of inflammatory activity in the arthritic TMJ.

Results
Sixtyfive percent of the TMJs in the patients and 4% of the TMJs in the healthy individuals were considered as arthritic, according to the reference standard definition in this study. In total, 58% of the investigated TMJs were considered as having an ongoing arthritis. There was no significant difference between men and women regarding TMJ synovial concentrations of TNF, IL-1beta or serotonin. Age and TMJ synovial fluid concentrations of TNF, IL-1beta or serotonin were not significantly correlated. In the total material, 17 (13%) out of the 127 joints that fulfilled the criteria for arthritis were pain-free. On the other hand, 54 (78%) of the 69 TMJs that did not fulfill the criteria for arthritis showed pain. Logistic regression with the TMJ resting and maximum opening pain intensity, number of jaw movements causing TMJ pain and laterotrusive movement to the contralateral side significantly explained presence of arthritis (p < 0.001) with an area under the ROC curve = 0.78 (n = 134; p < 0.001). The highest overall diagnostic sensitivity was found for the combination of the clinical variables 'TMJ resting pain' or 'TMJ pain on mandibular movements' or 'TMJ pain on maximum mouth opening' or 'Contralateral laterotrusion < 8 mm': 0.94. Its specificity was at the same time 0.29 (Table 4). On the other hand, the highest specificity was found for the combination 'TMJ resting pain intensity >4 (of 10)' and 'TMJ pain on at least three mandibular movements' and 'TMJ pain intensity on maximum mouth opening >2 (of 10)' and 'Contralateral laterotrusion < 8 mm': 0.97. The sensitivity of this combination was 0.08.

Conclusion
This study suggests a diagnostic model for TMJ arthritis by the use of 'possible', 'probable' and 'definite' TMJ arthritis. This model is based on clinical findings (pain-related variables and functional variables). The joint-related variables TMJ resting pain, TMJ pain on maximum opening, TMJ pain on mandibular movements and contralateral laterotrusion <8 mm showed a high diagnostic performance. The area under the ROC curve was 0.78, which can be considered to be acceptable. Probable TMJ arthritis is defined as TMJ resting pain or TMJ pain on maximum opening or TMJ pain on mandibular movements or contralateral laterotrusion <8 mm. These criteria gave a sensitivity of 0.94 and a specificity of 0.24. Definite TMJ arthritis is defined as TMJ resting pain and TMJ pain on maximum opening and TMJ pain on mandibular movements and contralateral laterotrusion <8 mm with a sensitivity of 0.22 and specificity of 0.89.
Title: Trajectories Of Pain Interference With Walking After Total Knee Arthroplasty In Two Subgroups Of Patients

Poster Number PTH129

Authors
M. Lindberg, C. Miaskowski, T. Rustoen, L. Rosseland, B. Cooper, A. Lerdal

Lovisenberg Diakonale Hospital, OSLO, Norway, University of California, San Francisco, San Francisco, CA, University of Oslo, Oslo, NORWAY, Oslo University Hospital, OSLO, Norway, Oslo University Hospital, Oslo, NORWAY, University of Oslo, OSLO, Norway, Lovisenberg Diakonale Hospital, OSLO, None

Aim of Investigation
Total knee arthroplasty (TKA) is a common procedure to relieve pain and improve function in patients with end stage osteoarthritis (OA). The procedure is known to be extremely painful. Although the procedure is considered highly successful, the long term outcomes vary. Between 10 – 34% of patients continue to experience pain one year after TKA, and this variability in long term outcomes is not fully understood. Pain may interfere with the ability to walk, which is an important outcome for patients undergoing TKA. No previous studies attempted to identify subgroups with different outcomes based on changes in pain interference with function during the first year following TKA. This study aims to identify subgroups with different trajectories of pain interference with walking during the first year after TKA, as well as identify demographic, clinical, symptom and psychological factors associated with poorer outcomes.

Results
The majority of the sample was female (n=138, 68%), lived with a partner (n=122, 60%), and had completed higher education (n=102, 51%). The mean age was 68 (SD 9.2) years and most of the patients were not working (n=130, 64%). The total sample had a mean pain interference with walking score of 5.9 prior to surgery that decreased over time. We identified two subgroups of patients with distinct trajectories of pain interference with walking over time. The majority of the patients (n=157, 78%) were classified in the 'Continuous improvement' class characterized by a gradual improvement in pain interference with walking over the 12 months after TKA. Patients in the 'Recurrent interference' class (n=45, 22%) reported gradual improvements in walking during the three first months, followed by a distinct worsening between 3 and 12 months, returning to preoperative levels 12 months after TKA.
Patients in the 'Recurrent interference' class were characterized by higher pain intensity, fatigue, and depression scores prior to surgery. In addition, patients in this class perceived their OA condition to have more severe consequences, reported more illness concern, and higher emotional response prior to surgery.

**Conclusion**
One in five patients reported no improvement in pain interference with walking 12 months after TKA. These findings may impact patient selection and follow-up after TKA. Future studies should develop and test a screening tool identifying patients with higher risk for poorer outcomes, as well as testing interventions targeting specific patient characteristics to improve outcomes after TKA.
Title: Pain In Knee Oa Was Not Found To Be Associated With Bone Marrow Edema Or Sensitization

Poster Number PTH130

Authors
M. Rodrigo-Domingo, C. Petersen, L. Arendt-Nielsen, K. Petersen, M. Boesen, R. Riis, O. Simonsen, S. Skou

Department of Research, Education and Innovation, Aalborg University Hospital, Aalborg, Denmark, Orthopedic Surgery Research Unit, Aalborg University Hospital, Aalborg, Denmark, Aalborg University, Center for Sensory-Motor Interaction, Aalborg, Denmark, Centre for Sensory-Motor Interaction, Department of Health Science and Technology, Aalborg University, Aalborg, Denmark, Department of Radiology & The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark, The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark, Department of Radiology, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark, Orthopedic Surgery Research Unit, Aalborg University Hospital, Aalborg, Denmark, Centre for Sensory-Motor Interaction (SMI), Department of Health Science and Technology, School of Medicine, Aalborg University, Aalborg, Denmark, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark, University of Southern Denmark, Research Unit for Musculoskeletal Function and Physiotherapy, Aalborg, Denmark, Aalborg University Hospital, Clinical Nursing Research Unit, Aalborg, Denmark

Aim of Investigation
Osteoarthritis (OA) is a disease affecting several tissue structures. The weak association between symptoms and radiographic severity, especially in early stages of the disease, could indicate that OA pain is multifactorial, which is why pain assessment needs to comprise a variety of measures. Most recently, bone marrow edema (BME) and neural sensitization have been highlighted as possible contributing factors to pain. Therefore, the aim of the present study was to explore associations between pain, BME and sensitization in patients with moderate and severe knee OA admitted to orthopaedic department and found not yet eligible for total knee replacement (TKR).

Results
Patients were on average 62.2 years old (SD: 8.1) and had experienced pain for 8.1 (SD: 9.96) years. Radiographic OA severity was grade III (17 patients) or grade IV (26 patients) on the Kellgren-Lawrence scale. The mean pain score was 5.02 (95% CI [4.18, 5.86]). Scores for sensitization were: mean PPT 966 KPa (95% CI [896, 1035]) and mean CPM 80 KPa (95% CI [57, 105]). The mean BME score was 7.88 (95%
CI [5.97, 9.76]). No correlations between pain and BME or sensitization, or between BME and sensitization were statistically significant. The correlation between PPT and CPM was -0.36 (p-value: 0.02). The multiple regression analysis showed no significant relationship between pain and BME, PPT or CPM (p-value: 0.16).

**Conclusion**
No significant associations were observed between pain, BME or sensitization in patients with knee OA not eligible for TKR, confirming previous results seen in patients with end-stage knee OA eligible for TKR. This calls for more research into further understanding of pain in OA and new para-clinical biomarkers in knee OA.
Title: Depression, Anxiety, And Pain Catastrophizing Among Patients Undergoing Total Knee Replacement In A Malaysian Public Hospital

Poster Number PTH131

Authors
S. Lee, J. Lee, J. Zubaidah, E. Lim, M. Cardosa

Hospital Kuala Lumpur, Kuala Lumpur, Malaysia, University Putra Malaysia, Seri Kembangan, Malaysia, University Putra Malaysia, UPM Serdang, Selangor, Hospital Selayang, Kuala Lumpur, Malaysia

Aim of Investigation
Total knee replacement (TKR) aims to provide pain relief and restore mobility in patients with debilitating knee osteoarthritis. Although psychological factors have been found to show bidirectional relationships with patients' pre and post operative pain and functioning, these factors are rarely addressed in patients undergoing TKR. This study aims to examine the prevalence of preoperative depression, anxiety and pain catastrophizing in patients undergoing TKR, and their associated factors.

Results
Eighty patients were recruited, which consisted of 64 females (81%) and 15 males (19%); mean age of 65 (range 36 to 87); ethnic background of 42.5% Malay, 35% Chinese, 21.3% Indian and 1.3% other ethnicity. The mean duration of knee pain was 85 months (range 6 to 432). 55 patients (70%) reported moderate to severe pain (pain score of 4 and above) and 46% reported having pain in other parts of the body in addition to knee pain. Females and those having pain in other parts of the body were significantly more likely to have moderate to severe pre-operative pain [(X2=4.16, p<0.05);(X2=5.89, p<0.05)]. High pain catastrophizing scores were reported by 7.9% of patients with Indian patients reporting significantly higher pain catastrophizing compared to other ethnic groups [F(3,72) = 3.06, p<0.05]. 32% of patients reported having anxiety, while 25% had depression. Patients with other pain conditions reported significantly higher level of preoperative knee pain, anxiety, and depression. Pain catastrophizing was positively correlated with usual pain score, anxiety, and depression (r ≥ .24, p < .01); with anxiety as a significant predictor for pain catastrophizing, but not pain score [Beta = .60 t(.30) = 4.2, p < .0001].

Conclusion
The findings indicated that a significant proportion of patients undergoing TKR have anxiety, depression
and pain catastrophizing. Therefore, it is important to screen these patients preoperatively for psychological variables, as recognising and addressing these factors may improve functional outcomes as well as reduce the risk of patients developing chronic pain after surgery.
Title: Danish Translation And Validation Of The Breakthrough Pain Questionnaire For Metastatic Bone Pain

Poster Number PTH132

Authors
R. Hansen, C. Frost, A. Johnsen, N. Sonne, A. Heegaard

University of Copenhagen, Department of Drug Design and Pharmacology, Copenhagen, Denmark, The Research Unit, Department of Palliative Medicine, Bispebjerg Hospital, Copenhagen, Denmark, Oncology Clinic, Section of Palliative Medicine, Rigshospitalet, Copenhagen, Denmark

Aim of Investigation
To translate into Danish and validate the Breakthrough Pain Questionnaire.

Results
The Breakthrough Pain Questionnaire consist of 10 questions that assess pain intensity, frequency, duration, triggering factors and pain relieving factors. The questionnaire was translated into Danish and following a discussion of minor issues the expert panel agreed on a final version. All included patients completed the questionnaire and only minor misconceptions were identified. Misconceptions and suggestions for improvements were discussed and revised by the project participants and an expert panel resulting in a final version of the Danish Breakthrough Pain Questionnaire.

Conclusion
The short form Breakthrough Pain Questionnaire was translated into Danish. The study of its validity suggests that the questionnaire can assess breakthrough pain experienced by patients with bone pain due to metastatic disease.
Titel: Clinical Response Of Cancer Pain Management: A Retrospective Study In A Tertiary Care Setting

Poster Number PTH133

Authors

Sriraj Hospital, Mahidol University, Bangkok, THAILAND

Aim of Investigation
To evaluate the efficacy of pain management in 3-month follow-ups for outpatients with cancer pain.

Results
Out of 432 new patients, 118 cancer pain patients were included in the study with the mean age of 59.8 ± 13.7 years (range 18-91 years). About half of patients had at least one co-morbidity. The common types of cancer were gastrointestinal cancer (22%), followed by lung cancer (16.9%). Over 90% of all cancer patients presented with distance metastasis. Mixed neuropathic/nociceptive pain (53.4%) and nociceptive pain alone (43.2%) were common pain features in cancer pain patients. The mean initial pain intensity described by verbal numerical scales was 7.7 ± 2.1 (range 3-10). Majority of patients (60.2%) received co-treatment. The main pharmacological therapies in all patients were opioids (99.2%) and anticonvulsants (90.7%). At three-month follow-up, nearly half of patients achieved good treatment response. However, 41% of good responders still had moderate pain. Interestingly, predictive factor associated with good treatment response was high initial pain intensity (p=0.001).

Conclusion
Approximately half of patients with cancer pain in the pain clinic could achieve good treatment response at 3-month follow-up. High initial pain intensity was the only predictive factor for good treatment response.
Aim of Investigation
Breakthrough pain (BTP) shows variable prevalence in different clinical contexts of cancer patients. BTP diagnostic tools with demonstrated reliability, validation and prognostic capability are lacking. We report the preliminary results of an ongoing impact study following the development of a diagnostic/prognostic tool, the IQ-BTP, for BTP recognition and its likelihood among cancer patients.

Results
The scoring system analysis showed that two thirds of the patients may be correctly classified as potentially having (or not having) BTP; proportions of correct classification for BTP likelihood classes 'High' and 'No BTP' was greater than 80%: most of the patients satisfying the criteria for having BTP were correctly recognized.

Conclusion
The IQ-BTP with its peculiar scoring system and with adequate feasibility may enable, in cancer patients, the detection of potential-BTP and its likelihood. The latter may have significant relevance to BTP epidemiology and management.
Title: The Proposed Classification Of Chronic Cancer Pain For Icd-11

Poster Number PTH135

Authors
M. Bennett, S. Kaasa, A. Barke

University of Leeds, Leeds, United Kingdom, University of Oslo, Oslo, Norway, Philipps University Marburg, Marburg, Germany

Aim of Investigation
Currently chronic pain syndromes are not represented in the International Classification of Diseases (ICD) in systematic manner. Among the chronic pain syndromes currently absent from the classification is chronic cancer pain, despite the fact that chronic pain is a frequent and debilitating accompaniment of cancer and needs its own treatment plan. The International Association for the Study of Pain (IASP) has long campaigned for improvements in the classification system.

Results
Chronic cancer pain designates all pain caused by cancer or its treatment. It is further subdivided into chronic cancer-related pain, which is pain that is caused by the cancer itself (the primary tumor or metastases), and chronic pain arising from its treatment, namely chronic painful chemotherapy-induced polyneuropathy, chronic post-cancer surgery pain and chronic post-radiotherapy pain. The treatment-related pain will be cross-referenced from the chapters on postsurgical pain and neuropathic pain, respectively.

Conclusion
In the context of the overall classification proposal, several improvements can be expected. For the first time, chronic cancer pain will be represented in the ICD. Although it may share characteristics with some of the other chronic pain diagnoses, the Task Force decided to list it as a separate entity because there are specific treatment guidelines. It is hoped that the better representation in the ICD will translate into improved pain relief and access to multimodal pain treatments for patients with chronic cancer pain.
Title: Safety And Efficacy Of Oxycodone/Naloxone Prolonged Release (Oxn Pr) Tablets In Daily Doses Up To Oxn180/90 Mg In Cancer Patients: Results From A Phase Iii Multicenter, Multiple-Dose, Randomized, Controlled Study With An Open-Label Extension Phase

Poster Number PTH136

Authors
M. Hopp, O. Loewenstein, W. Leppert, W. Kremers, B. Bosse, S. Ahmedzai

Mundipharma Research GmbH & Co. KG, Limburg, GERMANY, own practice, Mainz, GERMANY, Poznan University of Medical Sciences, Poznan, Poland, Mundipharma Research GmbH & Co. KG, Limburg, Germany, University of Sheffield, Sheffield, United Kingdom

Aim of Investigation
A multicenter, multiple-dose, randomized, double-blind, double-dummy, active-controlled, parallel-group study with an open-label extension phase was performed to determine the safety and efficacy of prolonged release oxycodone/naloxone tablets (OXN PR) in daily doses up to OXN 180/90 mg PR in cancer patients.

Results
Of the original 243 patients randomized (123 OXN PR and 120 Oxy PR), 21 of 27 and 14 of 19 patients, respectively, with malignancy pain completed the RCT phase and 25 of 35 patients completed the extension phase. The mean (SD) reduction in BFI from baseline to Week 5 was -40.8 (21.8) and -21.7 (29.8) in the OXN PR and Oxy PR groups, respectively, indicating a clinically significant difference between groups (p = 0.047). Mean (SD) BFI scores after 5 weeks were 31.0 (21.2) and 44.5 (30.7) for OXN PR and Oxy PR, respectively, indicating that OXN PR was close to the normal range, while the value for Oxy PR was still above normal. Pain scores remained stable in both groups with mean (SD) change from baseline at Week 5 of 0.1 (1.2) and 0.2 (0.7) in the OXN PR and Oxy PR groups, respectively. The majority of AEs in both groups were mild/moderate. Four severe AEs were reported in 4 (14.3%) patients in the OXN PR group and 9 severe AEs in 5 (22.7%) patients in the Oxy PR group, respectively; two severe AEs in each group were classed as treatment related. In the extension phase, the mean (SD) BFI score changed from a baseline value of 36.6 (26.3) to 23.1 (22.6) at 24 weeks. Pain scores remained stable throughout the 24-week extension phase. Twenty severe AEs were reported in 12 (34.33%) patients; 2 severe AEs in 2 patients (5.7%) were classed as treatment related.
Conclusion
We have previously shown that OXN PR provides significantly greater reductions in BFI compared with Oxy PR, with similar pain scores and AE rates in both groups, in doses up to Oxy 120 mg/day (1). This study shows that higher doses of OXN PR (up to 160/80 mg) were as effective as Oxy PR (up to 160 mg) in managing pain in cancer patients but with improved bowel function and a similar AE profile. The long-term extension phase showed continued benefits of OXN PR up to a dose of 180/90 mg. Reference: (1) Ahmedzai S et al. Pall Med 2011;26:50–60. This study was funded by Mundipharma Research GmbH & Co.KG. Medical writing support was provided by Christine McKillop of Medscimedia Ltd, UK, funded by Mundipharma Research GmbH & Co.KG.
**Title:** Efficacy And Safety Of Oral Morphine Vs. Oxycodone/Naloxone In Opioid-Naïve Cancer Patients: A Propensity Analysis

**Poster Number** PTH137

**Authors**
A. Roberto, M. Greco, M. Montanari, O. Corli
IRCCS Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy, Unità di Statistica Medica e Biometria, Milan, Italy, IRCCS Istituto di Ricerche Farmacologiche Mario Negri, Milan, ITALY

**Aim of Investigation**
The WHO Step III oral opioids Morphine (MOR) and Oxycodone/Naloxone (OXN) are commonly used to relieve moderate-to-severe pain; however, data are lacking on their direct comparison in the treatment of cancer pain. The aim of this study was to evaluate the efficacy and safety of prolonged-release MOR compared with OXN in opioid-naïve cancer patients with moderate-to-severe pain.

**Results**
One hundred twenty two patients for MOR and 138 for OXN were included in the comparative analysis. In both groups, similar 28-day WPI difference (3.8±0.25 MOR vs. 3.5±0.25 OXN, NS) and API (3.4±0.20 vs. 3.3±0.19; NS) were found, indicating comparable analgesic efficacy. Responder rates were also comparable (75.6% MOR vs. 82.5% OXN, NS). AEs rates were comparable between groups, but constipation was markedly more frequent after MOR (67.2% vs. 26.8%, p <0.0001). More patients prematurely switched from MOR (22.0%) than OXN (13.9%, p 0.08), despite lower mean daily MOR dosages both at baseline (45.7 mg vs. 50.9 OXN, p 0.06) and after 28 days (58.3 vs. 81.4 mg, p 0.001). Prevalence of OEI >5% was lower after MOR (10.3% vs. 22.5% OXN, p 0.009).

**Conclusion**
In this propensity analysis of patients with moderate-severe cancer pain, OXN showed similar analgesic efficacy compared to MOR, with significant less constipation, higher increase of dose and reduced rate of switch.
Title: Factors Affecting The Success Of Intrathecal Analgesia For Severe Cancer Pain: A 10-Year Retrospective Review In A Tertiary Center

Poster Number PTH138

Authors
E. KHOO, M. CARDOSA, N. Kim Swan

Hospital Selayang, BATU CAVES, SELANGOR, HOSPITAL SELAYANG, BATU CAVES, Malaysia, Hospital Selayang, Kuala Lumpur, Malaysia

Aim of Investigation
Intrathecal (IT) analgesia has proven to be useful in the management of intractable cancer pain that still remains a challenge despite pharmacological advances and development of evidence-based guidelines. This study aimed to determine factors that affect its success.

Results
44 patients were included; 45.5% were male, and the mean age was 55.3 years (range 22-84). 20.5% of patients had nociceptive pain, 25.0% neuropathic and 54.5% experienced a mixture of both pain types, with a mean pre-intervention pain score of 8.3 (SD 2.0). 6.8% had locally invasive disease and 93.2% had distant metastases. 47.7% had a permanent catheter while the rest had a temporary catheter. Morphine was used in 84.1% of patients with 97.7% needing a combination of 2 or more drugs. Median initial intrathecal opioid dose was 2.4 mg Morphine equivalent per day (range 0-12mg). The initial success rate was high at 92.9% but data analysis revealed no significant factors influencing this outcome. The definitive success rate was 65.9% and there was significant correlation with duration of pain. Although further analysis revealed that the regression model for this factor was significant, this was not so for the prediction equation.

Conclusion
Patients with advanced cancer pain often present with intractable pain and intrathecal analgesia results in immediate pain relieve in almost all patients. Our study revealed that duration of pain was correlated with definitive success of intrathecal analgesia, thus suggesting that timing of aggressive treatment of uncontrolled cancer pain is of utmost importance. Further studies will need to be done to determine the optimal timing for initiation of this intervention.
Title: Efficacy Of Pregabalin In The Treatment Of Pancreatic Cancer Pain: A Randomized, Controlled, Double-Blind, Parallel Group Study- Preliminary Results

Poster Number PTH139

Authors
C. Dürsteler, U. Rodriguez, L. Ilzarbe, G. Roca, J. Vallés, A. Montes

Hospital del Mar, Barcelona, Spain, Hospital Germans Trias i Pujol, Badalona, Spain

Aim of Investigation
Intense pain is a frequent clinical feature of pancreatic cancer. Its physiopathology is not yet well understood, but previous investigations suggest significant neuropathic pain involvement due to perineural invasion of intra and extra-pancreatic nerves (1). A recent work showed a substantial analgesic effect of pregabalin in chronic pancreatitis patients (2), but this results have not been confirmed in other pancreatic pain syndromes. Our aim was to evaluate the efficacy of pregabalin in pancreatic cancer pain.

Results
Our preliminary data show no statistically significant demographic differences between the two groups (treatment, placebo). Pain VAS score [mean(SD)] at the moment of diagnosis was 4.5(1.9). After beginning analgesic treatment, pain scores diminished progressively until the end of study [0.9(2.1)], with no statistically differences between groups. No inter-group differences in drug-related adverse-effects were observed, but placebo group received a much higher morphine-equivalent daily opioid dose [mean mg(SD)], compared with pregabalin group [270.6(148.3) vs. 20.9(27.1), respectively]. These differences were statistically significant on visits 3 (second month of treatment) and 4 (third month of treatment), with P values of 0.018 and 0.006, respectively. Pregabalin group showed also a significant lower level of anxiety and depression at the end of the study (P < 0.03 and P < 0.01, respectively).

Conclusion
Pancreatic cancer pain was adequately managed in both groups, 3 months after diagnosis. A strong opioid-sparing effect was observed in pregabalin-treated group, with no differences in adverse effects between both groups. Besides, pregabalin-treated patients had lower anxiety and depression levels at the end of the study. We have to wait until the end of the study to evaluate all final results, but it seems that early high-dose pregabalin treatment could be a good therapeutic option for patients with
pancreatic cancer pain. Acknowledgements/Discl

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Title: Pain Evaluation And Management In Special Populations Of The Oncological Patients

Poster Number PTH140

Authors
D. Nevzorova, E. Bakunina

Moscow Hospice №1 named after Vera Millionshikova, Moscow, Moscow area

Aim of Investigation
To evaluate the number of oncological patients experiencing moderate to severe chronic pain observed by the Moscow Hospice №1 in the year 2015, taking into the account national characteristic features, low public awareness on the causes of pain and its treatment, and the impediments of legal framework on prescribing and/or distributing opioid analgesics, and the quality of pain assessment and management.

Results
Out of 1157 patients, 53.6% were on medication with opioids to control moderate to severe pain; mean length of medication was 3 months. 735 patients were admitted to the hospice for the following indications: 30% of cases - poor pain control at home; increasing the dose of opioids led to psychological conflict with the family members and patient, so as was complicated to prescribe, due to unusually high doses. In some cases dose correction or managing side effects, or performing certain medical procedures were required. 40% were in terminal condition and wished to die at the hospice. 15% had no family and home care was complicated. 15% had psychological diseases or symptoms, which made the home care equally complicated.

Conclusion
In the current study the inadequate pain evaluation was revealed, both for acute and chronic pain as by patients and their families, so as by the medical professionals due to the range of cultural, socio-psychological, educational, political, religious and material and technical reasons. Ineffective pain management at home leaded to serious physiological, psychological, economical and social impact for patients and their families. The majority of patients were admitted at the hospice. 1/3 of patients were hospitalized due to social factors. Palliative physicians are highly experienced in managing pain, however, if the resources essential for pain evaluation and management are missing, it might be hard to relieve pain in 100% of patients.
Title: Electrophysiological Studies On An Animal Model Of Cancer-Induced Bone Pain: Differential Role Of Mechanical Sensory Neurons In Cancer Pain

Poster Number PTH142

Authors
Y. Zhu, E. Seidlitz, R. Ungard, N. Zacal, J. Huizinga, J. Henry, G. Singh

McMaster University, HAMILTON, Ontario

Aim of Investigation
Cancer-induced bone pain (CIBP) is often severe and directly induced by many processes, including pathological remodelling of the bone and the nervous system, yet little evidence is available regarding the underlying mechanisms leading to the development of CIBP. Although peripheral sensory neurons are involved in the development of CIBP, the precise contribution of peripheral sensory functional changes in pain perception has not yet been comprehensively defined. The aim of this study was to characterize the functional properties of primary sensory neurons in rats with and without prostate cancer tumours in bone to clarify which types of neurons undergo functional alterations in CIBP.

Results
Differences in intrinsic excitability and membrane properties of all three nociceptive DRG neuron types were observed between controls vs. model animals. These differences include: increased number of action potentials (APs) in response to dorsal root, soma, and receptive field stimuli; depolarized resting membrane potential; a decrease in amplitude and duration of evoked APs; and a significantly lower amplitude and duration of the afterhyperpolarization. In addition, Aβ-fiber low threshold mechanoreceptors exhibited an increased excitability to stimuli, a wider AP duration, and a lower AP amplitude. The pattern of the non-nociceptive neuron changes we observed are consistent with similar observations in models of peripheral neuropathy.

Conclusion
While previous studies have identified functional alterations in small diameter peripheral sensory neurons that correlate with bone tumours, none has provided direct evidence correlating behavioural nociceptive responses with properties of different sub-types of sensory neurons in an intact bone cancer model. This study provides evidence to suggest a potential contribution by all sub-types of mechanoreceptor neurons in CIBP including those normally considered to be non-nociceptive.
Furthermore, these results suggest that functional changes in peripheral neurons in CIBP may include aspects of nociceptive and neuropathic pain.
Title: Patients With Tumor Wounds: Evaluation And Characterization Of Oncologic Pain

Poster Number PTH143

Authors
A. COSTA, I. Kamada

Universidade de Brasília, Brasília, Brazil

Aim of Investigation
The objective of this study was to analyze the clinical and pain of oncology patients with tumor wounds, in treatment in specialized institutions of Brasilia.

Results
Of the 26 participants, 65.4% male and 34.6% female; 46.2% mulattos, 34.6% white and 19.2% black. The mean age of participants was 57.92 (± 12.47) and median of 56.50. With relation to labor activities, 42.3% were retired by age or sickness. In relation to the location of the tumor oncologic wounds, it was found that 84.7% of the sample were in the portion of the head and neck, statistics in the larynx (23.1%), skin (23.1%) and tongue (19.2%); and 15.3% were in other regions of the body. Regarding the oncology treatment, 65.4% performed antineoplastic chemotherapy (QtA) and radiotherapy in association with complications related to radiotherapy were radiodermites (47.6%). Already the frequency of pain was considered, by 63.2% of respondents, as daily, without specific time and without predominance of period. The result IBD showed that in corporal diagram of IBD, were highlighted the regions of pain location by participants, which correspond to the regions of the head, cervical, breasts, inguinal, anterior and posterior thorax, in addition to the left lower limb. With the IBD it was possible to observe the interference of pain in daily activities and labor, on a scale of zero to ten. The pain interferes, mainly, in general activity (6.05±4.88), work (7.0±4.7) and relationship (8.25±4.46). Lower scores were found in the humor, walking ability, sleep and appreciate life. The result of the MPQ revealed the verbal descriptors of four categories. In the sensory category composed by ten subcategories, the descriptors more chosen were: 'pulsing' (41.7%), 'throbbing' (41.7%), 'bystabbing pain' (75%), 'hook' (63.6%), 'itchy' (70%), 'heavy' (46.2%), 'Stretched' (25%). In the affective category composed by 5 subcategories, the descriptors more chosen were: 'tiring' (50%), 'exhaustive' (50%), 'sick' (66.7%), 'frightening' (57.1%) 'tormenting' (83.3%) and 'wretched' (71.4%). In the category of subjective, the descriptor more chosen was 'boring' (50%) and in the evaluative category composed by 4 subcategories, the descriptors chosen few were 'penetrates' (50%), 'jerking' (30%), 'tears' (30%), 'boring' (33.3%), 'gives nausea' (33.3%) and 'irksome' (33.3%). With
the 78 descriptors of the MPQ, the summation of category categories was 31.2, with minimum of 22 and maximum of 55 points.

**Conclusion**
Was completed that tumor wound was located in regions with body exposure, which changed the body image, as well as the idea of the patient regarding clinical condition and evolution of oncological disease. For the patients with neuropathic pain, control is complex and the use with drug association with adverse effects requires continuous follow up.
**Title:** Spatial Localization In Complex Regional Pain Syndrome Under Uni- And Multi-Sensory Guidance

**Poster Number** PTH144

**Authors**
J. Bultitude<sup>,2</sup>, K. Petrini

University of Bath, Bath, North East Somerset, Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB), University of Oxford, Oxford, United Kingdom

**Aim of Investigation**
Patients with Complex Regional Pain Syndrome (CRPS) can have problems with tasks that require spatial processing, such as localising their affected limb or attending to touch on the affected side of space. Also, some patients report that pain can be exacerbated by loud noises and ambiguous visual stimuli, suggesting changes in multisensory integration. The aim of this study is to investigate spatial localisation and multisensory integration in patients with CRPS.

**Results**
For each participant, estimates of variable error (VE: the sum of the variance of the end-points in x and y directions) were calculated separately for each condition (V, P/M, V-P/M). To evaluate localisation ability in CRPS, the VEs of individual patients were compared to bootstrapped (1000 samples) 95% Confidence Intervals (CIs) around the controls' means. One upper limb and one lower limb CRPS patient had VEs that were within the controls' 95% CI for all three conditions. The remaining six patients had VEs that exceeded the upper boundary of the 95% CI for the controls' means in at least one condition. Specifically, four had larger-than-normal VEs in the V condition, two had larger-than-normal VEs in the P/M condition, and five had larger-than-normal VEs in the V-P/M condition. This suggests that CRPS can be accompanied by deficits in localisation under both uni- and multi-modal guidance. Preliminary inspection of VE data when separated by Hand and Target Side suggests that more patients were impaired in P/M guidance for targets that appeared on the affected side compared to the unaffected side of space, regardless of which hand was used. Planned paired-samples t-tests with bootstrapping (1000 samples) showed that for control participants the VEs in the V-P/M condition were lower than in both the V condition (p=.002) and the P/M condition (p=.001). This is consistent with previous findings that uncertainty is reduced during multi-sensory compared to uni-sensory localisation. For the patients, VEs in the V-P/M condition were not significantly different to VEs in the V condition (p=.11) nor the P/M condition (p=.35). This is suggestive of a deficit in multisensory integration.
**Conclusion**

The results provide evidence for impaired spatial localisation in CRPS under conditions of visual-only, proprioceptive/motor-only, and combined visual and proprioceptive/motor guidance. Four of the five lower limb CRPS patients showed some form of localisation deficit, indicating that these changes are not limited to tasks involving the affected limb but generalise to broader spatial cognition. The results also provide preliminary evidence for deficits in multisensory integration in CRPS, although this conclusion should be treated with caution due to the small and heterogeneous sample.
Aim of Investigation
Complex Regional Pain Syndrome (CRPS) is often associated with impaired egocentric self-body perception of the affected area. The author had previously noted some patients appeared to have impaired allocentric body perception. Patients with more extensive allodynia, longer duration CRPS and greater egocentric self-body perception disturbance will be more likely to have cortical representational change and therefore might have more difficulty with egocentric/allocentric body perception and integration. We investigated whether body perception disturbance extends beyond the self to allocentric recalled external images of the body. We hypothesized that impaired allocentric pictorial body representation would be more likely in patients with longer disease duration, more extensive allodynia and greater egocentric body perception disturbance.

Results
45 patients (37 female, 8 male) of mean age 44 years (range 18-72) were assessed. The mean duration of CRPS was 7.4 years (range 0.25 – 25, 95%CI 5.3-9.6), and affected the upper limbs in 25% (n=11; right = 5, left= 6) and lower limbs in 75% (n=34; right = 11, left = 16, bilateral = 7). Tactile and/or pressure allodynia was present in 87%. The mean BBPS score was 35 (range 0-55, 95%CI 30-39) and the mean percentage of body surface area (%BSA) affected by allodynia was 7% (range 0.1-36%; 95%CI 4-9). 53% (n=24) patients had impaired recall of an external pictorial image of a full length person. 15 patients were able to accurately describe all areas of the body except the same limb on the image as affected by their CRPS. Nine patients in addition could not describe another part of the image; these additional areas were all also painful and/or had impaired egocentric self-perception. Among patients with impaired pictorial recall there was a statistically significant greater mean BBPS score (41 vs 28; p<0.001), larger mean percentage of body surface area allodynia (10 vs 3%; p=0.015) and longer mean duration of CRPS (10 vs 4.5 years, p<0.001). 83% of patients with impaired pictorial recall had a BBPS drawing score of 2 (maximal) and none had a score of 0 (normal); in comparison, 48% of patients with unimpaired recall had a score of 2 and 19% had a score of 0.
Conclusion
Body perception disturbance in CRPS extends beyond egocentric perception and may encompass allocentric body perception as demonstrated by impaired pictorial recall. The presence of longer disease duration, larger area of allodynia and greater self-body perception disturbance suggests that in some CRPS phenotypes there may be maladaptive neuroplasticity and failure of normal egocentric and allocentric body scheme integration.
Complex Regional Pain Syndrome (CRPS) is a chronic pain condition characterized by continuing (spontaneous and/or evoked) regional pain that is disproportionate in length of time or degree of pain after trauma or other lesions. Central sensitization is a primordial mechanism in the development of CRPS involving sensory as well as motor adaptive changes. CRPS is uncommon and practitioners are unfamiliar with the clinical presentation which manifests in a wide range visits with health-care professionals. CRPS is difficult for clinicians to manage as there is no gold standard for diagnosis or treatment. Thus, it has major socio-economic consequences. Early diagnosis and prompt instigation of rehabilitation is now widely recommended in order to achieve optimum patient outcomes. Therefore, there is a need to identify who will go on to develop CRPS. Atypical sensory responsiveness (ASR), is a generalized condition affecting single or several sensory systems and manifests as hypo/ hyper responsiveness to daily sensory innocuous stimuli. ASR interferes with quality of life and was found associated with hyper-sensitivity to pain. This study was designed to explore the association between CRPS and atypical sensory responsiveness and to test whether atypical sensory responsiveness could serve as a risk factor for CRPS.

**Results**
A statistically significant relationship was found between ASR and CRPS, where 12.8% (N=26) in the control group had ASR versus 34.1% (N=15) in the CRPS group (Chi-squared test, p=0.0005). Logistic regression modeling found that the risk for developing CRPS is 2.68 and 8.21 times higher for sensory
hyper- and sensory hypo-responsiveness subjects as compared to Non-ASR subjects (p= 0.03; 0.01 respectively).

**Conclusion**
ASR, particularly sensory hypo-responsiveness to daily innocuous stimuli may serve as a risk factor for developing CRPS. Further research is warranted.
Title: Does Crps Impair The Perception Of Somatosensory And Non-Somatosensory Stimuli?

Poster Number PTH147

Authors
L. Filbrich, A. Alamia, C. Verfaille, O. Barbier, X. Libouton, V. Fraselle, D. Mouraux, A. Berquin, V. Legrain

Université catholique de Louvain, Brussels, Belgium, Cliniques Universitaires Saint-Luc, Brussels, Belgium, Hôpital Erasme, Brussels, Belgium

Aim of Investigation
Patients suffering from the complex regional pain syndrome (CRPS) are presumed to be affected by cognitive deficits altering their ability to represent and perceive their body (for a review see Legrain et al., PAIN, 2012). Up to now, it is however unclear whether these cognitive deficits only affect the perception of stimuli applied to the body surface, or also stimuli presented in external space, e.g. visual stimuli. If the latter is the case, it also remains unclear if these deficits in spatial perception are limited to the space proximal to the patients' body or if they extend toward farther space.

Results
Preliminary results for the tactile TOJ task (n=9) did not reveal systematic cognitive deficits in the ability to perceive the location of tactile stimuli, neither for the uncrossed nor the crossed arm posture. On the contrary, results in the visual TOJ task (n = 8) suggest that the patients paid more attention to the visual stimuli presented in the same side of space as the unaffected limb, independently of whether the visual stimuli were presented close or far from the hands.

Conclusion
Our results extend previous studies, as they show that cognitive deficits in upper-limb CRPS patients can also affect the perception of the space external to the body. We did however not replicate previous findings which showed deficits in the processing of somatosensory information. These discrepant results could be explained by the duration of the CRPS. Funded by the Fund for Scientific Research of the French-speaking Community of Belgium (F.R.S.-FNRS).
Title: Spatially-Defined Motor Deficits In People With Unilateral Complex Regional Pain Syndrome

Poster Number: PTH148

Authors

University of South Australia, Adelaide, South Australia, Griffith University, Gold Coast, Queensland, University of Oxford, Oxford, United Kingdom, Università degli Studi di Milano-Bicocca, Milano, Italy

Aim of Investigation
A building body of evidence demonstrates spatially defined deficits in people with upper limb Complex Regional Pain Syndrome (CRPS). That is, thermoregulation and tactile processing are both disrupted according to where the hand is relative to the body midline. Here we wished to determine whether this midline effect also impacts on motor performance. Specifically, we aimed to determine whether motor accuracy and coordination is disrupted in people with unilateral CRPS of the upper limb, in a spatially defined manner. The specific objectives were to investigate and compare the accuracy and coordination of a simple motor task when it was performed on the ipsilateral, or usual, side of the body midline, and when it was performed on the contralateral side of the body midline.

Results
Full data were available for 13 participants [8 females, 6 affected left limb, mean (SD) age = 40.5 (12.7) years]. There was a main effect of both limb and side of the midline for the motor tasks. In Experiment 1, motor accuracy for the circle drawing task was poorer when participants used their affected limb than when they used their healthy one (p<0.001), and poorer when the task was performed on the affected side than when it was performed on the healthy side of their body midline (p<0.001), regardless of hand. In Experiment 2, motor coordination for the button pressing task was poorer when participants used their affected limb than when they used their healthy one (p<0.001), and poorer when the task was performed on the affected side of the midline than when it was performed on the healthy side of the midline, regardless of hand (p<0.001).

Conclusion
A spatial bias towards the healthy side of the body midline was evident for upper limb motor tasks performed by participants with CRPS. The results suggest that the midline-centred dysfunction in the processing of tactile input and the regulation of temperature that is present in this population also
extends to movement performance. These results provide further support for the concept of 'somatospatial' neglect in people with CRPS.
Title: Passive Transfer Autoimmunity In Crps

Poster Number PTH149

Authors
W. Kingery, W. Li, T. Guo, X. Shi, D. Clark
VAPAHCs, Palo Alto, CA, Stanford University, Palo Alto, CA

Aim of Investigation
Aim of investigation: We previously observed that B cells are required for the full expression of CRPS-like changes a mouse tibia fracture model of complex regional pain syndrome (CRPS). This study tested the hypothesis that serum antibodies from fracture mice or CRPS patients can induce regionally restricted pain behaviors in B cell deficient fracture mice.

Results
Results: When serum from WT fracture mice or CRPS patients was injected into muMT fracture mice, the mice gradually developed increased hindpaw von Frey alldynia and unweighting over the ensuing week and, consistent with the half-life of immunoglobulin, these pronociceptive effects resolved by 2 weeks post-injection. The pronociceptive effects of the CRPS serum antibodies were restricted to the fracture limb and not observed in nonfractured mice. When muMT fracture mice were injected with IgM from 3 weeks post-fracture WT mice it had the same pronociceptive effects as serum, but IgG had no effect. WT mice exhibited unilateral hindpaw alldynia and unweighting at 3 weeks post-fracture and these pain behaviors gradually resolve over the ensuing 21 weeks. Serum from 3 and 18 weeks post-fracture WT mice caused hindpaw alldynia and unweighting in muMT fracture mice, but 21 weeks post-fracture serum did not induce alldynia and had minimal effects on unweighting. After fracture there was a gradual increase in IgM-antigen complex levels in the ipsilateral hindpaw skin, sciatic nerve, and lumbar spinal cord of wildtype mice, peaking at 12 weeks and then declining, reaching control levels in the sciatic nerve by 21 weeks post-fracture. No IgG deposition was observed after fracture in WT mice and no IgM or IgG was observed in the muMT fracture mice.

Conclusion
Conclusions: When serum collected from CRPS patients was injected into 3 weeks post-fracture muMT mice, it exacerbated von Frey alldynia and unweighting in the fracture hindpaw, thus fulfilling Witebsky’s third criteria for an autoimmune disease; evidence that passive transfer of patient
autoantibodies can evoke CRPS-like changes in animals. CRPS patient serum had no effect on nociceptive thresholds in the contralateral paw, suggesting that circulating autoantibodies alone are insufficient to cause CRPS-like changes and that unique regional autoantigens expressed in the fracture limb are required to form the autoantigen-antibody complexes that initiate post-fracture CRPS-like changes.
Title: Effects Of 15 Weeks Of Resistance Exercise On Plasma Cytokine Levels In Patients With Fibromyalgia

Poster Number PTH150

Authors

Karolinska Institutet, Huddinge, Sweden, County council of ostergotland, Linkoping, Sweden, Karolinska Institutet, Stockholm, Sweden, University of Gothenburg, Gothenburg, Sweden, University of Linkoping, Linkoping, Sweden

Aim of Investigation
Worsening of symptoms after exercise is one of the key features of fibromyalgia (FM). Even though FM is not considered an inflammatory disorder, an imbalance between pro- and anti-inflammatory cytokines has been suggested as a possible pathogenic factor. Studies have reported impaired anti-inflammatory cytokine release after exercise in FM. The aim of this study was to evaluate the effect of a resistance exercise intervention on plasma cytokine levels in FM patients.

Results
The positive effects of resistance exercise on clinical variables have been reported elsewhere (Larsson et al. Arthritis Res Ther. 2015;17:161). Blood samples before and after training were available from 49 patients in the exercise group and 43 in the relaxation group. There were no differences between groups in global pain, PPT or any of the cytokines at baseline, except IL-8 that was higher in the exercise group (P = 0.027). IL-1β had increased in the relaxation group (P = 0.002) and IL-1ra had increased in both groups after the intervention (P’s = 0.004). ΔPPT was greater in the exercise group (P = 0.036) and ΔIL-1β (P = 0.037) was greater in the relaxation group. There were no other group differences in cytokine levels. ΔPPT showed moderately strong negative correlations to ΔVAS (rs = -0.40, n = 49, P = 0.004), ΔIL-2 (rs = -0.41, n = 49, P = 0.003), and ΔIL-6 (rs = -0.45, n = 49, P = 0.001) in the exercise group, but there were no significant correlations in the relaxation group or between cytokines, global pain intensity or background variables.

Conclusion
Resistance exercise in general had little effect on cytokine levels. However, increased PPT after training
was associated with reduction of IL-2 and IL-6. This may indicate that in patients with a positive effect of resistance exercise on mechanical sensitization this may to some extent be due to reduction of pro-inflammatory cytokines.
Title: Tnf-A Response Is Associated With The Clinical Pain Outcomes Of Fibromyalgia Patients: An Evaluation Done With Human Blood-Induced Microglia-Like Cells (Img)

Poster Number PTH151

Authors
M. Hosoi, M. Ohgidani, T. Kato, R. Iwaki, C. Hayaki, N. Sudo, S. Kanba

Dept of Psychosomatic Medicine, Kyushu University Hospital, Fukuoka, 福岡県, Department of Neuropsychiatry, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, Kyushu university, Fukuoka, Japan

Aim of Investigation
We have developed a technology to create human induced microglia-like cells (iMG) from human peripheral blood monocytes. Fibromyalgia, a type of chronic pain, is a refractory disease, the cause of which has not yet been unveiled due to its pathological complexity. In recent years, activation of immune cells in the brain called microglia has attracted attention as an explanation of the pathological mechanism of chronic pains. This study aims to observe microglia activation at the cell level in patients with fibromyalgia using iMG technology in an effort to examine the participation of microglia in its pathological mechanism.

Results
No significant difference was observed between the healthy group and the group with fibromyalgia in phagocytic capacity or cytokine responses that occurred during phagocytic activities. Interestingly, however, the TNF-α gene expression level and protein concentrations of the fibromyalgia group were significantly increased for ATP-stimulated iMG in comparison with the healthy group. Significant correlations were observed between the TNF-α expression level after ATP stimulation and clinic parameters that represent pain and mental manifestations.

Conclusion
These findings suggest that the microglia of patients with fibromyalgia are hypersensitive to ATP and that TNF-α produced by microglia may be one of the key factors that constitute the kernel of the complex pathology of fibromyalgia. Acknowledgement: This research is supported by a grant from the Research Project on Elucidation of Chronic Pain from the Japan Agency for Medical Research and development, AMED.
Title: Generalized Sensory-Affective Perturbations In Patients With Fibromyalgia

Poster Number PTH152

Authors
S. Nagi, U. Olausson, E. Lind, L. Koppel, B. Gerdle, H. Olausson

Linköping University, Linköping, Sweden

Aim of Investigation
Fibromyalgia is a frequent, debilitating syndrome that includes chronic widespread pain and a myriad of other symptoms; however, the underlying mechanisms remain elusive. In recent studies, a less known class of nerves in the skin, termed C-tactile fibers (CT), have been implicated in pain processing either directly or indirectly, as an allodynic substrate itself or by way of the malfunction of this network. In normal conditions, CTs have been associated with pleasantness associated with skin-to-skin contact between conspecifics – a hypothesis that has drawn considerable interest for its pertinence to physical and social well-being and the interoceptive system. Importantly, CTs exhibit a unique 'inverted U-shaped' response pattern to graded brushing velocities with slow brushing (1-10 cm/s) producing a robust discharge – a stimulus that is normally perceived as highly pleasant. While classical nociceptors have been the focus of earlier studies on fibromyalgia, little is known about the role of their low-threshold counterparts, the CTs. In the current study, we determined the sensory-affective profile of fibromyalgia patients across multiple body domains, including painful and non-painful regions.

Results
Pressure-pain threshold testing revealed generalized deep-tissue hypersensitivity. Likewise, abnormalities in thermal and thermal-pain thresholds were found across all sites. In addition, thermal allodynia was observed in some patients. Interestingly, the rating pattern of patients across brushing velocities deviated markedly from the typical hedonic-touch profile. In addition, a subset of patients found brushing to be allodynic, including at CT-optimal speeds. Akin to other observations, the impairment of hedonic touch was not limited to the painful site but was also reported for the contralateral site as-well-as the remote, non-painful site.

Conclusion
Widespread sensory-affective perturbations were found in patients with fibromyalgia. Hedonic-touch processing was impaired across painful and otherwise non-painful body sites. Consistent with the
proposed role of CTs in interoception, the generalized expression of sensory-affective perturbations in fibromyalgia may be indicative of an aberrant interoceptive system. Further investigations are warranted into the underlying mechanisms.
Title: Somatic Awareness And Tender Points In A Community Sample

Poster Number PTH153

Authors
A. Schrepf, D. Harper, D. Williams, A. Hassett, D. Clauw, S. Harte

University of Michigan, Ann Arbor, MI, UNIVERSITY OF MICHIGAN UM/Chronic Pain & Fatigue Research Ctr, ANN ARBOR, MI

Aim of Investigation
Somatic awareness (SA) refers to heightened sensitivity to a variety of physical sensations and symptoms. SA has been tied to the more general concept of negative affect as a putative manifestation of anxiety-specific symptoms. While negative affect and SA have been independently linked to pain, few attempts have been made to dissociate their relationship with pain outcomes. To address this, we used a validated measure of mood and anxiety symptoms that includes questions related to SA to predict the number of tender points found on physical examination in a large community sample.

Results
EFA revealed a three-factor structure similar to that found in other community and chronic pain samples: general distress (15 items), positive affect (15 items), and SA (15 items), accounting for 41% of the explained variance. Items loading on the SA factor included statements like, '...had a very dry mouth,' and '...felt numbness or tingling in my body.' The multivariate model using all three factors as predictors of tender points, while controlling for a number of potential confounding variables, revealed higher levels of SA (p = .002), but not general distress (p = .24) or positive affect (p = .29), to be significantly associated with the number of tender points. Each one point increase on the SA subscale (range 14-43) was associated with a 7% higher likelihood of finding a tender point during examination (OR=1.07, 95% CI = 1.03, 1.12). Additionally, older age, being female, the use of sedatives, use of opioids, use of anti-depressants, and abnormal joints/musculature were also associated with a greater number of tender points (all p < .05). Mediation analyses confirmed the results of the multivariate model: the relationship between general distress, positive affect, and tender points was mediated by levels of SA.

Conclusion
Our primary finding is that SA is strongly related to the number of tender points in a community sample.
Notably, neither general distress nor positive affect were associated with tender points in the model including SA, a result confirmed by mediation analyses. High levels of SA may tap into a neurobiological augmentation of interoceptive processes and external sensations, resulting in lower pain thresholds and increased sensory sensitivity. Our findings suggest that some of the relationships between affect and pain outcomes observed in previous studies may be driven primarily by SA. This would complement previous findings demonstrating that SA is a robust risk factor in the development of temporomandibular disorder. Furthermore, high levels of SA symptoms have been found in chronic pain populations that are characterized by central changes in pain processing such as fibromyalgia and migraine. More research is needed to determine whether the relationship between negative affect and chronic pain is dependent on SA.
Title: Asymmetrical-Fibromyalgia Syndrome (Fms): Clinical, Neurophysiological, And Pathological Comparison To Classic Symmetrical-Fms And Healthy Controls

Poster Number PTH154

Authors
R. Galhardoni<sup>,2</sup><sup>,3</sup>, H. Kaziyama<sup>,5</sup>, I. Raicher<sup>,7</sup>, G. dos Santos, J. Rodrigues, G. Tortella<sup>,2</sup><sup>,3</sup>, M. Marcolin, C.

Pain Center Department of Neurology University of São Paulo, São Paulo, Brazil, Transcranial Magnetic Stimulation Laboratory, Psychiatry Institute, Medical School of the University of São Paulo, Sao Paulo,, Brazil, School Medicine, University of City of São Paulo (UNICID), Sao Paulo,, Brazil, Pain Center Department of Neurology University of São Pauloi, Sao Paulo, Brazil, Physical Medicine and Rehabilitation, Orthopedics and Traumatology Institute ,Medical School of the University of São Paulo,, Sao Paulo, , Brazil, Pain Center Department of Neurology University of São Paulo, Sao Paulo, Sao Paulo, Pain Center, Cancer Institute of São Paulo, Sao Paulo,, Brazil, Pain Center Department of Neurology University of São Paulol, Sao Paulo, Brazil, Pain Center Department of Neurology University of São Paulol, Sao Paulo, Brazil, Pain Center Department of Neurology University of São Paulo, Sao Paulo, BRAZIL

Aim of Investigation
A significant proportion of patients fulfilling the diagnostic criteria of fibromyalgia syndrome (FMS) present asymmetrical ongoing pain and abnormalities on the physical examination that are not present in patients with 'classical' symmetric FMS. From the clinical perspective, this condition has been named FMS-Dysfunctional Pain Syndrome with Asymmetrical Exteroceptive Sensibility (DPSAES). Patients with DPSAES usually present higher negative impact in quality of life when compared to the more 'classic' FMS patients. The present study aimed at investigating potential clinical, QST, cortical excitability and intraepidermal nerve fiber densities between FMS patients with symmetric (classic) and asymmetric clinical presentation.

Results
When compared to patients with 'classical' FMS patients with asymmetric-FMS presented similar VAS scores, but higher scores in pain interference in daily activities (54.73±8.90 and 37.66±13.56; respectively; p<0.0001); higher negative impact in quality of life (73.67±13.90 and 58.38±13.97; respectively, p=0.004), and lower pressure pain thresholds on the most painful body side (27.74±7.96 and 35.86±8.37; respectively, p=0.007). Patients with asymmetric-FMS has asymmetric CE results and an
abnormally higher intracortical facilitation compared to classic-FMS. Skin samples were obtained and are under evaluation.

**Conclusion**

Patients with asymmetric-FMS have greater impact of FMS, greater interference of pain with daily activities, and asymmetric and abnormally high ICF in the hemisphere contralateral to the most painful side, which does not happen in classical FMS, where CE is symetrica and has low ICF (3.35±2.31 and 1.64±1.06; respectively, p=0.008). These results suggest that despite fulfilling the current FMS criteria, asymmetric-FMS may have different pathophysiological bases from classical-FMS and could be termed DPSAES).
Title: Specific Proteins Of The Trapezius Muscle Correlate With Pain Intensity And Sensitivity: An Explorative Multivariate Proteomic Study Of The Trapezius Muscle In Women With Chronic Widespread Pain

Poster Number PTH155

Authors
P. Olausson, B. Ghafouri, N. Ghafouri, B. Gerdle

Department of Medical and Health Sciences, Division of Community Medicine, Linköping University, Linköping, Sweden, Pain and Rehabilitation Center, Anaesthetics, Operations & Spec. Surgery Center, Region Östergötland, Linköping, Sweden

Aim of Investigation
Chronic widespread pain (CWP) including fibromyalgia syndrome (FMS) has a high prevalence and is associated with prominent negative consequences. CWP/FMS exhibit morphological and functional alterations in the central nervous system. The importance of peripheral factors for maintaining the central alterations are under debate. Hence, this study of CWP/FMS and healthy controls investigates the relationships between proteins of trapezius muscle biopsies, pain intensity and PPT.

Results
Twelve proteins representing five different groups of proteins were important regressors of pain intensity in CWP/FMS ($R^2 = 0.99$, $Q^2 = 0.91$, $p < 0.001$). In the regression of PPT in CWP/FMS it was found that 16 proteins representing six groups of proteins were significant regressors ($R^2 = 0.95$, $Q^2 = 0.81$, $p < 0.05$). Many of the important proteins were stress and inflammation proteins, enzymes involved in metabolic pathways, and proteins associated with muscle damage, myopathies and muscle recovery.

Conclusion
The altered expression of these proteins may reflect both direct and indirect nociceptive/inflammatory processes as well as secondary changes. The relative importance of the identified proteins and central alterations in CWP need to be investigated in future research. Data from this study give support to the suggestion that peripheral factors are of importance for maintaining pain aspects in CWP/FMS. Such information can be of guidance for designing treatment and rehabilitation interventions.
Aim of Investigation
Mounting evidence, mostly from studies with chronic musculoskeletal pain patients, indicates that pain-related fear plays a fundamental role in the transition from acute to chronic disabling pain. It has been shown that pain-related fear is acquired via associative learning (Meulders et al. 2011). In the clinic, however, spreading of fear and avoidance is observed beyond movements/activities that were associated with pain during the original pain episode. One possible mechanism accounting for this spreading of fear is stimulus generalization. Stimulus generalization is adaptive as it enables individuals to extrapolate the predictive value of one stimulus to novel, similar stimuli without actually having to experience them. From an associative learning perspective this implies that conditioned responses (CR) may extend to a range of novel stimuli resembling the original conditioned stimulus (CS), with more similar generalization stimuli (GSs) evoking stronger CRs. Yet, together with reducing the risk of missing positive threat alarms, which may contribute to avoiding harm in a swiftly changing environment, generalization bears an increased risk to respond to false threat alarms. As a consequence, when fear spreads in an unbridled way, stimulus generalization becomes maladaptive and may lead to dysfunctional avoidance behaviors and culminate in severe pain disability. In a previous study, we showed that pain-related fear indeed spreads selectively towards novel movements sharing proprioceptive features with the original painful movement in healthy participants, but fear generalized in a non-differential way in fibromyalgia patients (Meulders et al. 2015). In another study using a scenario contingency learning task with the simple verbal labels 'pain' and 'no pain' as outcomes, we found that chronic hand pain patients showed overgeneralization of pain-outcome expectancy to novel cues that were technically more similar to the original 'safe' cue as compared to healthy controls (Meulders et al. 2014). We argued that overgeneralization may play an important role in the etiology of chronic pain disability by spreading of undesired protective behaviors. Moreover, persistence of pain-related fear and expectancy to technically safe GSs despite corrective feedback might even be more debilitating and maintain chronic pain disability in the long run. Therefore, the present study aimed to test both differences in pain-related fear generalization to novel movements and in extinction of pain-
related fear generalization between fibromyalgia patients (FM) and HC. We hypothesized that 1) FM would show flatter generalization gradients than HC and that this is caused by higher responses to the GSs that are more similar to the original CS-, 2) FM would show resistance to extinction to unreinforced GSs, whereas generalized pain-related fear will subside quickly in HC.

Results
As predicted, there was a significant difference in the slope of the linear trend at the first trial of the generalization phase between both groups, indicating that FM showed flatter pain-US expectancy generalization gradients than HC. Planned comparisons further confirmed that this difference in steepness of the slopes is explained by differences at the CS- side of the generalization gradient (i.e. responses to novel movements that are more similar to the safe movements), but that no differences occurred at the CS+ side of the generalization gradient (i.e. responses to novel movements that are more similar to the painful movements). More particularly, FM reported significantly higher pain-US expectancies for the CS- and GS5 (the generalization movement that was most similar to the CS-) than the HC; the pain-US expectancy ratings for the other GSs and the original CS+ however did not differ between both groups. A similar data pattern was observed in the pain-related fear ratings, however the statistical analyses did not corroborate our findings in the pain-US expectancy ratings. At trial 4, there was also a significantly different slope in the pain-US expectancy ratings for the FM vs. HC. Planned contrasts further showed that pain-US expectancies in response to all GSs decreased significantly from trial 1 to trial 4 for the HC, but not for the CS+ that remained reinforced during the generalization phase, and not for the CS- (i.e. floor effect). The pain-US expectancy ratings for the FM also declined significantly from trial 1 to trial 4 for GS2-5, but not for the CS+, the CS-, nor the GS1. Interestingly, the decline in pain-US expectancies for GS2-4 was significantly smaller in the FM group than the HC, suggesting that there was resistance to extinction of pain-US expectancies to the novel, unreinforced generalization movements. Additionally, at trial 4, the pain-US expectancies for all GSs (GS1-5) were still significantly higher for the FM than the HC, which further supports the resistance to extinction of generalization hypothesis. A similar analysis was run on the pain-related fear ratings, however this analysis could only partly confirm our findings in the pain-US expectancy ratings. Fear in response to all GSs decreased significantly from trial 1 to trial 4 for the HC, but not for the CS that remained reinforced during the generalization phase, and not for the CS- (i.e. floor effect). The pain-related fear ratings for the FM also declined significantly from trial 1 to trial 4 for GS2-5, but not for the CS+, the CS- and the GS1. The decline in fear of movement-related pain was not significantly smaller in the FM group than the HC. Yet, at trial 4, the fear reported for all generalization movements was still significantly (GS1-2-4-5) (or borderline significantly, GS3) higher for the FM than the HC, which at least provides partial support for the resistance to extinction of generalization hypothesis.

Conclusion
To our knowledge, this is the first study that investigated the differences in generalization gradients of pain-related fear and pain-US expectancy between healthy controls and fibromyalgia patients, and subsequently compared the rate of extinction of generalization of both dependent measures. We replicated and extended our previous findings using a design in which the GSs either had a feature in common with the CS+ or CS- but no generalization gradients could be calculated (Meulders et al. 2015).
More specifically, we showed that pain-US expectancy generalization gradients are flatter in fibromyalgia patients than in healthy controls due to elevated pain-US expectancies for the novel, technically safe movements, whereas the shape of the fear generalization gradient did not significantly differ between fibromyalgia and healthy controls. These findings are also in line with the results of our study on pain-expectancy judgments in chronic hand pain patients (Meulders et al. 2014). With respect to extinction of generalization, we found at least partial evidence for our hypothesis: we showed that although the pain-US expectancy for all generalization movements declined for the healthy controls and for all but the GS1 in the fibromyalgia patients, this decline was still significantly smaller in the fibromyalgia group than in the healthy control group. Moreover after four unreinforced trials, pain-US expectancies for all generalization movements remained elevated in the fibromyalgia group compared to the healthy controls. A similar pattern was observed in the pain-related fear ratings, fear in response to all generalization movements declined for the healthy controls and for all but the GS1 in the fibromyalgia patients, this decline was however was not significantly different in the fibromyalgia group than in the healthy control group. Nevertheless, after four unreinforced trials, pain-related fear for most of the generalization movements remained elevated for the fibromyalgia group compared to the healthy controls. Given the status of overgeneralization as a plausible transdiagnostic pathogenic marker, we believe this research might increase our knowledge about the pathogenesis of musculoskeletal widespread pain. Furthermore, the persistence of unnecessary protective responses may be particularly maladaptive and contribute to the maintenance of chronic pain disability in the long run.
Title: Chronic Widespread Pain And Fibromyalgia Syndrome: The Influence Of Tender Points On Mental And Physical Health Status As Revealed By Sf-8 Score Analysis

Poster Number PTH157

Authors
M. Ildstad, S. Butler, A. Woodhouse, P. Borchgrevink, T. Landmark, M. Glette

St Olavs Hospital, Trondheim, Norway, Academic Hospital of Uppsala, Uppsala, Sweden, Norwegian University of Science and Technology (NTNU), Trondheim, NORWAY, National Competence Center for Complex Symptom Disorders, St. Olav’s University Hospital, Trondheim, Norway, St Olavs University Hospital, Trondheim, Norway, Norwegian University of Science and Technology (NTNU), Trondheim, Norway

Aim of Investigation
The American College of Rheumatology (ACR) 1990 criteria for fibromyalgia syndrome (FMS) require the presence of chronic widespread pain (CWP) and 11/18 tender points – however, the more recent ACR 2010 criteria no longer included tender point examinations. The relevance of tender points in FMS is thus uncertain. In this population-based study, we aimed to compare CWP with and without the presence of at least 11/18 tender points in relation to health related quality of life (HRQOL) as assessed by the SF-8 health survey.

Results
146 persons fulfilled the criteria for CWP. Of those, 57 subjects (39 %) had a minimum of 11/18 positive tender points, thereby meeting the ACR criteria for FMS. The group with CWP and at least 11 tender points had a significantly lower score on the SF-8 mental component summary, compared with CWP alone (t = -2.26, p = 0.026). The difference between the groups on the physical component did not reach statistical significance (t = -1.67, p = 0.097).

Conclusion
Surprisingly, the addition of a positive tender points count to CWP had non-significant effect on the physical aspects of quality of life. However, the presence of tender points seems to have a significant effect on the mental health component of quality of life as measures by the SF-8. More research is warranted in this area. Self-reported mental but not physical health was significantly poorer among
participants who fulfilled the ACR (1990) criteria for FMS compared with participants with CWP but not FMS.
Title: Evaluation Of Efficacy And Safety Of Ly2951742 In Randomized, Double-Blind, Placebo-Controlled, Single-Dose, And Dose Ranging Studies In Patients With Migraine

Poster Number PTH158

Authors

Eli Lilly and Company, Indianapolis, IN, Mayo Clinic, Phoenix, AZ, King's College London, London, UK, Eli Lilly and Company, Greenfield, IN

Aim of Investigation
Migraine remains poorly treated with few effective preventive medications available. LY2951742, a monoclonal antibody that binds to calcitonin gene-related peptide, was studied in the prevention of migraine headache in two different Phase 2 trials (ART-01 and CGAB). The results of the two studies are described.

Results
(1) For Study ART-01, patients were randomized to LY2951742 (N=107) or placebo (N=110). LY2951742 showed greater reduction in the mean change from baseline in the number of MHD at Month 3 (-4.2 vs. -3.0 days for LY2951742 vs. placebo, respectively, p=0.003). LY2951742 was also superior to placebo at Month 3, for MHD + pMHD, (-4.8 vs. -3.5 days, p=0.010), migraine attacks, (-3.1 vs. -2.3 attacks, p=0.005), and 50% response rate, (75% vs. 49% responders, p=0.0002), respectively. Treatment emergent adverse events seen more frequently with LY2951742 than placebo included injection site pain, upper respiratory tract infections, and abdominal pain.

(2) For Study CGAB, patients were randomized to LY2951742 (N=273) or placebo (N=137). Compared with placebo, LY2951742 120 mg showed greater reduction in mean change from baseline in the number of MHD at Month 3 (-4.9 vs. -3.6 days for LY2951742 vs. placebo, p=0.004). LY2951742 120 mg was also superior to placebo at Month 3 for MHD + pMHD, (-5.9 vs. -4.0 days, p<0.001), migraine attacks, (-3.5 vs. -2.7 attacks, p<0.003), and 50% response rate, (77% vs. 61% responders p=0.036), respectively. Treatment emergent adverse events that occurred more frequently with LY2951742 than with placebo included injection site pain, upper respiratory tract infections, nasopharyngitis, dysmenorrhoea, and nausea.
Conclusion

(1) In study ART01, LY2951742, 150 mg (biweekly), at Month 3, significantly decreased the number of MHD, MHD+pMHD, and migraine attacks, and was superior for 50% responder rate compared to placebo in subjects with migraine headaches.  

(2) In study CGAB, LY2951742, 120 mg (monthly), at Month 3, significantly decreased the number of MHD, MHD+pMHD, and migraine attacks, and was superior for 50% responder rate compared to placebo in subjects with migraine headaches. These results provide evidence that LY2951742 is efficacious in the prevention of migraine at the doses described. LY2951742 is safe and well tolerated.
Title: The Effectiveness Of Botox 200 Units In The Management Of Cervicogenic Headache

Poster Number PTH159

Authors
Z. Elchami, A. Mohamadin, A. Mirambel, S. delos Santos, A. Villamar

International Medical Center, Jeddah, Saudi Arabia, International Medical Center, Jeddah, -- SELECT --

Aim of Investigation
Since cervicogenic headache is commonly known as head pain that is referred from the bony structures or soft tissues of the neck, for this, treatment must be aimed at the problem in the neck. The aim of this study is to evaluate the effectiveness of Botox 200 units in the management of cervicogenic headache.

Results
An average improvement of 80% was seen in patients who were treated with Botox 200 units.

Conclusion
Significant improvement was appreciated in patients who received Botox injection 200 units for cervicogenic headache management.
Title: Musculoskeletal Dysfunctions In Patients With Episodic And Chronic Migraine: Diagnostic Study Validating An International Consensus Cluster Of Physical Examination Tests

Poster Number PTH160

Authors
K. Luedtke, W. Starke, T. Schoettker-Koeniger, A. May

University Medical Center Hamburg-Eppendorf, Hamburg, Germany, Hochschule für angewandte Wissenschaft und Kunst Hildesheim / Holzminden / Göttingen, Hildesheim, Germany

Aim of Investigation
The contribution of musculoskeletal dysfunction to migraine is not fully understood. Previous research evaluated selected musculoskeletal dysfunctions in migraine patients but methodological shortcomings did not allow for general conclusions. The objectives of this study were to a) test the feasibility and time required for the application of a cluster of tests recently identified as the minimum standard of physical examination tests for headache patients; b) evaluate the differences in musculoskeletal dysfunctions between migraine patients and healthy controls using the same international consensus cluster of physical examination tests.

Results
Ten out of 11 tests (with the exception of head forward posture) showed a statistically significant difference between migraine patients and controls. Post hoc tests indicated that these differences did not distinguish between episodic and chronic migraine. However, correlation analyses showed that test results were closely correlated with the number of headache days per month. The analysis of the number of tests considered positive by the physiotherapist showed a mean number of 4.8 positive tests in the migraine group compared to a mean number of 2.1 positive tests in the control group. This difference was statistically significant at p<0.001. The specificity of positive tests ranged between 0.80 to 0.90 while the sensitivity ranged between 0.32 and 0.70.

Conclusion
The recently published cluster of tests identified in an international consensus group is feasible for headache patients and takes approximately 30 minutes to conduct. 10 tests clearly distinguished between migraine patients and healthy control participants. A difference between episodic and chronic migraine patients was not identified in the current study population probably due to the high frequency
of headache days in the episodic migraine group. Migraine patients showed approximately twice as many positive tests as headache-free control participants when evaluated for cervical musculoskeletal dysfunctions.
Title: Functional Connections Between Rodent Meningeal And Nasal Nociceptors: Role In Headache Generation And Therapy?

Poster Number PTH161

Authors

Institute of Physiology and Pathophysiology, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany, International School for Advanced Studies - SISSA, Trieste, Italy, Department of Neurology, Keio University School of Medicine, Tokyo, Japan, Center for Animal Research and Education, Nagoya University, Nagoya, Japan

Aim of Investigation
Recent anatomical and functional data indicate nociceptive interactions between meningeal and extracranial structures such as the temporal muscle and neck muscles, which may result from collaterals of meningeal afferent fibers innervating both structures or from convergent afferent input to second order neurons in the trigeminal brainstem. Therefore a role for extracranial tissues in the generation of headaches is debated. Experiments were made to explore if similar interactions exist between nociceptive processes in the nasal cavity and meningeal nociception of the anterior cranial fossa.

Results
Anterograde tracing of the nasociliary nerve revealed dense networks of stained nerve fibers in the nasal mucosa and the dura mater of the anterior cranial fossa. Receptive fields of single Aδ and C fibers responding to mechanical and electrical stimuli were identified in the dura mater and along the dorsal half of the nasal cavity but the recordings did not indicate fibers with collaterals innervating both compartments. Stimulation of the nasal cavity with capsaicin but not vehicle increased CGRP release from the dura mater in vitro and meningeal blood flow in the anterior cranial fossa in vivo. The flow increase was diminished although not abolished by systemic application of the ganglion blocker hexamethonium. The pERK concentration and the number of pERK immunoreactive neurons in the trigeminal ganglion were increased after nasal capsaicin application compared to vehicle.

Conclusion
Meningeal afferents innervating the nasal cavity pass partly through the dura mater of the anterior cranial fossa. Noxious stimulation of nasal nociceptors activates trigeminal neurons and induces
intracranial nociceptive events such as neuropeptide release that increases meningeal blood flow. These effects are aggravated by an autonomic reflex. The nasal-meningeal interactions may explain how meningeal nociception and headache may be manipulated by intranasal application of substances.
Title: Clinical Association Between Brain MRI Findings With Epidural Blood Patch In Spontaneous Intracranial Hypotension

Poster Number PTH162

Authors
J. Choi, K. Kang, Y. Yoo, J. Moon, Y. Kim, S. Lee

Seoul National University Hospital, Seoul, Korea, Seoul National University Hospital., Seoul, Korea, Department of Anesthesiology and Pain Medicine, Seoul National University School of Medicine, Seoul, Korea, Seoul National University, Seoul, Korea

Aim of Investigation
Spontaneous intracranial hypotension (SIH) is characterized by spontaneous postural headache with neck stiffness, nausea, vomiting, tinnitus, and vertigo in patients with low cerebrospinal fluid pressure. Epidural blood patch (EBP) can be a treatment of choice in patients non-responsive to the initial noninvasive treatments. We compared brain magnetic resonance imaging (MRI) findings and clinical variables between patients with conservative management only and patients with added EBP, in order to help physicians plan the management modalities for SIH patients. In addition, clinical factors associated with MRI abnormalities in SIH, and the response to EBP between elderly and young patients were assessed.

Results
The incidence of abnormalities of brain MRI findings did not show significant differences between conservative treatment and EBP. However, the proportion of patients with severe pain was higher in patients who underwent EBP. In multivariate regression analysis, the incidence of positive brain MRI finding(s) for SIH increased in patients with older age, higher weight, and an absence in nausea/vomiting. EBP procedure was effective in both younger and elderly patients.

Conclusions
The results of our study indicated no difference between MRI findings in both conservative treatment and EBP modalities; however, there were differences in initial pain score. Therefore, clinical presentation of SIH patients may be critical and help physicians make a decision of EBP procedure.
Title: Somatosensory Cortex Hyperexcitability Is Associated With Headache Chronification In Tension-Type Headache: An Meg Study

Poster Number PTH163

Authors
W. Chen, F. Hsiao, S. Wang
Taipei Veterans General Hospital, Taipei, Taiwan, National Yang-Ming University, Taipei, Taiwan

Aim of Investigation
Tension-type headache (TTH) is the most common headache disorder. Although TTH is mild to moderate in severity, it may be disabling if the headache evolves from episodic TTH to chronic TTH, defined by 15 or more headache days per month. This study aims to elucidate the mechanism underpinning chronification of TTH.

Results
In response to paired-pulse stimulations, cSI activation was stronger in chronic TTH than in controls (first stimulation, 89.9±10.6 vs. 55.2±5.4; second, 80.5±9.8 vs. 43.4±4.1 pAm; both p < 0.05). The gating ratio of cSI activation (amplitude to the second vs. first stimulation) was higher in chronic TTH (0.93±0.04) and in episodic TTH (0.98±0.06) than in controls (0.76±0.03, p = 0.005 and 0.040, respectively). Patients with chronic and episodic TTH also showed increased resting-state spontaneous activities at specific frequency bands in all the somatosensory areas. In all TTH patients, headache frequency was positively correlated with cSI amplitudes (first: r=0.359, p=0.027; second: r=0.387, p=0.016). and inversely correlated cSII resting-state delta and theta spectral powers (delta: r=-0.391, p=0.032; theta: r=-0.383, p=0.037). Pressure pain thresholds did not differ between groups or correlate with headache parameters.

Conclusion
TTH is characterized by resting-state hyperactivation and disinhibition in cSI. TTH chronification is associated with cSI hyperexcitability and reduced cSII spontaneous activities at delta and theta bands.
Title: Long-Term Outcomes Of Neural Targeting Spinal Cord Stimulation: Final Results Of The Lumina Clinical Study

Poster Number PTH164

Authors

University Hospitals - Case Western Reserve University, Cleveland, OH, Carolinas Pain Institute, Winston-Salem, NC, Roanoke Chowan Hospital Pain Center, Ahoskie, NC, Comprehensive Pain & Rehabilitation, Pasagoula, MS, Jupiter Interventional Pain, Jupiter, FL, Pacific Pain Management, Ventura, CA, Florida Spine Specialists, Fort Lauderdale, FL, Spine Team Texas, Rockwall, TX, Interventional Pain Specialists of Wisconsin, Rice Lake, WI, Comprehensive Pain Clinic, Utica, NY, Balcones Pain Consultants, Austin, TX, Spine and Pain Institute, Kent, OH, Boston Scientific Corporation, Valencia, CA

Aim of Investigation
The effectiveness of spinal cord stimulation (SCS) is dependent by highly variable anatomically-related geometric parameters, such as vertebral level of lead placement, mediolateral lead placement and electrode spacing. The vertebral level where the lead is placed dictates the dermatomes that may be covered by the stimulation, and the varying thickness of the dorsal cerebral-spinal fluid along the axis of the spine further complicates the stimulation effect. A recently introduced Spinal Cord Stimulation (SCS) paradigm uses a 3-dimensional, anatomically-guided algorithm to customize stimulation to produce a desired stimulation field with robust specificity in which these parameters are optimized to the level of each individual (Neural Targeting SCS). We hypothesized that this new SCS modality would be able to generate highly effective pain relief in historically challenging pain areas, including low-back pain. We undertook a large multicenter observational study (LUMINA) to characterize the real-world clinical outcomes of Neural Targeting SCS in the treatment of chronic pain, including both leg pain, leg and back pain, and predominant back pain.

Results
The mean overall pain reduction in all subjects and a subset of subjects classified as 'severe' (NRS >8.0) decreased 4.2 and 5.3 points from baseline (7.17 and 8.75), respectively. All subjects (and 'severe' subset) reporting only low back pain displayed a decrease in mean low back pain of 4.1 and 5.6 points from baseline (7.21 and 8.60), respectively. Responder rates (RR) were greater than 70% for overall and
low back pain. Compared to a previous generation SCS system, statistically significant increases in response rates were observed using Neural Targeting SCS at 24 months post-implant (Overall Pain RR: 51% [previous generation] vs. 74% [neural targeting SCS]; Leg Pain RR: 63% [previous generation] vs. 81% [neural targeting SCS]; Back Pain RR: 41% [previous generation] vs. 71% [neural targeting SCS]).

Conclusion

This large observational study displayed long-term highly effective real-world overall and low-back pain relief out to 2 years using Neural Targeting SCS.
Title: Predictors Of Daily Pain Medication Use In Chronic Back Pain

Poster Number PTH165

Authors

Stanford University, Palo Alto, CA

Aim of Investigation
Although there is disagreement about the long-term benefit of pain medication as a primary pain coping strategy, evidence nevertheless suggests that many individuals with chronic pain rely on medications to manage pain or as a means of bolstering their levels of physical activity. Psychological factors, such as mood disturbance, may also modulate the use of pain medications for individuals with chronic pain, but few studies have examined how these factors may relate to pain medication usage at the daily level.

Results
Modeled together, higher-than-average daily pain intensity (β = .035, p < .001) and poorer-than-average daily mood (β = -.015, p < .001) and sleep (β = -.179, p = .009) independently predicted an increased likelihood of using pain medication on a given day. Similarly, higher-than-average pain intensity (β = .026, p < .001) and poorer-than-average mood (β = -.009, p = .005) but not sleep (β = -.097, p = .13) predicted an increased likelihood of overusing pain medications on the same day. Daily physical activity levels were unrelated to pain medication use and overuse (p > .35 in both cases).

Conclusion
The current study is among the first to highlight both pain and mood disruption as salient predictors of daily pain medication use and overuse in individuals with back pain. Future studies may expand these findings by exploring the role of other psychological factors (e.g., pain catastrophizing) at the daily level, as well as examining how these factors may affect use patterns in specific medication classes, such as opioid medications.
Title: Operative Management By Pedicular Screw Fixation Versus Conservative Management For Low-Back And Radicular Pain In Spondylolisthesis Grade-Ii And Grade-Iii

Poster Number PTH166

Authors
A. Das
Calcutta Medical Research Institute, Kolkata, India

Aim of Investigation
Patient with Grade-II and Grade-III spondylolisthesis often present with low back pain and radiculopathy, if not treated adequately may lead to chronic neuropathic pain. Very often patients are treated conservatively with multimodal analgesics, physiotherapy, but stabilization of spine is important for optimum pain relief. Aim of this study is to establish the operative management by pedicular fixation and stabilization of spine which offers better pain relief than conservative management methods.

Results
None of the patients in Group-I, at any time, had adequate pain relief VAS ≥5. They had sleep disturbances and depression. Radicular pain persisted in 16 patients for which the dose of gabapentine had to be increased. 22 patients had GI disturbances and 12 patients had drowsiness. In group-II patients had excellent pain relief VAS <2 in 16 patients at 2 weeks. 24 patients were free of radicular pain at 6 weeks, good pain relief VAS ≤4. In 6 patients mild radicular pain persisted at 6 months. There was no deformity in all patients. No neurological deficit found at 6 months.

Conclusion
To conclude conservative treatment offers temporary pain relief. Stabilization of spine by pedicular screw and rod in Grade-II and Grade-III spondylolisthesis yields better pain relief and functional outcome.
Title: Real-World Disability And Productivity Outcomes Following Spinal Cord Stimulation

Poster Number PTH167

Authors
R. Frey, R. Jutla, N. Mekel-Bobrov

Pacific Pain Management, Ventura, CA, Mind Your Body Institute, Seattle, WA, Boston Scientific Corporation, Valencia, CA

Aim of Investigation
Successful spinal cord stimulation (SCS) therapy in patients with chronic pain may not only improve pain intensity but may also reduce disability and increase activities of daily living (ADL). A recently introduced SCS paradigm using a 3-dimensional algorithm to customize stimulation (Neural Targeting SCS) has enabled SCS treatment of pain areas which have historically been challenging, such as low-back pain. This has potentially opened up new possibilities for functional improvement in patients suffering from predominant back pain. We undertook a large observational study to characterize real world disability and functional outcomes using Neural Targeting SCS out to 2 years post implant.

Results
To date, significant reductions in Oswestry Disability Index (ODI) scores and Numeric Rating Scale (NRS) scores, with increases in walking tolerance and an approximately 90% satisfaction rate, have been observed. Relative to baseline, these reductions include a 21.3 point decrease in mean ODI score, a 51% increase in mean walking time, and a 3.3 point drop in mean NRS score.

Conclusion
In subjects with moderate or severe low back and/or leg pain, Neural Targeting SCS provided reduced disability (as measured by ODI and walking tolerance), reduced pain intensity (as measured by NRS), and produced generally high satisfaction rates.
Title: Examining Correlates Of Low Back Pain In Singapore: A Retrospective Cohort Study

Poster Number PTH168

Authors
J. CHEMAT, S. Yang, F. Loy, S. Tjan

TAN TOCK SENG HOSPITAL, SINGAPORE, Singapore, Tan Tock Seng Hospital, Singapore, SINGAPORE, Tan Tock Seng Hospital, Singapore, Singapore

Aim of Investigation
Aspects of physical functioning and quality of life are known to be affected in patients with low back pain. However, there is little known about this relationship in low back pain patients in South-east Asia, including Singapore. This study was conducted to examine the (1) correlates of low back pain and (2) the impact of pain interference on physical functioning and quality of life in a sample of newly referred low back pain patients.

Results
A total of 257 participated in this study. Out of these, 47.3% were referred from the primary care and 52.3% from other healthcare settings. Patients had a mean age of 49.5 (SD = 16.9) years, 11.2 (SD = 2.9) years of education, with a mean pain score of 3.5 (SD=1.5). Primary care referrals had significantly lower pain scores (t=-2.06, p=0.04) than patients referred from other sources. Higher pain interference was moderately related to disability (r=0.72), physical functioning (r=-0.67), mental functioning (r=-0.63) and pain intensity (r=0.61). All significant at p<0.001. Higher pain interference correlated weakly with number of different specialist clinics visited, number of specialist clinic consults and number of rehab physician consults (r=0.17-0.21, p<0.01). In multiple regression analyses, after controlling for relevant demographic variables and pain intensity, pain interference explained 46.5 % of the variance of disability, 32.5% of the variance of mental quality of life and 42.6% variance of physical quality of life.

Conclusion
Physical functioning and quality of life were significantly affected in patients with low back pain. Pain interference significantly predicted physical function and quality of life. Managing pain interference rather than pain intensity itself appears more important in the subsequent management of patients with low back pain. One of the main limitations of this study is that only first visit patients' data were
analysed. A study analysing data from patients with follow-up appointments at the pain clinic may yield different results.
Title: Gray Matter Alteration Associated With Pain Catastrophizing In Patients Six Months After Lumbar Disc Surgery: A Voxel-Based Morphometry Study

Poster Number PTH170

Authors
O. Chehadi, T. Schmidt-Wilcke, O. Köster, B. Suchan, M. Hasenbring

Department of Medical Psychology, Ruhr Universität Bochum, Bochum, Germany, Department of Neurology, Universitätsklinikum Bergmannsheil, Ruhr Universität Bochum, Bochum, Germany, Dept. of Radiology, St. Josep Hospital, University Hospital of Bochum, Germany, Bochum, Germany, Department of Neuropsychology, Ruhr Universität Bochum, Bochum, Germany

Aim of Investigation
Patients suffering from chronic low back pain are more likely to display higher levels of disability and maladaptive coping strategies like pain catastrophizing compared with healthy individuals. Pain catastrophizing is defined as 'an exaggerated negative mental set brought to bear during actual or anticipated painful experience.' [1]. Recent evidence shows that chronic pain can lead to functional and structural alterations in the circuitry underlying the cognitive control of pain. The relation between structural brain alterations in these regions and pain catastrophizing as one type of dysfunctional cognitive control of pain is unclear.

Results
In a whole-brain analysis, pain catastrophizing was significantly negatively correlated with grey matter volume (GMV) in two clusters: a large cluster that included parts of the left cuneus, left precuneus and posterior cingulate and a smaller cluster in the right fusiform gyrus. This regions are known to play a role in conscious experience [2] and emotion processing [3]. Additionally, we found a positive correlation between pain catastrophizing and regional GMV in the right medial frontal gyrus, known to play a role emotion processing [3].

Conclusion
This study provides evidence for pain catastrophizing-related structural alteration. Our results are consistent with previous research and may provide potential insights into the neural substrates of obstructive emotion regulation in chronic low back pain, with a special emphasis on pain-related catastrophizing.

References


Title: Levels Of Physical Activity And Sedentary Behaviour Among Patients With Degenerative Disc Disease Who Are To Undergo Spinal Fusion Surgery

Poster Number PTH171

Authors
M. Lundberg, H. Lotzke, M. Jakobsson, H. Brisby, A. Gutke, M. Hagströmer, O. Hägg, R. Smeets

Department of Neurobiology, Care Sciences and Society (NVS), Karolinska Institutet, Huddinge, Sweden, Department of Orthopaedics, Sahlgrenska Academy, University of Gothenburg; Spine Center, Gothenburg, Sweden, Department of Orthopaedics, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, Department of Orthopaedics, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, -- SELECT --, Department of Health and Rehabilitation, University of Gothenburg, Gothenburg, Sweden, Spine Center, Gothenburg, Västra Frölunda, Sweden, Department of Rehabilitation Medicine, CAPHRI, Maastricht University, Maastricht, Netherlands

Aim of Investigation
The number of patients undergoing lumbar fusion surgery for degenerative disc disease (DDD) has increased worldwide. People who are to undergo spinal surgery are assumed to be less physically active than individuals without pain. Physical activity is of essence, both to avoid the negative health consequences of insufficient physical activity and to promote the analgesic effect from physical activity. Little is known about physical activity and sedentary behaviour among patients with DDD. The aim of the study was to describe levels of physical activity and sedentary behaviour among patients with DDD who are to undergo lumbar fusion surgery.

Results
On average the patients walked 7 535 (95% confidence interval, CI: 6863-8207) steps per day, equivalent to the recommendation for health set to 7000 steps/day. On average the patients spent 189 (95% CI: 157- 215) minutes on moderate-intensity physical activity level and 6 (95% CI: 2-10) minutes on vigorous-intensity physical activity level per week. Twenty-eight patients (42%) were physically active for less than 150 minutes of moderate-intensity physical activity per week, and 48 patients (73%) did not spend any time in vigorous-physical activity at all. Patients averaged 542 (95% CI: 518, 566) minutes of sedentary behaviour per day.
**Conclusion**

Nearly half of the study population did not reach the WHO’s recommendation for moderate-intensity physical activity per week. These patients might, therefore, have an increased risk of developing negative health conditions such as cardiovascular disease, obesity, cancer and diabetes. Furthermore, two third of the patients did not spend any time in vigorous-intensity physical activity which might reduce the analgesic effect on pain. These aspects must be considered when designing protocols for prehabilitation and rehabilitation for this patient group.
**Title:** Patient’s Beliefs About The Meaning Of Their Chronic Low-Back Pain And Its Relationship With Explanations Provided By Health Professionals In Primary Care: A Qualitative Study In Spain

**Poster Number** PTH172

**Authors**
F. Valenzuela Pascual, E. Briones Vozmediano, F. Molina Luque, J. Blanco Blanco, F. Rubí Carnacea, C. Climent Sanz, J. Soler González

University of Lleida, Lleida, Spain

**Aim of Investigation**
To identify the beliefs of chronic low back pain (CLBP) patients concerning the origin and meaning of their pain, and to explore how these beliefs may be influenced by the knowledge and explanations provided by health professionals in primary care.

**Results**
From the analysis of the data 4 categories were identified: 1) Beliefs about the origin and meaning of CLBP; 2) Expectations about the treatments to reduce the pain 3) Poor communication between health professionals and patients with CLBP; and 4) Perceived need for improving the knowledge of both patients and health professionals on CLBP. Describing our qualitative findings in these categories allows us to explain how patients and health professionals share the perception that CLBP is caused by tissue damage or structural alteration in their lower back. Both groups explained the need to find a biomedical cause that justifies the pain and will help to guide the treatment. The poor communication between health professionals and patients has important functional and emotional consequences for these CLBP patients. Our data further suggests that patients’ inaccurate beliefs about their CLBP are substantially influenced by the lack of knowledge of health professionals.

**Conclusion**
Our findings show that both patients and health professionals in our study demonstrated the need to know and understand the origin and meaning of CLBP. Furthermore, the expectations for treatment of both patients and health professionals were influenced by the meaning that patients and health professionals confer to the pain. We suggest that it is necessary to modify patients’ and health professionals’ beliefs about pain as a starting point for any type of treatment. One possible solution would be to construct and develop a biopsychosocial web-based educational intervention, teaching the
neurophysiology of pain to modify patients and health professionals' inaccurate beliefs about the origin and meaning of CLBP. Future research could explore web-based approaches for chronic pain management programs in primary care, and the acceptability of these interventions for unique cultural groups like patients and health professionals in Spain.
Title: Effects Of Pregabalin Treatment On Falls In Patients With Chronic Low-Back Pain

Poster Number PTH173

Authors
S. Caglar Okur, M. Vural, Y. Pekin Doğan, M. Mert, N. Sayiner Caglar

Istanbul Training and Research Hospital, Istanbul, Turkey, Bakirköy Sadi Konuk Training and Research Hospital, Istanbul, Turkey, Istanbul Training and Research Hospital, Istanbul, Turkey, Yeni Yüzyıl University Gaziosmanpasa Hospital Orthopaedics Department, Istanbul, Turkey

Aim of Investigation
Chronic low back pain (CLBP) is one of the most common health problems of industrialized countries. CLBP can be considered a mix of three pain components depending on the presentation: nociceptive, neuropathic origin, or augmented central pain processing. Pregabalin is one of the most recommended medications for neuropathic pain. Dizziness, vertigo, confusion, edema, weight gain are most frequent side effects of pregabalin. The aim of our study is to investigate the effect of pregabalin treatment on fall risk and gate balance in patients with CLBP and having neuropathic pain component.

Results
The two groups demographic data and clinical characteristics were similar at baseline (p>0.05). TFES and TGA were statistically significantly lower at group 1 for all assessment weeks except for TFES baseline value. There was a significant change at TFES and TGA scores of group 1 (p<0.001 for both). Statistically significant decrease at TFES and TGA scores were revealed from beginning to 4th week, also significant increase were revealed between 4th and 12th weeks (p<0.001). But TFES and TGA scores were significantly lower at 12th week in comparison with beginning (p<0.001). DN4 scores at 4th and 12th weeks were significantly lower at group 1 compared to group 2 even though there were not significant difference between groups at the beginning (p<0.001).

Conclusion
Pregabalin has proven to be effective in the treatment of neuropathic pain. But one of the main problems while using pregabalin is adverse events like dizziness and imbalance causing falls. In this trial we have found that pregabalin treatment is increasing fall risk as dose dependently at the first 4 weeks. We want to emphasize to be more careful about fall risk and to take preventive measures in particularly elderly patients while using pregabalin treatment.
**Aim of Investigation**

Toll-like receptor 4 (TLR4) is a key activator of inflammatory responses. Limited human work supports possible relevance of TLR4 activity to chronic pain status. Opioid analgesic medications used in chronic pain management are known to activate TLR4, and TLR4 activity may in turn alter responses to opioid analgesics. This study tested for associations between chronic pain intensity and TLR4 activation by a known TLR4 agonist, and evaluated whether endogenous opioids, which are also known to influence opioid analgesic responses, elicit TLR4 activity in a manner comparable to known TLR4 agonists.

**Results**

Release of IL-6, IL-8, and TNF-alpha elicited by LPS was not significantly different between the CLBP group and Healthy Controls (p's>.10). However, within the CLBP group, mean MPQ-Sensory back pain ratings were correlated positively and significantly with release of IL-6 (r = 0.63, p = 0.02) and IL-8 (r = 0.84, p<0.001) at the highest LPS concentration, with similar findings restricted to IL-8 release for VAS pain intensity (r = 0.67, p = 0.01) and unpleasantness (r = 0.60, p = 0.03). For the 15 samples targeting possible BE effects on TLR4, IL-6, IL-8, and TNF-alpha levels were found to decrease slightly even at the highest BE concentration. Relative to the Control Condition, LPS at the highest concentration elicited significantly larger increases in IL-6, IL-8, and TNF-alpha (indicating TLR4 activation) than did BE at the highest concentration (p's <.001).

**Conclusion**

Results suggest greater chronic back pain intensity may be linked in part to elevated TLR4-mediated inflammation among individuals not using opioid analgesics regularly. This is consistent with limited prior evidence suggesting links between elevated TLR4 activity and presence of diverse chronic pain conditions. BE, the most important endogenous opioid analgesic, did not elicit any TLR4 activity. This latter finding indicates that TLR4-related mechanisms are unlikely to contribute to previously reported
associations between elevated endogenous opioid activity and both lower chronic back pain intensity and reduced morphine responsiveness.
Date: 09/29/2016 03:15:00 PM

**Title:** Emotional Distress Leads To Repeated Healthcare Use For Low-Back Pain: An Observational Study

**Poster Number** PTH175

**Authors**
M. Huebscher, A. Traeger, N. Henschke, C. Williams, C. Maher, L. Moseley, H. Lee, J. McAuley

Neuroscience Research Australia, Sydney, Australia, Neuroscience Research Australia, Sydney, NSW, Institute of Public Health, University of Heidelberg, Heidelberg, Germany, Heidelberg, Germany, Hunter Medical Research Institute and School of Medicine and Public Health, University of Newcastle,, Callaghan NSW , Australia, The George Institute for Global Health, University of Sydney, NSW, Australia, Sydney, Australia, University of South Australia, Adelaide, Australia, Neuroscience Research Australia, REDFERN, NSW

**Aim of Investigation**
An important avenue to reducing the massive burden of non-specific low back pain is to reduce unnecessary health care use after an initial consultation. Unfortunately, the factors that cause people to seek additional healthcare are not known. Pain intensity and disability alone do not appear to account for future healthcare visits and other modifiable factors such as emotional distress may contribute. Our aim was to determine whether emotional distress reported at the initial consultation directly affects subsequent healthcare use or moderates the influence of symptoms over subsequent healthcare use.

**Results**
Participants had a mean (SD) of 1 (1.2) visit for low back pain over 3-months, and 9 (14) low back pain-related visits over 12-months. Higher reports of anxiety at the initial consultation led to increased short-term healthcare use (IRR 1.06, 95%CI 1.01 to 1.11) and higher reports of depression at the initial consultation led to increased long-term healthcare use (IRR 1.04, 95%CI 1.02 to 1.07). These effects were independent of pain intensity and disability. Neither anxiety nor depression moderated the influence of symptoms over subsequent healthcare use. Our findings suggest that a patient with a high anxiety score (8/10) would consult 50% more frequently over 3-months and a person with a high depression score (8/10) would consult 30% more frequently over 12-months than a patient with equivalent pain and disability but no reported anxiety or depression. In the samples included in this study, around 1 in 5 patients with acute low back pain reported anxiety scores higher than 8/10 and 1 in 10 reported depression scores higher than 8/10.
Conclusion
Emotional distress in the acute stage of low back pain increased subsequent consultation rates. Treatments targeted to individuals with high distress might lead to reductions in unnecessary health care use for low back pain.
Title: Predicting Placebo Response In Chronic Low-Back Pain Patients Using Personality Traits And Neuroimaging Biomarkers

Poster Number: PTH176

Authors
S. Berger, E. Vachon-Presseau, T. Abdullah, A. Baria, B. Petre, T. Schnitzer, A. Apkarian

Northwestern University, Chicago, IL, Northwestern University Feinberg School of Medicine, Chicago, IL, Northwestern University, Feinberg School of Medicine, Chicago, IL

Aim of Investigation
The placebo effect describes an improvement in symptoms caused by administering an inert treatment disguised as an active treatment. Most of the literature regarding placebo analgesia and its psychobiological parameters has been investigated in healthy participants in contexts involving acute pain, manipulations of expectation, and short treatment periods. Thus, the brain- and emotionally-based variables that influence placebo response in clinical populations remain unknown. Here we investigate the contribution of self-report measures, in combination with neuroimaging results, in predisposing individuals with chronic low back pain (CBP) to placebo response as part of a randomized double-blind clinical trial.

Results
The permutation test revealed that 24 people responded to at least 1 of the 2 treatment periods (nonresponders = 21). Factor analyses yielded 7 questionnaires that were initially entered into a full regression model; of these, 3 survived: Multidimensional Assessment of Interoceptive Awareness (MAIA, emotion and not-worry subscales) & Emotional Regulation Questionnaire (ERQ, suppression subscale). After entering neuroimaging results into the model, only MAIA emotion, ERQ suppression, and functional connectivity between frontal and sensorimotor networks were significant; the combination explained 48% of the variance & predicted response with 92% accuracy.

Conclusion
We show that placebo response in a clinical setting can be predicted using a combination of self-report and brain-based. We demonstrate that CBP patients showing response propensity have increased emotional awareness, decreased emotional suppression, and stronger functional connectivity between frontal and sensorimotor networks at baseline; this unique combination explains a large amount of the
variance dissociating responders from nonresponders. These results illustrate the importance of specific personality traits and imaging biomarkers for placebo response in CBP.
Aim of Investigation

Prognostic screening instruments have the potential to identify individuals at risk of persisting pain and disability and have shown promise in primary care. It is unclear however, whether prognostic screening in secondary care can add value above 'treat all' approaches to patient management. The aim of this study was to determine the ability of the Short-form Orebro Musculoskeletal Pain Screening Questionnaire (OMPSQ) to provide useful information about the prognosis of patients with low back pain in a secondary care setting. Specific objectives were to: 1. Investigate the performance of the OMPSQ in predicting 'poor outcome' at 4-month follow-up. 2. Describe the clinical value of screening with the OMPSQ.

Results

A total of 2439 referrals were screened for eligibility, and 612 patients fulfilled the inclusion criteria for initial telephone contact. 393 patients did not meet our inclusion criteria or were unable to be contacted and were excluded. Complete data were available for 81% of the 219 enrolled participants. Mean participant age was 49 (16) and 49% were female. 21% of participants reported pain for <3 months, 50% for 3-9 months and 29% for >9 months of episodic symptoms. 86% of participants (n=152) had the primary outcome ('poor outcome') at 4-month follow-up. The area under the receiver operating characteristic curve for the OMPSQ predicting poor outcome was 0.69 (95%CI 0.56-0.82). The model fit (Nagelkerke R2 =10%) indicated that the OMPSQ explained only a small amount of variation in poor outcome. Using the published cut-off score of 50 to classify patients as 'high risk', sensitivity was 72% and specificity was 40%. Our decision curve analysis indicated that there was no net benefit of screening patients if their predicted probability of having a poor outcome was less than 60%, and only a small net benefit for patients with predicted probabilities above this threshold. In order to produce a
net benefit from screening, cutoff scores would need to be much higher than 50 and may lead to many patients who had poor outcomes being denied intervention.

Conclusion
The OMPSQ performed poorly when predicting poor outcome at 4-month follow-up in a spinal secondary care setting. Prognostic screening in this setting is unlikely to provide any net benefit over and above treating all patients.
Title: Relationship Between Anterior Cingulate Cortex And Chronic Low-Back Pain: Measurement Of Metabolite Concentration Using Magnetic Resonance Spectroscopy

Poster Number PTH178

Authors

Dept. of Orthopaedic Surgery, School of Medicine, Fukushima Medical Univ., Fukushima, Japan, Dept. of Anesthesiology, Interdisciplinary Pain Management Ctr., Shiga Univ. of Med. Sci. Hosp., Otsu, Japan, Dept. of Anesthesiology, Shiga Univ. of Med. Sci. Hosp., Otsu, Japan, Dept. of Social Medicine, Medical Statistics, Shiga Univ. of Med. Sci. Hosp., Otsu, Japan

Aim of Investigation
Magnetic resonance spectroscopy (MRS) is a non-invasive analytical technique to measure the metabolic substances in brain. Recently, relationship between anterior cingulate cortex (ACC) and chronic pain has been reported. The purpose of this study was to analyze the influence of chronic low back pain (cLBP) to metabolic substance in ACC using MRS.

Results
The concentrations of N-acetyl aspartic acid (NAA) and glutamate + glutamine (Glu + Gln) were 8.795 ± 0.880 mmol/l and 1.909 ± 0.249 mmol/l. Less amount of NAA were measured in cLBP patients compared with normal subjects while controlling sex and age (partial regression coefficient B = -0.675, p < 0.001). Meanwhile, larger amount of Glu + Gln were calculated in cLBP patients (B = 0.152, p =0.004). There was a positive correlation between Glu + Gln concentration and depression score of HADS.

Conclusion
In this study, we detected the change of NAA and Glu + Gln concentration in ACC of cLBP patients. There is the possibility that these result reflects the decrease of normal neural activity and increase of glutamate from astrocyte in ACC. Furthermore, it is suggested there is a relationship between Glu + Gln and depression. These metabolic modulation in ACC might be associated with cLBP mechanisms. Further study is needed to reveal this relationship.
Title: The Role Of Invalidation In Pain, Depression, And Disability Among Individuals With Chronic Low-Back Pain

Poster Number PTH179

Authors

University of Alabama, Tuscaloosa, AL, University of Alabama, Falkville, AL, University of North Texas, Denton, United States, University of Alabama, Birmingham, United States

Aim of Investigation
Chronic Low Back Pain (CLBP) is a pervasive health issue affecting millions of people worldwide. Due to the frequent lack of identifiable organic pathology, many individuals with CLBP may experience disbelief, lack of support, and stigmatization by others regarding their condition. The aim of this study was to examine whether invalidation, as measured by the Illness Invalidation Inventory (3*I), was predictive of pain severity, disability, and depression in a community-dwelling sample of adults with CLBP.

Results
Significant bivariate associations were observed between the family members and medical professionals 'discounting' indices and all outcome variables (r's = .19 – .34, p's <.05) and between family members 'lack of understanding' index and participant disability (RMDQ and PDI) and depression (PHQ-9; r's = .23, p's < .05). In terms of work environment, significant associations emerged between the 'discounting' index and participant disability (RMDQ) and depression (PHQ-9; r's = .22, p's < .05), as well as between the 'lack of understanding' index and participant disability (RMDQ and PDI) and depression (PHQ-9; r's = .25 - .33, p's < .01). Regression analyses indicated that increased perceptions of discounting by family members and medical professionals each uniquely predicted increased pain severity (MPQ), disability (RMDQ and PDI), and depression (PHQ-9). Additionally, perceived lack of understanding and discounting in the work environment uniquely predicted increased pain severity (MPQ), disability (RMDQ), and depression (PHQ-9).

Conclusion
In line with previous research, our findings suggest that individuals with CLBP experience invalidation from multiple sources, and these perceptions of invalidation are associated with increased pain severity, depression, and disability. Further, specific dimensions of invalidation may be particularly relevant in
certain contexts. Collectively, findings point to the need for more consideration of evidence-based interventions to address invalidation from specific sources with the aim of improving the psychological and physical wellbeing of individuals with CLBP.
Title: Validating Invalidation: Construct Validity Of The Illness Invalidation Inventory Among Individuals With Chronic Low-Back Pain

Poster Number PTH180

Authors

University of Alabama, Tuscaloosa, United States, University of North Texas, Denton, United States, University of Alabama, Birmingham, United States

Aim of Investigation
The Illness Invalidation Inventory (3*I) was designed to assess individuals' perceived invalidation regarding chronic pain experiences. Although the original measure focuses on multiple sources of invalidation (spouse, family members, work colleagues, medical professionals, and social services), previous psychometric literature has focused on invalidation by family members and has supported the existence of two subscales referred to as 'lack of understanding' and 'discounting'. However, previous studies have only examined the psychometric validity of the 3*I among participant samples comprising heterogeneous pain conditions. No extant study has investigated the psychometric properties of the 3*I specifically among individuals with Chronic Low Back Pain (CLBP). Given the personal and societal impact (e.g., direct medical treatment costs and lost productivity) of CLBP worldwide, the lack of apparent organic pathology, and potential invalidation associated with this condition, the current study sought to examine the psychometric properties of the 3*I in a sample of individuals with CLBP.

Results
Exploratory factor analysis conducted on the 3*I family members subscale found two factors with high internal consistency (α > 0.7) that accounted for a cumulative 49.04% of the variance in scores. Consistent with previous findings, factor loadings suggest that these factors correspond to 'discounting' and 'lack of understanding'. Subsequent confirmatory factor analysis found that this two-factor model demonstrated good fit with the data, $\chi^2 (df = 19) = 25.96$, $p = .13$, CFA = .95, RMSEA = .05, TLI = .93, BIC = 109.22. Overall, the results of the current study are consistent with that of previous research (Kool et al., 2010, 2014) in terms of identifying a two-factor model of illness invalidation within the family members subscale of the 3*I.
**Conclusion**

The current study was the first to examine the psychometric properties of a key subscale (family members) within the 3*I among a sample of individuals with CLBP. This is likewise the first such study to be conducted with an American sample. The identified two-factor model reflects previous findings and further extends the psychometric validity of the 3*I across international samples and specific pain populations. Implications for future research regarding invalidation specific to CLBP are discussed.
Title: Conditioned Pain Modulation Is Reduced In Chronic Achilles Tendinopathy, But Left/Right Discrimination Remains Intact

Poster Number PTH181

Authors
M. Coppieters, N. Tompra, J. van Dieen

Vrije Universiteit Amsterdam, Amsterdam, Netherlands, The University of Queensland, Brisbane, Australia

Aim of Investigation
(1) To investigate the presence of altered central pain processing in persistent Achilles tendinopathy by assessing the conditioned pain modulation (CPM) effect in people with and without Achilles tendinopathy, and (2) to examine whether people with unilateral persistent Achilles tendinopathy present with impaired left/right discrimination.

Results
An increase in pressure pain threshold was observed in both the Achilles tendinopathy and control group during the cold pressor test (p<0.001). However, the CPM effect was stronger in the control group (mean difference=160.5kPa, SD=84.9kPa) compared to the Achilles tendinopathy group (mean difference=36.4kPa, SD=68.1kPa) (p<0.001). The deterioration in left/right discrimination at group level, if present, between affected and unaffected side, or compared to healthy participants, was negligible for accuracy (<1.5%) and recognition time (<50ms). There was no significant effect of side of pain (affected versus unaffected) or group (people with Achilles tendinopathy versus healthy) for accuracy (p>0.36) or recognition time (p>0.69).

Conclusion
The first part of this study revealed a reduced CPM effect in people with Achilles tendinopathy compared to people without Achilles tendinopathy. A reduced CPM effect reflects altered central pain processing, which is believed to contribute to the persistence of pain in other conditions. Altered central pain processing may also be an important factor in persistent tendon pain, which has traditionally been regarded to be dominated by peripheral mechanisms. The second part of this study showed that people with Achilles tendinopathy recognised the affected side as accurately and as fast as the non-affected side and their performance was comparable to healthy participants. The absence of impaired left/right
discrimination despite the chronicity of pain may be attributable to the typical intermittent nature of Achilles tendinopathy pain and/or maintained sports activity.
Title: Musculoskeletal Pain Awareness Of Health University Students

Poster Number PTH182

Authors
H. YUCEL
Bezmialem Vakif University Faculty of Health Sciences Department of Ergotherapy, Istanbul, Turkey

Aim of Investigation
Since university students are mostly in a static sitting position during the day, they are one of the groups who needs to be considered about musculoskeletal problems. The aim of this study was to present the awareness of musculoskeletal pain of the students.

Results
Four hundred and seventy one (90.57%) students had pain in any parts of their bodies. The incidence of pain according to body diagram; back pain in 471 students (90.57%), shoulder pain in 129 students (24.8%), leg pain in 91 students (17.5%), arm pain in 40 students (7.69%), neck pain in 35 students (6.73%), and anterior upper trunk pain in 18 students (3.46%). Four hundred and six (86.19%) students stated that they knew the initial cause of pain. These reasons, in order of frequency, were prolonged sitting bending body forward during lessons (254 students, 53.92%), heavy lifting and carrying (184 students, 39.06%), stay on the computer for a long time (103 students, 21.86%), standing (46 students, 9.76%), doing sport (31 students, 6.58%), watching TV (10 students, 2.12%). Besides pain, 63 students (13.37%) had mobility limitations, 54 students (11.46%) had hassle of getting out of bed, 37 students (7.85%) had difficulty in walking. To reduce pain, most students said that they prefer to rest (354 persons, 75.15%), and respectively, to use relaxant drugs and pain killer they found at home (85 persons, 18.04%), to apply traditional methods such as hot compresses and herbal products (58 persons, 12.31%), and to be seen by family physicians (4 persons, 0.84%).

Conclusion
It was remarkable that most students have pain and they behave symptomatic instead of expert resolving of the pain. Approaches should be considered to counteract the pain and students should be educated about what they could do as a reliever. Ergonomic solutions should be considered for students.
Aim of Investigation
A common feature in musculoskeletal pain is the recurrence of pain after the initial painful episode even after complete tissue healing. This may suggest that the nociceptive system undergoes changes following the tissue insult which do not return to normal. This study aimed to investigate whether individuals who have recovered from a recent musculoskeletal injury demonstrate signs of hypersensitivity of the pain system.

Results
The pain intensity and associated duration did not differ between legs or groups. The saline-induced pain evoked more frequent reports of referred pain, remote from the injection, in the foot region on the injured leg as compared to the non-injured leg and the control leg (P<0.05). The same applied when comparing the control leg with the non-injured leg (P<0.05). The group with a previous history of injury demonstrated an increased TSP-index compared with the control group (P<0.05).

Conclusion
The higher frequency of referred pain reported in the area of previous injury suggests that the nociceptive system remains altered and sensitized, particularly in neuroanatomical systems also excited by the initial tissue injury. Evidence of facilitated temporal summation of pain also existed when assessed remote from the original site injury, supporting a more general sensitization. Thus, increased sensitivity combined with a more general increased sensitivity of pain mechanisms appears to follow a painful injury. These findings may have implications for understanding the mechanisms behind recurring and chronic musculoskeletal pain conditions.
Date: 09/29/2016 09:30:00 AM

**Title:** Clinical Features Of Chronic Pain Patients With And Without Hypermobility Syndrome.

**Poster Number** PTH184

**Authors**
V. Bastoni, C. Gomes, P. Angrisani, M. Felippe, N. Yonekawa, L. Yeng, G. Teixeira, V. Faria, R. Cetra, V. Liggieri, C. Takiguti

CF-Dor, São Paulo, Brazil, CF-Dor, são paulo, Brazil, N/A, Sao Paulo, SP, N/A, Sao Paulo, Sao Paulo, Divisão de Medicina Física do IOT do Hospital das Clínicas FMUSP, Sao Paulo, BRAZIL, Centro de Funcionalidade e Dor, São Paulo, São Paulo, Center Functionality and Pain, São Paulo, SP

**Aim of Investigation**
Hypermobility Syndrome (HS) is a musculoskeletal disorder and a subtype of Ehlers–Danlos Syndrome (EDS), an inherited disorder of connective tissue collagen characterized by varying degrees of joint hypermobility and musculoskeletal pain. It is not universally recognized in pain medicine, and diagnosis is often delayed. Persistent pain in people with HS is relatively common, affecting functionality and quality of life. This study describes the clinical features of a group of HS and non HS in a group of chronic pain patients in an interdisciplinary tertiary pain clinic.

**Results**
Forty eight patients (45%) present hypermobility: 39 women (81%), mean age 46.2 years old. The average pain complaint period was 78.3 months (6.5 years). Twenty seven (56%) related neck pain. 38 (79%) low back pain, 27 (56%) upper limbs pain and 28 (58%) lower limbs pain. Fifty eight patients (55%) don’t have hypermobility: 37 women (64%), mean age 60.4 years. The average pain complaint period of time was 68.3 months (5.6 years). Eighteen (31%) related neck pain, 42 (72%) low back pain, 21 (36%) upper limbs pain and 43 (74%) lower limbs pain.

**Conclusion**
Hypermobility syndrome or Ehlers Danlos syndrome may compromise different tissues, and the patients are younger and have longer period of pain complaints comparing to the non hypermobility patients. The importance of recognition this syndrome is to provide the correct treatment, understanding how much treatments are missing and recognize this syndrome and its implication.
Aim of Investigation
Generalized joint hypermobility (GJH) is highly prevalent among patients diagnosed with chronic pain, although in the majority of these patients, the diagnosis is missing. The aim of this study is to analyze the incidence and the clinical features of hypermobility syndrome in a group of patients with chronic pain in an tertiary interdisciplinary pain clinic.

Results
Three hundred and two patients have hypermobility syndrome. Two hundred and thirty-two were female (76.8%). Mean age was 45.53 years old. All subjects presented myofascial pain syndrome, 10.3% (n=31) peripheral neuropathy and 12.6% (n=38) fibromyalgia. The average time of pain complaints was 36 months. The most common regions of pain were: dorsal and back in 78% of cases, scapular region in 60.5%, neck in 60.2%, lower limbs in 55.6%, upper limbs in 35.4%, head in 30.4% and pelvic girdle in 30.1%.

Conclusion
The majority of patients were women (a proportion of 3:1 women in relation men). Myofascial pain syndrome was present in all and 78% of these patients presented dorsal and back pain. Fibromyalgia was diagnosed in 38%.
Title: An Investigation Of The Relationship Between Post-Traumatic Stress Symptoms And Neck Pain Related Disability In Acute/Subacute Whiplash Injury

Poster Number PTH186

Authors
A. Maujean, M. Gullo, M. Sterling
Griffith University, Parklands, QLD, University of Queensland, Herston, QLD

Aim of Investigation
1) To explore the factor structure of the Posttraumatic Stress Diagnostic Scale (PDS) in a sample of acute to sub-acute whiplash-injured individuals following a motor vehicle crash. 2) To identify the symptom clusters that best predict long-term neck pain related disability in this population.

Results
Principal component analyses with oblique rotation generated two symptom clusters: Re-experiencing/Avoidance (Cluster 1) and Hyperarousal/Numbing (Cluster 2). Nine PTSD symptoms (e.g., recurrent dreams of the trauma, reliving the trauma and avoiding thoughts of the trauma) loaded exclusively on the Re-experiencing/Avoidance cluster and seven symptoms (e.g., sleeping difficulties, difficulty concentrating, and diminished interest in activities) loaded exclusively on the Hyperarousal/Numbing cluster. The Re-experiencing/Avoidance cluster consists of specifically trauma-related symptoms whereas the Hyperarousal/Numbing cluster consists of symptoms that are also commonly experienced as a result of pain associated with a whiplash injury. One PTSD symptom on the PDS scale (i.e. Inability to recall an important aspect of the trauma) had no salient loading on either clusters. Structural equation modelling analysis indicated that there was a significant positive relationship between the Hyperarousal/Numbing symptom cluster and long-term neck pain related disability while no significant relationship was found between the Re-experiencing/Avoidance symptom cluster and long-term neck pain related disability.

Conclusion
The factor structure generated by the PCA do not reflect the three symptom clusters (i.e., re-experiencing, avoidance, and hyperarousal) proposed by the DSM-IV diagnostic system but provides support for a two-cluster model as found in two earlier studies using samples of motor vehicle crash survivors. Given that only the Hyperarousal/Numbing symptom cluster predicted long-term neck pain...
related disability, this finding may have implications in terms of diagnosis, assessment and management of the psychological impact of whiplash-injured individuals following a motor vehicle crash.
Title: Living With Ongoing Whiplash Associated Disorder: Individual Perceptions And Experiences

Poster Number PTH187

Authors
C. Ritchie, M. Sterling
Griffith University, Gold Coast, Queensland, Griffith University, Parklands, QLD

Aim of Investigation
The aim of the present study was to explore participant perceptions and experiences of living with ongoing whiplash associated disorder (WAD).

Results
Twenty-seven (treatment=14, control =13) (mean VAS=3.8±2.1) interviews were recorded and transcribed verbatim. Thematic analysis yielded several key themes including mismatch of expectations, adaptation, and interactions with health professionals. Reflections of recovery were linked to both positive and negative sub-themes. Mismatch of expectations was expressed almost universally. Participants indicated that prolonged non-recovery was due to a mismatch in expectations about the injury, or symptoms, or interactions with health professionals, or treatment. Adaption: while active self-management strategies were presented as a means of adaption, some participants felt adaptive strategies were irrelevant and were resigned to just 'live with it'. Interactions with health professionals: the importance of positive affirmation of the whiplash condition by health professionals was emphasised by many, whereas the lack of acknowledgement led to confusion, self-doubt and resignation.

Conclusion
Living with a chronic whiplash injury is challenging and can be exhausting. The qualitative data explored in this study add to traditional quantitative measures to capture a more complete understanding of patient experiences of living with an on-going whiplash injury, and provide preliminary information that may help with the development of treatments and interventions. For example, an emphasis on patient-centred care with early identification of patient expectations of recovery, symptoms and therapy may help merge patient and health practitioner expectations for recovery. Additionally, helping individuals recognise symptom triggers and develop appropriate strategies to minimise these triggers may actively
engage patients in their recovery. Finally, acknowledgement of the whiplash injury by health professionals is seen by many as a necessary step in the recovery process.
**Title:** Ongoing Neck Pain Causes Alterations In Axioscapular Muscle Activity When Compared To Healthy Controls

**Poster Number** PTH188

**Authors**
S. Christensen<sup>,2</sup>, R. Hirata, T. Graven-Nielsen

Center for Neuroplasticity and Pain, SMI, Aalborg University, Aalborg, Denmark, University College North Denmark, Aalborg, Denmark

**Aim of Investigation**
Neck pain is a common complaint in the general population. Although the underlying cause of chronic neck pain is unknown, altered axioscapular muscle function has been suggested as a contributing factor. This study set out to investigate potential group differences in axioscapular muscle activity during arm movements when comparing two different subgroups of neck pain with healthy controls.

**Results**
VAS scores were significantly increased for both neck pain groups when compared to healthy controls (P<0.01). Preliminary results for the RMS EMG demonstrated decreased activity for both the ipsilateral middle and lower trapezius muscles when comparing the neck pain groups to controls (P<0.03). Only for the middle trapezius during the slow down movement was a difference between neck pain groups found with WAD showing decreased values compared to IONP (P<0.05). Furthermore, a decreased activity was found for the ipsilateral upper trapezius during the down movement when comparing the WAD group to IONP and controls (P<0.01)

**Conclusion**
In neck pain patients reorganized axioscapular muscle activity was found during arm movements supporting the theory that altered axioscapular muscle function is a feature of neck pain. For clinical practice these results supports the inclusion of the shoulder girdle in assessment and rehabilitation of neck pain patients.
Aim of Investigation
Increasingly, attention has been drawn to the role of persistent pain in the maintenance of post-traumatic stress symptoms consequent to whiplash injury. 'Mutual maintenance' models have been put forward to explain high rates of co-morbidity of pain and post-traumatic stress symptoms. It has been suggested that ongoing pain might contribute to the persistence of PTSD symptoms by acting as a "trigger" for memories of the traumatic incident. Clinical and anecdotal evidence supports the view that the symptoms of PTSD can be aggravated by stimuli that resemble aspects of the precipitating traumatic event. The present study tested the predictions of a mutual maintenance model of pain and PTSD in a sample of 105 (73 women, 32 men) individuals who had sustained whiplash injuries in rear collision motor vehicle accidents.

Results
Only H1 was supported. Symptoms of PTSD were less likely to resolve if pre-treatment levels of pain were high, X² = 4.5, p < .05. However, there was not significant relation between pre-treatment levels of PTSD and the probability of resolution of pain symptoms, X² = 1.1, ns.

Conclusion
The findings support the view that intense or ongoing pain symptoms might act as a trigger for memories of a traumatic accident, contributing to the persistence of symptoms of PTSD. The findings do not support the view that symptoms of PTSD contribute to the persistence of pain symptoms. Clinical and theoretical implications of the findings are discussed.
Title: Pain Distribution After Neck Traumas: An Analysis Of 745 Consecutive Patients With Persistent Neck Pain

Poster Number PTH191

Authors
J. Larsson, E. Malmström, H. Westergren

Department of pain rehabilitation, Skåne university hospital, Lund, Sweden

Aim of Investigation
Those who fail to recover from whiplash traumas risk persistent, widespread pain. Women and those whose trauma was long ago may be particularly prone to develop such symptoms, but research on the topic is so far scant. We aimed to assess whether age, gender, or time since trauma was related to widespread pain.

Results
The model fit was significant Chi-2(3) = 37.8, p < 0.0001 Women were 1.595 [CI: 1.138; 2.232] times more likely to be diagnosed with widespread than local pain p < 0.000, and 2.710 [CI: 1.656; 4.425] times more prone to have widespread compared with regional pain p = 0.027. Every month passed since the trauma increased the risk for widespread pain with 1.003 [CI: 1.001; 1.006] times compared with local pain, p = 0.027, and 1.005 times [CI: 1.001; 1.009] compared with regional pain, p = 0.011. Age did not account for any significant differences.

Conclusion
Time elapsed since the trauma correlated with widespread pain—a novel finding. In our discussion we provide a rationale for this, along with the increased risk of being a woman, which confirms the results of previous studies.
Date: 09/29/2016 09:30:00 AM

**Title:** Identification Of Substance P Mediated Depolarization In The Superficial Dorsal Horn Evoked By Single Electrical Stimulation Of Primary Afferents

**Poster Number** PTH192

**Authors**
K. Kaneko, T. Saotome, Y. Numata, T. Takasusuki, S. Yamaguchi, Y. Hori

Department of Physiology and Biological Information, Dokkyo Medical University, Mubu, Tochigi 321-0293 JAPAN

**Aim of Investigation**
Substance P (SP) plays a critical role in the development and maintenance of the neuropathic pain through the neurokinin-1 receptor (NK-1 receptor). To better understand effects of SP on nociceptive synaptic plasticity, we investigated the SP-mediated depolarization in the spinal superficial dorsal horn (SDH) by means of voltage-sensitive dye imaging.

**Results**
Mechanical alldynia was observed in the partial sciatic nerve-ligated mice. The electrical stimulation to the dorsal root remnant evoked fluorescence changes in the SDH. Fast inhibitory GABAergic and glycinergic transmission were blocked by bicuculline (10 μM) and strychnine (1 μM). Excitatory transmission was suppressed by 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX 10 μM, a non-NMDA receptor antagonist) and 2-amino-5-phosphonovaleric acid (AP-V 50 μM, an NMDA receptor antagonist).

Application of glycine and bicuculline increased the electrical stimulus-induced fluorescence changes. The addition of CNQX and AP-V to the perfusate decreased the fluorescence changes. The APV-sensitive depolarizing response was larger in sciatic nerve-ligated mice than in control sham-operated mice. In the presence of Gly, Bic, CNQX, and AP-V, electrical stimulus elicited a slight, but distinct, fluorescence change, which lasted a rather long time. This response was abolished by application of a NK-1 receptor antagonist CP99994 (1 μM). Thus, this long-lasting depolarizing response is mediated by SP released upon electrical stimulation of primary afferent fibers. The amplitude of the SP-mediated depolarizing response was larger in sciatic nerve-ligated mice than in control sham-operated mice. Additionally, the μ-selective opioid agonist [D-Ala2, N-Me-Phe4, Gly5-ol]-enkephalin (DAMGO 30 μM) decreased the SP-mediated depolarizing response.
Conclusion
The presently observed larger depolarizing responses mediated by NMDA receptor and NK-1 receptor in sciatic nerve-ligated mice might underlie the mechanisms of neuropathic pain. These optical imaging experiments might provide a useful tool for investigating the synaptic effects of SP in the SDH.
Title: Interferon-\(\Gamma\) Increases The Nmda-Induced Inward Current In Spinal Dorsal Horn Neurons Via Ccl2/Ccr2 Signaling

Poster Number PTH193

Authors

Department of Orthopaedic Surgery, Wakayama Medical University, Wakayama, Japan, Pain Research Center, Kansai University of Health Sciences, Osaka, Japan

Aim of Investigation
The development of neuropathic pain is believed to involve glia-neuron interactions. Expression of the pro-inflammatory cytokine interferon-gamma (IFN\(\gamma\)) is upregulated in the dorsal horn after peripheral nerve injury, and intrathecal IFN\(\gamma\) administration induces mechanical allodynia in rats. However the effects of IFN\(\gamma\) on the spinal dorsal horn are unclear. To elucidate how IFN\(\gamma\) affects nociceptive responses in the spinal dorsal horn, we analyzed the effects of IFN\(\gamma\) on postsynaptic action electrophysiologically.

Results
Perfusion of exogenous NMDA (50 \(\mu\)M) for 30 seconds onto the spinal cord slice induces slow inward currents at a holding potential of -50 mV. Bath application of IFN\(\gamma\) significantly increased the NMDA-induced current (147.3 \(\pm\) 10.7\%, \(n = 14\), \(p = 0.0002\)). This IFN\(\gamma\)-induced facilitation of NMDA current was inhibited by a selective IFN\(\gamma\) receptor antagonist (\(n = 10\)). Therefore IFN\(\gamma\) likely binds to IFN\(\gamma\) receptors and activates NMDA receptors in SG neurons. Since both neurons and microglia are reported as sites of IFN\(\gamma\) receptors, we investigated which receptor is responsible for the IFN\(\gamma\)-induced potentiation of NMDA-induced currents. The IFN\(\gamma\)-induced facilitation of NMDA currents was inhibited by minocycline, an inhibitor of microglia activation (\(n = 12\)). In addition, when we added the JAK inhibitor tofacitinib to the pipette solution, IFN\(\gamma\)-induced facilitation of NMDA currents was not affected even after 30 min (\(n = 7\)). Therefore IFN\(\gamma\) likely enhances neuronal NMDA-induced inward current via the microglial IFN\(\gamma\) receptor. Next we examined which mediator secreted by activated microglia effects on SG neuron. GDP-\(\beta\)-S, a non-hydrolysable analogue of GDP that competitively inhibits G-proteins, was added to the pipette solution. When IFN\(\gamma\) and NMDA were applied 30 minutes after the patch clamping with the pipettes containing GDP-\(\beta\)-S, IFN\(\gamma\)-induced enhancement of NMDA inward currents were significantly
These findings suggested that the IFNγ-induced increase of NMDA currents involves the activation of G protein-coupled receptors such as chemokine receptors. Specifically, the chemokine monocyte chemoattractant protein 1 (MCP-1, also known as chemokine ligand 2, CCL2) and its receptor C-C chemokine receptor type 2 (CCR2) are reportedly involved in the generation of neuropathic pain. IFNγ-induced enhancement of NMDA currents was blocked by a selective antagonist of CCR2, Teijin compound 1 hydrochloride (n = 6). In addition, bath-applied CCL2 enhanced NMDA-induced inward current (128.3 ± 6.4 %, n = 5, p = 0.006). This suggests that IFNγ increases the NMDA-induced inward current in SG neurons via CCL2/CCR2 signaling.

**Conclusion**

Our results show that IFNγ enhanced NMDA-induced inward currents in SG neurons through the activation of IFNγ receptors in microglia, and CCL2 was one of the mediators between microglia and neurons. Thus, IFNγ plays an important role as one of initiating agents of glia-neuron interactions that lead to neuropathic pain due to central sensitization.
Title: Involvement Of Rho Kinase In The Pkcγ Activation In The Spinal Cord Of Neuropathic Pain Model Mice

Poster Number PTH194

Authors
K. Ishikura, K. Kume, M. Ohsawa

UnivDept. Neuropharm., Grad. Sch. Pharmceu. Sci., Nagoya city Univ, Nagoya, Japan

Aim of Investigation
Spinal sensitization of nociceptive transmission is a major causal factor for the development and maintenance of neuropathic pain. Several intracellular events are involved in this sensitization, but the mechanism is still largely unknown. We and others recently revealed that the spinal activation of RhoA/Rho kinase (ROCK) signaling might be a key factor in the neuropathic pain. Moreover, many reports pointed the involvement of protein kinase C (PKC) in the pain. Until this time, many intracellular signalings are postulated to be involved in the neuropathic pain, although little is known how these signalings are integrated. The present study is designed to investigate the relationship between ROCK and PKCγ, both of which are well established in the neuropathic pain.

Results
Daily i.t. treatment with PKC inhibitor calphostin C partially, but significantly, attenuated the mechanical hyperalgesia in nerve-ligated mice, whereas the threshold in sham-operated mice was not affected. Daily i.t. treatment with ROCK inhibitor Y27632 fully reversed the mechanical hyperalgesia in nerve-ligated mice. Since previous reports indicated that the activations of glial cells are involved in the neuropathic pain, the expressions of astroglial marker GFAP and microglial marker Iba-1 in the spinal cord were examined. The expressions of GFAP and Iba-1 were increased in the ipsilateral dorsal horn of the spinal cord of nerve-ligated mice. This increased expression of GFAP was attenuated by Y27632, but not calphostin C. On the other hand, increased expression of Iba-1 was not affected by either Y27632 or calphostin C. Moreover, the expression of phosphorylated PKCγ was increased in the ipsilateral dorsal horn of the spinal cord from nerve-ligated mice.

Conclusion
This increased phosphorylation of PKCγ was completely blocked by Y27632, whereas calphostin C did not show any effect. Therefore, it is possible that ROCK signaling activates PKC signaling through the
modulation of astroglial function under neuropathic pain. These intracellular signaling activation might be important for the development and maintenance of neuropathic pain in the spinal cord.
Title: Paclitaxel Modulates Activity Of Spinal Cord Presynaptic Trpv1 Receptors Through Tlr4 Receptors Activation

Poster Number PTH195

Authors
P. Adamek, P. Mrozkova, J. Palecek

Institute of Physiology of The Czech Academy of Sciences, Prague, Czech Republic, Faculty of Science, Charles University in Prague, Czech Republic

Aim of Investigation
Paclitaxel is the frontline chemotherapeutic agent widely used in clinical practice for treatment of solid tumors, such as breast, ovarian and lung cancer. However, chemotherapy-induced peripheral neuropathy (CIPN) is a major dose-limiting adverse effect of paclitaxel therapy. We tested hypothesis that these undesirable adverse effects could be at least partially mediated due to activation of Toll-like (TLR4) and Transient Receptor Vanilloid 1 (TRPV1) receptors in the spinal cord.

Results
Acute application of paclitaxel (50 nM) on slices from naïve animals induced significant increase in the frequency of mEPSC. This effect was prevented by TRPV1 antagonist SB366791 (10 µM) pretreatment. The frequency and amplitude of the sEPSC and eEPSC was not affected by the paclitaxel treatment.
Paclitaxel (50 nM) also modulated responses to repeated application of low capsaicin concentration (0.2 µM), recorded as changes in mEPSCs frequency in spinal cord slices from naïve and CIPN animals. Under control conditions the second response to capsaicin was dramatically reduced, to only 33% of the first one. Acute application of paclitaxel significantly reduced the tachyphylaxis of the second response to capsaicin, which was under this condition 91% of the first one. This effect of paclitaxel was prevented by TLR4 antagonist LPS-RS (2 µg/ml; 44%) coapplication in experiments performed in slices from naive mice. The reduced tachyphylaxis of the second capsaicin response was present also in slices from CIPN animals, 1 and 8 days after single in vivo systemic paclitaxel treatment (8 mg/kg; 72% and 83% of the first response). Further information about the intracellular signalling pathways involved in signalling between the TLR4 and TRPV1 receptors after acute and in vivo paclitaxel treatment will be also presented.
Conclusion
Our results suggest that functional interaction between TLR4 and TRPV1 receptors and modulation of TRPV1 receptors functional properties may play an important role in the development of peripheral neuropathy following paclitaxel treatment. Targeting these receptors may represent a viable option for possible analgesic treatment. Our work was supported by grant support: GACR 1511138S, LH15279, GACR P304/12/G069, CZ.1.05/1.1.00/02.0109, RVO67985823, GAUK 138215
Title: Placebo Response In Central Neuropathic Pain: Subject-Level Predictors

Poster Number PTH196

Authors
F. Warner, J. Cragg, N. Finnerup, S. Andresen, J. Kramer

ICORD, University of British Columbia, Vancouver, Canada, Danish Pain Research Center, Aarhus University, Aarhus, Denmark, Spinal Cord Injury Centre of Western Denmark, Department of Neurology, Regional Hospital of Viborg, Viborg, Aalborg

Aim of Investigation
The primary aim of the current investigation was to identify factors that contribute to variability in placebo responses in randomized clinical trials (RCTs) for central neuropathic pain. The second aim was to investigate whether the location and type of pain, as well as the severity of damage in the spinal cord impacted placebo responses.

Results
Our preliminary analysis of 3 randomized clinical trials (n=84) revealed a significant placebo response (mean=0.55+/-.151; p=0.001). Pooled analysis of crossover-designed studies found that placebo responses were predicted based on age and the severity of damage in the spinal cord (n=52). Pain characteristics (e.g., location relative to damage in the spinal cord) were not found to be significant predictors.

Conclusion
Our analysis of subject-level data demonstrates that placebo responses are related to age and the extent of damage in the spinal cord. Additional analyses of subject-level RCT data are warranted to further elucidate the role of the spinal cord in facilitating changes in pain intensity due to placebo treatment.
Aim of Investigation
About 7~15% patients with hemorrhage stroke in lateral thalamus would suffer central post stroke pain (CPSP). But mechanism of CPSP is not clear. Although a hemorrhage rat model was well established for CPSP research. Due to the efficiency to test gene function in transgenic mice, it is valuable for establishing a mouse hemorrhage CPSP model that could help to distinguish more detail mechanisms of CPSP. In our previous study, we have shown that thalamic P2X7 receptors were directly involved in pain transmission and hypersensitivity in a rat model of CPSP. In this study, we tested the hypothesis that CPSP is caused by P2X7 receptor activation after thalamus hemorrhage damage in wide type and P2X7 knockout mice.

Results
Multiunit activities in medial dorsal nucleus of thalamus were enhanced and lengthened after noxious electrical stimuli on sciatic nerve in wild lesion mice group. In contrast with GABAergic inhibitory effect in sham lesion mice, spontaneous unit activity in medial dorsal nucleus could be enhanced by muscimol application in wild lesion mice. But in P2X7 knockout mice lesion group, patterns of alldynia in hind limbs, enhanced and lengthened noxious activities and muscimol enhanced response in MD neuron were not appeared.

Conclusion
Preliminary results suggest that the activation of P2X7 after thalamus hemorrhage damage is an important factor of CPSP. Our next step is to identify the effects of P2X7 cascades on CPSP.
Title: Methytransferase G9A/Glp Complex Controls Nr2B Expression By Methylating Grin2B In Neuropathic Pain

Poster Number PTH198

Authors
F. Wang, X. Shen, W. Wang, L. Lei, S. Xu, H. Wu, Y. Liu, S. Feng
Nanjing Medical University, Nanjing, Jiangsu, Nanjing Medical University, Nanjing, China

Aim of Investigation
Persistent activation of the receptors of excitatory neurotransmitters is an essential contributor to the central sensitization in response to nerve injury-induced hypernociceptive responses. One of the key compositions of this neural phenomenon is the over expression of the glutamate receptors in the neuropathic context. Cumulating evidence showed that the upregulation of the N-methyl-D-aspartate (NMDA) receptor subtype 2B (NR2B) after nerve injury is a pivotal factor facilitating pro-nociceptive transmission. However, the underlying mechanism of the pain-related NR2B upregulation is unknown. DNA methylation, a major characteristic process of epigenetic modulation, functions as a switch in controlling the gene expression through different types of methytransferases and demethylases. Previous studies demonstrated that the methytransferase G9a/Glp complex plays a critical role in cocaine-induced central plasticity. We herein proposed that G9a/Glp complex is involved in nerve injury-induced hypersensitivity regulation through NR2B expression by methylating its gene GRIN2B. The aim of this study was to test the hypothesis that the methytransferase G9a/Glp complex controlled over the expression of GRIN2B in the context of peripheral nerve injury-induced neuropathic pain.

Results
The expression of G9a, Glp, and NR2B were upregulated in the spinal cord dorsal horn at post-injury day 4 till day 49 (the last day of the behavioral test). Correspondingly, the GRIN2B CpG islands methylation is also increased. However, after the i.t. injection of both BIX 01294 and NUC 0638 since the post-injury day 7 for consecutive 4 days once daily, the expression of NR2B in contrast reached a new higher level, and the threshold of mechanical stimuli was reduced, even though the G9a/Glp levels were significantly downregulated followed with the decrease in GRIN2B methylation. Moreover, the continual i.t. infusion given at post-injury day 14 also produced the same results. These data suggested that the G9a/Glp complex itself plays an inhibiting role in preventing the excessive overexpression of NR2B by
methylating its gene GRIN2B, and the use of G9a/Glp inhibitors produced a disinhibitory effect on nerve injury-induced NR2B expression.

**Conclusion**
Spinal methyltransferase G9a/Glp complex controls NR2B expression at an elevated setpoint by methylating GRIN2B to prevent the over-sensitization from peripheral nerve injury-induced neuropathic pain.
The Effect Of Ciguatoxin At Sodium Channel Isoforms: A Link To The Pathobiology Of Ciguatera

Aim of Investigation
Ciguatera is a foodborne illness caused by consumption of fish contaminated with ciguatoxin, a toxin present in algae that is produced by the microorganism Gambierdiscus toxicus that bioaccumulates in large fish. It produces a range of gastrointestinal, neurologic and/or cardiovascular symptoms which last days to weeks, or even months. Ciguatoxins are known to modulate the activity of voltage-gated sodium channels (NaV), with P-CTX-1 being the most potent, and it thought that this activity underlies the peripheral pain symptoms observed in the clinic. Nine NaV subtypes (NaV1.1-1.9) are expressed in mammals with distinct tissue distributions and subsequent functional roles, with several subtypes (NaV1.7, 1.8 and 1.9) implicated to have a role in pain, however the activity P-CTX-1 at NaV channels has not been systematically assessed. Therefore the aim of this study is to assess the effect of P-CTX-1 on NaV1.1-1.9 and to identify which NaV isoforms mediate the painful neuropathy caused by P-CTX-1.

Results
P-CTX-1 caused concentration dependent potentiation of NaV responses in HEK293 cells, with surprisingly limited selectivity between NaV subtypes, although NaV1.3 and NaV1.8 were most potently affected (pEC50: 8.87±0.24 and 8.98±0.23 respectively). Despite limited selectivity in the FLIPR, P-CTX-1 (1 nM) was found to have differential effects at NaV1.1-1.8 assessed by automatic patch clamping. Interestingly, in cells expressing NaV1.8 a well-known pain target, P-CTX-1 elicits a hyperpolarising shift in the voltage dependence of activation but does not affect inactivation. All TTX-S isoforms displayed differential activation and inactivation kinetics in the presence of P-CTX-1. Surprisingly, a decrease in peak current was observed in NaV1.2 - 1.7 expressing cells. NaV channels may transiently open in response to small, slow depolarisation ramps, leading to a small inward current. These so-called ramp currents are increased significantly in most isoforms in the presence of P-CTX-1, the largest of these effects observed in NaV1.6 and 1.7 expressing cells. Application of P-CTX-1 (1 nM) to the receptive fields of sensory neurons caused spontaneous firing of action potentials in 100% of C fibers tested and 50% of
A-fibers tested. TTX-S channels, specifically NaV1.6 and NaV1.7, mediate spontaneous firing in A-fibers while both TTX-R and TTX-S channels mediated C-fiber responses. In vivo P-CTX-1 induced spontaneous pain is completely abolished by co-administration with TTX, as well as either a selective NaV1.6 or NaV1.7 inhibitors, in line with single fiber data.

**Conclusion**
P-CTX-1 is a non-selective NaV channel modulator that displays differential kinetics at NaV1.1 - 1.8. Most notably, P-CTX-1 increases ramp currents in NaV1.6 and NaV1.7, likely responsible for neural hyper-excitability and spontaneous firing observed ex vivo and in vivo. Indeed, the P-CTX-1 induced spontaneous firing sensory A fibers is mediated by NaV1.6 or NaV1.7. These isoforms also mediate P-CTX-1 induced spontaneous pain in vivo suggesting that this pain phenotype is A-fiber specific.
Title: Composite Piriformis-Sciatic Nerve Anomalies In The Etiopathogenesis Of Piriformis Syndrome And Sciatica Of Non-Discogenic Origin: A Case Report And Literature Review

Poster Number PTH200

Authors
A. Jha

College of Medicine, Texila American University, Georgetown, Guyana

Aim of Investigation
The aim of the present study is to highlight the anomalous union of the pre & post axial division of sciatic nerve and its relation with piriformis muscle, all of which may play a role in etiopathogenesis of piriformis syndrome leading to sciatica of non-discogenic origin.

Results
An unusual anatomical variation in the piriformis muscle and sciatic nerve was noted. Sciatic nerve division proximal to its entrance in the gluteal region was observed. The common peroneal component was passing through, and the tibial component was passing below a double piriformis muscle. Double piriformis muscles with two different arrangements of its two heads were also noted.

Conclusion
It is extremely important to be aware of these variations while planning a surgery in the gluteal region, as these nerves are more liable to be injured during surgeries. A detailed anatomical study of such variation aids in the understanding of increase in pain in various test positions. In sciatic neuropathies, level of sciatic nerve division plays a major role in the distribution of neurological deficits. Sciatic nerve division into tibial and common peroneal components at a higher level can result in manifestations pertaining to only one out of the two divisions in sciatic neuropathy. Description of such variations in relationship between sciatic nerve and piriformis muscle may be useful for diagnosis and treatment of piriformis syndrome and sciatica of non-discogenic origin. Attempted sciatic block at standard anatomical landmark may fail due to the anomalous union of the pre & post axial division of the sciatic nerve.
Title: Differential Immune Responses Depending On Genetic Heterogeneity Contribute To The Phenotype Of Neuropathic Pain Among Mouse Strains

Poster Number PTH201

Authors
K. Isami, S. Imai, A. Sukeishi, Y. Nakazato, H. Shirakawa, T. Nakagawa, K. Matsubara, S. Kaneko

Department of Molecular Pharmacology, Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan, Department of Clinical Pharmacology and Therapeutics, Kyoto University Hospital, Kyoto, Japan

Aim of Investigation
The differential neuro-immune responses due to diverse genetic factors can impact on neuronal adaptive responses associated with a phenotype of pain. However, the precise mechanisms are poorly understood. To address this issue, we compared the vulnerability of neuropathic pain in four strains of inbred mice with differential genetic backgrounds. Furthermore, we investigated how immune genetic heterogeneity can influence the pain phenotype via immune responses using these mice.

Results
After the nerve injury, the most severe neuropathic pain was observed in B6, while C3 showed lower responses than other strains. In C3, the immunoreactivity of CD206-positive anti-inflammatory M2 macrophages were remarkably increased in the dorsal root ganglia (DRG) after the nerve injury, while the number of Iba1-positive activated microglia in the spinal cord was smaller than that of B6. To determine whether the phenotype of peripheral immune cells affects spinal microglial activation, we generated BM chimeric mice between B6 and C3. Behavioral and immunohistochemical studies revealed that B6 donor chimeric mice showed significant severe mechanical allodynia and decreased ratio of M2/M1 macrophages in DRG only 3 days after the nerve injury, compared to C3 donor chimeric mice, suggesting that the differential phenotype of DRG macrophages partially participated in the early phase of neuropathic pain. By contrast, differential responses of spinal microglia depended on the phenotype of recipient mice, rather than the phenotype of DRG macrophages, which mainly contributed to the development and maintenance of neuropathic pain.
Conclusion
Taken together, our findings suggest that differential responses of immune/glial cells, especially microglia, contribute to the differential vulnerability of neuropathic pain on genetic heterogeneity.
Title: Ca\textsubscript{v}3.2 T-Type Calcium Channels Contribute To Oxaliplatin-Induced Neuropathic Pain In Mice

Poster Number PTH202

Authors
T. Miyazaki, R. Fukuda, M. Tsubota, A. Kawabata

Faculty of Pharmacy, Kindai University, Higashi-Osaka, Japan

Aim of Investigation
Chemotherapy-induced peripheral neuropathy is a major side effect of cancer therapy which is a dose-limiting factor and may result in interruption of the chemotherapy. Oxaliplatin, a third-generation platinum-based chemotherapeutic drug, is widely used for the treatment of advanced colorectal cancer, etc., whereas it frequently induces acute and chronic neuropathy. We have shown that the Ca\textsubscript{v}3.2 isoform of T-type calcium channels (T-channels), expressed on the primary sensory neurons, plays a role in processing of somatic and visceral pain and participates in the neuropathic pain induced by L5 spinal nerve injury or paclitaxel, an anti-cancer drug. In the present study, we asked if Ca\textsubscript{v}3.2 T-channels are involved in the oxaliplatin-induced neuropathic pain in mice.

Results
The mechanical nociceptive threshold significantly decreased 4 h after i.p. administration of oxaliplatin (acute phase), and the neuropathic allodynia lasted 8 days or more after oxaliplatin challenge (chronic phase). The oxaliplatin-induced acute allodynia was reduced by NNC55-0396 at 10 mg/kg or Z-944 at 20-30 mg/kg, but not by mibefradil at 10 mg/kg or RQ-00311651 at 20 mg/kg. On the other hand, the oxaliplatin-induced neuropathic allostodynia in the chronic phase was markedly reversed by the same doses of mibefradil, NNC55-0396, Z-944 or RQ-00311651, and also by TTA-A2 at 1-3 mg/kg. Further, the neuropathic allostodynia in the chronic, but not acute, phase was also suppressed by i.p. administration of ascorbic acid at 20 mg/kg. Finally, knockdown of Ca\textsubscript{v}3.2 by i.t. AS-ODNs abolished the oxaliplatin-induced chronic allostodynia.

Conclusion
These data strongly suggest that Ca\textsubscript{v}3.2 T-channels contribute to the oxaliplatin-induced chronic neuropathy, although the role of T-channels in the acute neuropathy is still open to question.
Title: Expression Of Anoctamin-1 Channel In L4, L5, And L6 Dorsal Root Ganglion Neurons After Spinal Nerve Ligation In Rats

Poster Number PTH203

Authors
G. Garcia, J. Murbartíán
Cinvestav (Sede Sur), Mexico City, Mexico

Aim of Investigation
Anoctamin-1 (Ano1) belongs to the family of calcium–activated chloride channels and it is expressed in dorsal root ganglion (DRG) neurons. Ano1 contributes to neuronal excitability in inflammatory and neuropathic pain. It is also known that decrease neuronal excitability is necessary for recovery of injury nerve. The aim of this study was to determine if the block of Ano1 contributes to recovery in injury nerves.

Results
The expression of Ano1 increased in uninjured L4 and injured L5 DRG neurons at 7 days after SNL. ATF3 and GAP43 increased their expression in L5/L6 DRG neurons from first day until 7 days after SNL. In the other hand, T16Ainh-A01 treatment, but not vehicle (DMSO 1%), reverted mechanical allodynia until 14 days post-treatment. Furthermore, we found that T16Ainh-A01 treatment decreased expression of Ano1 and ATF3, but increased expression of GAP43 in injured L5/L6 DRG neurons. T16Ainh-A01 treatment decreased only Ano1 expression in uninjured L4 DRG neurons.

Conclusion
These results suggest that the block of Ano1 probably enhances recovery of injured L5/L6 DRG neurons and decreased Ano1 overexpression in L4 after SNL.
Title: Atorvastatin Has The Antihyperalgesic Effect On Cisplatin-Induced Neuropathy

Poster Number PTH204

Authors
H. Park, S. Lee, H. Jung, Y. Han, Y. Kim, E. Kim

Department of Anesthesiology & Pain Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea

Aim of Investigation
Peripheral neuropathy produced by cisplatin treatment produce a persistent tactile allodynia in mice. Atorvastatin is traditionally used to treat hyperlipidemia and has been shown for antiemetic effects in cisplatin-induced neuropathic pain models. However, the antihyperalgesic effect on cisplatin-induced neuropathy remains unknown. Here we examined the effects of intraperitoneal atorvastatin on allodynia in peripheral neuropathic mice.

Results
Peripheral neuropathic mice showed a prominent allodynia. The control group showed no differences for mechanical allodynia. For the atorvastatin groups, the paw withdrawal thresholds to mechanical stimuli were significantly reduced versus the pre-administration values and versus the control group dose-dependently (P < 0.05).

Conclusion
Atorvastatin given IP yields attenuation of the mechanical alldynia in mice models of poly-neuropathic pain.
Title: Persistent Neuropathic Pain After Nerve Suture Surgery

Poster Number PTH205

Authors
A. Miclescu, J. Walan, M. Essemark, R. Karlsten, T. Gordh

Uppsala University Hospital, Uppsala, Sweden, Uppsala University, Uppsala, Sweden, Pain Clinic of Uppsala University Hospital, Uppsala, Sweden

Aim of Investigation
Iatrogenic nerve injury has been proposed as the main factor responsible for long term-postsurgical pain. The prevalence of chronic neuropathic pain after a known somatosensory lesion in the upper extremity nerves followed by suture surgery was determined.

Results
Three hundred eighty-two patients returned the questionnaire (response rate 35%). Post trauma or post-surgical pain was present in 186 patients (48%) from those 382 patients who responded to the questionnaire. A total of 87 patients (47%) of these 186 patients developed chronic pain after the operation. The most common symptom experienced by the patients was the enhanced sensitivity to cold in 69% of the patients that led to pain and discomfort at temperatures that normally were perceived as being innocuously cool. Other symptoms were diminished sensitivity to stimulation in 55% of the patients and allodynia to light pressure, cold presented in 50% of the patients. The majority of the patients with pain resulting from traumatic or surgical nerve injury (77% of the patients) had no medication for pain, despite the presence of pain more than 50 VAS.

Conclusion
Persistent neuropathic pain occurred in 48% of the patients following nerve suture surgery. Cold intolerance has a high prevalence both in the group of patients with pain and in the group without pain.
Title: Intratecal Treatment With Mesenchymal Stem Cells Reduced The Hyperalgesia Followed By Experimental Diabetics Neuropathy

Poster Number PTH206

Authors
J. Schiavuzzo, W. Viera, C. PARADA, A. Spejo, A. Oliveria
UNICAMP, Campinas, SP, UNICAMP, Campinas, Brazil, State University of Campinas, Campinas - SP, Brazil

Aim of Investigation
The aim of this study was to investigate if intrathecal injection of mesenchymal stem cells (MSC) modulates the hyperalgesia resulting from experimental diabetes.

Results
The intraperitoneal administration of STZ (25 mg/kg) for 5 consecutive days increased the blood glucose levels measured on days 0, 7, 14, 21 and 28 after the first STZ administration. Decrease of mechanical nociceptive threshold was detected from 7th to 28th day. This hyperalgesia was reversed by seven days of intrathecal administration of mesenchymal stem cells, but not of DMEM (P<0.05; ANOVA - One Away - followed by Bonferroni post hoc test).

Conclusion
The data of this study, although preliminary, suggest that intrathecal administration of mesenchymal stem cells (MSC) could be a promising treatment to control pain during diabetic neuropathy. The probable action mechanism of MSC is under investigation in our laboratory.
Title: Characterization Of Select Cytokine, Chemokine, Neuropeptide, And Neurotransmitter Levels In Plasma And Cerebral Spinal Fluid From Individuals With Painful Diabetic Peripheral Neuropathy, Non-Painful Diabetic Peripheral Neuropathy, And Controls

Poster Number PTH207

Authors
K. Johnson, R. Davis, C. Chang, J. Xu, X. Chai, K. Cox, T. McNearney

Eli Lilly and Company, Indianapolis, IN United States

Aim of Investigation
Insights into the physiology of diseases can potentially be gained by measuring levels of analytes in tissues and fluids from diseased individuals and appropriately matched controls. The aim of this study was to measure the concentration of select cytokines, chemokines, neuropeptides and neurotransmitters in the plasma and cerebral spinal fluid (CSF) from individuals with diabetic peripheral neuropathy (DPN) and matched controls.

Results
The concentration of fractalkine in the CSF from individuals with painful DNP were significantly greater compared to those with non-painful DPN (p<0.05). In addition, the concentration of fractalkine in CSF samples from both DPN groups correlated with the NRS pain score (r=0.59). The concentrations of glutamate in the CSF from the painful DNP group were significantly higher than levels in the control group (p<0.05). The glutamine levels in the plasma from the painful DNP and non-painful DPN groups were both significantly lower than levels from the control group (p<0.05). An interesting negative correlation was observed between glutamine concentration and hemoglobin A1c levels in the plasmas of the DPN groups (r= -0.54). Finally, plasma arginine levels were significantly higher in the painful DPN group compared to both the non-painful DPN group and matched controls (p<0.05). The analyses of all other analytes did not result in statistically significant differences between groups.

Conclusion
These results suggest that the roles of fractalkine, glutamate, glutamine and arginine should be investigated further in clinical pain disorders. These findings also provide clinical validation of preclinical studies in the literature suggesting that fractalkine, glutamate, glutamine and arginine are potential key mediators in persistent pain states.
Title: Pain Related Small Nerve Fiber Functions Assessed By Laser Speckle Contrast Analysis (Lasca)

Poster Number PTH208

Authors
I. Unal-Cevik

Hacettepe University Faculty of Medicine Dept. of Neurology, Ankara-TURKEY, Ankara, Turkey

Aim of Investigation
Peripheral neuropathic pain may be associated with small fiber neuropathy. Assessment of small fibers is possible with advanced techniques such as CHEPs, LEPs, microneurography or minimal invasive methods such as skin biopsy, all of which are performed only in very few specialized centers. Axon-reflex flare response is a vasodilation (hyperemia) induced by mechanical, electrical or chemical stimulation of the dermal nociceptive C-fibers. LASCA is a real-time method that visualizes tissue microcirculation with high resolution and speed. In this study intradermal small fibers were aimed to be sensitized (by histamine or capsaicin) and desensitized (by local anesthetic cream). The change in axon-reflex flare responses were quantified by LASCA.

Results
Healthy volunteers aged 27.75+3.77 years. Application of capsaicin caused mostly burning pain, whereas histamine induced mostly stinging pain and itch. Histamine induced more prominent flare response. Local anesthetic cream was able to reduce both the severity and duration of pain in both groups. It was also able to reduce the intensity of flare response but not abolish completely.

Conclusion
Pain related small fiber functions may be assessed with histamine or capsaicin evoked axon-reflex flare responses, visualized and quantified real-time by LASCA. This is an easy, quick, objective, quantitative, diagnostic method which may be used in pain patients. It may also enable us to evaluate the effects of different treatments on small nerve fiber functions. Acknowledgements: This work is funded by Hacettepe University, Scientific Research Projects Coordination Unit, Project numbers: 014 A 101 007-710 and THD-2015-9137.
Aim of Investigation
Chemotherapy-induced peripheral neuropathy (CIPN) is a dose limiting side effect in the use of the platinum-based antineoplastic drug oxaliplatin as a treatment for colorectal cancer. Currently there is no treatment available to reverse the neurotoxicity which presents as pain, sensory loss and cold allodynia in up to 80% of patients. The aim of this study is to investigate if pregabalin can reverse the mechanical allodynia caused by oxaliplatin in CIPN.

Results
In mice a neuropathic baseline was established 3 days post-oxaliplatin injection and remained stable for 14 days. Pregabalin had a dose response effect on mechanical allodynia. At day 15 pregabalin (3 mg/kg p.o.) reversed mechanical allodynia to baseline scores at 2 hours (H) post-dosing but not 1H. Following a 2 day wash out where scores returned to neuropathic baseline, pregabalin (10 mg/kg p.o.) reverted scores for mechanical allodynia to baseline scores at both 1 and 2H. Thermal allodynia was assessed and responded to pregabalin with a similar trend. Thermal testing was performed either immediately after vF or alone and our results were similar, showing no iatrogenic effects of vF on thermal sensitivity. Correlation analysis of the responses to thermal and mechanical stimuli showed no significant trend, indicating that oxaliplatin-induced peripheral neuropathy affects the mechanical and thermal modalities in different ways. In rats the effects of pregabalin (30 mg/kg) followed a similar trend.

Conclusion
A single dose of pregabalin can reverse mechanical allodynia in rat and mouse models of oxaliplatin-induced peripheral neuropathy. In the rat, oxaliplatin produces dose-dependent effects on mechanical and thermal alldony.
Title: The Streptozocin Model Of Diabetes, Induces Neuropathic Pain And Changes In Quality Of Life Measures Which Can Be Modulated By Social Interaction/Welfare

Poster Number PTH210

Authors
A. Fisher, P. Kennard, M. Burnett, N. Upton, L. Lione
Transpharmation, Hatfield, United Kingdom, University of Hertfordshire, Hatfield, United Kingdom

Aim of Investigation
Many diabetic patients experience chronic neuropathic pain leading to a reduced quality of life which poses a huge economic burden to the health system & society. There is a dire need to develop more efficacious analgesics as the majority of patients respond poorly to available treatments. The predictive validity of animal models for analgesia may be improved by reinstating specific innate rodent emotional wellbeing behaviours suppressed by pain (e.g. burrowing & sucrose preference). Streptozocin (STZ) given systemically to rats induces rapid & sustained changes that are translatable to diabetic patients i.e. hyperglycaemia, polydypsia & frequently neuropathic pain. The aim of this study, was to investigate whether the development of STZ induced diabetes in rats, over 18 days, reduces burrowing and sucrose preference (a measure of anhedonia) in line with the development of neuropathic pain (static allodynia) and whether these wellbeing behaviours could be improved by the analgesic, pregabalin (PGB) &/or social paired housing.

Results
STZ pairs showed polydipsia & polyphagia as early as 2 & 7 days post injection. By day 3 post STZ, diabetic animals possessed significant static alldynia (>70% had 68.2 ± 4.2% change from baseline, p<0.001), impaired burrowing (680 ±172g, p<0.001) & reduced sucrose preference (20 ± 13%, p<0.001) as compared with CTRL group (1650 ± 149g; 84 ± 2%). In STZ rats, the impaired burrowing & anhedonia emerged at the same time as static alldynia. However, the anhedonia disappeared (64 ± 4%, p>0.05) whereas the burrowing deteriorated further (102 ± 38g, p<0.001) after 9 days, whilst the alldynia remained consistent over 18 days. PGB (30 mg/kg p.o. at 1 & 2 hours post treatment) completely reversed alldynia (PWT 1 hour, 19 ± 2g, p<0.001) but not impaired burrowing (73.1 ± 52g, p>0.05) as compared with vehicle (VEH) treated rats (PWT 3.1 ± 0.3g, 86.7 ± 78.9g) between day 14 & 18 post STZ. The early decline (day 3-10) in burrowing, in STZ rats, is significantly reversed if they burrow in pairs (day
3; 1571 ± 159g, day 10; 848 ± 159g, p<0.01) whilst pairing offers no social benefit to CTRL rats burrowing performance (p>0.05).

Conclusion
PGB reversed the mechanical allodynia that developed following STZ injection, whereas the deficit in burrowing was left un-touched; suggesting different pathologies contribute to these two behaviours. Housing of CTRL rats with polydipsic STZ rats, in pain, alters their nociceptive responses & behaviour leading to hyperglycaemia, demonstrating rodents can recognize pain related responses in conspecifics. Social grouping of an STZ rat with a CTRL or STZ partner impacted on individual burrowing. If an STZ diabetic rat was paired with a CTRL rat it burrowed significantly more than an STZ diabetic rat that was paired with another STZ diabetic rat. Similarly, if a CTRL rat was paired with another CTRL rat it burrowed significantly more than a CTRL rat that was paired with an STZ diabetic rat. This alteration in burrowing, depending on home cage partner, suggests burrowing is measuring affective well-being of both CTRL & STZ diabetic rats & that social grouping of an STZ rat with a CTRL partner can have a positive impact on its welfare. We conclude that allodynia, anhedonia (as measured by the reduction in sucrose preference) & impaired burrowing in STZ diabetic rats may offer affective sensitive & objective quality of life measures of pain &/or diabetes. Furthermore it is clear that social pairing of diabetic rats can have a positive impact on welfare whilst the pairing of CTRL rats with diabetic rats in pain can have a negative impact.
Title: Attenuation Of Hyperalgesia In Neuropathic Rats By Induced Pluripotent Stem Cells

Authors
H. Kim, H. Lee, E. Choi, D. Kang, S. Do

Konkuk University, Seoul, Korea

Aim of Investigation
Neuropathic pain is one of the most difficult to treat pain condition due to its complex etiology and pathogenesis. Damages of the somatosensory system often lead to molecular and cellular changes which lead to disturb inhibitory tone. Recently, stem cell-based therapeutic approach is being pursued as potential alternative curative treatment options for neuropathic pains. Induced pluripotent stem cells (iPSCs) are one of the promising sources of stem cells, due to a lower risk of immune rejection, expansion and differentiation capacity. The aim of this study was to determine whether the transplantation of iPSc has an antihyperalgesic effect and to investigate the sequential alteration of clinical, histological and genetical expression pattern changes in crushing injury-induced neuropathic rats.

Results
Crushing injured groups showed lower withdrawal threshold to von Frey and higher ADT score than the control group (p<.05). However, compared to injury group, a mechanical threshold of the iPS group was increased from 2 weeks to the end point of experiments (statistically significant at 4 weeks, p<.05). CNAP amplitude of iPS group was similar to control groups but lower than injury group at 5 weeks. On histopathological examination, the severity of neurodegenerative features such as hydropic changes and inflammatory cell infiltration to the endoneurium was reduced in the iPS group compared to that in the injury alone group. Further immunohistochemical staining revealed that Schwann cell activation and maintenance of nestin-positive structures were prominent in the iPS group. Neuroinflammation related gene, including IL-1β and cannabinoid receptor 2 (CB 2) expression levels were significantly increased in the iPS group (p<.01). The expression levels of the purinergic receptor, P2RX2 which predominantly expressed in nociceptors, showed statistically significant decrease in the iPS group compared to injury group at both 2 and 5 weeks (p<.01). In addition, gene expression levels of Na v1.3 and N-type calcium channel were also reduced in the iPS group at 2 weeks (p<.1).
Conclusion

The result indicates that transplantation of iPS could contribute to attenuate crushing injury-induced hyperalgesia in mechanical and thermal sensitivity. Our result also indicates that iPS treatment yielded the decrease of CNAP amplitude as well as the downregulation of neuropathic pain-related genes which include purinergic receptor and ion channels. Furthermore, iPS enhances neuroprotective properties by hastening the Wallerian degeneration and Schwann cell activation. Importantly, our findings provide preliminary evidence of iPScs application to treat neuropathic pain. Acknowledgements: This research was supported by Basic Science Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Science, ICT & Future Planning (NRF-2014R1A1A3052557)
Title: A Randomized, Placebo-Controlled, Double-Blind Study Of The Safety, Tolerability, Pharmacokinetics, And Pharmacodynamics Of Single And Multiple Doses Of Mirogabalin In Healthy Asian Volunteers

Poster Number PTH212

Authors
J. Mendel, S. Warrington, V. Dishy, S. Ohwada, L. Johnson, K. Brown, H. Ishizuka

Daiichi Sankyo Development, Gerrards Cross, Buckinghamshire, United Kingdom, Hammersmith Medicines Research, London, United Kingdom, Daiichi Sankyo Pharma Development, Edison, NJ, Daiichi Sankyo Co., Ltd., Tokyo, Japan, Daiichi Sankyo Co. Ltd., Tokyo, JAPAN

Aim of Investigation
Mirogabalin, a novel, preferentially selective α2δ-1 ligand, is currently under investigation as an analgesic agent for patients with neuropathic pain conditions. Single and multiple ascending-dose studies in healthy subjects in the US indicated that mirogabalin was well tolerated at doses up to 30 mg/day. However, as drug exposure, safety, and tolerability in Asian subjects may differ from that of other races, the current study was designed to evaluate of the pharmacokinetics (PK) and tolerability of various doses of mirogabalin in healthy subjects of different ethnicities.

Results
In total, 53 subjects were randomized to treatment and completed the study. In the single ascending-dose phase, 6 subjects (all Japanese) received mirogabalin 10 mg, 22 subjects (5 Japanese, 6 Korean, 5 Chinese, 6 Caucasian) received mirogabalin 20 mg, and 9 subjects (3 Japanese, 2 each Korean, Chinese, and Caucasian) received placebo. The multiple dose phase included 16 Japanese subjects (6 each received mirogabalin 10 mg BID and 15 mg BID [instead of the planned 20 mg BID]; 4 received placebo). Overall, both single doses and multiple doses of mirogabalin were tolerated, although 15 mg BID was associated with an increased incidence of nervous system disorders. Overall, the most frequently reported TEAEs were somnolence (n = 17, 32%), headache (n = 11, 21%), and dizziness (n = 9, 17%), and most TEAEs were of mild or moderate intensity. There were no reports of suicidal ideation or behavior during the study. PK data indicated that mirogabalin was rapidly absorbed (t<sub>max</sub>, 1 hour) and rapidly eliminated (t<sub>1/2</sub>, 3-4 hours). Exposure appeared to increase proportionally as doses increased. Single-dose PK parameters were similar between ethnic groups. PD assessments
indicated changes in LARS scores consistent with increased somnolence and sedation with mirogabalin. No appreciable effects of mirogabalin were noted on POMS, DSST, VSS, or BARS scores.

**Conclusion**
Single-dose mirogabalin PK parameters are similar between Japanese subjects and other Asian subjects. Mirogabalin has an acceptable safety and tolerability profile in Japanese subjects at doses of up to 15 mg BID for 7 days. The most common TEAEs were consistent with the previous safety profile and known mechanism of action of mirogabalin. Currently, mirogabalin is being investigated for various pain indications both in the United States and Japan. Acknowledgements: Funded by Daiichi Sankyo Development, LTD. MJ, VD, SO, LJ, KB, and HI are/were employees of Daiichi Sankyo. VD and KB have stock ownership in Daiichi Sankyo.
Date: 09/29/2016 03:15:00 PM

**Title:** Pharmacokinetics And Safety Of A Single Oral Dose Of Mirogabalin In Japanese Patients With Varying Degrees Of Renal Impairment

**Poster Number** PTH213

**Authors**

Daiichi Sankyo Co., Ltd, Tokyo, Japan, Daiichi Sankyo Co., Ltd., Tokyo, Japan, Keikokai Medical Corporation P-One Clinic, Tokyo, Japan, Kasaoka Daiichi Hospital, Okayama, Japan, Daiichi Sankyo Co. Ltd., Tokyo, Japan

**Aim of Investigation**
Mirogabalin, a novel, preferentially selective α2δ-1 ligand, is in phase 3 development for the treatment of various neuropathic pain conditions, including diabetic peripheral neuropathic pain (DPNP) and post herpetic neuralgia. Mirogabalin is primarily excreted unchanged in urine. Because individuals with DPNP often have reduced renal function, it is imperative to determine the effect of renal impairment on mirogabalin pharmacokinetics (PK). In Caucasian subjects, increased mirogabalin exposure was observed with worsening renal function, leading to a dose adjustment in subjects with moderate or severe renal impairment. The current study aims to determine the effect of varying degrees of renal impairment on mirogabalin PK in Japanese subjects, which will guide dose recommendations in this ethnic group.

**Results**
Enrolled subjects (16 men; 14 women) were older adults (61.7-70.5 years), with body weight ranging from 59.5 to 69.3 kg. All 30 (6 per renal function category) subjects were available for PK and safety evaluation. For subjects with normal renal function, mild, moderate and severe impairment, and ESRD, median t<sub>max</sub> was 1.3, 2.0, 1.7, 2.0, and 4.0 hours, respectively. Based on the geometric least-squares (LS) mean ratio, in subjects with severe renal impairment and ESRD, C<sub>max</sub> values were 50% and 30% higher than those of subjects with normal renal function, respectively. C<sub>max</sub> was not notably different in the other categories compared with subjects with normal renal function. The AUC<sub>last</sub> increased with severity of renal impairment; the geometric LS mean ratios of AUC<sub>last</sub> in comparison with subjects with normal renal function were 1.3, 1.9, 3.6, and 5.3 for patients with mild, moderate, and severe impairment, and ESRD, respectively. In accordance with this AUC<sub>last</sub> increase, CL/F, CL<sub>R</sub>, and the cumulative percentage of mirogabalin dose excreted into urine were all found to decrease with severity.
of renal impairment. There were no deaths; no severe TEAEs, serious TEAEs, or TEAEs that led to study discontinuation were reported. The most frequently reported TEAEs were dizziness (ESRD, n = 3), somnolence (ESRD, n = 2), and vomiting (ESRD, n = 2). No notable changes were found in laboratory parameters or physical evaluations.

**Conclusion**

In Japanese subjects, mirogabalin exposure increased with worsening of renal function. These observations are consistent with those made in Caucasian subjects. Based on these data, a mirogabalin dose adjustment will be considered in Japanese subjects with moderate to severe renal impairment and ESRD. Administration of a single, oral, 5-mg mirogabalin tablet was considered well tolerated in Japanese subjects with normal renal function and mild to severe renal impairment.

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Title: PL37, A Dual Enkephalinase Inhibitor As A Novel Oral Treatment For Painful Diabetic Neuropathy (Pdn): A Randomised, Double-Blind, Placebo-Controlled Phase 2A Trial

Poster Number PTH214

Authors
M. Wurm, B. Frank, T. Ouimet

PHARMALEADS SA, PARIS, Other, The Walton Centre NHS Foundation Trust, Liverpool, UNITED KINGDOM, Phamaleads, PARIS, Other

Aim of Investigation
Neuropathic pain (NP), and more specifically painful diabetic neuropathy (PDN) is difficult to treat with no newly licensed oral medication in the last 15 years. Despite intensive drug development efforts, molecules with new mechanisms of action remain sparse despite strong demand to adequately manage this debilitating condition with a growing prevalence. PL37 is the most advanced compound of a novel pharmacological class, the Dual ENKephalinase Inhibitors (DENKI), which protect enkephalins from their rapid physiological degradation by the metalloenzymes neutral endopeptidase (NEP) and aminopeptidase N (APN), thereby prolonging the analgesic action of enkephalins. The aim of this ‘proof of concept’ study of PL37 was to assess the efficacy, safety and tolerability of PL37 in PDN insufficiently treated by pregabalin or gabapentin.

Results
Changes in mean pain intensity scores will only be available after database lock (June 2016), safety data already shows that the drug is safe and well tolerated. Results will be presented at the congress.

Conclusion
The analgesic effect of PL37 orally administered three times a day in addition to a stable dose of either pregabalin or gabapentin was investigated on a patient population suffering from PDN and the results of this international trial will be presented here for the first time. Currently available data on this phase 2a trial confirm that use of PL37 for the treatment of PDN is safe and causes no major side effects in patients insufficiently relieved by their gabapentin or pregabalin treatment.
Title: Sampling And Analysing Images From Corneal Confocal Microscopy

Poster Number PTH215

Authors

Danish Pain Research Center & Stereology and Electron Microscopy Laboratory, Aarhus, Aarhus, Danish Pain Research Center, Aarhus, Denmark, Aarhus University Hospital, Dept. of Neurology & Danish Pain Research Center, Aarhus, Denmark, Stereology and Electron Microscopy Laboratory, Aarhus, Denmark

Aim of Investigation
Corneal Confocal Microscopy (CCM) is a novel but established technique estimating the density of corneal nerves. The method potentially detects the presence and severity of neuropathy in patients with varying conditions. Cornea Nerve Fiber Length (CNFL, the total length of nerves mm⁻¹) is one of the most reliable CCM measures. However, the quality of the acquired images and the methods used to choose and analyze the images can significantly influence the outcome. Many studies use a subjective method to select 6-8 images, containing a) few nerve fibers, b) many nerve fibers, and c) representative images. In a series of pilot measurements, we tried four different ways to select images and got four widely different results where the patients were either within or outside normal range (ranging from 16.3 to 32.1 mm⁻¹ in the same patient). Therefore, it is pivotal to ensure the quality of current selection and analysis methods. The aim of this study is therefore to develop a minimally biased method to select images and to use mathematically well-defined principles to analyze nerve fibres, and compare the results with the current method.

Results
Mean UENS score was 13.2 (out of 42, ranging from 6-30). Mean IENFD was 5.48 (ranging from 0.31-11.6). Mean CNFL where images were selected using the traditional method was 13.7 mm⁻¹ (ranging from 3.05-20.1). After adjusting for area out of focus, mean CNFL using CC Metrics was 15.3 mm⁻¹ (ranging from 3.78-22.8mm⁻¹) and 14 mm⁻¹ using ACC Metrics (ranging from 3.65-19.7mm⁻¹). 1-way ANOVA testing revealed no difference between the different methods (p=0.14).

Conclusion
This study addresses the high risk of selection bias when selecting images for CCM analysis. The preliminary results of this study containing analysis from 14 idiopathic SFN with mild to moderate
symptoms of neuropathy do not reveal a significant change in CNFL when comparing current selection method to our new sampling and analysis method. We did, however, observe larger differences within some individual patients. Our sampling method may be less subjective and less biased compared to current methods. A direct sensitivity/specificity comparison between the methods in a larger cohort study is needed. The full analysis of all included patients in our database will be presented at the 16th World Congress on Pain.
Title: Immune Mechanisms Of Neuropathic Pain: Role Of Antibodies To Norepinephrine

Poster Number PTH216

Authors
M. Kukushkin, S. Igonkina, L. Vetrile

Institute of General Pathology and Pathophysiology, Moscow, Russian, N/A, Moscow, RUSSIA

Aim of Investigation
Noradrenergic descending inhibitory system plays an important role in the pathogenesis of neuropathic pain. Reuptake blockers of norepinephrine used for the treatment of neuropathic pain. Data on the participation of antibodies to neurotransmitter-norepinephrine in the pathogenesis of neuropathic pain are absent. The aim of the present study is to examine the role of antibodies to noradrenaline in immune mechanisms of neuropathic pain.

Results
The development of neuropathic pain syndrome in animals induces production of autoantibody to norepinephrine. Active immunization of animals with the conjugate of norepinephrine-protein leads strong production of antibodies to norepinephrine and also evokes amplification and prolongation of the pain syndrome.

Conclusion
Our data suggest that antibodies to norepinephrine are involved in immune mechanisms of the pathogenesis of neuropathic pain. Antibodies to norepinephrine have pronociceptive effect on neuropathic pain.
Title: Go-Sha-Jinki-Gan (GJG) Attenuated Allodynia Via Suppression Of The TNFα Derived From Microglia In Chronic Constriction Injury Model Mice

Poster Number PTH217

Authors

Department of Kampo Medicine, Osaka University Graduate School of Medicine, Osaka, Japan, Immunology Frontier Research Center, Osaka University, Laboratory of Brain-Immune Interaction, Osaka, Japan, Department of Pain Medicine, Osaka University Graduate School of Medicine, Osaka, Japan, Executive Vice President, Osaka University, Osaka, Japan

Aim of Investigation
Elderly patients in general indicate a higher incidence of chronic and neuropathic pain conditions. In the 15th World Congress on Pain, based on experiments in chronic constriction injury (CCI) model mice, we reported that the Japanese traditional herbal medicine Go-sha-jinki- gan (GJG) is a promising treatment for neuropathic pain of elderly patients. However, several problems still remain to be resolved regarding the molecular mechanism of the analgesic effect of GJG. Here, we focused on the effect of GJG on neuro-inflammation in neuropathic pain, in particular on its effects on the relationship between Iba1 (a marker for activated microglia) and TNFα in microglia of the spinal cord.

Results
GJG significantly reduced allodynia and hyperalgesia (von Frey test, p<0.0001; cold-plate test, p<0.0001; hot-plate test p<0.05; two-way repeated measures ANOVA). GJG showed analgesic effects in the early phase of neuropathic pain in CCI mice. IHC showed that GJG suppressed the number of activated microglia in the ipsilateral dorsal horn. Double IHC staining indicated that TNFα was expressed in Iba1-positive cells on day 3 post-operation. GJG significantly decreased the number of TNFα/Iba1 double positive cells in CCI mice (p<0.0001, one-way ANOVA). Western blot analysis showed that GJG decreased the expression levels of Iba1, TNFα, and p–p38 in the ipsilateral spinal cord of CCI mice. To confirm the relationship between GJG and TNFα in pain alleviation, we intrathecally injected (i.t.) TNFα into the GJG treated CCI mice. The cold threshold in CCI mice was significantly increased by GJG treatment (i.t. PBS CCI vs. i.t. PBS GJG-treated CCI, p<0.0001, one way ANOVA) and was decreased by TNFα treatment (i.t. PBS CCI vs. i.t. TNFα CCI, p=0.044). The analgesic effects of GJG were opposed by i.t. TNFα, and no
significant difference was observed between the cold threshold of the i.t. TNFα GJG-treated CCI group and that of the i.t. PBS CCI group (p=0.511, one way ANOVA). A synergistic interaction between GJG and TNFα in increasing neuropathic pain was observed (p=0.013, one way ANOVA).

**Conclusion**
We clearly demonstrated that GJG attenuated hyperalgesia and allodynia in CCI mice via suppression of the TNFα derived from microglia. GJG is thus a promising drug for the treatment of neuropathic pain induced by neuro-inflammation.
Title: Ema401, A Novel Angiotensin II Type 2 Receptor Antagonist For Treatment Of Peripheral Neuropathic Pain: Design Of Two Phase II Studies

Poster Number PTH218

Authors
T. Inamura, S. Pandhi, F. von Raison, A. Shah, G. Flesch, F. Callegari

Novartis Pharma K.K., Tokyo, Japan, Novartis Pharma AG, Basel, Switzerland, Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA

Aim of Investigation
Peripheral neuropathic pain (PNP), prevalent in 3–8% of the population, continues to be a major unmet medical need due to the limited efficacy and tolerability of the existing therapies. EMA401 is a first-in-class angiotensin II type 2 receptor (AT2R) antagonist, which acts on peripheral Angiotensin II/NGF/TRPV1-convergent pathways to reduce augmented neuropathic pain signaling. Evidence of its safety and analgesic action has been demonstrated in robust preclinical (e.g. diabetic neuropathy) and classical clinical models (e.g. post-herpetic neuralgia) of PNP. In a randomized, placebo-controlled, multicenter study, patients administered EMA401 (100mg p.o. b.i.d.) for 4 weeks reported significant improvement in pain intensity compared with placebo (ACTRN12611000822987). EMA401 was well-tolerated and central nervous system side effects such as somnolence or confusion (typically associated with existing therapies) were not observed in earlier clinical studies conducted in healthy participants or patients. Two Phase II studies are currently being designed to evaluate efficacy and safety of different doses of EMA401 in two PNP conditions.

Results
The study design of two phase II clinical trials will be presented at the congress.

Conclusion
New therapies effective in PNP are an important unmet medical need. Two multicenter, randomized, placebo-controlled, phase II studies will explore the potential of EMA401 in PNP. Future clinical development of EMA401 is targeted towards establishing EMA401 as a novel treatment option for PNP.
Title: Ema401, A Novel Angiotensin II Type 2 Receptor Antagonist, In Patients With Post-Herpetic Neuralgia: Subgroup Analysis From A Randomized Placebo-Controlled Trial

Poster Number PTH219

Authors
S. Pandhi, A. Shah, F. Callegari, A. Sarkar, T. Inamura, F. von Raison

Novartis Pharma AG, Basel, Switzerland, Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, Novartis Healthcare Pvt. Ltd., Hyderabad, India, Novartis Pharma K.K., Tokyo, Japan

Aim of Investigation
To analyze the impact of treatment with EMA401 on physical function and sleep in patients taking or not taking concomitant medications for post-herpetic neuralgia (PHN).

Results
A total of 183 patients were enrolled in the study. Baseline demographic data were comparable between both groups (mean age, EMA401 group: 62.5 years and placebo group: 63.4 years; Females, EMA401 group: 53.3% and placebo group: 56%). Of the total population, 41 patients in EMA401 group and 36 patients in placebo group were on concomitant medications for PHN. Overall, improvement in terms of physical function and sleep was observed in patients receiving EMA401 compared with placebo as assessed by the BPI and ISI respectively. The performance of EMA401 versus placebo as measured by the BPI and ISI is similar for both subgroups of patients taking or not taking any concomitant medications for PHN.

Conclusion
Treatment with EMA401 resulted in improvement in function and sleep of PHN patients, whether receiving concomitant medications for PHN or not.
Title: The Expression Of Sigma-1 Receptor In Dorsal Root Ganglia Neurons In Rats With Streptozotocin Induced Diabetic Neuropathy

Poster Number PTH220

Authors
S. Kostic, N. Filipovic, D. Sapunar

University of Split School of Medicine, Split, Croatia

Aim of Investigation
Sigma 1 receptor is a molecular chaperone found mainly in the endoplasmic reticulum and the plasma membrane of various tissues including the nervous system. It is activated under pathological conditions to modulate the function of ion channels and several neurotransmitters. Sigma 1 receptor has a role in central sensitization and pain hypersensitivity and it has been shown that σ1R antagonists effectively attenuate painful behavior in neuropathic and inflammatory pain models. Even though its role and distribution in DRG neurons has been studied in different pain models, to our knowledge the expression of sigma 1 receptor in neuronal population of rats with diabetic neuropathy has not been explored. In the present study, we aim to investigate the expression and distribution of sigma 1 receptor in sensory neurons in rats with streptozotocin induced diabetic neuropathy.

Results
DM1 animals developed hypersensitivity to both cold and heat, and the number of withdrawal responses to von Frey fibers, as well as the needle pin prick test on the 7th and 14th postinjection day was significantly increased, compared to control group. To investigate changes in DRGs and spinal cord dorsal horn caused by diabetes induction, immunofluorescence analysis of sigma-1 receptor will be performed, in neuronal groups characterized by expression of calcitonin gene-related peptide (CGRP), isolectin-B4 (IB4) and neurofilament-200 (NF-200). Our preliminary results showed a trend toward down-regulation of sigma 1 receptor in N52 positive and IB4 positive DRG neurons, two weeks in rats with diabetes, compared to control animals.

Conclusion
Our preliminary findings indicate decreased expression of sigma-1 receptor in specific types of DRG neurons of diabetic rats.
Date: 09/29/2016 03:15:00 PM

Title: Perineal Pain As A Predictor Of Depressive Symptoms Over The First Six-Month Postpartum

Poster Number PTH221

Authors

National Taiwan University (NTU) and NTU Hospital, Taipei, Taiwan, Central Taiwan University of Science and Technology, Taichung, Taiwan, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan, National Taiwan University Hospital, Taipei, Taiwan

Aim of Investigation
We investigated the association between pain and previous postnatal pain with depressive symptoms during the 6-month postpartum period.

Results
After adjusting for covariates, women who reported perineal pain at 4–6 weeks postpartum had an increased risk of concurrent depressive symptoms at 4–6 weeks postpartum compared to women without perineal pain (risk ratio [RR]: 1.9, 95% confidence limits [CL]: 1.2, 3.2); women who reported perineal pain at 4–6 weeks postpartum also had an increased risk of depressive symptoms at 6 months postpartum compared to women without perineal pain (RR: 1.9, 95% CL: 1.1, 3.3). Higher levels of perineal pain at 4–6 weeks postpartum was a significant predictor of depressive symptoms at 6 months postpartum (β= 0.63, p = 0.02); higher levels of any pain at 3–5 days postpartum was a significant predictor of depressive symptoms at 3 months postpartum (β= 0.31, p = 0.0498).

Conclusion
Our study provides robust evidence that perineal pain prevalence 4–6 weeks postpartum is associated with depressive symptoms at 4–6 weeks; the prevalence or severity of perineal pain 4–6 weeks postpartum predicts depressive symptoms at 6 months postpartum.
Title: Intravenous Dexamethasone As An Adjunct To Patient-Controlled Epidural Analgesia With Levobupivacaine And Fentanyl In Labor: A Randomized, Double Blind, Placebo Controlled Study

Poster Number PTH222

Authors
S. Mitra, P. Dube, J. Singh, R. Saroa, R. Mehra

Government Medical College & Hospital, Chandigarh, India

Aim of Investigation
To assess the effect of intravenous dexamethasone vis-à-vis saline (as placebo) in reducing the hourly average consumption of epidural levobupivacaine and fentanyl mixture in laboring parturients.

Results
Hourly drug consumption was significantly lower in the Dexamethasone Group than Placebo Group (10.34 ml±1.79 vs. 11.34±1.83, p<0.05). Dexamethasone Group also required significantly less number of bolus doses than the Placebo Group. There were no other significant differences between different outcome measures within the two groups.

Conclusion
Intravenous administration of 8mg of dexamethasone significantly decreased hourly average drug consumption and the number of boluses through the epidural route, thus providing the epidural drug dose sparing effect.
Title: Labor Pain Exceeds The Worst Imaginable Before Labor Onset

Poster Number PTH223

Authors
Y. Iizuka, Y. Nakajima, N. Masaoka, K. Ohashi
Graduate School of Medicine, Osaka University, Suita, Osaka, Japan, Tokyo Women’s Medical University
Yachiyo Medical Center, Yachiyo, Chiba, Japan, Tokyo Women’s Medical University Yachiyo Medical Center, Yachiyo, Chiba, Graduate School of Medicine, Osaka University, Suita, Osaka

Aim of Investigation
After the onset of labor, the labor pain increases in intensity and frequency. However, the change of its intensity during labor remains unclear. Some previous studies were conducted retrospectively, and the other studies used a small number of assessments during labor. In this study, we prospectively examined the intensity of labor pain every hour from the onset to the end of labor every hour.

Results
Of 33 participants, only the NRS 0-10 were used in 8 cases (the first study) and two scales were used in 25 cases (the second study). The assessment started from the period with up to 5cm of cervical dilation which deems the end of the latent phase. All participants did not receive obstetrical analgesia and anesthesia. The mean age of participants was 32.3 years (SD=5.2) and 22 were primiparae. The mean duration of labor was 10.8 hours (SD=6.1). The time duration between the start of measure and delivery was 6.3 hours (SD=5.3). In the first study, the mean intensity of labor pain at the starting point was 6.9 (5.0-9.0), and that at the maximum point was 9.9 (9.0-10.0). Of 8 participants, 5 showed the score of 10 before the full dilation of cervix and indicated score of 10 during the remaining first stage. The intensity of labor pain was immediately declined to 2.3 (1.0-6.0) after delivery. These results indicated that the NRS 0-10 was not suitable for assessing the intensity of labor during the first stage so that we conducted the second study. In the second study, the mean intensity of labor pain at the starting point was 6.4 (3.0-10.0) and that at the maximum point was 15.0 (9.0-20.0). The intensity of labor pain was immediately declined to 3.1 (0.0-8.0) after delivery. Of 25 participants, 16 indicated scores of 10 or more.

Conclusion
The NRS 0-10 was a common tool to assess the intensity of labor pain in the previous prospective study,
but could not assess it accurately. Of 33 pregnant mothers, 21 (63.6%) experienced severe labor pain scored 10 (Worst Pain Imaginable) or more during the first stage of labor, suggesting that women in labor might overcome strong and repeated labor pain which they could not image at the onset of labor.
Title: A Comparative Study Of Intramuscular Acetaminophen Versus Intramuscular Pentazocine As Labour Analgesia In Zaria, North Western Nigeria

Poster Number PTH224

Authors
J. Ekweani, A. Adesiyun, E. Ogboli Nwasor, S. Avidime

Ahmadu Bello University Teaching Hospital, Zaria, Kaduna State

Aim of Investigation
To compare the efficacy of intramuscular acetaminophen versus intramuscular pentazocine on women in labour as well as the effects of both drugs on APGAR scores of their newborn.

Results
The mean age was 28.1 years ± SD 5.2 years. The majority of the subjects (53.5%) were Hausa-Fulani and 70.1% were Muslims; 64% were booked for antenatal care while 58.5% had received secondary school education. The average duration of labour was 5.4 hours. Acetaminophen was administered to 91 (48%) subjects while pentazocine was administered to 97 (52%). Sixty-nine percent and 80% experienced adequate pain relief in the acetaminophen and pentazocine groups respectively at one hour. The pain scores was statistically significant at one hour but comparable in both groups afterwards: p=0.01, 0.52, 0.338 and 0.389 at 1st, 2nd, 3rd and 4th hours on the linear/visual analogue scale and comparable on the verbal rating scale. There was no difference in the 1st and 5th minute APGAR scores of the babies delivered (p=0.24 and 0.63 respectively). Patients’ satisfaction was comparable but the pentazocine group experienced more side effects.

Conclusion
Intramuscular acetaminophen gave comparable labour analgesia with fewer side effects when compared with pentazocine.
Title: A Comparative Study Of Continuous Infusion Of Combination Of Fentanyl Citrate With Bupivacaine Hydrochloride, Levobupivacaine Hydrochloride, And Ropivacaine Hydrochloride For Labour Epidural Analgesia

Poster Number PTH225

Authors
P. Jain, R. Sharma, A. Gupta, J. SOOD

Sir Ganga Ram Hospital, New Delhi, India, Sir Ganga Ram Hospital, New Delhi, India, New Delhi, -- SELECT --

Aim of Investigation
To compare continuous epidural infusion of combination of fentanyl citrate with bupivacaine hydrochloride, levobupivacaine hydrochloride and ropivacaine hydrochloride in labour analgesia with respect to: • Analgesic efficacy • Degree of motor blockade • Mode of delivery • Patient satisfaction

Results
NRS scores were comparable among all the three groups. The degree of motor blockade by modified Bromage score was statistically significant with levobupivacaine and ropivacaine group as compare to bupivacaine group at 60, 90 and 120 minutes The patient satisfaction score was comparable in all the three groups There was no statistically significant difference in the mode of delivery between 3 groups.

Conclusion
Motor blockade with levobupivacaine and ropivacaine was significantly less than bupivacaine while maintaining the analgesic potency.
Title: Cdk5 Modulates Functional Responses Of Trpa1

Poster Number PTH226

Authors

National Institute of Dental and Craniofacial Research, Bethesda, MD, University of Maryland School of Dentistry, Baltimore, MD

Aim of Investigation
TRPA1 is a polymodal transient receptor potential channel that is one of the key receptors in nociceptive signaling. TRPA1 is involved in mechano- and chemo-sensations, and its function is affected by different kinases. Cyclin-dependent kinase 5 (Cdk5) is a serine/threonine kinase whose activity plays an important role in regulating nociceptive signaling and in mediating inflammatory hyperalgesia. We have previously reported that Cdk5 is able to phosphorylate the TRPV1 channel, which in turn influences thermal nociception. However, the role of Cdk5 in modulating TRPA1 responses is not known. The aim of the current study was to identify the precise role of Cdk5 in TRPA1 modulation of orofacial nociception and agonist-induced responses.

Results
In response to different concentrations of mustard oil, transgenic mice with either increased or reduced Cdk5 activity showed opposite responses, demonstrating that Cdk5 activity modulates aversion to this TRPA1 agonist. Mice with increased Cdk5 activity displayed reduced consumption of water containing mustard oil, suggesting greater aversive behavior than wild type animals. In contrast, mice with reduced Cdk5 activity displayed enhanced consumption of water containing mustard oil, suggesting decreased aversion. In dissociated trigeminal ganglia neurons, the percentage of responding neurons to low doses of mustard oil was greater in neurons from p35 overexpressing mice than from wild type. Conversely, sensory neurons from p35 knockout mice showed a smaller percentage of responders to mustard oil than wild type.

Conclusion
We present behavioral and cellular data indicating that Cdk5 modulates functions of TRPA1. Increased or decreased Cdk5 activity in genetically engineered mice substantially influence TRPA1-mediated avoidance behavior. Calcium imaging analysis using dissociated trigeminal ganglia neurons showed that...
p35 levels are crucial for receptor sensitivity and kinetics. Acknowledgments: This work was supported by the Division of Intramural Research, National Institute of Dental and Craniofacial Research, National Institutes of Health (A.B.K.) and NIH grant R01 DE023846 (M.K.C.)
Title: Pain And Immunological Changes In Trigeminal Neuralgia And Trigeminal Neuropathic Syndrome

Poster Number PTH227

Authors
V. Fedirko, I. Vasileva, M. Lisjany

Romodanov Institute of Neurosurgery, Kyev, Ukraine, Romodanov Institute of Neurosurgery, Kyev, --

Aim of Investigation
Though neurovascular compression and focal nerve root demielination are accepted generally as the cause of Trigeminal Neuralgia (TN) development, there are no explanation why they manifests, have remissions and recurrences in existing neurovascular compression. Trigeminal Neuropathic Pain (TNP) someone estimates like atypical TN and there is no explanation of its etiology and pathogenesis.

Results
HV were revealed in 932(74%) from 1260 investigated patients. Autoimmune changes including increase of myelin basic protein (MBP) induced proliferation (RBTL) and anti MBP-autoantibody level was registered in 579(89%) from 650. Immune correction and antiviral treatment leads to pain decrease in 65% totally. MVD resolved pain in TN cases in 96% postoperatively. Combined MVD and immune correction improved follow up results in TN group up to 89%.

Conclusion
Pain manifestation or recurrences in both TN and TNP cases depends on immunological status and herpes viruses activation. Immune changes correction and antiviral treatment lead to the pain regress. Symptoms of TN develops due to vascular compression of nerve root and autoimmune changes in the presence of HV reactivation. MD and antiviral treatment resolves pain in TN.
Date: 09/29/2016 09:30:00 AM

**Title:** The Role Of Comorbidities In Neuropathic Orofacial Pain: Sensory Evidences

**Poster Number** PTH228

**Authors**

Pain Center Dept of Neurology of Clinics Hospital of Medicine School of USP, Sao Paulo, Sao Paulo, Pain Center Dept of Neurology of Clinics Hospital of Medicine School of USP, São Paulo, BRAZIL, McGill University, Montreal, QC, Hospital da Clínicas - FMUSP, Sao Paulo, BRAZIL, University of São Paulo School of Medicine, Sao Paulo, BRAZIL, University of Sao Paulo, Sao Paulo, Brazil

**Aim of Investigation**
Comorbidities can present influence in local conditions. In general, there are inflammatory mechanisms underlying them. The objective of this study was to investigate sensory abnormalities in neuropathic orofacial pain and their association with comorbidities.

**Results**
The evaluation of cold detection threshold (CDT) was positive correlated with the presence of neurologic disease (rho=0.197 p=0.001), inflammatory diseases of the upper and lower airways (rho=0.142 p=0.018) that is an increase of CDT in the presence of both comorbidities and a decrease of CDT with systemic osteoarthrosis (SO)(rho=-0.140 p=0.02). Independent mixed model measure analysis for CDT revealed significant main effect for VAS (F1,267=8.30, raw p=0.004), age (F1,271=50.25, raw p=<0.0001), orofacial pain(F1,255=9.96, raw p=0.001), SO (F1,264=6.35, raw p=0.012) and no difference for gender (F1,271=0.56, raw p=0.45), BMI (F1,259=0.09, raw p=0.77), inflammatory diseases of the upper and lower airways (F1,264=1.92, raw p=0.16), neurologic disease (F1,264=0.00, raw p=0.96). Warm detection threshold (WDT) increase in the presence of inflammatory diseases of the upper and lower airways (rho=0.168 p=0.005) and the opposite happens with SO (rho=-0.155 p=0.009). The mixed model for WDT revealed significant main effect of VAS (F1,270=4.79 raw p=0.02), age (F1,274=15.83, raw p<0.0001), orofacial pain (F1,255=5.08, raw p=0.02), BMI(F1,255=9.36, raw p=0.002), SO (F1,255=5.9, raw p=0.01), inflammatory diseases of the upper and lower airways (F1,255=9.05, raw p=0.002).

**Conclusion**
In conclusion, systemic osteoarthrosis seems to have an influence on CDT and WDT and inflammatory diseases of the upper and lower airways appears to affect WDT. Thus, reinforce the philosophy that is
necessary a global approach of the patient. Not only local but also systemic comorbidities must be taken into account in the assessment and treatment of neuropathic orofacial pain.
Title: Effect Of 8% Lidocaine Application To The Face And Hand Skin On Tactile Sensory And Pain Thresholds

Poster Number PTH229

Authors

Nagasaki University, Nagasaki, Japan, Nihon University, Matsudo, JAPAN, KU Leuven, Leuven, BELGIUM

Aim of Investigation
The aim of the present study was to examine the effect of 8% lidocaine applied to the face and hand skin on tactile sensory and pain thresholds of symptom-free men and women.

Results
All TDT increased after application of both LDC and SAL, and significant LDC effects on the TDT were not found. All FPT increased after application of LDC, but the FTP at the CS of men and at both the CS and TS in women, decreased after application of SAL. Significant LDC effects on the FPT were found in men's CS (P < 0.01) and women's TS (P < 0.01).

Conclusion
The increase of TDT and the decrease of FPT found in this study are considered to illustrate habituation and sensitization, respectively. Application of LDC affected sensitization more than habituation, indicating its effect of pain control in the skin.
Title: Perceptual Distortion Of The Tongue Evoked By Lingual Nerve Block And Topical Application Of Capsaicin In Healthy Participants

Poster Number PTH230

Authors
M. Honda, L. Baad-Hansen, O. Komiyama, T. Iida, M. Kawara, P. Svensson

Nihon University, Matsudo, JAPAN, Aarhus University, Aarhus, DENMARK

Aim of Investigation
Patients with burning mouth syndrome (BMS) may occasionally report that the painful tongue feels swollen and differently although clinical inspection does not reveal abnormalities. Perceptual distortion may be an important phenomenon to consider in persistent orofacial pain conditions. The aim of this study was to test if reports of perceptual distortion could be evoked in healthy participants by transient deafferentation (lingual nerve block) and burning pain (topical capsaicin).

Results
In the lingual nerve block session, MDT at the tongue at 5 min up to 1 h was significantly higher than baseline (P < 0.001). Perceived size of the tongue from the template matching procedure at 5 min (P < 0.05), 15 min (P < 0.001), 30 min (P < 0.01), and 1 h (P < 0.01) were significantly higher than baseline in the lingual nerve block session. Perceived size of the tongue from the NRS scores at 5 min (P < 0.01), 15 min (P < 0.001), 30 min (P < 0.001), and 1 h (P < 0.001) were also significantly higher than baseline values in the lingual nerve block session. There were no significant effects on MDT and perceptual distortion estimates at any time points for the lower lip, lower front teeth or right thumb in the lingual nerve block session. In the capsaicin session, although the perceived size from the NRS scores at the lip at 5 min was significantly higher than baseline (P < 0.001), there were no significant effects on MDT or perceived sizes for the tongue, lower front teeth or right thumb at any time points. In the control session, neither MDT nor perceived sizes changed significantly over the 3 h period for any of the four areas.

Conclusion
The present results suggest that lingual nerve block evoked perceptual distortions of the tongue whereas capsaicin-evoked pain did not. Perceptual distortions of the tongue may be influenced by
somatosensory changes rather than nociceptive activity. Further studies on perceptual distortion phenomena in BMS patients may be warranted.
**Title:** Erk Phosphorylation In Medulla And Upper Cervical Cord Neurons Projecting To Thalamus And Parabrachial Nucleus In Rats

**Poster Number** PTH231

**Authors**
H. SAITO, A. Katagiri, N. Gionhaku, K. Iwata

Nihon University School of Dentistry, Tokyo, Chiyoda-ku, Nihon Univ. Sch. of Dentistry Dept. of Physiology, Chiyoda-ku, TOKYO, Nihon University School of Dentistry, Tokyo, Japan, Nihon Univ. Sch. of Dentistry Dept. of Physiology, Chiyoda-ku, Tokyo

**Aim of Investigation**
Three distinct ascending pathways from the trigeminal spinal subnucleus interpolaris/caudalis (Vi/Vc) transition zone and upper cervical spinal cord (C1-2) to the ventral posteromedial thalamic nucleus (VPM) and medial thalamic nuclei (mediodorsal, posteriormedian, centrolateral, centromedial and parafascicular thalamic nuclei) and parabrachial nucleus (PBN) are known to be involved in orofacial nociception. To evaluate functional significance of projection neurons regarding orofacial nociception, we studied distribution pattern of Vc and C1 projection neurons expressing phosphorylated extracellular signal-regulated kinase (pERK) and Neurokinin 1 receptor (NK1) in rats.

**Results**
The number of NK1-IR and pERK-IR neurons was larger in PBN projection neurons than VPM and medial thalamus. pERK- and NK1-IR VPM projection neurons were mainly distributed in the middle Vc, few medial thalamus projection neurons showed pERK- and NK1-IR, and pERK- and NK1-IR PBN projection neurons were observed from mid-Vc to Vc/C1-2.

**Conclusion**
Percentage of pERK- and NK1-IR projection neurons sending axons to these regions was approximately 10%, suggesting that the majority of nociceptive neurons receiving C-fiber afferents might be classified as interneurons. Furthermore, the rostro-caudal distribution differences of pERK- and NK1-IR projection neurons in Vi/Vc and Vc/C1-2 may reflect functional differences between 3 projection areas regarding orofacial pain.
Title: Altered In Vitro Production Of Cytokines In Temporomandibular Disorder (Tmd)

Poster Number PTH232

Authors
C. King, M. Ribeiro-Dasilva, S. Wallet, R. Fillingim

Cincinnati Children’s Hospital Medical Center (CCHMC), Cincinnati, OH, University of Florida, Gainesville, FL

Aim of Investigation
Case-control differences in inflammation have been reported in several chronic pain conditions including Temporomandibular Disorder (TMD). These studies have shown a heightened pro-inflammatory profile at rest and following a painful stressor, which suggests that these conditions could be associated with augmented inflammatory tone. Research is needed to evaluate the mechanisms underlying these observations, which could be due to a heightened reactivity of peripheral immune cells (e.g., monocytes) and the regulation of cytokine production in these immune cells through glucocorticoid signaling. Thus, the current study tested the hypothesis that individuals with TMD would show a) a greater production of cytokines from isolated monocytes following exposure to lipopolysaccharide (LPS, a bacterial endotoxin) and b) a reduced inhibition of LPS-induced cytokine production by glucocorticoids compared to controls. Exploratory analysis of the associations between immunological variables and clinical outcomes were also conducted.

Results
Compared to controls, isolated monocytes from TMD cases exhibited a greater production of TNFα, IL-6, and IL-1β (pro-inflammatory cytokines) but a blunted production of IL-10 (anti-inflammatory cytokine) following exposure to LPS. Additionally, isolated monocytes from TMD cases were less sensitive (e.g., required slightly higher levels of glucocorticoids to inhibit LPS-induced cytokine production) to the suppress effect of glucocorticoids. Associations between immunological variables were mixed whereby higher GCPS scores were associated with a) cytokine production (higher levels of IL-1β; lower levels of IL-10) following LPS and b) cytokine production following a co-incubation of LPS and DEX (higher levels of TNFα, IL-6, and IL-1β across different doses of DEX).

Conclusion
The current study suggests that the innate immune system could be 'primed' in TMD patients. Further
studies are needed to replicate this finding in larger cohort in addition to determining relationships with potential biological and psychological factors.
Title: Management Of A Case Of Rare Orofacial Syndrome For Pain Management

Poster Number PTH233

Authors
T. DOCTOR, D. shah
B.J.MEDICAL COLLEGE, AHMEDABAD, GUJARAT, INDIA, Gandhinagar, GUJARAT, B.J.MEDICAL COLLEGE, AHMEDABAD, GUJARAT, INDIA, Ahmedbad, Gujarat

Aim of Investigation
To relieve the constant mastication movement and provide pain relief

Results
After performing the diagnostic block with Inj.Bupivacaine 0.25% on Right side face for Mandibular branch of Trigeminal Nerve, patient had only 5-10 frequency of movement of Jaw so the therapeutic block was planned and performed with Inj.Phenol 6% with inj.Bupivacaine 0.125% under guidance on next day which resulted in complete relief of pain symptoms and improvement in function. Pt was able to eat, drink and sleep well. Pt was put on tablet carbamazepine, anticonvulsant, antidepressants, vitamins and rehabilitation therapy. Patient recovered completely and able to work, eat etc...

Conclusion
Proper investigations, modalities of treatment can treat the rare syndromes like Tardev's disease? with oro facial manifestations. Patient is able to live nearly normal life with symptomatic relief and functional improvement. Multi modality of pain management treatment made the successful attempt to treat the challenging rare disease.
Title: Burning Mouth Syndrome Patients’ Pain Modulation Profile

Poster Number PTH234

Authors

Rutgers School of Dental Medicine, Newark, NJ, University of Rochester Medical Center, Rochester, NY

Aim of Investigation
To assess the Pain Modulatory System of patients suffering from Burning Mouth Syndrome (BMS).

Results
MTS and HS CPM induced by hand immersion to water bath at 46.5 °C as a 'conditioning stimulus' was significantly lower in BMS patients compared to controls (P ≤ 0.05). No significance differences between BMS and healthy controls were found in MTS and HS CPM induced by hand immersion to water bath at 37°C.

Conclusion
This preliminary study suggests that Burning Mouth Syndrome patients present less efficient modulation of pain compared to healthy controls.
Aim of Investigation

Painful conditions are usually defined based on the anatomical location of the pain (e.g., back pain versus temporomandibular disorder [TMD]), which does not consider etiology. Recently, we developed a classification system for pain based on an array of biopsychosocial risk factors that identified three clusters of individuals, which we called the adaptive cluster (AC), the pain-sensitive cluster (PSC), and the global symptoms cluster (GSC). Individuals in the PSC had had greater sensitivity to experimental pain than individuals in the AC, and individuals in the GSC had greater pain sensitivity compared to individuals in the AC and greater psychological distress compared to individuals in the other two clusters. Individuals in the PSC and GSC had higher odds of chronic TMD, while initially TMD-free individuals in the GSC had greater risk of developing first-onset TMD relative to other clusters. However, the stability of these clusters over time is currently unknown. The purposes of the present study are (1) to investigate changes in cluster classification at three time points in a cohort of initially TMD-free individuals, and (2) to evaluate the association between TMD and cluster classification and determine if this association varies over time.

Results

Overall 60.3% of study participants were classified to the same cluster at V2 as they were at V1, and 62.9% were assigned to the same cluster at V3 as they were at V2. When individuals developed first-onset TMD,
onset TMD, they were more likely than controls to transition to (or remain in) the PSC or GSC. Among incident TMD cases in the GSC at V1, 78.8% remained in the GSC at V2. In contrast, among incident TMD cases in the PSC at V1, 43.4% transitioned to the GSC, 49.1% remained in the PSC, and only 7.5% transitioned to the AC at V2. Similarly, among incident cases in the AC at V1, 46% remained in the AC, 28% transitioned to the PSC, and 26% transitioned to the GSC at V2. Participants who developed first-onset TMD were more likely than controls to belong to the GSC at V1 (Chi-square, p=0.002), and they were more likely than controls to belong to either the PSC or GSC at both V2 and V3 (Chi-square, p<0.0001). However, there were no significant differences between the proportions of persistent and transient cases in each cluster at any of the three time points.

**Conclusion**

Most participants remained in the same cluster over the course of the study. However, participants who developed first-onset TMD were more likely to transition to clusters associated with greater experimental pain sensitivity and psychological distress. Controls were less likely to belong to the PSC and GSC. No differences between persistent and transient cases were observed with respect to cluster membership at any of the three time points.
Title: Effect Of Lidocaine On Tonic And Frequency-Dependent Block Of Action Potential Propagation In Peripheral Sensory Axons

Poster Number PTH236

Authors
A. Minocha, M. AlQatari, M. Koltzenburg

University College London, London, United Kingdom

Aim of Investigation
Local anaesthetic drugs such as the prototypical lidocaine can modulate the excitability of neurons with different potencies depending on resting membrane potential and firing frequency of a cell. This is often referred to as (1) state-dependent block, (depending on the polarization of the resting membrane potential), (2) frequency-dependent block (at physiological activation rates) and (3) tonic block (at low rates of neuronal activation). In heterologous expression systems local anaesthetic drugs profoundly depress currents in all isoforms of voltage gated sodium channels (VGSC) at frequencies as low as 5 to 10 Hz. The aim of this study was to investigate how these clear biophysical findings translate to the effects on action potential propagation in situ.

Results
Tonic block of sensory fibres increased with greater concentrations of lidocaine. At low stimulus frequencies there was no or little block at 100 μM and the block was always complete at 3000 μM. Increases of exposure length from 5 to 20 mm had only small effects on the dose response relationship for a tonic block. At a constant exposure length of 7 mm and 500 impulses there was no drop of amplitude at 0.25 or 20 Hz with SIF. Furthermore, there was only a very small change in the dose response function of lidocaine over this range of stimulation. The IC<sub>50</sub> was 468 ± 27 at 0.25 Hz and 417 ± 13 at 20 Hz. In the absence of drug a significant effect on the CAP was only observed at frequencies above 100 Hz. At 200 Hz there was a drop by 21 ± 6% which occurred mainly within the first ten stimuli. In the presence of lidocaine there was a further drop and compared to 0.25 Hz stimulation there was a leftward shift of the dose response function and a reduction of approximately 50% of the IC<sub>50</sub>.

Conclusion
Local anaesthetic drugs do not significantly impair action potential propagation in myelinated sensory
fibres at physiological firing rates and drug concentration that show profound use-dependent reduction of sodium currents in heterologous expression systems. Exposure length beyond 5 mm has little effect on the tonic blockade of action potential propagation. This indicates that in the peripheral nerve high exposure of sodium channel blockers need to be achieved over a short exposure distance to significantly affect signalling between peripheral terminals and their central connections.
Title: Ongoing Oral Pain Model Of Burning Mouth Syndrome: Relationship To Pain Catastrophizing

Poster Number PTH237

Authors
J. Payano Sosa, S. Burrowes, M. Rangel, S. Khan, T. Meiller, D. Seminowicz

University of Maryland Baltimore, Owings Mills, MD, University of Maryland, Baltimore, Baltimore, MD, University of Maryland Baltimore School of Dentistry, Baltimore, MD, University of Maryland, Baltimore, MD

Aim of Investigation
Burning mouth syndrome (BMS) is a chronic neuropathic pain condition that is most prevalent in postmenopausal women. It is characterized by a burning sensation in the superficial oral mucosa, with no clinically evident lesions. BMS patients have described similarities in their ongoing burning pain and the burning experienced when the oral mucosa is exposed to TRPV1 agonist, capsaicin. As there are no current BMS pain models in the literature, this project aims to (1) create a novel model of BMS pain in healthy controls through the use of oral capsaicin to safely induce the burning sensations experienced in BMS patients and (2) study the impact of pain catastrophizing on ongoing oral pain. We hypothesized that our BMS model (1) would mimic a neuropathic pain sensation in healthy controls and (2) that greater pain intensity and unpleasantness would be associated with increased pain catastrophizing.

Results
In cohort 2, pain catastrophizing was negatively correlated to burning intensity among BMS subjects, though the average burning intensity ratings were sustained above a 7.3 and burning unpleasantness above 6.9 across oral capsaicin trials. This was particularly significant in the rumination scale score correlation with burning intensity and unpleasantness. Although capsaicin triggers a similar burning state as BMS exposure to capsaicin, we observed that capsaicin triggers lower responses in healthy subjects' burning intensity (average 4.1) and unpleasantness (average 3.8) in cohort 2 when compared to BMS subjects in cohort 1. In addition, in healthy subjects, PCS was negatively correlated with burning intensity and unpleasantness in cohort 1 as was seen in cohort 2.

Conclusion
The negative relationship between PCS and oral capsaicin burning intensity and unpleasantness ratings seems reliable, despite the small sample size. This negative relationship might be due to an anticipatory
effect whereby a BMS subject with a high PCS score (an amplified reaction to pain) expected burning pain of a higher degree than what was actually experienced. This might be explained by a dynamic alteration of pain perception over time in BMS, where the maximum pain perceived in the lifetime of the individual is redefined as this chronic burning sensation BMS subjects experience daily. Another explanation could be that those with higher PCS scores are more familiar with pain and therefore might have developed better strategies for coping with it. To mimic a BMS subjects' response we will need to determine how to sustain the burning sensation across trials as seen in BMS subjects. While burning pain of reasonable intensity did last for up to 10 minutes in healthy subjects, the data suggests that the sensations were only maintained during the oral capsaicin application window itself. This oral pain model where the oral pain experience is sustained across trials in healthy subjects will lay the groundwork for understanding induction of BMS.


**Title:** Psychiatric Comorbidities In Patients With Atypical Odontalgia

**Poster Number** PTH238

**Authors**

Graduate School of Tokyo Medical and Dental University, Tokyo, Japan, Tokyo Medical and Dental University Hospital, Tokyo, Japan

**Aim of Investigation**
Atypical odontalgia (AO) is a condition characterized by tooth pain or pain at the site of tooth extraction with no apparent radiographic or tooth pathology. Although in many cases of AO regard as 'psychogenic', there are many unclear points about the association between pain and psychiatric diseases. The aim of this study was to investigate the clinical features and the association between pain and psychiatric disorders in AO.

**Results**
Our study included 325 patients (48 men, 277 women; mean age of onset was 53.58±13.78 years). 121 of 325 patients had a history of psychiatric disorders; forty-nine patients with depression, forty-one with anxiety disorder, twelve with somatoform disorder, ten with insomnia, ten with bipolar disorder, four with schizophrenia, a patient with personality disorder, a patient with eating disorder. (Some cases were overlapped.) 72 of 121 patients with psychiatric disorders had headaches. There were no significant gender differences of headaches in patients who had comorbidities of psychiatric disorders. 90 of 325 patients had comorbidities of oral psychosomatic disorders; seventy-one patients with burning mouth syndrome, seventeen with oral cesthespathy, ten with phantom bite syndrome, four with temporomandibular joint disorder and two with halitophobia. Female patients had more comorbidities of oral psychosomatic disorders except of AO, and it is statistically significant. (χ² =4.833, df=1, p=0.028<.05) There were no significant differences between patients who had comorbidities of psychiatric disorders and patients with oral psychosomatic disorders except of AO.

**Conclusion**
38.5 % (121/325) had psychiatric disorders and 27.7 % (90/325) had comorbidities of oral psychosomatic disorders in AO. There were no correlation between AO and headaches in this study.
Title: Spatial And Temporal Brain Responses To Noxious Heat Thermal Stimuli In Burning Mouth Syndrome

Poster Number: PTH239

Authors:
T. Shinozaki, Y. Imamura, K. Iwata, A. Okada-Ogawa, N. Noma

Nihon University, chiyodaku, Japan, N/A, Tokyo, JAPAN, Nihon Univ. Sch. of Dentistry Dept. of Physiology, Chiyoda-ku, Tokyo, Nihon Univ. Sch. of Dentistry Dept. of Oral Diagnostic Sci, Chiyoda-ku, Tokyo, Nihon Univ. Sch. of Dentistry Dept. of Oral Diagnostic Sci, Chiyoda-ku, Tokyo

Aim of Investigation
Burning mouth syndrome (BMS) is an idiopathic orofacial pain condition. Although the pathophysiology of BMS is not clearly understood, central and peripheral neuropathic mechanisms are thought to be involved. We compared brain response to noxious heat stimuli in 16 right-handed women with primary BMS and 15 sex- and age-matched right-handed healthy female controls.

Results
result1 Overall brain activity evoked by noxious heat Brain activity was more significantly facilitated in BMS patients than in controls, although there were no significant differences in perceived pain intensity between both groups. BMS patients showed an excessive brain activity during the palm stimulation and the entire brain areas were shown to be activated as a cluster. Subtraction of brain activity in controls from that in BMS patients showed more significantly activated areas in BMS patients, which included left S2 cortex, left dorsolateral prefrontal cortex (dIPFC), left insula, left visual cortex (VC), right posterior cingulate cortex (PCC), hippocampus, parahippocampal gyrus, and cerebellum during the palm stimulation. Further, noxious stimulation of the lip led to a significantly greater activation in left premotor cortex (PMC), left orbitofrontal cortex (OFC), bilateral medial prefrontal cortex (mPFC), left dIPFC, left anterior cingulate cortex (ACC), left insula, bilateral VC, left caudate nucleus, and midbrain in BMS patients.

result2 Time dependent changes in brain activity there was a significant correlation between the temporal changes in pain ratings and the increase in brain activity at the bilateral parahippocampus during repetition of the thermal stimulus sequence at the palm in BMS patients. Contrarily, there was a significant correlation between the changes in pain perception and reduction in brain activity at the parahippocampus and right temporal pole when the thermal stimuli were repeatedly applied at the palm in controls.
Conclusion
An fMRI study with a psychophysical test of BMS patients and pain-free controls revealed pathophysiological changes in brain activity in BMS patients. Specific brain responses in BMS patients to repetition (1st to 4th) of thermal sequence (warm and noxious heat stimuli) probably reflect BMS pathophysiology. Repetitive tonic heat stimulus revealed involvement of both the central and peripheral nervous systems. The cingulate cortex (ACC, MCC, and PCC) appeared to be specifically involved in trigeminal pain processing/modulation in BMS patients.
Title: Temporomandibular Disorders Examined With A Multidisciplinary Approach: A Case-Control Study

Poster Number PTH240

Authors
S. Kvinnsland, E. Helgeland, L. Willassen, K. Staniszewski, T. Berge, A. Johansson, B. Schjødt, R. Bell, A. Paulsberg, J. Geitung

Department of Clinical Dentistry, University of Bergen, Bergen, Norway, Department of Oral and Maxillofacial Surgery, Haukeland University Hospital, University of Bergen, Bergen, Norway, Centre for Pain Management and Palliative Care, Haukeland University Hospital, Bergen, Norway, Department of Radiology, Akershus University Hospital, University of Oslo, Oslo, Norway, Department of Radiology, Haraldsplass Deaconess University Hospital, Bergen, Norway

Aim of Investigation
Aims of Investigation Temporomandibular disorder (TMD) involves muscles and joint derangement (TMJD). The symptoms include jaw dysfunction and moderate to severe pain. A control group was recruited to be compared with the patients evaluated in the Norwegian Ministry of Health project on multidisciplinary investigation of TMD/TMJD patients (N=60).

Results
Results Thirty eight healthy individuals have been examined to date. The mean age in the control group was 45.5 years and consisted of 40 women and 5 men. The TMD group with 60 patients had a mean age of 45 years and consisted of 51 women and 9 men. Preliminary results comparing the control group with the TMD group indicate that jaw function is significantly better in controls, including clinical parameters. The TMD group had lower maximum opening capacity (p<0.0001), higher tenderness to palpation over TMJ (p<0.05) and masticatory muscles (p<0.0001), and had more TMJ sounds (p<0.001). In addition, TMD patients scored significantly higher on MFIQ, 13.8 versus 0.34 (p<0.0001). The HADS questionnaire, Roland Morris scale and questions regarding catastrophizing showed significantly less dysfunction for the controls (p<0.0001).

Conclusion
Conclusions Preliminary results indicate significant differences between the groups with regards to jaw function, jaw muscle tenderness, HADS scores, Roland Morris disability scale scores and catastrophizing.
Title: Pain And Tmd In Rowers: Pilot Study Of Two Therapeutic Modalities

Poster Number PTH241

Authors
E. Abe, S. Oliveira, H. Barboza, J. Costa-Frutuoso, M. Vasques, M. Mori, M. Frigério, D. Laganá

University of Sao Paulo, Sao Paulo, Brazil, Fluminense Federal University, Rio de Janeiro, Rio de Janeiro, Association for the Study of Pain of the State of Rio de Janeiro, Rio de Janerio, RJ, Federal University of Sao Paulo, SAO PAULO, Brazil, University of Sao Paulo, SAO PAULO, Brazil

Aim of Investigation
The aim of this study was to evaluate the orofacial pain in rowers with temporomandibular joint disorder (TMJD), comparing the effect of use occlusal splint with therapeutic exercise against therapeutic exercise.

Results
Comparing before and after moments, the occlusal splint group (OSG) observed statistical significance (p < 0.05) for the T-Student test, combined with the RDC/TMD test showing decrease in excruciating pain and mandibular range. There was no statistical significance intergroup according the Anova test.

Conclusion
The use of occlusal splint associated with therapeutic exercise seemed better than the isolated therapeutic exercise, however larger samples and new study designs shall present better results for rowers suffering from pain and TMJD.
Title: Pain-Associated Mediators And Genes In Acetic Acid-Induced Oral Ulcerative Mucositis

Poster Number PTH242

Authors
T. Nodai, K. Ono, S. Hitomi, M. Ito, R. Hosokawa, K. Inenaga

Department of Oral Reconstruction and Rehabilitation, Kyushu Dental University, Fukuoka, Japan,
Division of Physiology, Kyushu Dental University, Fukuoka, Japan

Aim of Investigation
Rat oral ulcerative mucositis models treated with acetic acid have been used to examine therapies for oral ulcer patients. However, relationships of pathophysiological changes of mediators and gene expression with pain induction are not well understood. In the present study, to clarify the mechanisms underlying oral ulcerative mucositis-induced pain, we examined daily changes of putative pain-associated mediators in the oral mucosa, with measurements of pain-related behaviors, and performed DNA microarray analysis for the trigeminal ganglion in the model.

Results
On day 1 after acetic acid treatment, the treated oral mucosal area showed slight redness and swelling, but not ulceration and pain induction. On day 2, oral ulcer was obviously developed together inducing spontaneous and mechanical pain. In the treated mucosal area, the bacterial loading and prostaglandin E₂ were up-regulated from day 2 without significant changes on day 1. Bradykinin was up-regulated from day 1. DNA microarray analysis demonstrated 32 significant regulated genes (>1.5-fold changes of expressions). These genes had links to defense/wound/immune response pathways in gene ontology process. In quantitative RT-PCR, the up-regulations of top 3 genes, Hamp, Reg3b and Serpina3n, were validated and significantly suppressed by pre-treatment of antibiotic drugs that exhibited pain relief.

Conclusion
In the acetic acid-treated rat model, oral ulcerative mucositis-induced pain is caused by bacterial infection and followed prostanoid production through destruction of oral epithelial barrier (ulceration). In the response to the infectious inflammation, innervated sensory neurons genetically produce antibacterial and anti-peptidase factors to cure the mucositis. Bradykinin mainly works in acid injury-associated mucosal inflammation before ulceration and does not directly in pain induction.
**Title:** Referred Pain And Sensations Due To Standardized Palpation Of The Masseter Muscle In Healthy Participants

**Poster Number** PTH243

**Authors**
M. Masuda, T. Iida, F. Exposto, L. Baad-Hansen, O. Komiyama, M. Kawara, P. Svensson

Nihon University School of Dentistry at Matsudo, Matsudo, Japan, Nihon University School of Dentistry at Matsudo, Matsudo, Chiba, Aarhus University, Aarhus, Denmark, Aarhus University, Aarhus C, DENMARK, Nihon University, Matsudo, JAPAN, Aarhus University, Section of Orofacial Pain and Jaw Function Dept of Dentistry, Aarhus, DENMARK

**Aim of Investigation**
The aim of this study was to compare mechanical sensitivity and referred pain / sensations evoked by three different mechanical stimuli applied to the masseter muscle.

**Results**
Referred pain / sensations were evoked in 50% of the healthy participants when the 2 kg stimuli were applied, in 18.8% when the 1.0 kg stimuli were applied and in 12.5% when the 0.5 kg stimuli were applied. Four participants had referred pain / sensations in both sessions, 2 participants had referred pain / sensations in the 1st session, but not in the 2nd session, and 2 participants only had referrals in the 2nd session. The ANOVA of frequency of referred pain / sensations evoked by each test site showed no significant differences between gender, session or test sites. However, there was a significant difference between stimuli (p < 0.05) with increased referred pain for the 2 kg stimulus when compared with the 0.5 kg. The ANOVAs of NRS scores of pain and unpleasantness as well as after-sensation duration for the three mechanical stimuli showed no significant difference for session or gender (p > 0.05). However, there was a significant difference between stimuli for NRS scores of pain and unpleasantness as well as for after-sensation duration (p < 0.05). Finally, there was a significant difference of test site for the 1.0 kg and 2.0 kg stimulus on NRS scores of pain and unpleasantness, and a significant difference of test site for the 2.0 kg stimuli in terms of after-sensation duration (p < 0.01).

**Conclusion**
Our results indicate that referred pain in the orofacial region is a frequent phenomenon in healthy individuals upon standardized palpation of the masseter muscle. Interestingly, the referred sensations
were not test site-dependent whereas the NRS scores of perceived pain and unpleasantness were. This observation could indicate differences in mechanisms underlying mechanical pain sensitivity and referred pain / sensations from the masseter muscle and could have implications for muscle pain diagnosis according to the DC/TMD.
Title: Comparison Between Lidocaine And Mepivacaine Efficacy In The Management Of Myofascial Pain

Poster Number PTH244

Authors
H. Albagieh, N. Alsammahi

King Saud University, Riyadh, Saudi Arabia

Aim of Investigation
The aim of this study is to compare efficacy of mepivacaine versus lidocaine as a local anesthetic injected into the trigger points in the orofacial region, to alleviate local and referred pain.

Results
At one week post-treatment evaluations, all groups showed statistically significant improvements, however, none of the treatment methods proved to be superior to the others when intergroup comparisons were made. All groups complained from increase pain following second injections, but rapid relief following the third. At one month post-treatment evaluations, statistically significant improvements were detected both in Lidocaine and Mepivacaine TrPs and they were found to be equally effective. Using the Analysis of Variance test with repeated measurements, it was observed that the groups presented had no significant difference in the means of solution used. There was a significant decrease for both groups from the time before treatment and after.

Conclusion
Both Lidocaine and Mepivacaine injections into TrP were effective in relieving pain among all participant with myofascial pain. Mepivacaine gave comparable results to Lidocaine.
Title: A Survey On Phantom Limb Phenomena And Identification Of Risk Factors For Developing Phantom Limb Pain In Lower Limb Amputees In UMMC

Poster Number PTH245

Authors
M. Mansor, F. Abdul Aziz
University of Malaya, Kuala Lumpur, Malaysia, Tuanku Mirzan Armed Forces hospital, Kuala Lumpur, Malaysia

Aim of Investigation
The main aim of this study is to determine the prevalence of phantom limb pain among lower limb amputees, to identify the risk factors which may contribute to the development of phantom limb pain and to describe the characteristics of phantom limb pain.

Results
Out of 101 patients who had undergone major lower limb amputations in UMMC, 51 patients' data were analysed. The rest of the patients' data could not be analysed because 29 were not contactable, 16 passed away and 5 were aphasic due stroke and cannot be interviewed. Prevalence of phantom limb pain was 63%, prevalence of phantom sensations was 69% and prevalence of stump pain was 55%. The most common descriptions by patients are itchiness, pricking, tiring, numb and electric shock like pain. The mean worst pain rating was 4.5 over 10 with half of the patients took medications to ease the pain. However, in this study, no link was found between the possible risk factors such as medical diseases, aetiology of amputation, pre and post amputation pain, extent of amputation, level of amputation, the type of anaesthesia and the development of phantom limb pain.

Conclusion
Phantom limb pain remains a common problem for amputees with a significant impact on their quality of life. More studies with bigger sample size are needed to identify the risk factors of developing phantom limb pain so that this phenomena can be prevented and treated more effectively.
Aim of Investigation
Limb amputation is often done in patients with severely infected wounds which cannot be controlled by conservative means. Prevalence of phantom limb pain after amputation has been reported to range from 30% to 85%, and there are many factors which could contribute to this pain. The aim of this study was to determine the prevalence of phantom pain in patients undergoing lower limb amputation in Selayang Hospital, Malaysia, and its associated risk factors.

Results
A total of 115 patients underwent either above or below knee amputation; 66 were male (57.4%) the mean age was 58.9 years (SD 11.4, range 26-91). 74 patients (64.9%) had below knee amputations and 38 (33.3%) above knee amputations. 97.4% of patient had some form of chronic illness, most commonly diabetes mellitus (93.0%) and hypertension (64.3%). Pre-operatively, 21 patients (18.1%) had moderate pain and 2 patients (1.8%) had severe pain at rest; postoperatively, the number of patients reporting moderate pain increased to 22 (21.0%) and those with severe pain to 11 (10.5%). The prevalence of phantom limb pain was 29.6% (95% CI: 21.1%, 38.0%). Univariate analysis revealed that patient age and resting pain score after surgery were associated with phantom limb pain (p=0.041 and 0.001 respectively), but with multivariate analysis, only resting pain score after surgery was significant. The odds of having phantom limb pain were 14.81 times greater for those who experienced severe pain postoperatively compared to patients who had no pain (p=0.006). However, there was no significant difference between those with no pain compared to those with mild pain (p=0.740) and those with moderate pain (p=0.067).

Conclusion
Almost 30% of patients in our hospital experienced phantom limb pain after lower limb amputation.
Severe pain in the postoperative period was associated with a higher risk of having phantom limb pain. This can be prevented by good postoperative pain management and should be emphasised in the education and training of doctors involved in managing this group of patients as this may possibly reduce the incidence of phantom limb pain.
Aim of Investigation
Neuropathic pain is thought to be accompanied by changes in the central nervous system (Woolf, 2011). In amputees, reorganization within the somatosensory cortex has been observed to be associated with the presence of pain (Flor et al., 1995), though the evidence is not unequivocal (Makin et al., 2015). However, the involvement of spinal and brain stem structures in generating and maintaining phantom limb pain has rarely been considered (Finnerup et al., 2012). In this study we used a combination of electrical and thermal stimuli with functional magnetic resonance imaging (fMRI), to assess whether brain stem and spinal cord activity is altered in patients with neuropathic pain and/or phantom limb pain following amputation.

Results
A significant main effect of GROUP was observed within the C6 cord mask for electrical stimulation $F(1,15)=5.972, p=0.027$. Post-hoc t-tests revealed that difference was driven by significantly lower percentage blood flow signal in the patient group primarily in response to stimulation on the affected body side (left) compared to controls. For thermal stimulation on the unaffected (right) body side, there was a significant GROUP x REGION interaction with $F(1,6)=4.499, p=0.001$, which post-hoc t-tests revealed was due to increased activity in the C7 mask in the patient group. No difference in activity between the groups was observed in either the PAG or RVM brain stem masks.

Conclusion
To our knowledge this is the first demonstration of direct evidence for altered nociceptive processing within the human spinal cord in patients with neuropathic/phantom limb pain. It is interesting to note that the observed changes in the cord were not mirrored in the putative pro-/anti-nociceptive brain
stem structures (PAG/RVM). Future investigations will examine the localization of spinal cord responses, using recently developed group analysis techniques (Fonov et al., 2014).
Title: A Feasibility Study On Preoperative Electro Acupuncture On Postoperative Nausea And Vomiting And Pain In Patients Undergoing Gynecologic Laparoscopic Surgery

Poster Number PTH248

Authors
M. Zheng, S. Li, Z. Zheng, J. Guo, W. Wu

Affiliated Hospital of Nanjing University of Traditional Chinese Medicine, Nanjing, China, RMIT University, Bundoora, Vic, Australia, Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing, China

Aim of Investigation
A majority of the studies about perioperative acupuncture delivered the treatment 30 minutes before surgery, intraoperatively or postoperatively. Very few studies have examined if acupuncture could be delivered the day before the surgery. Our study aimed to investigate the feasibility and effectiveness of preoperative electroacupuncture (EA), delivered 24 hours before surgery, on postoperative nausea and vomiting (PONV) and postoperative pain in patients undergoing gynecologic laparoscopic surgery.

Results
The two groups were comparable in their age, anesthesia type (total intravenous anesthesia), surgical procedure, duration of surgery and their anesthetic medication use (p > 0.05, respectively). 15% and 20% of the patients experienced PONV in the EA and the UC groups, respectively. PONV reduced to zero over 24 hours in both groups and there was no statistically significant difference between the two groups at any time point. The EA group rated their postoperative pain statistically significantly lower than the UC group did at 6 hours post-surgery (EA: 1.9 ± 0.8; UC: 2.9 ± 0.9, p = 0.001). The two groups did not differ in pain at 12 and 24 hours. There was no difference in the use of anti-emetics or in pain medications between the two groups. The EA group had a shorter time to pass first flatus than the UC group did (EA: 20.3 hours ± 6.1; UC: 26.4 ± 5.2, p = 0.002). The common EA related adverse effects were pain at the needling sites and bruising. All were minor, and did not require medical attention. The patients tolerated the EA treatment well.

Conclusion
It is feasible and safe to deliver one-session EA treatment within 24 hours preoperatively to preempt postoperative pain. One-session preoperative EA may also accelerate motility of the gastrointestinal
track. Properly powered studies are needed to further test the effectiveness of preoperative EA on PONV.
Title: Delayed Pain Treatment Impacts Central Networks In Women With Chronic Pelvic Pain

Poster Number PTH249

Authors
J. Brawn, J. Bijsterbosch, L. Buck, C. Becker, I. Tracey, K. Vincent


Aim of Investigation
Women with chronic pelvic pain (CPP) experience huge diagnostic delays for potential underlying pathologies like endometriosis. In the US, on average, there is a twelve-year delay, whilst in the UK and Norway the delay is approximately eight and seven years, respectively (Hadfield et al. 1996; Husby et al. 2003). Potentially this leaves women without effective pain treatment and ultimately prolongs their suffering. Given the known delay in treatment and diagnosis experienced by women with CPP, we aimed to determine whether experiencing pain for longer resulted in functional connectivity changes in the brain.

Results
Women were divided into 2 groups based on duration of pain: 24 months or less and longer than 24 months. Comparing the functional connectivity between the groups, women with the longer duration had a statistically significant increase in hippocampus and PAG connectivity (p(corr) = 0.0346). No other regions displayed near-threshold changes in functional connectivity. There was no difference between the groups in age, however, the group with longer duration of pain had higher State-Trait Anxiety Inventory (State: p = 0.0160; Trait: p = 0.0051), Beck Depression Inventory (p = 0.0144), and Pain Catastrophising Scale (p = 0.0239) scores. The extent to which differences in psychology may explain the connectivity changes was explored. Across all 26 women, both State Anxiety and Pain Catastrophising were significantly positively correlated with functional connectivity between the hippocampus and PAG (State: r = 0.4159 p = 0.0346; Catastrophising: r = 0.4551 p = 0.0195), however there was no significant relationship with Trait Anxiety or Beck Depression scores.

Conclusion
We observed significantly greater coupling between the hippocampus and PAG in women with pelvic pain for longer than 24 months. Moreover these women also report greater psychological distress and
pain catastrophising, potentially explaining some of the connectivity changes. These findings support the need for prompt and effective analgesia for all women presenting with pelvic pain symptoms whether or not an underlying pathology is looked for or identified.
Title: Disruption Of The Menstrual Cycle Is Common In Women With Chronic Pain.

Poster Number PTH250

Authors
L. Buck, K. Vincent

University of Oxford, Oxford, United Kingdom

Aim of Investigation
Regular menstrual cycles in post-menarchal women reflect a healthy hypothalamic-pituitary-ovarian (HPO) axis. It is well known that psychological stress can disrupt this axis both acutely and chronically leading to cycle irregularity or a period of amenorrhoea (1). High levels of opiate use, both for chronic pain and recreationally, can lead to suppression of ovarian endocrine function, amenorrhoea or even premature ovarian insufficiency (2). However, it is not known whether chronic pain in itself is a sufficient stressor to disrupt HPO axis activity. The ultimate aim of this ongoing observational study is to investigate the extent to which hormone production is altered in women with chronic musculoskeletal or pelvic pain and whether clinical symptoms relate to the extent of HPO and hypothalamic-pituitary-adrenal (HPA) suppression. The interim analysis described here uses menstrual cycle length and regularity as a surrogate for a healthy HPO axis.

Results
The mean age of the sample was 39. 13 women (42%) described irregular or absent cycles in the last 6 months (somewhat irregular (8-20 days before or after expected) n=4, irregular (>20 days before or after expected) n=3, or absent n=6). All women with irregular cycles described prolonged cycle length. Comparing women with regular cycles to those with irregular/absent cycles, there was no significant difference in age (39 vs 34); duration of pain (13.6 vs 12.9 years); severity of pain (7.9 vs 8.2); state anxiety (41 vs 40); or depression (16 vs 13). There were also no significant differences in any of these variables when women with regular cycles were compared to those with amenorrhoea for the last 6 months.

Conclusion
In healthy women, menstrual cycle irregularity and amenorrhoea rates are approximately 15% and 3% respectively (3,4). Thus, we describe strikingly high rates of menstrual cycle irregularity (42%) and amenorrhoea (19%) in a cohort of women with chronic pain of reproductive age. This likely reflects
Title: Peculiarities Of Pain Syndromes In Pregnant Women

Poster Number PTH251

Authors
I. Romanenko, I. Romanenko, V. Romanenko, Y. Romanenko

Lugansk State Medical University, Rubizhne, Ukraine, Bohomolets National Medical University, Kiev, UKRAINE, Kiev Regional Clinical Hospital, Kiev, UKRAINE

Aim of Investigation
To study clinical features of pain of various localization and degree of severity in pregnant women at I-II trimesters of uncomplicated pregnancy.

Results
Recurrent headaches were found in 13.51% of women, pain in the neck – in 16.2%, pain in the thoracic spine area – 20.3%, low back pain – 24.3%. Pain in different parts of the spine (cervical, thoracic, lumbar) was observed in 22.9% of cases. Most often women were suffering from pain in the thoracic and lumbar areas of spine (48.7%). 14.9% of the patients had complaints on pain in the joints. Periodic pains in the heart area bothered 18.9% of women; in 6.7% of cases it was combined with headaches. Intensity of pain was measured by the majority of patients as moderate (66.2%). The rest 33.8% of women experienced pain of mild intensity. Average intensity of headache was 4.8±0.8 points on VAS, back pain – 2.9±0.4 points, joint pain – 2.4±0.5 points, pain in heart area – 3.8±0.7 points. A direct correlation between average intensity headache and heart pain was found (r=0.50, p=0.001).

Conclusion
The study showed the frequent combination (68.9%) of pregnancy with pain syndromes of various origin, nature and localization, which should be reflected in the formulation of clinical diagnosis. Successful treatment of these patients is possible in case of utilization of comprehensive clinical and gynecological examination.
Title: Persistent Post-Operative Pain And Its Influence On Perioperative Pain Management

Poster Number PTH252

Authors
F. Veal, A. Thompson, L. Bereznicki, G. Peterson

The Unit for Medication Outcomes Research and Education, University of Tasmania, Hobart, Australia

Aim of Investigation
Persistent post-operative pain (PPP) is common, with a prevalence of between 30-50% amongst surgical patients. The quality and consistency of existing studies identifying risk factors for PPP have been variable, making the findings difficult to apply in clinical practice. There is little known about what pre-surgical patient factors anaesthetists perceive as increasing the risk of PPP and what, if any, influence this has on the way they manage perioperative pain. This study aimed to fill these gaps in our understanding, regarding these important issues.

Results
175 (2.5%) anaesthetists completed the survey. The majority of respondents were consultants (75.4%); the median years practicing in anaesthetics was 13 (range 1-40) and 90.9% of respondents worked in more than one surgical speciality. Pre-surgical factors that anaesthetists associated with an increased risk of PPP were somatic persistent pain (82.9%), depression (76.0%), anxiety (75.4%), pain catastrophising (69.7%), visceral persistent pain (68.6%) and the severity (62.3%) and duration (66.9%) of pre-operative pain. Re-operation on the same site (50.3%), socioeconomic status (25.1%) and education level (25.7%) were less frequently cited by anaesthetists as risk factors for PPP. The most common influences on perioperative pain management were clinical judgment (86.3%), patient factors (85.7%) and operation factors (82.9%). Hospital or department protocols (62.9%) and Australian (44.0%) or International (22.9%) guidelines were less frequently used to inform practice. Perceptions regarding an increased risk of uncontrolled acute pain or PPP also influenced perioperative management. For patients at increased risk of PPP, anaesthetists were for example, more likely to use a short course of gabapentinoinds (66.9% vs 46.3% p<0.01), perioperative ketamine (72.6% vs 67.4% p<0.01) and post-operative ketamine (69.1% vs 58.3% p<0.01) compared to those patients identified as high risk for uncontrolled acute pain. Patients at high risk of uncontrolled acute pain would be more likely to receive a regional anaesthetic (78.3% vs 70.9% p<0.01), patient controlled analgesia (70.3% vs 50.3% p<0.01) and parecoxib (62.9% vs 47.4 p<0.01) than those at high risk of PPP. In terms of strategies to reduce
the severity or incidence of PPP, nearly two thirds of respondents agreed identification of predictors of
PPP and subsequent production of an assessment tool for PPP risk (62.3%) would be useful and almost
half (48.0%) of respondents thought that pre-surgical screening of pain catastrophising, anxiety and
depression would be beneficial.

**Conclusion**
Clinical judgment, patient and operation factors were the most common factors influencing
perioperative pain management by anaesthetists. There was however, a lack of consensus about which
factors increased the likelihood of PPP. Because anaesthetists’ perioperative management differed
depending on perceived PPP risk and acute pain risk, there is an impetus to increase the certainty
regarding which factors increase the risk of PPP and acute pain so that more consistency in
perioperative management can be achieved. The need for prospective large-scale studies using the
same study protocols to identify factors associated with PPP has been previously identified, although
these have yet to be carried out. In the meantime, all pre-surgical patients should be routinely screened
for pain catastrophising, anxiety, depression and pre-existing pain on admission to ensure that
anaesthetists are working with as much information as possible to adequately inform their perioperative
management of those at greatest risk of PPP.
Title: Anger Expression And Its Relation To Depression, Anxiety, And Pain In Patients Treated For Breast Cancer

Poster Number PTH253

Authors
R. Sipilä, T. Hintsa, T. Tasmuth, A. Estlander, E. Kalso

Div of Pain Medicine, Dept. of Anaesthesiology, University of Helsinki, Helsinki University Hospital, Helsinki, Finland, Institute of Behavioural Sciences, University of Helsinki, Helsinki, Finland, Div of Pain Medicine, Dept. of Anaesthesiology, University of Helsinki, Helsinki University Hospital, HUS, Finland

Aim of Investigation
Pain after breast cancer treatment is a well-recognized and described problem. Psychological distress, depression, anxiety, and also feelings of anger are understandable and common reactions related to breast cancer diagnosis. Anger has been shown to affect somatic wellbeing, quality of life and pain. However, there are no previous studies of the effects of anger on depression and anxiety in breast cancer patients or how anger and mood associate with experimental, acute clinical and persistent pain in this group of patients. The aim of the present study was to assess anger expression in women treated for breast cancer and examine its relation to depressive symptoms, anxiety, and pain. We examined the association between anger expression and pain, and whether these associations are independent of depressive symptoms and anxiety.

Results
Anger-In correlated moderately with depressive symptoms (r=.30, p= <0.001), state anxiety (r=.26, p= <0.001), and trait anxiety (r=.40, p= <0.001) before surgery and also at 12 months (r=.26, p= <0.001; r=.24, p= <0.001; and r=.33, p= <0.001) respectively. Whereas Anger-Out had only mild correlations before surgery (depressive symptoms r=.11, p=0.001; state anxiety r=.15, p= <0.001; and trait anxiety r=.15, p= <0.001) and there were no significant correlations at 12 months. Women with elevated levels of Anger-In had higher scores on depressive symptoms and anxiety preoperatively and 12 months after surgery compared with patients reporting lower Anger-In. Anger-Out and Anger-Control were associated with higher level of depressive symptoms and anxiety only at the preoperative phase. Results of univariate t-test analyses indicated that women with high Anger-In had higher scores in experimental test for heat pain (t=-2.17, p=.031). Women with high Anger-Out expected to have higher pain postoperatively (t=-2.715, p=.007) and they needed significantly more oxycodone to achieve satisfactory
pain relief for the first time after surgery (t=-2.754, p=.006). Anger-Control was not associated with any of the pain variables. The association between Anger-Out and pain variables remained significant in linear regression analyses after controlling for depression and anxiety whereas Anger-In did not.

**Conclusion**
These preliminary results indicate that Anger-In was related to lower psychological wellbeing but not pain when controlled for depressive symptoms and anxiety. Whereas, Anger-Out expression was associated independently with higher need of oxycodone to have satisfactory pain relief for the first time and higher expectation of postoperative pain. Anger-Control was not associated with pain.
Title: Preliminary Study Of Post-Thoracotomy Pain Syndrome: Ptps Incidence In Our Institution

Poster Number PTH254

Authors
Y. Takahashi, A. Hara, T. Matsunaga, I. Kawagoe, M. Iseki
Juntendo University School of Medicine, Tokyo, Japan

Aim of Investigation
Pain is caused by surgery, trauma, inflammation and infection, which gradually decrease or disappear with time. Whereas acute pain is a normal sensation that alerts us to possible injury; chronic pain often persists months or even longer over normal recovery period. Previous data showed that incidence of postoperative pain varies with surgeries from 5 to 50%. A reported incidence of PTPS is rather high around 30-50%. PTPS negatively impact on reducing quality of life as well as increasing the subsequent costs to the health care. Along with over 60,000 thoracotomies for lung cancer were performed annually in Japan, the number of cases is increasing linearly. However not only little is known about PTPS, but also there is no nationwide survey on PTPS in Japan. The aim of this study was to review the incidence of PTPS in our institution.

Results
Fifteen cases were included in this study. The mean age and standard deviation was 67±14. There was no significant differences between two groups in patient characteristics. Five patients were allocated into PTPS group and ten patients were allocated into NR group. Although there was no significant differences between two groups in smoking index (Brinkman Index), pre-existing pain, Pain DETECT, HADS, PDAS, PCS, there were significant differences in length of incision (P=0.04) and duration of surgery (P=0.04)/anesthesia (P=0.04).

Conclusion
The incidence of PTPS two months after thoracic surgeries was 33%, and 13% of patients experienced severe pain (NRS≥5). These results are consistent with results of previous reports. The length of incision and duration of anesthesia/ surgery are found to be predicting factors, assuming that greater surgical stress would cause more inflammation and develop central sensitization which prolong pain. The number of included patients was comparatively small in this study, hence further investigation should be needed.
Title: A Comparison Of Pain Profiles Of Peripheral Nerve Blocks Versus Spinal Anaesthesia In Patients Undergoing Diabetic Foot Surgery

Poster Number PTH255

Authors
S. Lim, H. Lai, L. Foo, C. Yong, P. Loh, M. Hasan, C. Wang

University of Malaya, Kuala Lumpur, Wilayah Persekutuan, University of Malaya, Petaling Jaya, Selangor, University of Malaya, Kuala Lumpur, Malaysia

Aim of Investigation
Diabetic patients often present with diabetic foot ulcer requiring surgery such as wound debridement, ray amputation, trans-metatarsal amputation, below knee and above knee amputation. These surgeries are usually done under general anaesthesia, spinal anaesthesia (SAB) or peripheral nerve block (PNB). The prevalence of painful diabetic neuropathy ranges from 6 to 27% (Hartemann 2011). Many of these patients present for diabetic foot surgery and some of them may even undergo a series of surgeries that progress to limb amputation. In this study, we compared the immediate post operative pain profile of patients who underwent diabetic foot surgery under PNB or SAB. We also assessed the chronic pain profile at 6 months after surgery to compare the incidence chronic pain in the PNB group to the SAB group.

Results
In this study 120 patients were recruited and randomly divided to 2 groups (PNB and SAB). 17 patients were excluded for analysis (3 patients were converted to general anaesthesia, 8 patients had missing or incomplete data, and 6 patients were repeatedly recruited). 103 patients were available for final data analysis, of which PNB group had 47 patients while SAB group had 56 patients. Demographic analysis showed that both group were similar in characteristics. Baseline data showed no difference in the prevalence of chronic pain, preoperative pain score, preoperative S-LANSS score and proportion of patients with neuropathic pain between the PNB and SAB group. The overall prevalence of chronic pain was 22.3% and neuropathic pain was 36.9% in our cohort. PNB group received a mean dose of 153.4 ±30.3 mg of ropivacaine while SAB group received a mean dose of 10.9 ±1.2 mg of 0.5% heavy bupivacaine and a mean dose of 15.2 ±5.3 mcg of intrathecal fentanyl. Patients in PNB group had a longer duration of pain free time after the surgery (9.00 hours in the PNB group vs 4.49 hours in the SAB group, P = 0.0001). They also had a lower recorded pain score when first pain appeared (2.09 in the PNB
group vs 4.20 in the SAB group, P = 0.0003). However, patients in the PNB group took a longer time to be able to move affected limb (8.57 hours in the PNB group vs 3.85 hours in the SAB group, P = 0.0001). 68% of the initial cohort of 103 patients completed the 6 month follow-up. 25 patients were not contactable and 8 patients had passed away (mortality rate 10.3%). Analysis of pain score (1.12 in the PNB group vs 1.27 in SAB group, P = 0.803), S-LANSS score (3.91 in the PNB group vs 3.22 in the SAB group, P = 0.582), and proportion of patients with neuropathic pain at 6 months post-operation (9.1% in the PNB group vs 10.8% in the SAB group, P=1.000) did not show any statistically significant difference.

Conclusion
PNB provided better pain control postoperatively with a significantly longer pain free duration and lower pain score at first post-surgical pain compared to SAB. Despite having better pain control in the immediate post operative period, the PNB group did not show a statistically significant difference in prevalence of neuropathic pain at 6 months. This may suggest that PNB was not able to reduce incidence of post surgical neuropathic pain. Proportion of patients will neuropathic pain at 6 months post-surgery was 10%, which was much lower than the initial 36.9%. Diabetic foot surgery definitely played a role in reduction of diabetic foot pain. However, nociceptive pain from infection and inflammation may have resulted in overestimation of S-LANSS score in the initial period. In summary, PNB provided superior postoperative pain relief compared to SAB in patients undergoing diabetic foot surgery but this did not translate into a lower incidence of neuropathic pain after 6 months.
Title: Mrgb2 Contributes To Mechanical And Thermal Allodynia In An Animal Models Of Inflammatory And Neuropathic Pain

Poster Number PTH256

Authors
D. Green, V. Tiwari, X. Dong

Johns Hopkins Medical Institute, Baltimore, MD, Departments of Neuroscience and Neurosurgery, School of Medicine, Johns Hopkins University, Baltimore, MD

Aim of Investigation
Although the mechanisms of postoperative pain are still incompletely understood, research has shed light on one potentially important immune cell. As one of the key effector cells in the inflammatory process, mast cells are an important contributor to pain pathophysiology. The role of mast cells in mediating postoperative pain is incompletely understood, although studies using mast cell stabilizers demonstrate that this immune cell is involved in contributing to nociception in animal models of postoperative pain. Thus, there is a compelling need for fundamental research aimed at understanding the mechanisms of mast cells in postoperative pain.

Results
Male C57bl/6 wild-type (WT) or MRGB2KO (n=6/group) were tested 24 h after incision surgery. Behavioral testing was done utilizing the radiant heat test and Von Frey filaments. At 24 hours postsurgery we saw significant reduction in both mechanical and thermal allodynia in MRGB2 KO mice but not WT. In the CCI model of neuropathic pain, similar results were observed. Behavioral testing was done 14 days after surgery, and we saw significant reduction in both mechanical and thermal alldynia in MRGB2 KO mice but not WT.

Conclusion
Results indicate that mast cells contribute to postoperative alldynia via MRGB2 and contribute to the thermal and mechanical alldynia seen in a neuropathic pain model. Further study of the mechanisms underlying the role of this receptor in mediating incision induced pain may provide potential strategies for the development of novel analgesics to treat debilitating postoperative and neuropathic pain.
Title: Discrete Role Of Trpv4 Channel At A Model Of Postsurgical Pain In Mice

Poster Number: PTH257

Authors
M. Gonçalves, P. Geppetti, I. Marone, S. Materazzi, J. Ferreira

Universidade Federal de Santa Catarina, Florianópolis, Brazil, University of Florence, Florence, -- SELECT - - University of Florence, Florença, Italy, Federal University of Santa Catarina, Florianópolis, SC, Brazil

Aim of Investigation
Pain after surgical procedures is a common condition affecting about 50% of patients who usually receive unsatisfactory treatments. A better understanding of the mechanisms underlying postsurgical pain might ameliorate patient outcome. The ion channel transient receptor potential vanilloid 4 (TRPV4) is an osmoreceptor involved in many types of pain, including neuropathic pain whereas there is no information regarding TRPV4 in models of postsurgical pain. Topical hypertonic saline (a stimulus able to engage TRPV4) makes worse postsurgical pain in patients with nasal surgery. Mast cell degranulation (often produced by surgical procedures) by releasing tryptase activates the protease-activated receptor 2 (PAR2) inducing pain-like behaviors via TRPV4 sensitization in nociceptors. Thus, we hypothesized that TRPV4 contributes to the hyperalgesia associated with models of postsurgical pain.

Results
No difference in paw withdraw thresholds was found between WT and TRPV4-/- mice before surgery. Surgical procedure decreased paw withdrawal threshold values (mechanical hyperalgesia) at 2, 24 and 48 h when compared to baseline in WT mice. However, TRPV4-/- mice showed reduced mechanical hyperalgesia when compared to WT mice at 24 h after surgery. Application of hypertonic saline spray to the paw evoked nociception behavior in WT mice at 2 h after surgical incision, but not in TRPV4-/- mice. WT mice presented a significant edema only at 2 h but no differences were observed between TRPV4-/- and WT mice. The behavior of nest building usually is reduced by pain and stress, then that parameter was also evaluated. The results about nest building showed no differences between groups (the experiment was performed at the first day, 12-24 h after surgery). There was an increase of spontaneous pain only at 2 h after surgery in WT mice, with no more differences in other evaluated times. The TRPV4-/- group presented increased spontaneous pain only at 2 h after surgery as well.
Conclusion
In a model of postsurgical pain the TRPV4 channel has a role in the mechanical hyperalgesia and in nociception evoked TRPV4-selective stimuli. The channel contribution appears to be limited to the early phase after incision.
Title: One-Year Opioid Consumption Trajectories In 8,975 Patients Undergoing Total Hip Or Knee Arthroplasty

Poster Number PTH258

Authors
M. Petersen, C. Joergensen, H. Kehlet, E. Aasvang

Multidisciplinary Pain Center, Rigshospitalet, Copenhagen, Denmark, Section of Surgical Pathophysiology, Rigshospitalet, Copenhagen, Denmark, Copenhagen University Rigshospitalet, Copenhagen, DENMARK, Section of Surgical Pathophysiology, Rigshospitalet, Copenhagen, Denmark

Aim of Investigation
Total hip (THA) and knee arthroplasty (TKA) is performed to increase function, activity and reduce pain. With improvement a subsequent reduction in analgesic consumption would be expected, however the available data are sparse and indicate that a subset of patients experience an increase in analgesic consumption similar to incidence of persistent post arthroplasty pain (10-20%). Chronic analgesic consumption and especially opioids are known risk factors for increased morbidity and mortality. The purpose of the current study was to describe the trajectories in patients analgesic consumption after THA and TKA, to evaluate the efficacy of surgery and identify areas for future research to reduce pain and analgesic consumption.

Results
The study included 8,975 patients who underwent primary arthroplasty (4,849 THA, and 4,126 TKA), whereof 23.8% of patients used opioid prior to surgery. For patients with preoperative opioid consumption 10.2% and 17.6% of THA/TKA had an increased consumption 8-12 months postoperatively. Overall for the patients with preoperative opioid consumption 24.4% had a decreased consumption and 59.0% had no consumption 8-12 months postoperatively. Patients with no preoperative opioid use had a significantly lower (p<0.001) frequency of increased opioid consumption in the late postoperative phase, 6.3% and 9.9% for THA/TKA respectively.

Conclusion
This large study shows that increased opioid consumption occurs in a significant proportion of THA and TKA patients calling for optimization of surgical outcomes and identification of risk patients.
Title: Patient Coping And Expectations About Recovery Predict The Development Of Chronic Post-Surgical Pain, Pain Interference, And Reduced Quality Of Life After Traumatic Open Extremity Fracture Repair

Poster Number: PTH259

Authors

Department of Anesthesia, HSC-2V9 Faculty of Health Sciences, Hamilton, ON, McMaster University, Hamilton, Ontario, Hamilton General Hospital, Hamilton, Ontario, Greenville Health System University Medical Center, Greenville, United States, University of Manitoba, Manitoba, Canada, University of Montreal, Montréal, Canada, McMaster University, Hamilton, Canada

Aim of Investigation
In North America, chronic non-cancer pain affects approximately 30% of the population, with similar rates in Europe and Australia. Surgery and trauma are frequently cited as triggering events responsible for the development of chronic pain. Although several risk factors for persistent post-surgical pain have been identified many, such as age, are non-modifiable and thus not amendable to intervention. However, there are emerging data that suggest patients' beliefs may be associated with clinical outcomes. The aim of the current study was to explore the role of patients' beliefs regarding their recovery from severe physical trauma, and the development of persistent post-surgical pain, pain interference, and quality of life.

Results
Of 1,111 open fracture patients with data available for analysis, 725 (65%) reported pain at 1-year. Addition of SPOC scores to an adjusted regression model to predict persistent pain improved the c-statistic from 0.66 to 0.73 (p<0.001 for the difference) and found the greatest risk was associated with high (≥78) SPOC scores (OR 5.29, 95% CI 3.75 to 7.46). Thirty-six percent (406 of 1125) reported pain interference at 1-year. Addition of SPOC scores to an adjusted regression model to predict pain interference improved the c-statistic from 0.66 to 0.74 (p<0.001 for the difference) and found the greatest risk was associated with high SPOC scores (OR 5.83, 95% CI 4.12 to 8.26). In our adjusted multivariable regression models, SPOC scores at 6-weeks post-surgery accounted for 11% of the variation in SF-12 physical component summary scores and 13% of SF-12 mental component summary.
scores at 1-year. All associations were conserved with 1-week SPOC scores, but the magnitude of associations for SPOC scores at 6-weeks was significantly larger across all models.

**Conclusion**
Patient's coping and expectations of recovery, as measured by the SPOC questionnaire, is a strong predictor of persistent pain, quality of life, and pain interference after traumatic open extremity fracture. Future studies should explore whether these beliefs can be modified, and if doing so improves prognosis.
**Title**: Lidocane 5% In Chronic Neuropathic Pain After Breast Surgery: Randomised Controlled Trial

**Poster Number** PTH260

**Authors**
P. Sansone, M. Pace, M. Passavanti, V. Pota, N. Pezone, L. Ferrante, C. Aurilio

Second University of Naples, Napoli, Italy, Hospital of Marcianise, ASL Caserta, Napoli, Italy

**Aim of Investigation**
The prevalence of chronic pain after surgery for breast cancer, has been known to develop in 20–68% of patients. The pain is often located in the axilla, the shoulder, the arm or the chest wall. PMPS is often described as a typical neuropathic pain consisting of burning pain, shooting pain, pain evoked by pressure and deep blunt pain. Like other neuropathic pain conditions, the treatment is often difficult. The aim of our RCT was to evaluate the efficacy of Lidocaine patch 5% in patients with chronic pain after breast surgery.

**Results**
All patients completed the study, no adverse events were recorded, NRS (baseline): Lido 5.4 +/- 1.32 vs Plac 6.0 +/- 2.20. At 4 wks (4.7 +/- 0.47 vs 5.2 +/- 2.83) and at 8 wks (2.4 +/- 0.73 vs 5.8 +/- 2.42). A significant reduction in the frequency of pain interference with sleep also occurred in Lido group.

**Conclusion**
Lidocaine patch 5% may be considered to be an effective and safe drug for the treatment of pain after breast surgery.
Postoperative Epidural Analgesia For Joint Replacement Surgery: Inj. Bupivacaine With Fentanyl-Intermittent Versus Continuous Analgesia

Title: Postoperative Epidural Analgesia For Joint Replacement Surgery: Inj. Bupivacaine With Fentanyl-Intermittent Versus Continuous Analgesia

Poster Number PTH261

Authors
T. DOCTOR, D. Patel

B.J.MEDICAL COLLEGE, AHMEDABAD, GUJARAT, INDIA, Gandhinagar, GUJARAT, B.J.Medical College, ahmedbad, India, B.J.MEDICAL COLLEGE, AHMEDABAD, GUJARAT, INDIA, Ahmedbad, GUJARAT

Aim of Investigation
To evaluate efficacy of inj. bupivacaine with or without fentanyl as intermittent versus continuous epidural analgesia for post operative pain relief in joint replacement surgeries

Results
demographic databetween group A and group B for age, height, weight were statistically insignificant. There was male dominance in Group B as compared to female dominance in Group A. Within the group pulse rate changes were significant after 2hrs in Group A and was statistically significant at 15min, 2.5hrs, 6, 18 and 48hrs. In between the group A & Group B, SBP was statistically significant at 15min, 2.5hrs, 6hr, 12hr, 18hr, 24hr and 30hr. DBP changes were significant from 2.5hrs to 30hrs between the groups. Mean visual analogue score 4-5 was observed at 2.5hr and 6hr in group A. Mean VAS 3-4 at 2hr, 3hr, 12hrs in Group A as compared to Group B at 2hr, 2.5hr only. Mean VAS 2-3 was observed at 3hr, 18hr and 24hr in Group A while Group B only at 3hrs. Mean VAS 0-2 was observed in Group A at 30hr, 36hr, 42hr & 48hrs only while Group B had at 6hr, 12hr, 24hr, 30hr, 36hr, 42hr and 48hrs. We observed much lower VAS scores in Continuous group as compared to intermittent group A. Mean ±SD 2.23 ±1.40 as compared to Group B 1.40 ± 1.25 which was significantly high (p<0.001). Duration of analgesia was maximum in group B 7.03 ±0.51 as compared to Group A intermittent 5.66 ±0.05 (p<0.001) Satisfaction score was higher in Group B, score 2-24%; score 3 76% as compared to Group A score 1 20%, score 2 36% & score 3 in 11patients Side effects observed were itching 12%, vomiting 4%, Nausea (8%), sensory block (4%), accidental removal of catheter (4%) in group A while in Group B sensory block (8%), hypotension (8%)

Conclusion
we conclude that epidural given as a continuous infusion of low concentration of 0.125% Inj. Bupivacaine
with inj. Fentanyl 1 μg/kg is costly but superior technique and good alternative for pain management in joint replacement surgeries with less side effects, better patient satisfaction and quality of pain score (VAS) with/without rehabilitation program as compared to intermittent technique
Title: The Role Of Continuous Administration Of Desogestrel In Reducing Pain And Ovarian Endometrioma Volume In Women With Ovarian Endometriosis

Poster Number PTH262

Authors
M. Grigore, D. Gafitanu

University Of Medicine And Pharmacy, Iasi, Romania, University of Medicine and Pharmacy, Iasi, Romania

Aim of Investigation
The aim of the study was to investigate the effect of continuous low-dose oral desogestrel on endometrioma diameter and pain induced by this disease (dysmenorrhea and dyspareunia).

Results
During the follow-up we noticed a significant decrease (p<0.001) of dysmenorrhea and pain induced by this disease. A significant reduction in endometrioma mean diameter (p<0.001) was observed during the follow-up. Seven patients stop the treatment because of the irregular uterine bleeding that appeared. No new endometrioma occurred during the treatment.

Conclusion
Daily administration of desogestrel seems to be effective in reducing pain and endometrioma mean diameter.
Title: Factors Affecting Patient Involvement In Pain Research: A Survey Of Attitudes And Perceptions In Patients With Chronic Pelvic Pain

Poster Number: PTH263

Authors
M. Stasiowska, J. Cambitzi, R. Cregg

National Hospital for Neurology and Neurosurgery, UCLH, London, United Kingdom, University College London, London, UNITED KINGDOM

Aim of Investigation
Participant recruitment and retention is key in conducting successful medical research. Chronic pelvic pain (CPP) has a significant negative impact on biological, psychological and social aspects of patients' lives, making it difficult for them to participate in medical research. The aim of our survey was to explore the reasons why patients with CPP participate in medical research and what factors affect participant recruitment, retention and compliance.

Results
54 patients took part in our survey. 63% were female, 37% male. The majority of patients (84%) were between the ages of 31 – 70 years. Overall involvement in clinical research More than 80% of patients expressed a positive interest in participating in research about CPP. Reasons included:
- Better understanding of their condition and improved treatment and symptom management.
- To find better treatments for other patients with similar problems.
- Participation in clinical research involving live patients (as opposed to laboratory or animal studies) provides better quality data and improves knowledge about the disease process.
- A way of giving back to the medical community and other patients, for the care and support they received during their treatment.

Reasons for not getting involved in medical research included:
- Many years of unsuccessful pain management and treatment.
- A wish to seek more holistic and alternative forms of non-invasive treatment.
- Worry about aggravating their current chronic pain.
- Lack of adequate knowledge about the proposed study aims, type of medication/intervention and follow-up period.
- Concern about the randomisation and withdrawal process.
- Living far away and not being able to travel in order to fully participate in research.
- Communication problems which affect follow-up, such as a lack of telephone or reliable internet access.
- Interference with work and social/family life.
- Existing multiple food and drug allergies.
- Contemplating pregnancy or breast-feeding.

Type of medical research Patients were
most amenable to research, which required undergoing additional examinations (Yes 46.3%, Maybe 29.6%, No 24.1%) (including pelvic examinations) or investigations, including the use of ionizing radiation (Yes 44.4%, Maybe 35.2%, No – 20.4%). Research into new injection treatments (Yes. Maybe, No) and medication (Yes 30.2%, Maybe 43.4%, No 26.4%) was less popular. Causes for new injection or medication trials being the least popular type of research included: - Concerns about side effects affecting ability to drive, work and enjoy life. - Interaction with other medications. - Problems with multiple food and drug allergies. Follow-up Regular telephone follow-up was the preferred method for the majority of patients (Yes 66.7%, Maybe 16.7%, No 16.7%), followed by self administered questionnaires (Yes 60.2%, Maybe 18.5%, No 21.3%) and lastly regular attendance in clinic (Yes 42.6%, Maybe 33.3%, No 24.1%). The majority of patients preferred to return their questionnaires on-line (74%) compared with pre-paid postage (24%).

Conclusion
Patients with CPP are motivated to participate in medical research in order to promote knowledge and understanding of their condition, and help others and themselves receive better quality and effective treatment. Surprisingly patients are not averse to undergoing repeated assessments, including internal pelvic examinations and investigations, but are cautious about any new treatments with potential systemic side effects. We can improve patient recruitment rates by providing clear and concise information about research opportunities, and maximize participant retention and follow-up by using convenient forms of communication such as telephone interviews and electronic questionnaires.
Date: 09/29/2016 09:30:00 AM

**Title:** Superior Hypogastric Plexus Block For Chronic Urogenital Pain

**Poster Number** PTH264

**Authors**
S. EL-TALLAWY<sup>,2</sup>

King Khalid University Hospital, College of Medicine, King Saud University, KSA, Riyadh, KSA, Faculty of Medicine, Minia University, Minia, Egypt

**Aim of Investigation**
This study was designed to evaluate the clinical and urodynamic assessments of the superior hypogastric plexus block (SHPB) in patients complaining of intractable cystitis.

**Results**
The study showed that pain relief was satisfactory in (66.667%) of patients (VAS < 3). The remaining (33.333%) required another block after 1 week with good pain relief in (20.833%), and (12.5%) showed no signs of improvement. The distressing frequency of micturition showed significant improvement after the block. Cystometric parameters showed increase in the maximum cystometric capacity (ml) and bladder compliance (ml/cm H2O) from (217+54.01 to 377+62.836) and (15.7+9.78 to 32.55+11.72) respectively. The detrusal instability decreased from (79.2% to 33.3%) after the block. No serious side effects were reported during the study.

**Conclusion**
Clinical and urodynamic assessments showed that the superior hypogastric plexus block is an effective method for the relief of pain and distressing symptoms due to intractable cystitis.
Title: Severity Of Pain, Disability, And Depression At The Time Of Referral To United Kingdom Specialist National Pain Service: How Measures Differ Between Widespread And Local/Regional Chronic Pelvic Pain As Classified By The European Association Of Urology On

Poster Number PTH265

Authors
J. Cambitzi, R. Cregg, M. Tavakkoli Zadeh, A. Al-Massari

National Hospital for Neurology and Neurosurgery, UCLH, London, United Kingdom, UCLH, London, United Kingdom, NHS, London, United Kingdom, University College London, London, United Kingdom

Aim of Investigation
To apply Axis One of the European Association of Urology (EAU) 2014 classification of Chronic Pelvic Pain syndromes to a sample of 713 Pelvic Pain patients and compare degrees of pain, pain interference, anxiety, depression, positive outlook, catastrophising and self efficacy, in patients referred to specialist pelvic pain service over a period of two years.

Results
In total 890 patients were seen in the clinic. Seven hundred and thirteen filled out the questionnaire. Age range was 16 to 89 years with an average of 44 years. There were 220 men and 493 women, 30% were men. Ethnicity 604 (85%) patients were caucasian. One hundred and forty four patients saw the GP 5 or more times in the last 3 months. Out of that figure 55 patients saw their GP more then 10 times. In the last 6 months 142 patients saw the hospital consultant 5 or more times. Out of that figure 59 saw the specialist on 10 or more occasions. Twenty four patients attend Accident and Emergency department 5 or more times and out of that figure, 10 patients attended A and E more then 10 times. We found statistically significant difference between the groups as described below: BPI: G1(25.1 +/- 0.65 SEM) > G2 (21.9 +/- 0.38) P=0.0001 BPI Interference: G1 (6.34 +/- 0.19 SEM) > G2 (5.07 +/- 0.11) P<0.0001 PSEQ: G1 (18.62 +/- 1.2 SEM) << G2 (25.7 +/- 0.68) P<0.0001 PCS: G1 (30.6 +/- 1 SEM) >= G2 (28.5 +/- 0.50) P=0.071 DAPOS D: G1 (13.2 +/- 0.50) > G2 (11.46 +/- 0.23) P=0.0006 DAPOS A: G1 (8.10 +/- 0.34 SEM) > G2 (7.10 +/- 0.15) P=0.004 DAPOS PO: G1 (8.84 +/- 0.25) = G2 (9.1 +/- 0.12) P= 0.27 The above data suggests BPI, PSEQ, PCS, DAPOS A and D measures of pain, dysfunction, disability, anxiety and depression rise with increases in area of the pelvic pain. The DAPOS positive outlook was found to be equal in both groups. There was a tendency to see more catastrophising in the group of patients with a wider spread of pain.
Conclusion
We observed that there is a tendency to see increasing levels of anxiety, disability, pain experience associated with the number of sites where the pain is perceived, when the EAU axis 1 classification was applied to 713 patients. Our data supports the current classification system by axis when it comes to collecting and pooling PROMs used in our institution. References European Association of Urology Guidelines on Chronic Pelvic Pain 2014 Engeler D, Baranowski A, Borovicka J, et al. http://uroweb.org/wp-content/uploads/26-Chronic-Pelvic-Pain_LR.pdf Giamberardino MA, Costantini R, Affaitati, et al. Viscero-visceral hyperalgiesia: Characterization in different clinical models. Pain 2010 151:307–322
Title: Vulvodynia Management: An Empirical Investigation

Poster Number PTH266

Authors
M. Alappattu, G. Lamvu

University of Florida, Gainesville, FL, Veterans Affairs Orlando Medical Center, Orlando, FL

Aim of Investigation
Vulvodynia is a condition that affects 16% of females in the United States and defined as burning pain that occurs in the absence of relevant visible findings or a specific clinically identifiable, neurologic disorder. Published guidelines for vulvodynia exist with recommendations that patients receive the following treatments: topical medications, oral medications, injections, physical therapy, and psychotherapy. Despite these recommendations, no empirical information exists related to how closely physicians follow these guidelines. Thus, the aim of this investigation is to report the type and frequency of treatment for vulvodynia prescribed by physicians using data from the National Vulvodynia Registry (NVR).

Results
Approximately 900 women across the eight sites were screened for eligibility into the NVR and 344 women provided consent to participate in the NVR. Of the 344 women, 291 with complete treatment prescription data were included in this investigation. The mean age of the sample was 34.6 year (SD=12.3). The most commonly prescribed treatment for vulvodynia was topical vaginal creams (82.8% of cases), followed by physical therapy (50.5% of cases), oral medications (44% of cases), psychotherapy (11.7% of cases), dilators (8.9% of cases), injections (4.5% of cases), vaginal suppository (3.8% of cases), and surgery (2.1% of cases). In terms of multiple treatments, 2.4% of patients were not prescribed any additional treatment, 26.8% were prescribed one treatment, 38.1% were prescribed two treatments, 26.4% were prescribed three treatments, 5.5% were prescribed four treatments, and 0.3% were each prescribed five and six treatments.

Conclusion
These data suggest that physicians who manage vulvodynia do not uniformly follow all recommended treatment guidelines, particularly with regard to physical therapy, oral medications, and psychotherapy. The most closely followed recommendation was topical vaginal creams and less than one percent of
patients received all recommended treatments. A potential reason for the lack of uniformity in
treatment prescription is that the treatment guidelines are general in their recommendations and little
information is known about responders to particular types of vulvodynia treatment. Future work in this
area should expand our understanding of the clinical decision making when prescribing vulvodynia
treatments and identifying characteristics of women with vulvodynia who respond favorably to specific
treatments.
Title: Mindfulness Meditation Induced Analgesia Is Not Mediated By Endogenous Opioids

Authors

Wake Forest School of Medicine, Winston-Salem, NC, Wake Forest University, Winston-Salem, NC, University of North Carolina Charlotte, Charlotte, NC, Cincinnati Children's Hospital, Cincinnati, OH

Aim of Investigation
Endogenous opioidergic systems have been repeatedly shown to mediate the cognitive attenuation of pain. Mindfulness meditation, a cognitive practice, premised on sustaining non-judgmental awareness of arising sensory events, reduces pain through neural mechanisms that are suggestive of opioidergic involvement. For instance, mindfulness-based pain relief is associated with greater activation in prefrontal, anterior cingulate, and insular cortices, brain regions containing high concentrations of opioid receptors. However, mindfulness meditation is also associated with deactivation of the periaqueductal gray matter, a brain area critically involved in mediating opioid-driven descending inhibition of pain. The aim of the proposed randomized, double blind psychophysical and pharmacologic study is to determine if meditation requires endogenous opioids to reduce pain.

Results
Mindfulness meditation during saline infusion significantly reduced pain intensity and unpleasantness ratings when compared to the control + saline group (p < .001). Importantly, mindfulness meditation during naloxone infusion produced significantly greater reductions in pain intensity and unpleasantness ratings than the control groups (p < .001). Thus, naloxone failed to reverse meditation-induced analgesia. There were also no significant differences in pain intensity (p = .69) or pain unpleasantness (p = .75) reductions between the meditation + naloxone and the meditation + saline groups.

Conclusion
This is the first study to demonstrate that mindfulness meditation-induced analgesia does not require endogenous opioids to reduce pain. These findings provide supplementary evidence that meditation attenuates the subjective experience of pain through unique mechanisms. Taken together with our previous findings, we will propose a new model for the mechanisms supporting meditation-induced
analgesia. We postulate that mindfulness meditation engages multiple, executive level neural mechanisms (i.e., orbitofrontal cortex; perigenual anterior cingulate cortex) to reduce the elaboration of ascending nociceptive input at the level of thalamus and other low-level sensory processing regions (i.e., primary somatosensory cortex). These findings are also important for the millions of chronic pain patients seeking a fast-acting, non-opioid based pain therapy. Since opioid and non-opioid mechanisms of analgesia interact in a synergistic manner, the present work suggests that the combination of mindfulness-based and pharmacologic/non-pharmacologic analgesic strategies that rely on opioid signaling may be particularly effective in the treatment of pain due to a lack of cross tolerance effects.
Title: Accept Or Change? A Randomized Controlled Trial Of Brief Mindfulness Training Versus Hypnotic Suggestion For Acute Pain In The Hospital Setting

Poster Number PTH268

Authors
E. Garland, Y. Nakamura

University of Utah, Salt Lake City, UT

Aim of Investigation
This poster reports one of the first randomized, head-to-head comparisons of mindfulness to hypnotic suggestion in the management of acute pain in the hospital setting. Although hypnosis and mindfulness have been shown to be viable mind-body interventions for pain control, there have been few (if any) head-to-head comparisons of these techniques. We conducted a randomized controlled trial comparing the relative efficacy of hypnotic suggestion and brief mindfulness training in comparison with an educational control.

Results
Patients receiving the hypnotic suggestion and mindfulness interventions reported significantly greater reductions in pain intensity (25% and 22% respectively, Group X Time F(2,197)=9.9, p <.001) as well as in pain unpleasantness (25% and 31% respectively, Group X Time F(2,197)=13.6, p <.001) than patients receiving the education intervention. Additionally, hypnotic suggestion was associated with significantly greater decreases in desire for opioids than mindfulness or education (Group X Time F(2,195)=5.2, p = .006).

Conclusion
Findings suggest a modest superiority of hypnosis to mindfulness in the amelioration of acute pain intensity, whereas mindfulness produced greater reductions in pain unpleasantness. Further, there have been no tests of mindfulness as a treatment for acute clinical pain in the hospital setting. Results indicate that a single brief, scripted training session either focusing on mindfulness or hypnotic suggestion may produce clinically significant benefits to patients in the busy hospital environment.
Title: Different Effects Of Moxibustion Applied To Acupoint Zusanli (St36) And Non-Acupoint Areas In The Perception And Modulation Of Pain In Humans

Poster Number PTH269

Authors
Y. Li, J. Lei, J. Kuang, J. Li, C. Sun, J. Wu, H. You

Key Laboratory of Thermo-Fluid Science and Engineering of MOE, Xi'an Jiaotong University, Xi'an, Shaanxi, China, Center for Biomedical Research on Pain, College of Medicine, Xi'an Jiaotong University, Xi'an, Shaanxi, China

Aim of Investigation
The aim of the present work was to reveal differences of traditional Chinese therapy: moxibustion, applied to Zusanli (ST36) acupoint and non–acupoint areas in the perception of pain and its modulation in humans.

Results
The average skin temperature during the moxibustion at ST36 area within the radius of 0.5 cm did not exhibit significant difference compared with that of within the non–acupoint area (P > 0.05). Contrastingly, the average skin temperature within the ST36 area with the radius of 2 cm was significantly higher than the temperature measured within the non-acupoint area (P < 0.05). All volunteers reported warm, hot, and, burning sensation during the exposure to the moxibustion applied to the ST36 acupoint and the non–acupoint areas. Around 66.7 % of the volunteers felt tolerable pain during the period of moxibustion. No significant difference was found in the perception of heat and pain at the ST36 acupoint areas compared with the treatment of non–acupoint areas.

Conclusion
Despite no significant differences in specificity of pain sensitivity at acupoint and non-acupoint areas, the heat transfer from the acupoint area to its surrounding tissue is better than those in non-acupoint area. It is suggested that moxibustion therapy applied within the acupoint, but not non–acupoint, may recruit more heat–sensitive afferents in treating pain.
Title: Acupuncture Assisted Anaesthesia In A Malaysian General Hospital

Poster Number PTH270

Authors
K. Bhojwani, M. Wen, Y. Yan
Raja Permaisuri Bainun Hospital, Ipoh, Perak, Shuguang Hospital, Shanghai, Shanghai, China

Aim of Investigation
Acupuncture assisted anaesthesia (AAA) is a technique that involves inserting a thin needle into the body at acupuncture points (acu-points) to produce analgesic effect and reduce physiological changes during surgery, hence mimicking modern anaesthesia. Since 2012, the Ministry of Health (MOH) Malaysia has promoted the integration of traditional and complementary medicine, including acupuncture, into MOH hospitals as part of the 'Pain Free Hospital' initiative. The aim of this study was to evaluate the feasibility of this technique including the quality of perioperative analgesia and patient satisfaction.

Results
23 patients were included; ages ranged from 17-74 years and 8 patients (35%) were males. There were 9 Malays and 9 Chinese patients (41% each), 3 Indians (14%) and 1 Vietnamese patient (5%). Types of surgery done included excision of breast lump (39%), cranioplasty or burr hole (17%), excision of thyroid nodule (13%), hernioplasty (4%), chemoport insertion or removal (13%) neck, and lymphnode and preauricular lump excision (13%). 87% were done as day cases. All surgery proceeded well with no complications. All patients required sedation with midazolam (dose range 1-5 mg) and fentanyl (dose range 25-100 mcg) For each operation, less than 10 mls of local anaesthesia was used, mainly for skin infiltration – 2 to 3 times less than if the surgery were to be done under local anaesthesia alone. Post-operatively, 22 patients(96%) reported no or mild pain while 1 patient(4%) reported moderate pain ; all resolved with oral analgesics (paracetamol, celecoxib and/or tramadol) and no one experienced nausea or vomiting. All patients reported that they were 'satisfied' or 'very satisfied' with the technique.

Conclusion
AAA is a feasible technique for selected operations, with high patient satisfaction and minimal perioperative pain and discomfort. While we do not expect AAA to replace conventional anaesthesia, it will certainly widen our armamentarium as anaesthesiologists as we will be able to offer this as an
alternative option to suitable patients. The method is also very cost effective as the needles are cheap and the use of supplementary drugs is minimal. More cases need to be done and prospective studies should be conducted to determine the validity and utility of this technique.
Date: 09/29/2016 03:15:00 PM

**Title**: Analgesic Effect Of Transcutaneous Electrical Nerve Stimulation Via An Opioid Mechanism In Rat Inflammatory Pain Model

**Poster Number** PTH271

**Authors**

Showa University, School of Medicine, Shinagawa-ku, Tokyo, Japan

**Aim of Investigation**
Transcutaneous electrical nerve stimulation (TENS) is a treatment for alleviating pain by stimulating nerves with electrodes attached to the skin. It has been reported that the release of endogenous opioids in the central nervous system is involved in the mechanism of the analgesic effect of TENS. Some studies have demonstrated that electrical stimulation induces the secretion of different opioid peptides according to the frequencies. In this study, we investigated whether TENS promotes the release of β-endorphin, the endogenous ligand of the μ-opioid receptor, in intact rats. We also determined the involvement of β-endorphin in the analgesic effect of TENS on acute and chronic inflammatory pain.

**Results**
A significant increase in β-endorphin was observed in the LF-TENS group compared with the control group, although there was no significant change in the HF-TENS group. In the acute study, pain-related behavior was promoted in the For group, however, the promotion was significantly inhibited in the ForT group. In the chronic study, the pain threshold was significantly decreased in the AA group compared with the Control group, but on day 14 the decrease was inhibited in the AAT group. The administration of naloxone antagonized the analgesic effects of TENS in both inflammatory pain models.

**Conclusion**
These results suggest that LF-TENS treatment has an antinociceptive effect on acute and chronic inflammatory pain in association with β-endorphin secretion.
Title: Radiotherapy Suppresses Bone Cancer Pain And Inhibits Activation Of Camp And Cgmp Signaling In Rat Dorsal Root Ganglion And The Spinal Cord

Poster Number PTH272

Authors
H. Tan, G. Zhu, Y. Dong, X. Song

Department of Anesthesiology, Peking University Cancer Hospital & Institute, Beijing, China, Center for Clinical Research and Translational Medicine, Lianyungang Oriental Hospital, Lianyungang, China, Department of Anesthesiology, Peking University Cancer Hospital & Institute, Beijing, China

Aim of Investigation
Radiotherapy is one of the major clinical approaches for treatment of bone cancer pain. Activation of cAMP and cGMP signaling are important roles in neuropathic and bone cancer pain. We investigated effects of radiotherapy on bone cancer pain and accompanying abnormal activation of cAMP-PKA and cGMP-PKG signaling.

Results
Radiotherapy significantly suppressed TCI-induced thermal hyperalgesia and mechanical allodynia. The mRNA level of PKA and PKG in DRG, cAMP concentration and PKA activity in DRG and in the spinal cord, as well as concentrations of IL-1β and TNF-α in the spinal cord were significantly increased after TCI. These alterations were significantly reversed by radiotherapy.

Conclusion
This study demonstrates that radiotherapy can suppress bone cancer pain and inhibit the abnormal activation of cAMP-PKA and cGMP-PKG signaling and the proinflammatory cytokines in DRG and the spinal cord in rats.
Title: New Therapeutic Approach For Allodyna In Patients With Acute Spinal Cord Injury: Preliminary Results

Poster Number PTH273

Authors
A. Duprat Ramos, I. Barreto Bassi, A. Silva de Miranda

Fundação Hospitalar do Estado de Minas Gerais - FHEMIG João XXIII Emergency Hospital, Belo Horizonte, Brazil, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais

Aim of Investigation
Allodynia is defined as a pain in response to a nonnociceptive stimulus due to loss of sensory specificity. Currently there is no specific treatment for this condition. The aim of this work was to report the outcome of patients with mechanical allodynia, after being submitted to a hand technique, admitted to the neurosurgical sector from a trauma reference emergency hospital in Brazil.

Results
Four patients with allodynia complaint were enrolled in the study. All of them were male, with thoracolumbar spinal cord injury (SCI) caused by fire gun, GCS 15 and admitted in 2014. In the same year, the total number of patients with SCI with different causes admitted in the EH was 312 (243 men and 69 women). From this total number, 30 was caused by gun fire (28 men and 2 women). Four men from the 28 total had the allodynia. The mean age was 23 years old (range 30-19) and none of them underwent surgery. All patients (n=4) had pain level of 10/10 according to the VAS before the hand technique application. After the physical therapy technique, all patients had their pain reduced for a low level, mean intensity 2/10 (range 0-4) and the allodynia did not returned during the entire hospitalization. The physical therapy session ends when patients did not complaint anymore of painful sensation caused by touch, pressure, pinch or mechanical brush. In all cases the allodynia led to limitations in functional activities as personal hygienical care and in routine medical procedures.

Conclusion
Our preliminary data indicates that the proposed therapy might be a potential therapeutic approach for the management of mechanical allodynia in patients with SCI caused by fire gun. The decrease of allodynia following the hand technique improved the functional limitations of patients during the hospitalization.
Aim of Investigation
Isoflurane is one of principal inhaled anesthetics used on medicine and basic research nowadays. Acupuncture (A) and Electroacupuncture (EA) are accepted as a good treatment for neuropathic pain (NP), however pre-clinical studies are still necessary to improve knowledge on this field. Due to the difficulty to apply these treatments on rats awake and freely movements, most studies use restrain or anesthesia to apply the treatment on rats; however, both conditions could cause some bias. To test the hypothesis that anesthesia can interfere on exploratory behavior and could promote neuronal injury, we perform open field test and measure S100β level on serum blood of rats submitted to NP model treated with A or EA, with and without anesthesia.

Results
On open field test, the number of external crossed squares demonstrated interaction between the independent variables anesthesia x treatment, and effect of the independent variable anesthesia (P≤0.05). On rearing behavioral, there were interactions between anesthesia x acupuncture, and effect of independent variable pain and anesthesia (P≤0.05). On latency output of the first square and on quantity of fecal bolus there was effect of independent variable anesthesia (P≤0.05). On S100β measure, the analyses demonstrated there were interaction between the independent variables: pain x treatment (P≤0.05) and pain x anesthesia (P≤0.05). It was also observed significant effects of the independent variable of anesthesia (P≤0.01).

Conclusion
our results show the effect of isoflurane decreasing locomotion, exploratory behavior and increasing
symptoms of anxiety on open field test. On S100β level, our result demonstrates that animals submitted to pain and treatment showed an increase on S100β level, however which was submitted to pain and anesthesia showed a decrease on S100β level. Animals submitted to anesthesia also presented a decrease on serum blood S100β level in comparison to the groups without anesthesia, showing that isoflurane could prevent some brain damage.
Title: New Challenges And Integrated Approaches For Neuromodulation Of Chronic Pain And Depression With Intranasal Photobiostimulation

Poster Number PTH275

Authors
L. Ailioaie, C. Ailioaie
'Al.I.Cuza ' University, Iasi, Romania, Iasi, Romania, Gr. T. Popa University of Medicine and Pharmacy and St. Mary' Emergency Hospital, Iasi, ROMANIA

Aim of Investigation
Implementation of new intranasal photobiostimulation techniques with two laser wavelengths for the neuromodulation of chronic pain and depression in juvenile idiopathic arthritis (JIA) were investigated. JIA is one of the most common chronic immune-mediated inflammatory diseases (IMIDs) of childhood, with unknown etiology and a complex genetic component. Chronic pain and inflammation are the most devitalizing marks and constitute a threat for the child's quality of life. The laser energy is absorbed by the figurative elements of the circulating blood in the plentiful capillaries inside the nasal cavity, and will be distributed throughout the body and the brain, inducing a systemic effect, bringing great benefits, without side effects or drug complications, and triggering quick results for the redox regulation and the resolution of mitochondrial damage caused by inflammation.

Results
After the first 3 months from the initiation of the study, there was an improvement of the ACR Pedi 30 by 57.14% in Group I, compared to only 35.71% in the placebo group. In the end of the study, in Group I there was an improvement of the ACR Pedi 30 by 82.14%, compared to 46.42% in Group II, with significant statistical differences. The improvement in the quality of life, quantified by SQL score, had significant statistical differences between the two groups. In the end of the study, both SQL and ACR Pedi significantly and strongly correlated in Group I (p = 0.0001).

Conclusion
Neuromodulation of chronic pain and depression using intranasal photobiomodulation is a very new, non-invasive and painless integrative therapy. It is a good option in the field of Pediatrics, in the multidisciplinary management of chronic pain and depression in JIA.
Title: Acupuncture Changes Hyperalgesia Induced By Sciatic Nerve Compression

Poster Number PTH276

Authors
R. Vercelino, L. Spezia Adachi, C. de Oliveira, V. Scarabelot, S. Cioato, I. da Silva Torres

Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil, Federal University of Rio Grande do Sul, Porto Alegre, Brazil

Aim of Investigation
Pain and loss of function are intimately associated with neural damage, and any injury or disease of nervous system can results in neuropathic pain (NP). Acupuncture shows goods results in pacientes with NP, but the effect of needling on pain syndromes yet poorly understood. The association of electric current with acupuncture needles is know as electroacupuncture. Electroacupuncture can promove more analgesic effects than needles only in NP. The objective of this study was to evaluate the effect of treatment of acupuncture (AC) and electroacupuncture (EA) for 8 days on the thermal and mechanical hyperalgesia induced by NP in rats.

Results
Interaction was observed time x treatment (Wald $\chi^2 = 35.785; 21$), $P <0.023$ in the Randall Selitto test, and also in the hot plate test (Wald $\chi^2 = 146.241; 24$), $P <0.000$.

Conclusion
Treatment with AC and EA was able to partially reverse hyperalgesia generated by the pain model, and the effect lasted for 24 hours.
Title: Case Report: Bioregulatory Medicine Through Biopuncture: An Excellent Alternative For Improving The Functionality And Quality Of Life In Patients With Severe Mixed Chronic Pain In Failed Back Surgery Syndrome (FBSS) And Adverse Effects Due To Chronic Use

Poster Number PTH277

Authors
H. Zuleta Angulo
Unidad Medica Villa Country, Barranquilla, Colombia

Aim of Investigation
The following case report assesses the effect of medications with bioregulatory properties, applied primarily by biopuncture, in a patient with Failed Back Surgery Syndrome (FBSS). It is aimed to demonstrate that this treatment is an effective and safe alternative to conventional therapies by improving functionality and quality of life while reducing the risk of side effects

Results
1. Pain: a) Progressive improvement from severe constant pain to a slight to moderate pain. (b) Reduction of allodynia b) Progressive reduction of the area of pain. c) Reduction or withdrawal of conventional medicines; thus reduction of risk of adverse effects. 2. Disability: Progressive improvement from being bed-bound (86%) to moderate disability (31%). 3. Sleep: Improvement in quality and duration of sleep. No more intake of sleeping medication. 4. Scars: Substantial improvement in mobility; elimination of alldynia. 5. Adverse Effects and/or incidents associated with the treatment: No treatment-related adverse effects. 6. Adherence to treatment: Excellent 7. Acceptance of treatment by the patient: Excellent 8. No more need for invasive treatment (spinal neurostimulation)

Conclusion
The presented case demonstrates the potential of a personalized treatment protocol with medications with bioregulatory properties applied primarily by biopuncture. In this particular case the use of medications with bioregulatory properties reduced chronic pain and disability and increased functionality and quality of life. It reduced the risk of side effects from conventional medicines with no reported side effects caused by itself. This positive outcome may be explained by the concept of Extracelluar Matrix (ECM) and related concepts. Medications with bioregulatory properties may neutralize the acid pH of the ECM, produced by pro-inflammatory cytokines and the actions of mast cells.
that control the peripheral sensibility, the neurological plasticity responsible for central sensitization and for chronic pain, the core ailment in patients with FBSS. Therefore this case may suggest that treatment with medications with bioregulatory properties applied by biopuncture could be considered a safe and effective alternative in the treatment of the FBSS
Title: Application Effect Of Acupuncture (Ac) And Eletroacupuncture (Ea) In Rats With And Without Anesthesia In A Model Of Neuropathic Pain (Np)

Poster Number PTH278

Authors
C. de Oliveira, L. Spezia Adachi, R. Vercelino, V. Scarabelot, S. Cioato, A. Souza, C. Wolnei, I. da Silva Torres

Federal University of Rio Grande do Sul, Porto Alegre, Brazil, Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil, Federal University of Rio Grande do Sul, Porto Alegre, RS

Aim of Investigation
Use of acupuncture and electroacupuncture shows promising effects on the treatment of neuropathic pain. Animal studies are needed to clarify the mechanisms involved in this treatment. The AC and EA in animals can be performed with or without anesthesia, but the anesthetic could promote synergistic analgesic effect of the intervention. This study aimed to compare the effects of the application of AC and EA with and without anesthesia in an animal model of mechanical allodynia induced by NP.

Results
On Basal measure, all groups presented pain threshold with no statistically difference to control group (P≥0.001). Post-surgery, the control and sham groups were different from pain groups, showing that the neuropathic pain was established (P<0.001). Immediately after the last session of treatment, both treatments (A and EA) enhances the mechanical pain threshold of animals exposed to a neuropathic pain +A or EA, but this result was not statistically different from neuropathic pain no-treatment groups (Np and NpAn). However, when all groups receive isoflurane anesthesia, the increase on pain threshold was significant different from Np and NpAn groups (P<0.001). This result remained 24h and 48h after the last session of treatment. The generalized estimation equation presented interaction time x treatment (χ2=1419.33; 52) P<0.001.

Conclusion
AC and EA can increase the pain threshold in neuropathic pain model, but not reverse completely. The use of low flow of anesthesia together with AC and EA can potencialize the effect of intervention. This study show that the use of anesthesia can influence the analgesic effect of this intervention in pain animal models.
Title: Vibroacoustic Sound Therapy In Children’S Chronic Pain Management

Poster Number PTH279

Authors
C. Ailioaie, L. Ailioaie

'Al.I.Cuza' University and Laser Clinic, Iasi, +/-, 'Al.I.Cuza ' University, Iasi, Romania, Iasi, Romania

Aim of Investigation
The study aimed to investigate the effects of vibroacoustic sound therapy on pain management in subtypes of juvenile idiopathic arthritis (JIA).

Results
In Group I, changes in SDAI score resulted in the reduction of the disease activity, and the decrease of pain, anxiety and chronic fatigability, as well as increased feelings of well-being, with statistically significant differences compared to the witness group (p<0.001).

Conclusion
Vibroacoustic sound therapy is a noninvasive, safe therapy that has demonstrated its ability to decrease pain, reduce anxiety and the symptoms of illness by a noticeable diminution of the SDAI score, decreasing the disease activity with great statistically significant difference to the witness group.
Title: Peripheral Afferent Mechanisms For Inhibition Of Bladder Micturition Contractions By Stimulating The Perineal Skin In Rats

Poster Number PTH280

Authors
H. Hotta, A. Onda, H. Suzuki, S. Uchida

Department of Autonomic Neuroscience, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan

Aim of Investigation
Variety of noxious stimulation and some of non-noxious stimulation applied to perineal skin can inhibit micturition contractions of the urinary bladder. However, the types of somatic afferent fibers involved in such reflex inhibition have still to be accurately determined. We aimed to examine afferent mechanisms for the reflex inhibition of the bladder contractions induced by stimulation of the perineal skin.

Results
Activation of only Aβ fibers (0.2 V) produced an inhibition of bladder contractions 6-10 min after stimulation ended (late inhibition), at any frequencies tested. Additional activation of Aδ fibers (1 V) produced additional early inhibition (immediately after stimulation) at 1 and 10 Hz. Further, additional activation of C fibers (10 V) at 10 Hz produced complete inhibition, consistently in all rats tested: bladder contractions stopped for more than 10 min. This strong inhibition was persisted even after local application of capsaicin to the stimulating nerve. Noxious heat stimulation produced an excitation during stimulation followed by a complete inhibition of bladder contractions (for more than 10 min); both effects were attenuated by capsaicin treatment.

Conclusion
Activities of Aβ fibers (at 0.1-10 Hz), Aδ fibers (at 1-10 Hz), and C fibers (at 10 Hz) contribute to inhibition of bladder contractions at late, early, and both early and late phases, respectively. Not only TRPV1 positive, but also TRPV1 negative, skin afferent fibers, including low threshold mechanoreceptor C fibers, can contribute to the inhibitory effect by perineal stimulation.
Aim of Investigation
The efficacy of acupuncture in clinical trials is difficult to demonstrate due to the absence of a double-blind milieu. Vulvodynia is a chronic pain condition, which affects up to 14 million women in the United States, and is characterized by vulvar pain and dyspareunia (painful sexual intercourse). The aims of this multi-needle, multi-session feasibility study for the treatment of vulvodynia were to determine: 1) feasibility of enrolling and retaining subjects; 2) challenges to protocol implementation; and 3) the range in subjects' acceptability scale scores.

Results
Four subjects were enrolled, two subjects were randomly assigned to each of the two groups, and four subjects (100%) completed the 10-session study protocol without missing any sessions. Double-blind needles were inserted, retained, removed, and rotated according to the study protocol. Two of the 4 subjects' and 3 of the 4 of the acupuncturist's needle-type guesses were correct. All participants guessed they received penetrating needles. Subjects' mean confidence was 7.8±1.7; acupuncturist mean confidence was 4±1.4 in their needle-type guesses. A challenge to maintaining the blind was the acupuncturist noting one mild bruise on both subjects receiving penetrating needles. One subject in the penetrating needle group did not like acupuncture (60% acceptability score); 3 subjects liked acupuncture (100% acceptability scores).

Conclusion
There is a 50/50 chance of maintaining the blind; guesses should be around 50% correct for both groups. In this small sample, subjects with vulvodynia remained blind to the needle type and were confident of their guesses; the acupuncturist did not maintain the blind and was not confident in her guesses. To enhance the acupuncturist's potential to maintain the blind, we will eliminate needle rotation to reduce
potential for bruising. Protocol acceptability is adequate. We will next demonstrate the feasibility of training and observing another acupuncturist in the revised study protocol.
Title: Association Of Vitamin D Supplementation And Chronic Non-Specific Musculoskeletal Pain: A Systematic Review And Meta-Analysis

Poster Number PTH282

Authors
M. Gaikwad, S. Vanlint, M. Mittinty, L. Moseley, N. Stocks

School of Medicine, University of Adelaide, Adelaide, Australia, School of Public Health, University of Adelaide, Adelaide, Australia, University of South Australia, Adelaide, Australia

Aim of Investigation
Chronic nonspecific musculoskeletal pain (CNMP) is a complex idiopathic condition which causes significant disruption to patients' lives, their relationships and functionality. The etiology of CNMP is not fully understood which makes diagnosis and management challenging. We have previously identified that general practitioners consider vitamin D testing and supplementation to be an important part of management. We aimed to determine the current state of evidence concerning the effectiveness of vitamin D supplementation in the management of CNMP, through systematic review and meta-analysis of the available literature.

Results
The initial search identified 107 studies, of which 10 were potentially relevant, with 7 studies excluded because they did not meet selection criteria. This left only three studies, which were included in the meta-analysis. We found no effect, nor a trend towards an effect, of vitamin D supplementation (SMD: 0.004; 95% CI: -0.248 to 0.256) on pain in CNMP patients.

Conclusion
Despite the fact that there is a growing interest in using vitamin D supplementation for pain management the current systematic review conducted using RCTs does not support this hypothesis. Although the number of studies in this systematic review are small, the results suggest that vitamin D supplementation is not helpful for treating CNMP patients.
**Title:** E-52862, A First In Class Sigma-1 Receptor Antagonist, In Chronic Acute Post-Operative Pain Following Open Abdominal Hysterectomy: An Exploratory Phase II Clinical Trial

**Poster Number** PTH283

**Authors**
M. Sust, A. Montes, A. Morte, V. Domingo-Triado, S. Manrique, A. Martínez, A. Montero, S. Casals, A. Vaqué, J. Cebrecos, N. Gasc

Laboratorios Dr. Esteve, S.A., Barcelona, Spain, Hospital del Mar, Barcelona, Spain, Pain Clinic Lluis Alcanyís Hospital, Valencia, SPAIN, Hospital Vall d’Hebrón, Barcelona, Spain, Hospital Universitario Cruces, Baracaldo, Spain, Hospital Universitari Arnau de Vilanova, Lleida, Spain, Laboratorios del Dr. Esteve, S.A.U., Barcelona, Spain

**Aim of Investigation**
Postoperative pain management aims to reduce pain intensity and increase patient comfort to allow an improvement of the postoperative outcome. Better pain control is achieved through multimodal analgesia. E-52862 is a first-in-class selective sigma-1 (σ1) receptor antagonist that has demonstrated its effect potentiating opioid analgesia in different animal pain models without exhibiting undesirable effects. In a phase I study when E-52862 was co-administered with morphine, a decrease in the total number of opioid-related adverse events was observed as the dose of E-52862 increased. The aim of the present proof-of-concept study was to investigate the effects of perioperative administration of E-52862 on postoperative pain in patients undergoing open abdominal hysterectomy.

**Results**
In total, 121 patients were randomized to treatment. No clinically or statistically significant treatment differences were observed on PCA morphine consumption in the first 24 and 48 hours. At 24 hours, total morphine consumption was 27.1 mg and 24.4 mg for E-52862 and placebo groups, respectively, being the difference of 2.6 mg. Alike, at 48 hours, total consumption was 38.42 mg and 35.11 mg for E-52862 and placebo groups, respectively, being the difference of 3.3 mg. During the first 24 hours, the mean pain intensity was below in E-52862 arm than in placebo [2.77 vs 3.25 points, respectively (p=0.0588)]. In the immediate postoperative period (first 8 hours) and just before the second administration of E-52862 (18 hours), the difference in mean pain intensity was statistically significant in favour of E-52862 patients (p=0.0465 and p=0.0469, respectively). After 24 hours, the pain was well controlled in both groups. There was a similar number of patients reporting treatment-emergent adverse events (TEAEs) in
both treatment groups. Most of the TEAEs were of mild or moderate intensity. The most common TEAEs were nausea, headache, vomiting and dizziness. Significantly less patients in E-52862 group reported nausea, vomiting and dizziness, common associated morphine adverse events. Moreover, a reduced consumption of antiemetic medication was identified in the group of patients treated with E-52862 (35%) versus patients receiving placebo treatment (52.5%).

**Conclusion**

A single 400 mg dose of E-52862 before hysterectomy shows a clinically relevant reduction of opioid-associated adverse events (nausea, vomiting, and dizziness), a meaningful reduction for the need of concomitant antiemetic medication, and a statistically significant reduction in pain intensity up to 24 hours post-surgery. The analgesic effect was obtained with a similar total amount of morphine in both treatment groups. The maintenance of full morphine analgesic activity concomitant with a reduction in opioid-induced adverse events, represents an enhancement of the benefit-risk of the opioid (morphine) overall clinical profile.
Title: Ceftriaxone And Clavulanic Acid Analgesia In An Inflammatory Pain Model May Be Related To Microglial Modulation

Poster Number PTH284

Authors

Universidad Nacional Autonoma de Mexico, Mexico city, Mexico, Universidad Nacional Autónoma de México, Mexico, Distrito Federal, Universidad Nacional Autónoma de México, Mexico, Mexico

Aim of Investigation
Betalactam molecules (BLMs) are a group of drugs mainly used clinically for their antibiotic properties. However ceftriaxone (CFX) and clavulanic acid (CA), two members of this family with different pharmacokinetic and pharmacodynamic properties, have been demonstrated to have analgesic properties when chronically administered in both inflammatory and neuropathic pain. This effect has been thought to be due to glutamatergic modulation; nonetheless, acute administration of BLMs has also been proven to downregulate inflammatory cytokines such as TNF or IL1b and to regulate microglial activation. The present study was undertaken to determine if acute administration of BLMs has analgesic properties and if those actions could be related to an anti-inflammatory or microglial modulating effect.

Results
CFX administration did not induce an acute analgesic effect (p>0.05), however an important effect was found at 24, 48 and 72 hours after induction of inflammation (p<0.001). A microglial modulating effect was also found when compared to control and diclofenac as less microglial cells were activated (p<0.001). CA administration did induce an acute analgesic effect (p<0.05) that lasted for only 1 hour after administration on the first day. However CA administration 24, 48 and 72 hours after inflammation induction did induce an analgesic effect which was significant compared to control and non significant when compared to CFX. A microglial modulation was also found for CA that was similar to CFX. Neither CFX nor CA groups showed a significant difference in cytokine concentration. (p>0.5)

Conclusion
Although CFX has previously shown analgesic effects, its relation to a microglial modulation has not
been reported. Also, CA acute and chronic analgesic and microglial modulating properties may give a possible translational alternative to this group, as its clinical antibiotic spectrum is negligible.
Title: Betalactam Molecules Acute Analgesic Effect On A Neuropathic Pain Model May Be Related To Dopamine Activity

Poster Number PTH285

Authors
M. Sotomayor-Sobrino, A. Ochoa-Aguilar, R. Lazo-Gomez, L. Balcazar-Ochoa, R. Ventura-Martinez

Universidad Nacional Autónoma de México, Mexico, Distrito Federal, Universidad Nacional Autonoma de Mexico, Mexico city, Mexico, Universidad Nacional Autónoma de México, Mexico, Mexico

Aim of Investigation
Ceftriaxone (CFX) and clavulanic acid (CA) are both part of a group known as betalactam molecules (BLMs), which are commonly used in the clinic as antibiotics. However, ceftriaxone has recently been demonstrated to have antiallodynic and antihyperalgesic properties when chronically administered in murine neuropathic pain models. This effect has been thought to be due to glutamatergic modulation as BLMs administration upregulates glutamate transporter 1 (GLT1) in astrocytes. Nonetheless an acute analgesic effect has also been proven in both inflammatory and neuropathic pain models, which would indicate a possible alternative mechanism. On the other hand, although CA has not yet been proven to share the analgesic attribute, it has been shown to act as an anxiolytic agent apparently due to an enhanced dopamine release. Taking this into account, the aim of our investigation is to elucidate if CA has acute antihyperalgesic properties in a chronic neuropathic pain model comparative to CFX and if administering a dopamine D2 blocker could inhibit this effect.

Results
Acute treatment with either dose of IP administered CFX produced an increase in PWT (p < 0.05) each time it was measured when compared to control. Acute treatment with IP administered CA 1 and 10 mg/kg also increased PWT. This was significant when compared to both control and CFX groups (p < 0.001), however this effect was only found for 60 minutes. After 90 minutes, we did not find any analgesic effect on any dose(P > 0.05.). Haloperidol co-administration inhibited both CA and CFX analgesic effects throughout the 3 hours of the experiment.

Conclusion
Both CA and CFX induce antiallodynic effects when acutely administered in a neuropathic pain model. Administering haloperidol, a non-selective dopamine antagonist, can block this effect. CA induces a
greater effect than CFX, however this only lasts for 1 hour after administration. This difference in latency may be due to CA’s pharmacokinetics so further experiments are being performed by our group to elucidate the cause.
**Title:** Cyx-6: A Novel G-Protein Biased Mop Agonist/Dop Antagonist Evokes Potent Antinociception Following Intracerebroventricular (icv) Administration In Rats

**Poster Number** PTH286

**Authors**

M. Imam, A. Kuo, Y. Cai, T. Li, M. Smith

Centre for Integrated Preclinical Drug Development, The University of Queensland, Brisbane, Queensland, Australia, School of Biomedical Sciences, The University of Queensland, Brisbane, Queensland, Australia, School of Pharmacy, Nanjing Medical University, Nanjing, China, School of Pharmacy, The University of Queensland, Brisbane, Queensland, Australia

**Aim of Investigation**

Biased signaling of G-protein coupled receptors is a recent concept and an evolving area of drug discovery research that has opened immense opportunities to develop selective target oriented therapeutic agents with a reduced side-effect profile. Previous work by others suggests that biased signaling at the μ-opioid (MOP) receptor may evoke antinociception in rodents without activating signaling pathways thought to be responsible for producing undesirable opioid-related side-effects. CYX-6 is an endomorphin-2 analogue (Dmt-Pro-Tmp-Tmp-NH2) that has shown biased G-protein signaling at the MOP receptor, antagonism at the δ-opioid (DOP) receptor and it does not recruit β-arrestin2 in vitro. This in vitro signaling profile has the potential to produce antinociception with reduced opioid-related side-effects. Hence, the aim of the present study was to evaluate whether the promising in vitro signaling profile of CYX-6 at MOP and DOP receptors resulted in a molecule where antinociception was retained in vivo following Intracerebroventricular (icv) administration in a rat model.

**Results**

Single icv bolus doses of CYX-6 (3-20 nmol) evoked dose-dependent antinociception and vehicle was inactive. The potency of CYX-6 at 20 nmol was similar to that of morphine at 100 nmol in the warm-water tail flick test. The duration of antinociception produced by CYX-6 at 20 nmol and morphine at 100 nmol were similar at approximately 3h. The ED50 of icv CYX-6 for evoking antinociception in rats was estimated at 12.6 nmol.
Conclusion
Following supraspinal administration in rats, CYX-6, a selective MOP agonist and DOP antagonist, evoked antinociception in rats with a potency 5-fold higher than that of morphine.
Date: 09/29/2016 03:15:00 PM

**Title:** Adyx003: A Randomized, Double-Blind, Placebo-Controlled, Phase II Trial To Assess The Safety And Efficacy Of A Single Preoperative Dose Of Ayx1, An Egr1 Decoy, For Postoperative Pain After Total Knee Arthroplasty.

**Poster Number** PTH287

**Authors**
D. Manning, K. Hebert, S. Harris, A. Das, J. Gimbel, T. Melson, I. Gilron, J. Mamet

Adynxx Inc, San Francisco, CA, Adynxx, Inc., San Francisco, CA, ADas Consultants, Guerneville, CA, OASIS Hospital. Arizona Research Center, Phoenix, AZ, Shoals Medical Trials, Inc., Sheffield, AL, Queen's University, Anesthesiology, Kingston, ON

**Aim of Investigation**
Inadequate pain relief and development of chronic pain still burdens patients after surgery. We designed the investigational drug AYX1, an EGR1 transcription factor decoy, to reduce acute pain and prevent the development of postoperative chronic pain and tested it in subjects undergoing total knee arthroplasty (TKA). A previous study (ADYX002) showed that the efficacy of AYX1 injection (330mg/3mL) in TKA was limited to injections made at or below the L4/5 lumbar interspace. The current study tested the hypothesis that higher doses/volumes of AYX1 with broader lumbar cerebrospinal fluid distribution will have enhanced efficacy independent of spinal injection site for patients undergoing TKA.

**Results**
From May 6, 2014 to May 4, 2015 after central IRB (Western IRB) approval, 120 subjects were enrolled, 116 were dosed and 115 completed the 42-day study. AYX1 660mg/6 mL plus SOC significantly reduced pain with walking during the outpatient period compared to placebo plus SOC (LS mean 2.0 [SEM 0.2] vs. 2.9 [0.3], p=0.026); the 1100mg/10 mL dose did not reach significance (2.4 [0.2] vs. 2.7 [0.4], p=0.423). AYX1 660mg/6 mL also significantly reduced pain at rest during the outpatient period compared to placebo (1.5 [0.2] vs. 2.4 [0.3] p=0.033). Neither dose significantly reduced pain from 0-48 hours. Opioid utilization was similar across treatment groups. Post-hoc analysis, defining a responder as a subject who reached a NRS pain level of <3, showed a greater percentage of AYX1 treated subjects responding at each time point after 48 hours for both pain with walking and pain at rest. The incidence of pain ≥3 at day 42 for both walking (5% vs. 32%) and at rest (3% vs. 21%) was markedly reduced in AYX1 660mg/6 mL-treated subjects compared to placebo. All AYX1- and all but two placebo-treated subjects reported adverse events. Adverse events were, in general, consistent with a population undergoing TKA with


spinal anesthesia and opioid-based analgesia. Eleven subjects experienced a total of 13 serious adverse events. None of these serious adverse events were considered AYX1-related.

Conclusion
A single preoperative intrathecal administration of AYX1 660mg/6mL added to a SOC postoperative analgesic regimen was well tolerated and significantly reduced both movement-evoked pain and pain at rest from day 7 through 28, independent of injection site, and the treatment effect persisted through the 42-day follow-up period. The decreased efficacy of the 1100mg/10mL dose in the 7-28D period (0-48H vs. 7-28D) was consistent with shorter half-life and reduced effects at elevated doses/volumes of AYX1 in preclinical studies. A greater proportion of AYX1-treated subjects achieved NRS scores <3 earlier than placebo-treated subjects for pain with walking and at rest, suggesting a change in the course of post-operative pain. The lower proportion of subjects with pain ≥3 at day 42 in the 660mg/6mL group compared to placebo is strongly predictive of AYX1’s ability to prevent postoperative chronic pain.
Title: Golgi Plays An Important Role In Morphine Tolerance Developing

Poster Number: PTH288

Authors
R. Tsai, C. Wong, C. Li, C. Lai, Y. Cheng

Da-Yeh University, Changhua, Taiwan, Cathay General Hospital, Taipei, Taiwan, Dayeh University, Changhua, Taiwan, National Central University, Taipei, Taiwan

Aim of Investigation
Long-term morphine treatment leads to tolerance. We previously demonstrated that ultra-low dose naloxone restores the antinociceptive effect of morphine in morphine-tolerant rats via suppresses microglia activation. We further investigated that, ultra-low dose naloxone suppressed neuro-inflammation through prevention of heat shock protein 90 (HSP90) cleavage in morphine-induced activated microglia EOC13.31 cells. We found that, morphine enhanced EOC13.31 cell activation and induced HSP90 fragmentation, and the fragments of HSP90 cluster near the Golgi. We suggest that, Golgi perhaps play an important role in morphine tolerance development.

Results
Our results showed that morphine enhanced microglia activation and migration, induced HSP90 fragmentation and histone deacetylase 6 (HDAC6) expression. Moreover, morphine-induced α-tubulin deacetylation and HSP90 fragmentation were HDAC6-dependent. Pretreatment with naloxone (1 nM) not only inhibited morphine-evoked microglia activation, but also prevented HSP90 fragmentation and gather around Golgi by inhibiting HDAC6 expression.

Conclusion
We demonstrated a novel phenomenon that ultra-low dose naloxone inhibits morphine-induced microglia activation by prevent HSP90α fragmentation. Our results broaden the molecular basis of morphine-induced microglia activation.
**Title:** E-52862, A First In Class Sigma-1 Receptor Antagonist, In Oxaliplatin-Induced Peripheral Neuropathy: An Exploratory Phase II Clinical Trial

**Poster Number** PTH289

**Authors**

Laboratorios del Dr. Esteve, S.A.U., Barcelona, Spain, Hospital Universitari de Bellvitge, Barcelona, Spain, University Hospital of Patras, Rion-Patras, Greece, Medicxact, Madrid, Spain, Hospital Clínic, Barcelona, Spain, Sant Gerardo Hospital, Monza, Italy, Azienda Ospedaliera Di Padova, Padova, Italy, Laboratorios Dr. Esteve, S.A., Barcelona, Spain

**Aim of Investigation**
Colorectal cancer is one of the leading causes of cancer and cancer-related death. Oxaliplatin (OXA)-based regimens have become the standard therapy for colorectal cancer. However, its administration is commonly hampered by the occurrence of peripheral neuropathy. E-52862 is a first-in-class selective sigma-1 receptor antagonist that has demonstrated analgesic activity in animal models, particularly chemotherapy-induced neuropathic pain, at doses devoid of side effects. The aim of this study was to evaluate the suitability of E-52862 to prevent and treat acute and chronic oxaliplatin (OXA)-induced neuropathy.

**Results**
124 patients were randomized (62 E-52862, 62 placebo), 63 patients withdrew prematurely before ending of 12 planned OXA cycles. Acute neuropathy: a) Sensory thermal sensitivity: E-52862 reduced, at pre and post-cycle assessments, both cold pain threshold (p=0.018 and p=0.001, respectively) and supra-threshold cold stimulus-evoked pain intensity (p=0.032 and p=0.036, respectively). The effects of E-52862 were present from the first cycle over all cycles and across the whole chemotherapy period. b) Specific OXALIPLATIN-induced neuropathy questionnaire: E-52862 markedly reduced the signs and symptoms due to acute motor neurotoxicity. Chronic neuropathy: a) NCI-CTCAE grade ≥3 (severe symptoms that limit self-care activities of daily living): 3.0% patients of E-52862 and 18.0% of placebo group developed severe neuropathy (p=0.046). b) TNS: low scores were obtained for both placebo and E-52862, with no significant differences between groups. Safety: 1279 adverse events (AEs) were recorded in 62 patients of the E-52862 group and 1146 AEs in 58 patients of the placebo group. Most of
these AEs occurred during the chemotherapy period. Few AEs were assessed as related to E-52862 [38 (3.0%) in 16 patients] or placebo [40 (3.5%) in 7 patients].

**Conclusion**
E-52862 showed evident efficacy in acute and probable efficacy chronic oxaliplatin-induced peripheral neuropathy. E-52862 is well tolerated in patients with colorectal adenocarcinoma treated with oxaliplatin.
Title: E-52862, A First In Class Sigma-1 Receptor Antagonist, In Painful Diabetic Neuropathy: An Exploratory Phase II Clinical Trial

Poster Number PTH290

Authors

Laboratorios Dr. Esteve, S.A., Barcelona, Spain, N/A, Madrid, SPAIN, SC Kristef Med SRL, Craiova, Romania, Centrul Medical Sanatatea Ta SRL, Bucuresti, Romania, Spitalul Pelican Oradea, Oradea, Romania, Hospital Universitari de Girona, Girona, Spain, Laboratorios del Dr. Esteve, S.A.U., Barcelona, Spain

Aim of Investigation
Painful diabetic neuropathy (PDN) is a common complication of diabetes. It has major implications on quality of life, morbidity and costs from a public health perspective. Despite many decades of drug development, current treatment of this chronic neuropathic pain is still an unmet need. E-52862 is a first-in-class selective sigma-1 (σ1) receptor antagonist that has demonstrated robust analgesic activity after administration in animal pain models of diabetes type 1 and type 2 at doses devoid of side effects. The aim of this proof-of-concept study was to explore the effects of daily administration of 400 mg of E-52862 in patients with painful diabetic neuropathy during 28 days.

Results
In total, 163 patients were randomized to treatment. After 28 days of treatment, the average pain intensity values assessed by NPRS showed a reduction of 2.6 and 2.4 points, for E-52862 and placebo, respectively. Similar differences between treatment groups were obtained for worst NPRS pain intensity values and the items of SF-BPI. In parallel, a high percentage of patients with a reduction from baseline of at least 50% measured by the NPRS average pain (50% responders) after 28 days of treatment was seen in both treatment groups: 38.8% and 34.6%, for E-52862 and placebo, respectively, with a statistically significant difference favouring E-52862 at Day 7 being observed (11.5% versus 3.1%, p=0.021). The exploratory subgroups analysis indicated interesting results favouring E-52862 that deserve further discussion. There were no serious Treatment Emergent AEs (TEAEs) reported and only one patient discontinued due to a non-related TEAE in the E-52862 group. Moreover, there was a low incidence of patients reporting at least one TEAE and it was similar between treatment groups: 34.1% in
the E-52862 group and 26.9% in the placebo arm. From these TEAEs a very low incidence was assessed as related to the study drug (12.9% in the E-52862 group vs 10.3% in the placebo arm). The most frequently occurring TEAE was nausea (E 52862 group: 8 patients [9.4%] experienced 15 TEAEs, placebo group: 0 patients). No clinically significant trends were observed among laboratory test parameters, vital signs, ECG or physical examination.

**Conclusion**
The magnitude of effect of E-52862 in reducing pain intensity observed in the study was at least comparable to published data from other standard of care approved medications for DPN. E-52862 was shown to be very well tolerated in this study, allowing the performance of further development taking into consideration the results of the subgroup analysis.
Title: E-52862, A First In Class Sigma-1 Receptor Antagonist, In Chronic Post-Surgical Neuropathic Pain: An Exploratory Phase II Clinical Trial

Poster Number PTH291

Authors

Laboratorios Dr. Esteve, S.A., Barcelona, Spain, UNIVERSITY OF GRANADA (SPAIN), GRANADA, Spain, Clinica Ruber, Madrid, Spain, Hospital Gregorio Marañon, Madrid, Spain, N/A, Palma De Mallorca, SPAIN, N/A, Castelldefels, SPAIN, Laboratorios del Dr. Esteve, S.A.U., Barcelona, Spain

Aim of Investigation
Chronic post-surgical neuropathic pain (CPSNP) is a common complication of surgery and the second most common cause of neuropathic pain. The incidence of CPSNP is underestimated and differs among the various types of surgery. The management and prevention of CPSNP remains inadequate to date, which has a major impact on both patients and society. E-52862 is a novel selective sigma-1 receptor antagonist that has demonstrated robust analgesic activity after administration in different animal models of pain, particularly neuropathic pain, at doses devoid of side effects. The aim of this study was to explore the efficacy, safety and tolerability of daily oral administration of 400 mg of E-52862 in patients with CPSNP during 28 days.

Results
In total, 116 patients were randomized to treatment. After 28 days of treatment, the pain intensity values assessed by NPRS showed a reduction in the average pain of 1.56 and 0.89 points, for E-52862 and placebo, respectively (p: 0.029); and in the worst pain of 2.00 and 1.04 points, for E-52862 and placebo, respectively (p: 0.035). Similar differences between treatment groups were obtained in the items of SF-BPI and 50% and 30% responder’s rate. Planned analysis by surgery location, showed a reduction in the non-spinal surgery subgroup after 28 days of treatment in average pain [1.86 and 0.83 points, for E-52862 and placebo, respectively (p: 0.077)] and worst pain [2.34 and 0.93 points, for E-52862 and placebo, respectively (p: 0.006)]. Treatment emergent adverse events (TEAEs) were reported by 50 (90.9%) patients in the E-52862 group and 46 (76.7%) patients in the placebo group. TEAEs were mostly mild or moderate in intensity and reversible. Study drug-related TEAEs were reported by 65.5% and 38.3% of the patients in the E-52862 and placebo group respectively. They were mostly central
nervous system and gastrointestinal system disorders being dizziness, headache and nausea the most frequent.

**Conclusion**

The results of this study are of relevant clinical significance considering the study population (chronic patients with moderate/severe pain), the magnitude of change in pain relief measurement, and the lack of effective available treatments in this condition. The adequate safety, tolerability, pharmacokinetics, and pharmacodynamics profile of E-52862 demonstrated in this study support its further development in this condition.
Title: Comparison Of Rat And Mouse Formalin Model To Study The Effects Of MGL Inhibitors In Formalin-Induced Nocifensive Behavior

Poster Number PTH292

Authors
J. Holappa, C. Stenfors, K. Ängeby Möller, J. Immonen, H. Svärd, M. Karimaa, M. Pakarinen, J. Sallinen
Orion Pharma, Turku, Finland, N/A, Turku, FINLAND, Karolinska Institutet, Södertälje, Sweden

Aim of Investigation
Modulation of the endocannabinoid system by inhibiting the degradation of endocannabinoids may represent a valuable therapeutic option in the treatment of pain. Increase of endocannabinoid levels in tissues is less likely to cause psychoactive side-effects as has been seen with direct acting cannabinoid agonists, whilst maintaining the beneficial analgesic effects of cannabinoid CB1/CB2 receptor activation. Inhibition of monoacylglycerol lipase (MGL) to increase 2-arachidonoyl-glycerol (2-AG) in the brain is one such approach. Previously, MGL inhibitors have been shown to decrease formalin-induced nocifensive behavior in mice and rats. The aim of this study was to compare MGL inhibitor-mediated antinociceptive effects between rats and mice in the formalin model and to explore the difference in sensitivity of the model between these two species in relation to the increased AG levels.

Results
Single oral administration with selective blockers of MGL raised brain AG, but not AEA levels in a dose dependent manner both in rats and mice. Furthermore, the formalin-induced licking of the paw was also decreased dose-dependently, and correlated well with the increase in AG levels in the brain. In our studies a larger increase in AG levels was needed in mice compared to rats in order to decrease formalin-induced licking behavior.

Conclusion
This study supports the use of the formalin model to detect MGL inhibitor-mediated antinociceptive effects in mice and rats. However, the formalin model performed in rats appears to be more sensitive in detecting antinociceptive effects related to the increased AG levels, than when it is performed in mice. Thus, this model may serve as a valuable model in the lead optimization phase of a drug development program.
Title: Bupivacaine Lozenges For The Treatment Of Pain Due To Oral Mucositis In Patients With Head And Neck Cancer: A Phase II Randomized, Controlled Study

Poster Number PTH293

Authors
S. Mogensen, C. Treldal, J. Bentzen, C. Kristensen, T. Mogensen, J. Petersen, O. Andersen

Clinical Research Centre, Copenhagen University Hospital, Hvidovre, Hvidovre, Denmark, N/A, Copenhagen OE, DENMARK, Department of Oncology, Herlev Hospital, Herlev, Denmark, Department of Oncology, Rigshospitalet, Copenhagen, Denmark, N/A, Greve, DENMARK, Clinical Research Centre, Copenhagen University Hospital, Hvidovre, Hvidovre, -- SELECT --

Aim of Investigation
The aim was to investigate the efficacy of bupivacaine (25mg) lozenges (L) as local oral pain treatment in addition to standard pain treatment compared to standard treatment (ST) in head and neck cancer (HNC) patients with oral mucositis (OM). The primary endpoint was pain in mouth or pharynx 1 hour post administration of the lozenges compared to the average pain during the day for ST-group in a seven day treatment period.

Results
32 HNC patients completed the study. The L-group had a lower level of pain (VAS 35mm in L-group vs. 51mm in ST-group, p=0.0032). The difference in the mouth (pharynx excluded) was even more pronounced (VAS 18mm in L-group vs. 36mm in ST-group, p=0.0002). No serious adverse events were reported among the patients treated with the bupivacaine lozenge.

Conclusion
The results show that the bupivacaine lozenge has a clinically significant pain relieving effect in patients with oral pain due to mucositis compared to standard treatment.
Title: Is Opioid Constipation Still A Problem?

Poster Number PTH294

Authors
R. Vrads, T. Mahler, G. Handberg

Pain Centre South, Odense University Hospital, Odense, Denmark, University of Southern Denmark, Institute for Health Services Research, Faculty of Science, Odense C, Denmark, Pain Centre South, Odense University Hospital, Odense C, Denmark

Aim of Investigation
The aim of the study was to analyze the extent of opioid-induced constipation in a group of chronic pain patients attending our multidisciplinary pain centre and if the patients were constipated did they receive an acceptable laxative treatment.

Results
22 patients were included in the study of which 19 patients participated in the interview. 12 (63,2 %) of the 19 patients reported constipation of which 11 (91,7 %) were treated with laxative. 8 (72,7 %) patients were satisfied and 3 (27,3 %) unsatisfied with the treatment. 7 (36,8 %) patients reported not to be constipated and none of them were in laxative treatment. 1 patient was constipated but did not receive any laxative treatment. 22 patients fulfilled the BFI. 20 (91 %) patients with normal or moderate BFI implying no or moderate degree of constipation were all treated with less than 60 mg morphine a day and the 2 patients with severe constipation according to the BFI received more than 60 mg a day.

Conclusion
In this study 2 out of 3 pain patients in opioid treatment were constipated according to the interview. Previously studies have reported as low as 40 % opioid users are constipated. Moderate to severe constipation may reduce quality of life and in this study almost 1 out of 3 patients is not satisfied with his or hers laxative treatment. In this study there is a tendency towards: The less opioid the less constipation. We conclude that opioid induced constipation is still a clinical problem. It is not a problem for all patients treated with opioid but for those who have a problem, the constipation should be addressed. Sufficient treatment of iatrogenic constipation is a central issue for god clinical praxis.
Title: Effects Of Intraarticular Injection Of Anti-Nerve Growth Factor Neutralizing Antibody On Pain In Osteoarthritis Rat

Poster Number PTH295

Authors
k. aso, M. Izumi, M. Ikeuchi

Department of Orthopedic Surgery, Kochi Medical School, Kochi University, Nankoku, Japan

Aim of Investigation
More recently, nerve growth factor (NGF) has been recognized as an important mediator of chronic knee pain caused by osteoarthritis (OA). Recent human clinical trials showed that a therapy blocking NGF remarkably reduced joint pain in knee OA. However, effects of local administration of anti-NGF antibody in OA rat have not been clarified. Aim of this study was to examine the intraarticular injection of anti-NGF neutralizing antibody on pain in OA rat. Specifically, we evaluated pain-related behavior and the histological changes of OA by administration route (intraarticular (IA) versus intraperitoneal (IP)).

Results
MIA injection decreased mechanical threshold in the knee joint and the hind paw. Anti-NGF neutralizing antibody IP injection significantly reversed mechanical hyperalgesia of the knee joint and hind paw at day 35, 35 (2 hours after injection), 36, 42 and 21 (2 hours after injection), 28 (2 hours after injection), 35, 35 (2 hours after injection), 36, 42, respectively. IA injection significantly reversed mechanical hyperalgesia from day 14 (2 hours after injection) to 42. Analgesic effect of IA injection was greater than IP injection. The OARSI histological scores of anti-NGF (IP), anti-NGF (IA) and control were 1.8 (1, 2.9), 4.5 (2.8, 5) and 1.3 (0.5, 2.7). The OARSI score of anti-NGF (IA) was significantly higher than control.

Conclusion
Our results showed anti-NGF neutralizing antibody inhibited mechanical hyperalgesia induced by MIA injection in the knee joint and the hind paw. The analgesic effect of anti-NGF neutralizing antibody IA injection was greater than IP injection. These results suggest that inhibition of local NGF is important in order to reduce of OA pain. Histological analysis showed IA injection group had higher histological scores for OA than control. OA progression in IA injection group probably caused by increased activity due to pain reduction. Another possible explanation is subchondral microfractures occurred in rapidly progressive OA, because NGF plays an important role in promoting bone formation and healing. In
conclusion, anti-NGF neutralizing antibody IA injection was more efficacious for the treatment of OA knee pain than IP injection, but IA injection of high concentration probably lead to progression of knee OA. The cause for rapidly progressive OA requires further investigation.
**Title:** Compatibility And Stability Of Opioids In Combination With Commonly Used Supportive Drugs Administered By Continuous Subcutaneous Infusions For End Of Life Care

**Poster Number** PTH296

**Authors**
A. Dickman, E. Roberts, P. Weir, J. Ellershaw

Marie Curie Palliative Care Institute Liverpool, Liverpool, United Kingdom, Quality Control North West, Stepping Hill Hospital, Stockport, United Kingdom

**Aim of Investigation**
To determine the chemical compatibility and stability of commonly encountered opioid-containing drug combinations administered by continuous subcutaneous infusion (CSCI) in end-of-life care.

**Results**
All 25 combinations were identified as compatible and stable over the 24 hours. The combinations tested remained clear and free from visible particulate matter and the pH remained constant over the monitored period. There was some evidence of a transient reduction in concentration of certain drugs, which is indicative of adsorption to the PVC administration lines.

**Conclusion**
This research is the first step towards providing technical information required by healthcare staff for the mixing of injectable medicines in the same syringe. From our work it can be concluded that 25 combinations of commonly encountered opioid-containing drug combinations are chemically and physically stable and compatible for infusion over 24 hours.
Title: Utilizing Time Series Analyses Of Pain And Sleep Interference To Predict Therapeutic Response To Pregabalin In Patients With Painful Diabetic Peripheral Neuropathy

Poster Number PTH297

Authors

J. Alexander, Jr., R. Edwards, A. Savoldelli, L. Manca, R. Grugni, E. Whalen, B. Emir, S. Dubrava, M. Brodsky, B. Parsons

Pfizer, New York, NY, Health Services Consulting Corporation, Boxborough, MA, Fair Dynamics Consulting, srl, 20154 - Milano MI, Italy, Pfizer, Groton, CT

Aim of Investigation

Predicting medication therapeutic response based on trajectories of changes over time in pain levels and sleep interference have the potential to improve patient outcomes. The bidirectional relationships between pain and sleep interference have been documented; however, practical implications for therapeutic interventions and patient management remain challenging. Our goals were to identify patient subgroups in both randomized clinical trial (RCT) populations and observational study populations based on their baseline pain levels, baseline sleep interference levels, patient characteristics, and initial response to pregabalin.

Results

Cluster analyses identified 4 clusters for the RCT and 6 clusters for the Observational study with clusters ranging in size from 68 to 180 for the RCT patients and 287 to 777 for the Observational Study patients. Multivariable analyses showed that different explanatory variables were significant in different clusters including different combinations of lagged pain and sleep interference. AUCs of the models for each individual clusters ranged from 0.8508 to 0.9692 for the 10 clusters. For development of the ARMAX models, we used the 1,031 patients (out of 2,790) of the 6 clusters identified in the Observational Study data that matched with the RCT data. CEM results showed favorable global imbalance scores of 0.2545 to 0.3143 for 5 of the clusters and 0.6771 for the last cluster. The remaining 1,759 patients in the Observational study provided the validation dataset. ARMAX models showed R-squared ranging from 0.90 to 0.94 and Root Mean Square Errors ranging from 0.38 to 0.43. Two-sample t-tests comparing observed and estimated probability distribution frequencies at each pain level and % change in pain (responder) all performed well with p-values ranging from 0.40 to 0.80. Lagging prior pain was a
significant covariate for all 6 clusters; lagging sleep interference was a significant covariate in 2 of the clusters as well. Other covariates differed by clusters.

**Conclusion**
Results suggest that patients first need to be sorted into meaningful subgroups in order to better understand how pain and sleep interference patterns can be used to predict responses to pregabalin. They also showed the overlap between patients participating in RCTs in the US and Canada and those who participated in a non-randomized study in Germany. Results still need to be validated in other datasets but the findings show the potential for improving patient care by identifying patient profiles that take into account more complex dynamics related to their pain and sleep interference along with other patient characteristics.
Title: Management Of Pain In Surgical Patients Post-Discharge: Who Is Responsible For Provision Of Advice?

Poster Number PTH298

Authors
F. Veal, A. Thompson, L. Perry, L. Bereznicki, G. Peterson

The Unit for Medication Outcomes Research and Education, University of Tasmania, Hobart, Australia

Aim of Investigation
Up to 80% of patients experience acute pain following surgery. A number of studies have identified that poor pain control following discharge from hospital may contribute to persistent post-operative pain (PPP). This study aimed to identify how patients take analgesics following surgical discharge and if in-patient counselling affects the way patient’s self-manage pain.

Results
500 surveys were mailed and 169 (33.8%) were returned. The median age of the participants was 57 years (range 18-92); 53% were female. Analgesic use was reported by 95.4% of participants in the week following discharge, with 67.8% of patients using more than one class of analgesic. Non-pharmacological strategies were utilised by 35.5% of participants. Sources of medications were varied and included: the hospital at discharge (54.6%), community pharmacy (28.2%), prescription from a general practitioner (25.9%), already in the home (6.5%) or a supermarket (5.6%). Moderate-severe pain was reported by 47.3% participants; 63.7% of these reported using fewer analgesics than directed and 11.3% using more analgesics than directed. The majority (89.3%) of patients were provided or recalled being provided, advice regarding management of their pain after discharge. Nurses (46.7%), doctors (35.5%), pharmacists (30.2%) and anaesthetists (13.6%) provided advice regarding pain management; 32% of respondents were provided advice by more than one health care professional. Most participants received information about what analgesics to take (72.2%) and how many to take (66.9%), with fewer being provided advice about when to contact the hospital (52.7%) or what activities they could or could not undertake (54.4%). Most (78.7%) of the patients stated that they followed the advice given, with those not, most likely to report taking their analgesics differently to directed. People who experienced moderate-severe post-discharge pain were less likely to have received or recalled receiving pain management advice (OR 0.2 95% CI: 0.05-0.83 p=0.03). Only 25% of those patients who had moderate-severe post-discharge pain were seen by the acute pain service (APS) during their stay.
Conclusion
It was concerning to see a high proportion of patients underusing their analgesics despite experiencing moderate-severe pain. Although the vast majority of participants reported receiving advice regarding pain management, this appears to have been conducted in an inconsistent manner. There may be benefits to patients if hospitals were to encourage delivery of advice more consistently, in terms of both content and who it is delivered by. Increasing the role of the APS to include discharge counselling may potentially improve the consistency of advice provided and may allow for patients to self-manage their pain better. Additionally, having increased involvement by the APS at discharge could potentially allow for early identification of those patients at high risk of experiencing uncontrolled post-discharge pain or PPP and their discharge analgesics could be tailored more appropriately to account for this risk. Early intervention, consistent pain management counselling on discharge and more tailored discharge analgesics may aid in reducing the severity or incidence of post-discharge pain and PPP.
Aim of Investigation
An audit of the outcome data from a Qutenza (8% Capsaicin) patch service within a tertiary centre. Qutenza is a relatively new treatment for peripheral neuropathic pain (PNP). Studies have shown that a single application of the high concentration patch for 60min can produce pain relief for 12 weeks or more in some cases. Some of the advantages of using the high dose Capsaicin patch over standard low concentration cream are better patient compliance, longer duration of effect, less systemic side effects and less drug-drug interactions. The improved side effect profile and potential disease modification increase the patient satisfaction/compliance and make it attractive for treatment of PNP.

Results
The audit ran over an 18 month period and more than 60 treatment episodes. Patients treated had various types of PNP including: postsurgical pain, postherpetic neuralgia, chemotherapy-induced neuropathy, idiopathic small-fibre neuropathy and post-amputation pain. The treatment was generally well tolerated by the majority of patients. However, a minority experienced significant discomfort requiring the use of cool packs and in some cases Tramadol. The possibility of significant discomfort had been explained to the patients beforehand and only two patients were dissatisfied with the discomfort level. As per reports in the international literature, there was a variable response to Qutenza therapy, with approximately half of the patients reporting a good response. Of those reporting benefit, we recorded improvements in VAS, BPI, EQ5D and medication consumption.

Conclusion
The Imperial Qutenza service had a successful first year. The response rates are comparable to those published in randomised controlled trials and systematic reviews. The service is feasible and affordable
to set up and has provided an extra therapeutic modality within our multidisciplinary tertiary pain clinic for our patients with PNP. It has benefited a significant proportion of patients including some of those with pain that has been unresponsive to all other treatments including appropriate medications and injection-based therapy. Our experience is consistent with the concept of disease modification with Qutenza therapy.
Aim of Investigation
The use of prescription opioids to treat chronic non-cancer pain remains controversial. Due to increased attention from professional and regulatory boards, and the general public, patients once prescribed high-dose opioids are now being told to reduce or discontinue these medications. As a wide range of biological and psychosocial factors influences a patient's opioid use, no universal approach has been identified for opioid reduction/elimination. Our goal was to identify predictors of opioid cessation after participation in an inpatient, interdisciplinary chronic pain program through a prospective, observational study combined with retrospective chart review.

Results
Baseline NIH-PROMIS measures, hospital length of stay, and absolute MEQ decrease did not differ between groups. Baseline MEQ at hospital admission was 152.1 (139.1) mg in patients reaching opioid cessation, and 644.6 (1190.9) mg in those who did not, p-value = 0.06. Both univariate and multivariate logistic regression analyses of predictors associated with complete opioid cessation after SCIPP participation showed a significant association with baseline MEQ (OR 0.64, 95% CI 0.43-0.95, p-value < 0.03). Every 100mg MEQ increase in baseline opioid dose predicted a 36% decreased odds of complete opioid cessation. On further sensitivity analyses, patients taking less than 100mg MEQ at baseline had a 3.93 (95%CI 1.09-14.2) increased odds of complete opioid cessation at discharge (p-value=0.04). Using PROC MIXED for ANOVA, no statistically significant differences in the rate of change in depression, anxiety, physical functioning, pain impact, and global health scale scores were found from pre- to post-SCIPP treatment between groups.

Conclusion
Baseline MEQ at admission is a significant predictor of complete opioid cessation after participation in an intensive inpatient pain program. No differences in baseline NIH PROMIS scores or their change from pre- to post- treatment may have resulted from lack of statistical power. Maximizing success with
inpatient opioid tapering may require pre-admission opioid dose reduction. Future studies should focus on the role of MEQ at the start of a taper on longitudinal outcomes.
Title: Do Hypnotic Medications Improve Post-Surgical Outcomes? A Systematic Review And Meta-Analysis

Poster Number PTH301

Authors
E. O'Hagan, M. Huebscher, C. Miller, C. Gordon, S. Gustin, J. McAuley

Neuroscience Research Australia (NeuRA), Randwick, New South Wales, Neuroscience Research Australia, Sydney, NSW, Australia, The Woolcock Institute of Medical Research, Camperdown, NSW, Australia, Sydney Nursing School, The University of Sydney, Sydney, NSW, Australia, School of Psychology, University of New South Wales, Sydney, NSW, Australia, Neuroscience Research Australia, Redfern, NSW, Australia

Aim of Investigation
Up to 80% of patients report acute pain post-surgery. If not managed effectively, post-surgery pain can lead to chronic problems. Sleep disruptions following surgery may play a role in the transition from acute to chronic pain and the development of long-term functional limitations. Hypnotic agents or muscle relaxants are used to manage sleep post-surgery, however, the effects of these medications on post-surgery patient outcomes have not been evaluated in a systematic review. This systematic review investigated the effects of hypnotic medications post-surgery on pain intensity and sleep quality.

Results
The search retrieved 5454 articles, from which 70 articles were considered for full text review and 23 fulfilled the inclusion criteria. Risk of bias was unclear in 11 of the studies and low in 12 studies. Pain was an outcome in 19 studies, sleep in 6 studies and both pain and sleep in 3 studies. A meta-analysis, of 5 studies showed that benzodiazepines combined with a usual analgesic regime, were effective at decreasing pain compared with the usual analgesic regime alone (SMD 0.44, 95% CI, 0.19 to 0.70). When compared with placebo, benzodiazepines showed no effect on pain (SMD 0.10, 95% CI, 0.24-0.44; 4 studies). Due to substantial heterogeneity regarding the type of interventions (different combinations of hypnotics and other pain medications), the comparison group (ie. usual analgesic regime or alternate analgesic regime (for example bupivacaine in combination with an opioid) or placebo) and the timing of outcomes assessed it was not possible to pool the results from the remaining studies.
Conclusion
This systematic review showed that benzodiazepines when used in combination with usual analgesics are more effective at reducing pain than usual analgesics alone. Due to the high heterogeneity between studies and inconsistent reporting, the available evidence is insufficient to conclude whether hypnotic medications post-surgery are (a) more effective than placebo, (b) more effective than an alternate analgesic regime (c) or whether they improve sleep outcomes. Future research that addresses these issues is likely to have an impact on these results and improve our understanding of the utility of hypnotics post-surgery.
**Aim of Investigation**

Oxaliplatin is a platinum derivate used in the treatment of colorectal cancer. Administration of this drug produces transient cold-induced dysesthesia and paresthesia at peripheral territories. These symptoms may arise immediately following the first infusion in up to 90% of patients. After repeated administration, about 20% of patients develop chronic dose-limiting neuropathy that compromises quality of life and can lead to treatment arrest. Preliminary results obtained in the lab showed the prevention of oxaliplatin-induced acute neuropathy by the Class I HDACs inhibitor MS-275. The first aim of this study was to analyze the effect of the MS-275 on a mouse model of oxaliplatin-induced chronic neuropathy. Secondly, we investigated the impact of MS-275 on the antiproliferative effect of oxaliplatin both in APCMin/+ mice, a murine model of colorectal cancer, and in human colorectal cancer cell lines.

**Results**

The results showed that Class I HDACs inhibition prevents the cold and mechanical hypersensitivity induced by repeated oxaliplatin injections in mice. MS-275 also prevents oxaliplatin-induced erythrocytopenia. Furthermore, MS-275 did not alter the antiproliferative effect of oxaliplatin in vivo. Moreover, MS-275 per se exerts an antiproliferative effect upon human cancer cells.

**Conclusion**

Our results showed the preventive effect of a Class I HDAC inhibitor in the development of oxaliplatin-induced chronic neuropathy. Moreover, MS-275 didn't alter the antiproliferative effect of oxaliplatin neither in vivo nor in vitro, suggesting that the use of MS-275 could present a double benefit for colorectal cancer patients receiving oxaliplatin treatment.
Title: The Rare Arg181Cys Mutation In The µ Opioid Receptor Can Abolish Opioid Responses

Poster Number: PTH303

Authors: F. Skorpen, S. von Hofacker, M. Bjørngaard, A. Skogholt, O. Dale, S. Kaasa, P. Klepstad

Department of Laboratory Medicine, Norwegian University of Science and Technology, Trondheim, Norway, Haukeland University Hospital, Bergen, Norway, Sunniva Centre for Palliative Care, Haraldsplass Deaconess Hospital, Bergen, Norway, Volda Hospital, Volda, Norway, Norwegian University of Science and Technology, Trondheim, Norway, Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway, 6. European Palliative Care Research Center, Norwegian University of Science and Technology, Trondheim, Norway, Department of Oncology, St Olav's University Hospital, Trondheim, Norway, Department of Anaesthesiology and Intensive Care Medicine, St Olav's University Hospital, Trondheim, Norway

Aim of Investigation
Genetic variability contributes to variable clinical response to opioids. This study emerged from the observation of three Norwegian patients who showed no or extraordinary poor response to very high doses of opioids. The patients were reported to our research group by experienced anesthesiologists. We suspected a genetic defect and applied a 'most likely candidate gene' approach to investigate this possibility.

Results
DNA sequencing disclosed a homozygous, inactivating Arg181Cys mutation in hMOR in a male patient who showed no effects from opioids. During introduction to total intravenous anesthesia (TIVA) this patient received a total dose of remifentanil of 3,000 µg, which is 60 times the dose usually needed for surgical anesthesia. Two female patients with advanced cancer disease both had extraordinary poor pain relief from very high doses of opioids and were found to be heterozygous for the mutation. Six heterozygous patients identified among the European cancer patients all used high doses of opioids and/or reported inferior effect on their pain. About one in every 100 Norwegians is heterozygous for the mutation. The likelihood of reporting two heterozygous patients 'by chance' (i.e. if the heterozygous state does not alter opioid efficacy) is only 1 in 10,000, strongly indicating that heterozygotes can be identified on the basis of their poor response to opioids.
Conclusion
The Arg181Cys mutation occurs at clinically relevant frequencies in several European populations and produces a signaling dead hMOR which may abolish or significantly reduce opioid effects in affected individuals. Anesthesiologists and practitioners in pain medicine should be aware of this mutation as a possible explanation for inefficiency of opioids and consider genotyping in relevant cases. Individuals homozygous for the mutation may need a highly personalized approach to pain therapy.
Title: Induced Side Effects Enhance Response To A Non Steroidal Anti-Inflammatory Drug: An Experimental Analgesic Rct

Poster Number PTH304

Authors

Centre Hospitalier Universitaire Vaudois, Université de Lausanne, Lausanne, Switzerland, Harvard Medical School, Boston, MA, Karolinska Institute, Stockholm, Sweden, Wilfrid Laurier University, Waterloo, Canada

Aim of Investigation
Medication side effects might lead to unblinding in randomized clinical trials (RCT). On one hand, beliefs to be on active medication could enhance active treatment responses, thereby increasing drug-placebo differences. On the other hand, the absence of perceived side effects could lead to beliefs to be on placebo, with ensuing decreased expectations and lessened therapeutic benefits. These hypotheses were tested through an experimental double-blind RCT of a nonsteroidal anti-inflammatory medication (NSAID) with an induced side effect.

Results
Groups did not differ significantly in demographics, state anxiety, temperature producing moderate pain, nor pre-treatment relief expectations. Analgesia was observed in all groups; the ANOVA revealed a significant interaction, F (1,96) = 4.046, p = .047, without main effects. Diclofenac alone was not better than double-placebo. The addition of atropine increased pain relief more than threefold among participants given diclofenac (d= 0.77), but did not enhance the response to placebo (d= 0.09). The induced side effect increased beliefs that one had received active medication, but this belief enhanced pain relief only in the diclofenac group.

Conclusion
These findings could have important implications for the design of RCTs because the double-blind nature of an RCT instills uncertainty in subjects regarding whether they received the active drug or placebo. The doubt produced by double-blind instructions, when not diminished by noticeable side effects, may decrease the effectiveness of the drug.
Title: Analgesic Efficacy And Mode Of Action Of Ema300, A Small Molecule Angiotensin II Type 2 (AT2) Receptor Antagonist For Neuropathic Pain

Poster Number PTH305

Authors
N. Khan, A. Muralidharan, M. Smith

The University of Queensland, Australia, Brisbane, Australia, The University of Queensland, Brisbane, QLD, Centre for Integrated Preclinical Drug Development/ The University of Queensland, Brisbane, QLD, Australia

Aim of Investigation
Neuropathic pain is often difficult to alleviate with currently available first-line treatments due to poor efficacy and/or dose-limiting side-effects [1]. Recently, EMA401, a highly selective, orally bioavailable, small molecule angiotensin II type 2 (AT2) receptor antagonist showed promising efficacy in patients with postherpetic neuralgia in a randomised, double-blind, placebo-controlled Phase 2 clinical trial [2]. Hence, this study was designed to further investigate the mode of action of AT2 receptor antagonists, in a rat model of peripheral neuropathic pain.

Results
CCI-rats but not sham-rats developed mechanical allodynia (PWTs ≤ 6g) in the ipsilateral hindpaws by day 7-10 post-surgery that persisted until study completion at day 14-15 post-surgery. A single i.p. bolus dose of EMA300 at 10 mg/kg produced significant relief of mechanical allodynia (P < 0.05) at 1 h post-dosing in CCI-rats, whereas vehicle did not. Single i.p. bolus doses of vehicle did not significantly alter (P > 0.05) PWT values in sham-rats. Together, our IHC and western blotting data confirm our previous findings that EMA300 alleviated mechanical allodynia in CCI-rats by attenuating augmented AngII/AT2 receptor signaling in the ipsilateral lumbar DRGs of CCI-rats [3]. Of particular interest, we now show for the first time that at the time of peak effect EMA300 restored mature NGF isoform (mNGF) levels in the ipsilateral lumbar DRGs to match the corresponding levels in sham-rats, but without affecting CCI-induced upregulation of TrkA or upregulated expression of GFAP. Thus our findings suggest that augmented AngII/AT2- receptor signaling regulates mNGF expression levels in the ipsilateral lumbar DRGs. Additionally, at the time of peak effect, EMA300 significantly attenuated the up-regulated expression levels of pp44/42-MAPK and pp38-MAPK in the ipsilateral lumbar DRGs in agreement with our previous work [3].
Conclusion

Conclusions: In CCI-rats, augmented angiotensin II/AT2 receptor signaling in the ipsilateral lumbar DRGs reduced mNGF expression levels in the ipsilateral lumbar DRGs and this was reversed by EMA300 at the time of peak pain effect. Our present findings showing that AngII/AT2 receptor signaling modulates mNGF expression levels in the ipsilateral lumbar DRGs of CCI-rats are highly novel and provide new insight on the AT2 receptor as a clinically validated novel target for alleviation of neuropathic pain.

Title: Preventive Effect Of Pulsed Radiofrequency On Mechanical Allodynia Of Chronic Constriction Injury Rats: A Preliminary Study

Poster Number PTH306

Authors

Department of Anesthesiology and Intensive Care Medicine, Osaka University Graduate School of Medici, Suita, Osaka, Japan, Osaka University Graduate School of Medicine, Osaka, Japan, Osaka University Graduate School of Medicine, Suita, Osaka, Japan, Department of Anesthesiology and Intensive Care Medicine, Osaka University Graduate School of Medici, Suita, Osaka , Japan, Osaka University Graduate School of Medicine, Osaka, JAPAN

Aim of Investigation
Pulsed radiofrequency (PRF) delivers electrical field and heat bursts to neural tissue without causing neural injury. Recently, PRF treatment is recommended as the most evidence-based treatment for cervical radicular pain. But there is no report about the effect of preemptive analgesia. In regards to the effectiveness of interventional pain management, it has been reported that preoperative sciatic nerve block in the young animals provides a preemptive analgesic effect on mechanical allodynia. We investigate the preventive effect of PRF for neuropathic pain in rats.

Results
In the group 1, the withdrawal threshold for the paw ipsilateral to the operated paw reduced significantly from the baseline at time point 1 (50.0 ± 0.03 vs. 20.0 ± 2.45g, mean ± SE, baseline vs. time point 1, p=0.08, Steel's test), and PRF treatment improved mechanical hypersensitivity (20.0 ± 2.45 vs. 44.1 ± 6.57g, time point 1 vs. time point 2). The variation of threshold between baseline and time point 2 was 5.80 ± 2.92g (mean ± SE, Steel-Dwass test). In the group 2, the withdrawal threshold did not decreased significantly compared with the baseline value (47.3 ± 3.98 vs. 41.95 ± 6.37g, baseline vs. time point 2, p=0.23). The variation of threshold between baseline and time point 2 was 5.36 ± 2.44 g. There was no significant difference in variation of threshold between group 1 and group 2 (p=0.998).

Conclusion
PRF was effective for neuropathic pain induced by cuffing of sciatic nerve. The results of this study
suggest that the PRF administration before neural injury may prevent the generation of neuropathic pain. We need further study to elucidate the mechanism of it.
Title: Investigating The Neural Circuits Of Spinal Cord Stimulation

Poster Number PTH307

Authors
A. Sdrulla, W. Fan

Oregon Health & Science University, Portland, OR

Aim of Investigation
Chronic pain is a significant public health problem, affecting some 100 million Americans. Neuromodulation approaches such as spinal cord stimulation (SCS) provide important alternative strategies for treating chronic pain conditions when other therapies have failed. Despite widespread clinical implementation, the mechanisms underlying the analgesic actions of SCS remain poorly understood. The 'gate control theory' continues to be the leading explanatory model, postulating that stimulation of low-threshold Aβ-fibers (Aβ-ES) in the dorsal columns activates inhibitory interneurons in the superficial dorsal horn (SDH), 'closing the gate' on ascending nociceptive transmission. However the gate control theory fails to explain how SCS reverses long-term potentiation of wide dynamic range neurons, why SCS is ineffective for 'nociceptive' pain, why only some patients benefit, or the fact that analgesia persists for prolonged periods after stimulation is discontinued. Additional or alternative mechanisms for SCS's effects are therefore needed. Our experiments take advantage of state-of-the-art imaging of genetically encoded calcium indicators expressed specifically in dorsal horn neurons to delineate the effect of Aβ-ES on activity in real time over the entire SDH.

Results
We found that in the baseline condition, without Aβ-ES conditioning, there is a gradual increase in the response to C-fiber intensity stimulation at 0.05 HZ, a phenomenon similar to wind-up (normalized maximum ΔF/F0 at 60 minutes 2.61 ± 0.65, mean ± SEM, n=10 cells from 3 animals, ). This C-fiber evoked wind-up was eliminated by Aβ-ES conditioning (1.17 ± 0.26 at 60 minutes, n=17 cells from 3 animals; p=0.03 comparing control and Aβ-ES at 60 minutes, Mann-Whitney U test) . C-fiber stimulation at lower frequency (0.017 Hz) did not evoke wind-up (1.24 ± 0.21 at 60 minutes, n=20 cells from 4 animals), and Aβ-ES conditioning stimulation did not alter the C-fiber evoked responses in SDH neurons (0.98 ± 0.11 at 60 minutes, n=46 cells from 3 animals).
Conclusion
We found that SDH neurons display wind-up with prolonged low frequency (0.05 Hz) C-fiber intensity stimulation, and using slower stimulation frequencies (0.017 Hz) or giving Aβ-ES conditioning prevented this increase. Although others have shown that Aβ-ES prevented wind-up and long-term potentiation in neurons in deeper laminae, our results are novel as they extend those findings to the superficial dorsal horn, raising the possibility that changes seen in deeper layers reflect changes more superficially. Our studies set the stage for future experiments aimed at characterizing the specific subtypes of excitatory or inhibitory neurons modulated by Aβ-ES.
Title: Audit Of Peripheral Nerve Block – Setting Up A New Service In Resource Limited Setting In Karachi, Pakistan.

Poster Number PTH309

Authors
S. Sultan, M. Iqbal, V. Vankwani

The Indus Hospital, Karachi, Sindh, The Indus Hospital, Karachi, Pakistan

Aim of Investigation
Regional anaesthesia and peripheral nerve blockade is associated with improved patient outcome and increased patient satisfaction. Competency in regional anaesthesia needs formal training and close monitoring as the neurological and other complications associated with peripheral nerve blockade can have disastrous consequences. The Indus Hospital is a charity based, free of cost hospital located in Korangi, one of Karachi's impoverished areas in Pakistan.

Results
Over time the volume of local anaesthesia agent decreased. The failure rate decreased with improvement in sensory and motor blockade time.

Conclusion
We demonstrate a comprehensive audit process for a new service in a developing country. The training of specialists and supervision of procedure overtime results in improved patient care. We also demonstrate the need to follow-up patients after a peripheral nerve block to detect any complication and propose a fast track pathway for management.
Title: Influence Of The Electrodes Positions Of Transcutaneous Electrical Nerve Stimulation On Primary Dysmenorrhea: A Single Case Study

Poster Number PTH310

Authors
I. Yoshie, K. Hideki, K. Shomoto
Graduate School of Health Science, Kio-University, Kitakatsuragigun, Japan, Takarazuka University of Medical and Health Care, Takarazuka-city, Japan

Aim of Investigation
The reports of transcutaneous electrical nerve stimulation (TENS) for the primary dysmenorrhea were seen in various articles, but the influence of the electrodes positions on the pain relief were not clear. The aim of this single case study was to research the influence of the three types of electrodes positions on the pain relief with the primary dysmenorrhea.

Results
The value of VAS reduced in 54mm (pre: 76mm, post: 22mm) at ①, reduced in 78mm (pre: 92mm, post: 14mm) at ②, reduced in 25mm (pre: 64mm, post: 39mm) at ③. Moderate reduction of pain (affective) was shown in MPQ-SF.

Conclusion
It was proposed that a mean reduction in VAS of 30.0 mm represents a clinically important difference in pain severity by the previous study. In this single case study, the dermatomes same as the level that rule nerve of the uterus and the partly same dermatomes were shown to be more possible to clinically important pain relief than the unrelated dermatomes.
**Title:** Epidural Alcohol Neurolysis – A Good Option For Cancer Pain Management

**Poster Number** PTH311

**Authors**
K. PODDAR

FORTIS HOSPITAL, KOLKATA, India

**Aim of Investigation**
Aim is to assess the feasibility, safety and efficacy of the Epidural Alcohol Neurolysis in cases of Cancer Pain.

**Results**
70% patients showed >70% pain relief and 30% patients reported 50% relief. Opioid consumption was reduced to less than 25%. Duration of pain relief was 1 month to 3 months. Activity and sleep scores were good. There were no miserable adverse effects. Most side effects were minor like Burning pain during alcohol injection.

**Conclusion**
The goal of cancer treatment is generally pain reduction and function recovery. Up to 73% of patients are in pain at the time of diagnosis. Thus, a major treatment focus is to optimize the quality of life (QOL) by managing symptoms, especially by providing adequate pain control. The Epidural Alcohol neurolytic block is a good alternative option for the treatment of cancer pain. However, large, well-controlled studies and refinement of the technique using other radiological methods are needed to improve the safety and efficacy of this neurolytic technique.
Title: Spinal Cord Stimulation – An Analysis Of Response To Therapy And Surgical Consequences. A Single Center, Retrospective Study.

Poster Number PTH312

Authors
S. Hara, J. Jørgensen, T. Fredriksen, Ø. Nygaard

Department of Neurosurgery, St. Olav's University Hospital, Trondheim, Norway, Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway, National Advisory Unit on Spinal Surgery Center for Spinal Disorders, St. Olav's University Hospital, Trondheim, Norway

Aim of Investigation
Previous reports have demonstrated that long-term treatment of chronic pain with spinal cord stimulation (SCS) may be cost-effective compared with conventional medical treatment in selected patient populations. However SCS is associated with biological and hardware-related complications and need for repeated re-operations, which both the providers and receivers of SCS should be aware of. This single center study analyzes the individual course of therapy from trial stimulation throughout follow-up in terms of response to therapy and subsequent surgical interventions.

Results
A total of 245 patients with refractory chronic pain conditions were included. The most frequent diagnosis was failed back surgery syndrome (N=106), followed by angina pectoris (N=38) and CRPS (N=21). Eighty percent of the patients (N=196) received an IPG. The trial-to-implantation ratio was dependent on diagnosis. Spinal cord injury had a lower ratio of 47% while all patients with multiple sclerosis received an IPG. Twenty four patients (12.2%) were later lost for further data analysis. Of the remaining 172 patients, 70 patients discontinued the therapy due to either loss of effect (74%), spontaneous improvement of pain (12%), infections (7%) or other causes (7%). A considerable number of devices (46 of 70) were removed even after 24 months of therapy, suggesting that a positive long-term effect of SCS up to 24 months does not ensure a further stable effect. The incidence of complications was comparable with previous reports. The infection rate was 4.0% and this was typically an early complication occurring within weeks of surgery, while electrode migration (6.5%) occurred weeks to months and electrode breakage (3.4%) months to years after implantation. The re-operation rate for survivors during the mean follow-up period of 91.0 months was 2.5±2.8 (range 0-12).
Conclusion
Eighty percent of the selected patients received a permanent internal pulse generator after successful trial stimulation. Of the responders, 40.7% discontinued the therapy later in the course at a steady rate. The most common reason for discontinuation was loss of effect. A positive long-term effect of SCS during the first 24 months did not ensure a further effect. Future research on this specific group of patients who discontinued the therapy is needed to help understand the mechanisms of late therapy failure.
Title: Preliminary Sham-Controlled Randomised Clinical Trial Outcome Of Repetitive Transcranial Magnetic Stimulation Treatment For Fibromyalgia

Poster Number PTH313

Authors
B. Fitzgibbon, K. Hoy, E. Guymer, G. Littlejohn, P. Fitzgerald

Monash University, Melbourne, Australia

Aim of Investigation
Fibromyalgia is a complex chronic disorder with limited effective treatment. One promising new treatment option is repetitive Transcranial Magnetic Stimulation (rTMS); a non-invasive technique that can change the activity of neurons in the brain. Preliminary studies support the use of rTMS for pain relief in people who suffer from fibromyalgia, however treatment courses have been brief (~2 weeks) therefore potentially limiting the therapeutic benefit. The aim of the current study is to investigate the clinical efficacy of a 4-week rTMS treatment course applied to the left dorsolateral prefrontal cortex (DLPFC) in a double blind randomised placebo-controlled pilot trial in patients who suffer from fibromyalgia.

Results
Within the active group, we observed a significant reduction in pain unpleasantness from baseline (6.6[1.4]) to final treatment (4.5[1.4]), t (7) = 4.12, p = .004 (2-tailed, 95% CI = .91 - 3.34, cohen's d = 1.5).
We also observed a reduction in pain interference measured by the Brief Pain Inventory from baseline (6.86[1.50]) to final treatment (4.25[2.86]), t (7) = 4.55, p <.01 (2-tailed, 95% CI 1.25 – 3.96), and a reduction in total score on the Fibromyalgia Impact Questionnaire from baseline (62.60[14.95]) to final treatment (37.63[21.46]), t (7) = 5.70, p <.001 (2-tailed, CI = 14.60 – 35.34). Similar reductions were seen for anxiety from baseline (18.75[9.60]) to final treatment (10.38[8.48]), t (7) = 3.63, p <.001 (2-tailed, CI = 2.92 – 13.83) and pain catastrophisation from baseline (20.38[10.18]) to final treatment (7.13[6.75]), t (7) = 3.57, p <.001 (2-tailed, CI = 4.47 – 22.03). Within the sham group, significant improvements were observed for pain unpleasantness from baseline (6.33[1.53]) to final treatment (4.67[1.15]), t (2) = 5.00, p = .04 (2-tailed, CI = .23 – 3.10, cohen's d = 1.23) and for pain severity measured by the Brief Pain Inventory from baseline (5.83[1.13]) to final treatment (4.25[1.64]), t (2) = 5.27, p = .03 (2 tailed, CI = .29 – 2.88).
Conclusion
The results of this preliminary analysis demonstrate a 4 week rTMS treatment course applied to the DLPFC to significantly reduce pain unpleasantness in a small sample of patients with fibromyalgia. While this was reported in both the active and sham group, the active group revealed a number of additional improvements in our secondary measures. While a larger sample is needed, the results of the current analysis supports the potential role of a 4 week rTMS course as a pain management option for fibromyalgia. Additional data is being collected and will be presented.
Title: Intravenous Ketamine Infusion For The Treatment Of Anaesthesia Dolorosa: A Case Report

Poster Number PTH314

Authors
A. Mattar, M. Ong-Lam

The University of British Columbia, Vancouver, British Columbia

Aim of Investigation
Anaesthesia dolorosa (AD) is a rare complication of trigeminal neuralgia, occurring after traumatic injury to the trigeminal nerve during surgical interventions aimed at providing symptomatic relief. It is characterized by unilateral facial/oral pain and signs of trigeminal dysfunction that include combinations of allodynia, hyperalgesia, hypoalgesia, and hypoesthesia within the distribution of the injured nerve. AD can lead to intractable neuropathic pain, often more difficult to treat than the original trigeminal neuralgia. Much of the research on AD treatment has focused on repeat surgical procedures, and more recently on motor cortex stimulation. Studies on pharmacologic interventions reveal limited evidence for the use of gabapentin, and negative trials on the effectiveness of morphine and dextromethorphan, an NMDA-antagonist. In recent years, ketamine, another NMDA-antagonist, has received increased attention for its efficacy in treating neuropathic pain, particularly in centralized, complex regional pain syndromes. To our knowledge, the use of ketamine for treatment of AD has not been studied. Here we report a clinical case study, in which a patient with post-surgical AD achieved symptomatic relief of her neuropathic pain following an infusion of IV ketamine.

Results
CS received a 9-day infusion of IV ketamine, running at a sub-anaesthetic dose of 30 mg/hour. Her pain improved at infusion rates of 15 mg/hour and greater. Her pain reduced to 5/10 after 4 days of infusion, and then 3/10 by the time of discharge. This was better analgesia than she had obtained at any previous point. This allowed her to reduce her methadone dose to 30 mg/day at the time of discharge, and then further to 26 mg/day in the following weeks. Her pain control was sustained for approximately 1 month. It then returned gradually to its pre-infusion level of 9/10, approximately 60-days post-infusion. The ketamine infusion was tolerated well. CS did develop a transient elevation of liver transaminases, dysuria, and hematuria, all of which were mild and resolved spontaneously once the ketamine infusion was stopped. In hospital she also incidentally developed costochondritis, treated with a short course of gabapentin. CS returned to hospital in February 2016 for a second ketamine infusion. Once again her
pain abated to 4/10, this time at a lesser dose of 20 mg/hour, suggesting replicability of the therapeutic effect of ketamine and an increased dose response.

Conclusion
Here we describe successful treatment of AD with an IV ketamine infusion. To our knowledge this is the first such report in the literature. The analgesic effect was profound and long lasting, with only minor side effects that resolved spontaneously and were not troublesome. This suggests that ketamine may have a role as a treatment option for intractable neuropathic pain that occurs with AD.
Date: 09/29/2016 03:15:00 PM

**Title:** Investigating The Use Of High-Concentration 8% Capsaicin Patch In Patients With Chronic Cancer-Related Peripheral Neuropathic Pain.

**Poster Number** PTH315

**Authors**
S. Ramnarine, B. Laird, L. Williams, M. Fallon

Edinburgh Cancer Research Centre, University of Edinburgh, Edinburgh, United Kingdom
Centre for Population Health Sciences, University of Edinburgh, Edinburgh, United Kingdom

**Aim of Investigation**
Cancer-treatment related peripheral neuropathic pain is a challenging clinical problem as current interventions have significant toxicities and limited efficacy. This study examines the analgesic effect of high-concentration (8%) transdermal capsaicin patch in patients with chronic cancer-treatment related peripheral neuropathic pain.

**Results**
19 patients with a median age of 61.5 (IQR 49-69) were included. All had peripheral neuropathic pain for a median of 2 years (IQR 1-3) following treatment for various types of cancer: gynaecological (n=2), breast (n=6), colorectal (n=8), multiple myeloma (n=2) or other (n=1). The median baseline total BPI score was 56 (IQR 50-69). At 4 weeks post-treatment, 37% (7/19) patients demonstrated a clinically significant improvement in pain (≥ 30%). Of these 7 responders, 5 patients experienced > 50% reduction in pain. 16% (3/19) patients exhibited a possible partial improvement (average 17%). Of the patients reassessed at 12 weeks, 50% (7/14) demonstrated significant improvement in pain (≥ 30%) from baseline. From baseline to 12 weeks, the treatment also resulted in: reduction in worst pain score, -1.3 (95% CI:-2.5, -0.06; p=0.04), improvement in function or reduced interference, -10.9 (95% CI: -21.5, -0.4 p=0.04) and a decrease in the HADS depression subscale, -1.7 (95% CI:-3.4, 0.02; p=0.053). Total HADS score at 4 weeks and 12 weeks correlated with total BPI at the same time points, 4 weeks (r =0.68) and 12 weeks (r =0.70). The HADS depression subscale also correlated with BPI at 12 weeks (r =0.73). All correlations were statistically significant (p<0.01).

**Conclusion**
In patients with chronic, resistant, cancer-treatment related peripheral neuropathic pain, high-
concentration 8% capsaicin patch maybe provide some benefit in pain severity, function and mood with the effect continuing at 12 weeks post-treatment. This may warrant further long-term follow up in a larger cohort of patients.
Title: A Comparative Study Of Caudal Epidural Block With Steroid And Normal Saline Versus Steroid With Bupivacaine For Treating Chronic Low Back Pain.

Poster Number PTH316

Authors
S. Lawange, Bliss Pain Relief Center, Nagpur, Maharashtra, Bliss Pain Management Centre and Orange City Hospital and Research centre, Nagpur, Maharashtra, India, Bliss Pain Management Centre and Orange City Hospital and Research centre, Nagpur, Maharashtra, India

Aim of Investigation
1) To assess the effectiveness of both combinations administered via caudal epidural route for treating low back pain. 2) To compare the effectiveness of both combinations. 3) To assess the short and long term efficacy of both.

Results
Initial short term relief in Study group (Steroid and NS) was less when compared to Control group (Steroid and bupivacaine) this was probably due to action of local anaesthetic. Long term pain relief and improvement in disability score was comparable and same in both the groups. A stable haemodynamic status was observed in Study group after injecting the drug whereas a significant number of patients in Control group in the form of bradycardia and hypotension. Not a single patient in study group suffered from haemodynamic instability.

Conclusion
Caudal epidural injection with normal saline and steroid is a better, safe and effective alternative when compared with bupivacaine and steroid combination in patients suffering from chronic low back pain. The pain relief in both groups was mainly due to methylprednisolone.
Title: The Use Of Group Therapy For Chronic Pain Patients In A Multidisciplinary Setting.

Poster Number: PTH317

Authors
B. Hesjedal, A. Paulsberg, T. Meyer
Haukeland University Hospital, Bergen, Norway, Haukelands University hospital, Bergen, Norway

Aim of Investigation
Aim of investigation was to find out if group therapy can contribute to reduced fear of movement, improved physical function and reduced anxiety and depression. The overall major aim of the group therapy was to stimulate the development of coping strategies.

Results
We have now completed 2 of 3 groups with a total of 14 patients. 11 of the patients have completed the questionnaires. The final results of the project will be presented in the poster. The preliminary results show a change in Tampa scale which indicated less fear of movement in 36,36% of the patients, and more fear of movement in 45,45% of the patients. 18,18% were unchanged. In Pain Catastrophizing Scale 27,27% had less pain dramatizing after completion, and 72,72% had more pain dramatizing after completion. Coop/Wonca indicates a positive change in physical function in 27,27% of the patients, a negative change in 54,54% of the patients. 18,18% of the participants, had no change. HAD indicates reduced anxiety levels in 54,54% of the participants, and a reduction in depression scores in 63,63% of the patients. 36,36% of the patients had more fear, and 36,36% of the patients had more depression. 9,9% of the patients had no change in fear. 18,18% of the patients reported that the body awareness exercises had reduced their pain both during and after the group therapy. The participants both supported and challenged each other and this appeared to facilitate coping.

Conclusion
Group therapy in a Pain clinic setting may reduce fear of movement, and levels of anxiety and depression in some patients, and increase the levels in others. The results may reflect that 16 hours treatment is not enough to see change in a patient group with a long history of chronic pain who have tried multiple treatment modalities earlier. The overall impression was also that the patients developed better coping strategies as a result of the group therapy. The body awareness exercises reduced pain and muscular tension in some of the patients. Our final conclusions may still change, and will be
presented on the poster. We are still treating the last group and are collecting follow up data from them. Key words: Group therapy, coping, chronic pain.

Poster Number PTH318

Authors
H. Shigetoh, M. Osumi, S. Morioka

Department of Neurorehabilitation, Graduate School of Health Sciences, Kio University, Marugame, Kagawa, Neuro Rehabilitation Research Center, Kio University, Kitakatsu-rgun, Nara

Aim of Investigation
Manual traction is one of the treatment for pain relief. Recent investigation have demonstrated that the effect of manual traction can be brought by several factors includes peripheral nerve, central nerve, personal factors like psychological, and expectation. So, it is not clear whether the pain relief were brought by specific effect of the manual traction. This study aimed to reveal whether manual traction and touch were effective for the pain relief using signal detection theory, and to compare the pain relief effect among the manual traction and touch.

Results
Signal detection analysis demonstrated that all conditions tended to alter value of sensitivity (A') than response bias (B'). Effect sizes of sensitivity (A') were as follows; manual traction×A-delta fiber(-0.64), touch×A-delta fiber(-0.56), manual traction×C fiber(-0.50), touch×C fiber(-0.40), while effect sizes of response bias (B') were as follows; manual traction×A-delta fiber(0.33), manual traction×C fiber(-0.25), touch×C fiber(0.11), touch×A-delta fiber(0.10). In addition, effect sizes of hit rate were as follows; manual traction×A-delta fiber(-0.62), touch×C fiber(-0.59), manual traction×C fiber(-0.45), touch×A-delta fiber(0.38). Regarding to sensitivity (A') and response bias (B'), there were no significant difference between pre-intervention and post-intervention in all conditions. Also, amount of change sensitivity (A') and response bias (B') were no significant difference between manual traction and touch in both frequencies.

Conclusion
These results suggests that the effect of manual traction and touch tended to be brought by the change of pain sensitivity but not bias. From the result of effect size of hit rate, manual traction might be more effective for pain relief than touch in A-delta fiber.
Title: Cardiovascular Safety Of Naloxegol In Noncancer Pain Patients With Opioid-Induced Constipation

Poster Number PTH319

Authors
M. Sostek, W. White, U. Diva, R. Tummala

AstraZeneca Pharmaceuticals LP, Gaithersburg, MD, USA, University of Connecticut School of Medicine, Farmington, CT, USA

Aim of Investigation
Naloxegol (NGL), a peripherally acting mu-opioid receptor antagonist (PAMORA), is an FDA-approved treatment for opioid-induced constipation (OIC) in adults with chronic noncancer pain. A health authority query regarding an imbalance in major adverse cardiovascular events (MACE) from one study with another member of the PAMORA class led to an evaluation of the cardiovascular (CV) safety data from the NGL clinical trial program.

Results
Over two-thirds of patients across the 4 studies combined (N=2135) had ≥1 CV risk factor; >40% had a history of CV disease, diabetes, or ≥ 2 CV risk factors. Treatment groups were well balanced for baseline CV risk. At 1 h post-first-dose, respective mean (SD) changes in rate-pressure product from baseline were –235.5 (1021.1), –235.6 (1102.1), and –176.9 (1245.6) mmHg•bpm for pooled K4/K5 placebo, NGL 12.5 mg, and NGL 25 mg groups; –84.3 (1344.0) mmHg•bpm for K8 UC; and –134.7 (1305.3) mmHg•bpm for K8 25 mg NGL. There were no clinically meaningful differences in ECG parameters across treatment groups. Pooled across studies, the rate of MACE per 100 patient-years of exposure was 1.13 (95% CI 0.31, 2.89) for placebo/UC vs 0.75 (95% CI 0.24, 1.75) for NGL at all doses, with a relative risk (NGL vs placebo/UC) of 0.66 (95% CI 0.14, 3.34). Overall, 10 events in 9 patients were adjudicated as MACE; incidence was similar across all treatment groups in all studies. One K7 patient who received 25 mg NGL and 1 K8 UC patient were each adjudicated with hospitalization due to heart failure.

Conclusion
Conclusions These findings from a pooled clinical trial experience of approximately 2000 patients with OIC indicate that the selective PAMORA NGL has a CV safety profile comparable to that of placebo and/or usual care. There is no evidence that NGL increases CV risk among patients with OIC.
Acknowledgments/Disclosures This research was funded by AstraZeneca Pharmaceuticals LP (Gaithersburg, MD, USA). M. Sostek, U. Diva, and R. Tummala are employees and shareholders of AstraZeneca Pharmaceuticals LP, and M. Sostek holds stock options from AstraZeneca. W.B. White was a safety consultant to AstraZeneca Pharmaceuticals in 2014.
**Title:** Effectiveness Of Low Level Laser Therapy In Knee Osteoarthritis

**Poster Number** PTH320

**Authors**
L. Tun, M. Htun, W. Shein

University of Medicine, Mandalay, Mandalay, Myanmar, University of Medical Technology, Mandalay, Mandalay, Myanmar

**Aim of Investigation**
To study the effectiveness of low level laser therapy in knee osteoarthritis

**Results**
There were no significant differences in baseline characteristics of patients between the two groups. There were significant improvements in range of motion of knee, modified WOMAC pain, stiffness, function and total scores after completion of 3 weeks treatment period in LLLT group A \((p<0.05)\). This improvement was maintained in follow-up assessments at week 4 and week 5 in group A. However, in sham laser therapy group B, significant improvements were found with regard to range of motion of knee, modified WOMAC pain, function and total scores after completion of 3 weeks treatment period \((p<0.05)\). There was no significant improvement in modified WOMAC stiffness score in group B \((p=0.1866)\). Intergroup analysis showed there were more significant improvements of range of motion of knee, modified WOMAC pain, stiffness, function and total scores in LLLT group in comparison with sham laser therapy group at week 3, 4 and 5 respectively \((p<0.05)\). Moreover there was significant reduction of acetaminophen intake in LLLT group in comparison with sham laser group \((p<0.05)\).

**Conclusion**
LLLT (given over joint line of knee for three weeks) is more effective than sham laser therapy in terms of relieving pain, increasing range of motion of knee and improving function in patients with knee OA.
Title: Effects Of Thoracic Epidural Analgesia In The Management Of Pain Due To Multiple Ribs Fracture: Initial Experience Of 25 Cases.

Authors
M. Khandoker

Northern International Medical college and hospital, Dhaka, Asia

Aim of Investigation
Ribs fracture is a very common incidence in trauma patients. It produces severe pain in chest which interfere normal respiratory function and ambulation. As a result of inadequate ventilation patient developed hypoxia, retened sputaum and even atelectasis and pneumonia may be developed. In USA incidence of ribs fracture is 10 to 15 percent of all traumatic injuries. No data is available in Bangladesh, but not uncommon. Most of the cases are managed by systemic analgesia. Thoracic epidural analgesia with local anaesthetic drugs mixed with narcotic drugs produce immediate & prolonged relieve of pain and improve ventilation. We treated 25 cases of multiple ribs fracture with thoracic epidural analgesia. Our aim of study is to observe the effectiveness of thoracic epidural analgesia to our patients with ribs fracture and to establish this treatment option in our country.

Results
Initially pain intensity in VAS score was 7-8. Immediate & adequate pain relieve in 19 patients after epidural block. VAS score reduced to 0-1. Moderate pain relieve occur in 5 patients, VAS & VRS reduce to 3-4. Catheter displaced in 1 patient and refused to take again. Pulse, Blood pressure & blood sugar level reduced. Early ambulation occurs & total duration of hospital stay reduced.

Conclusion
Thoracic epidural analgesia provide adequate pain relieve, it also improve ventilation, reduced incidence of morbidity & mortality. It should be treatment option for this type of patients in the developing country, but skilled manpower & monitoring facilities should be available.
Title: Occipital Nerve Stimulation For Treatment Of Intractable Headache. Value Of Transcutaneous Electrical Nerve Stimulation To Help The Selection Of Patients.

Poster Number PTH322

Authors

University Hospital, Nantes, France, Nantes University Hospital, Saint Herblain, France, University Hospital, Créteil, France

Aim of Investigation
Occipital nerve stimulation (ONS) is a surgical approach to treat patients with medically intractable chronic headache disorders. However, no predictive factor has been yet determined to select candidates for surgery.

Results
Both TENS trial and chronic ONS therapy at short and long terms were found to be efficacious (57-76% improvement compared to baseline on the various clinical variables). A good or very good response to TENS was associated with a better efficacy of ONS, suggesting that TENS may be predictive of the outcome of subsequent ONS therapy.

Conclusion
Implanted ONS is a valuable therapeutic option for refractory chronic headache disorders. A good or very good response to TENS could be used to select patients for implantation. This could particularly useful in patients with chronic migraine, in whom it may be difficult to indicate an invasive technique of cranial neurostimulation.
Title: Safety And Validation Of An Ambulatory System For Internet-Controlled Transcranial Stimulation (TDCS) For Pain Relief At-Home.

Poster Number PTH323

Authors
L. Garcia-Larrea, C. Bradley, C. Perchet, C. Trouba, M. Courtet, N. André-Obadia

INSERM - University Claude Bernard, Lyon, France, NeuroPain - Inserm, Lyon, France, Neurosciences Research Center of Lyon - NEUROPAIN, BRON, France

Aim of Investigation
Non-invasive cortical stimulation has demonstrated usefulness as an ancillary therapy for chronic pharmaco-resistant neuropathic pain (NP). Due to its simplicity and reasonable cost, transcranial direct-current stimulation (tDCS) is particularly attractive among the different techniques to choose from. Treatment through non-invasive stimulation is currently performed in hospital settings, where the patient typically receives a maximum of 5-10 repeated sessions. Regrettably, repetition of stimulating sessions leads to crowding of hospital services, while short therapy duration may lead to insufficient dose administration. This prevents performance of clinical trials over long periods of stimulation, which would be necessary to assess the efficacy of this therapy in the long run. Here we aim to report preliminary data on the use of a system allowing at-home direct-current cortical stimulation (tDCS) with remote scheduling and physician monitoring, via an Internet connection ensuring secure stimulus launching and data storage in 'the cloud'.

Results
Ten patients have undergone the whole procedure so far, all with probable or definite NP. The procedure was learned correctly during the first week and was in general well tolerated thereafter. Performance at home was satisfactory, although problems with internet connection and/or electrode impedance caused delay or skipping of the stimulation in ~15% of cases. Two patients withdrew after 3 weeks of stimulation because of gastrointestinal symptoms probably unrelated to tDCS (nausea, diarrhoea). Both patients experienced subjective pain relief before withdrawal, decreased ongoing analgesic medication, and asked to repeat the procedure several months later. Subjective benefit after the stimulating period could last up to 5 months, the scores for improvement of quality of life (QoL) being in general higher than the numerical scores of pain relief, which remained modest (~20%). Each
patient responded affirmatively to the question: 'Would you be willing to undergo the whole procedure again?'.

**Conclusion**
The at-home tDCS system proved to be well tolerated and technically robust. Although the sample is definitely too small to draw conclusions on efficacy, a majority of patients declared themselves satisfied to a higher extent following active rather than placebo sessions. QoL ratings and medication intake appeared as more robust markers of efficacy than were numerical scales of pain intensity. These results open the way to a possible system of loan similar to that used with TENS devices.
Title: Exploring The Effects Of 10-Khz Spinal Cord Stimulation On The Excitability Of Dorsal Column Axons And Superficial Dorsal Horn Projection Neurons In The Rat Spinal Cord

Poster Number PTH324

Authors
M. Smith, D. Lee, K. Bradley, S. McMahon

King’s College London; Faculty of Life Sciences & Medicine, London, United Kingdom, Nevro Corporation, Santa Clarita, CA

Aim of Investigation
Spinal Cord Stimulation (SCS) is increasingly used to treat chronic pain although the underlying biological mechanisms remain unclear. Traditional SCS uses low frequencies and is known to activate dorsal column axons. Recently, there has been considerable interest in high frequency SCS that does not produce paresthesia and might provide superior pain relief [1]. Here, we used anaesthetized rats to ask if 10-kHz SCS affected the excitability of primary sensory neurons running in the dorsal columns or other neuronal populations close to the stimulation site such as superficial dorsal horn projection neurons, which are essential for the development of persistent pain states in animals [2].

Results
We tested 38 dorsal column sensory neurons with 10-kHz SCS for 3 hours and none of these units showed either any signs of intermittent activation by the SCS or conduction block. When the 3-hour data points were compared to baseline, there was no significant effect on the conduction velocity (-2.9% ± 0.01%) or activation thresholds (7.8 ± 1.65%). In contrast, compared to the baseline responses from 16 electrical stimuli of the hind limb, 90-minutes of 10-kHz SCS at 20% MT significantly decreased the raw activity of specific responses while sham treated neurons remained unchanged with no significant differences. Furthermore, at 90-minutes with each unit compared to its own baseline at 0-minutes, sham treatment increased total (42.5 ± 41.5%) and C-fibre, putative nociceptive, activity (103.1 ± 59.0%), while SCS treatment at 20% MT decreased both total (-32.0 ± 18.9%) and C-fibre activity (-20.5 ± 19.8%).

Conclusion
Although traditional SCS is thought to act through activation of dorsal column neurons, our initial results show high-frequency SCS uses a different mechanism. Our current results imply that 90-minutes of 10-
kHz SCS (at ~20% MT) reduces the responsiveness of superficial dorsal horn projection neurons, predominantly in lamina I, that are believed to be critical for developing both chronic inflammatory and neuropathic pain [4], possibly suggesting a mechanism for high-frequency SCS–induced analgesia.

References:  
Title: A Case Series Of Radio-Frequency Ablation Of Lumbar Sympathetic Trunks As A Minimally Invasive Adjunctive Intervention For Patients With Chronic Visceral Pain Associated With Colonic Dysmotility

Poster Number PTH325

Authors

Department of Anesthesiology & Pain Medicine, Kohnodai Hospital, NCGM, Chiba, Japan, Department of Anesthesiology, National Center for Global Health and Medicine, Tokyo, Japan, Department of Anesthesiology, Saitama Medical University Hospital, Saitama, Japan

Aim of Investigation
Treatment of chronic visceral pain associated with colonic dysmotility remains challenging. The macroscopic anatomical pass of pain caused by colon dysmotility is routed through superior or inferior mesenteric plexus, splanchnic nerves, and sympathetic nerve trunks. Nociceptive information mainly enters dorsal root ganglions (DRGs) at levels more cephalad than second lumbar vertebra (L2), finally passing through communicating branches of sympathetic nerve trunk. The aim of this study is thus to evaluate our approach as a minimally invasive interventional option to treat chronic non-malignant visceral pain by radio-frequency ablation (RFA) of lumbar sympathetic trunks at levels of cephalad edge of L2 or L1.

Results
Seven RFAs of lumbar sympathetic trunks were performed to two patients with chronic abdominal pain. The pain reduced to moderate or much better. Doses of oral morphine could be reduced by the intervention while the patients did not want to completely quit the use of morphine. The duration of efficacy of this intervention appeared to be 4 – 6 weeks. One patient requested RFA three times and chose oral morphine medication without redoing this intervention thereafter. Another continues to request the RFA application.

Conclusion
We suggest that RFA of lumbar sympathetic trunks is a minimally invasive adjunctive intervention that can be performed repeatedly for patients with chronic abdominal pain to whom oral opioid is prescribed.
Title: Pharmacokinetics Of Buprenorphine Following Administration Via Transdermal Patches In Japanese And Caucasian Subjects

Poster Number PTH326

Authors

CPC Clinical Trial Hospital, Kagoshima, Japan, Mundipharma K.K., Tokyo, Japan, Mundipharma Research Ltd, Cambridge, United Kingdom

Aim of Investigation
Buprenorphine Transdermal System (BTDS) patches are available in different dosage forms for either 3-day or 4-day, or 7-day wear. This study investigated the pharmacokinetic characteristics of 3-day and 7-day application of transdermal buprenorphine in Japanese and Caucasian individuals.

Results
In line with earlier investigations, buprenorphine was delivered over the entire duration of patch wear in all Japanese and Caucasian subjects. Dose proportionality of buprenorphine plasma concentrations over time was confirmed for 3-day application of BTDS 5 mg, 10 mg, 20 mg, 30 mg, and 40 mg in Japanese subjects. No differences in the rate or extent of systemic exposure to buprenorphine were observed between Japanese and Caucasian populations. Following 3-day application of 20 mg BTDS, mean AUCt of 19,076 pg.h/mL and 20,079 pg.h/mL, and mean Cmax of 273.4 pg/mL and 278.0 pg/mL were observed in Japanese and Caucasian subjects, respectively. Following 7-day application of 20 mg BTDS mean, AUCt of 35,639 pg.h/mL and 40,478 pg.h/mL, and mean Cmax values 243.8 pg/mL and 261.4 pg/mL were observed in Japanese and Caucasian subjects respectively.

Conclusion
BTDS patches enable controlled delivery of buprenorphine over an extended period of up to 7 days. No differences in either the rate or extent of buprenorphine exposure were noted between healthy Japanese and Caucasian individuals. This study was funded by Mundipharma K.K.
Title: A Method To Detect Opioid Tolerance In Opioid Consuming Patients For Perioperative Pain Control

Poster Number PTH327

Authors
N. Nozaki-Taguchi, S. Isono
Chiba University Hospital, Chiba, Japan

Aim of Investigation
Acute pain management in chronically opioid-consuming patients has become a common clinical situation, due to an increase in opioid prescription from early stage cancer patients to non-cancer patients. These patients are opioid tolerant. Routine dose of post-operative opioids may not be enough to treat their new pain; post-operative pain. We seek for a clinical method to detect opioid tolerance, for a better perioperative management.

Results
Data were obtained from 30 opioid-naïve patients (control), 5 weak opioid-using patients and 5 strong opioid-using patients. In all patient groups, BP, HR and RR showed statistically but not clinically significant decrease after fentanyl administration. In control patients, both PT and NRSP significantly increased after fentanyl administration (PT: 5.8 to 8.2, NRSP: 15.4s to 21.7s). While PT showed reliable increase, change in NRSP seemed to produce strong effect in some and slight effect in most patients. Accordingly degree of changes between PT and NRSP showed no correlation. Result was also the same in weak opioid (tramadol) using patients. However, in patients using strong opioids (oxycodone or fentanyl), PT and NRSP showed no significant change after fixed dose of iv fentanyl showing tolerance in opioid effect.

Conclusion
This simple method to measure fentanyl effect is likely to be an useful method to measure patients' tolerance to opioid effect. Further study is necessary to clarify whether we can measure the degree of tolerance that may lead to calculation of perioperative opioid dose.
Title: Comparison Of Analgesic Efficacy Of Dexmedetomidine Versus Fentanyl As An Adjunct To Thoracic Epidural With Bupivacaine In Patients Undergoing Upper Abdominal Surgery

Poster Number PTH328

Authors
N. Bharti, S. Pokale, I. Bala, V. Gupta
PGIMER, Chandigarh, India, PGIMER, Chandigarh

Aim of Investigation
This randomized, double blind study was designed to compare the analgesic efficacy and safety of dexmedetomidine with fentanyl as an adjunct to bupivacaine for thoracic epidural administration in patients undergoing hepaticojejunostomy.

Results
The groups were comparable with respect to demographic data, duration of surgery, intraoperative analgesic requirements, recovery times and post-operative pain scores. The total consumption of rescue analgesia via PCEA pump was significantly less in dexmedetomidine group as compared to fentanyl group (p=0.049). Though, the heart rate was lower in dexmedetomidine group as compared to fentanyl group at any point of time, the systolic, diastolic and mean arterial pressures were comparable among groups during both intraoperative and postoperative period. None of the patients developed significant bradycardia or hypotension. Two patients in fentanyl group had vomiting and one patient had pruritus. None of the patients had excessive sedation, respiratory depression or hypoxia.

Conclusion
We conclude that addition of dexmedetomidine to epidural bupivacaine provides effective intraoperative and postoperative analgesia without any significant adverse effect.
Title: Dexmedetomidine Added To Bupivacaine For Fascia Iliaca Compartment Block (Ficb) For Post-Operative Pain Relief Following Proximal Femoral Fracture Surgery

Poster Number PTH329

Authors
B. Bhattarai, M. Agrawal, B. Sah, G. Khanal, K. Pokharel, A. Ghimire

BP Koirala Institute of Health Sciences, Dharan, Nepal

Aim of Investigation
To find out the postoperative analgesic effect of dexmedetomidine added to bupivacaine for fascia iliaca compartment block for postoperative analgesia following proximal femoral fracture surgery under spinal anaesthesia.

Results
Demographic variables were comparable between the two groups. Pain VAS was less in Group BD compared to Group B at all observation time points but significant only at 2 h and 6 h. Patients in Group BD had significantly longer duration of analgesia compared to Group B (13.40± 6.15 h versus 7.27± 1.46 h, p< 0.001). The median rescue analgesic doses required during first 24 h postoperatively in Group BD was less than that in Group B (1 versus 2). Group BD patients were more sedated than Group B patients. Hemodynamic parameters and complication rates were comparable between the two groups.

Conclusion
Dexmedetomidine added to bupivacaine for FICB significantly prolongs the duration of analgesia following proximal femoral fracture surgery without significant undesirable effects.
Title: Modulation Of Morphine-Induced Antinociception In Acute And Chronic Opioid Treatment By Ketamine, Norketamine, And Hydroxynorketamine

Poster Number PTH330

Authors
T. Lilius, E. Kangas, V. Jokinen, H. Viisanen-Kuopila, J. Laitila, M. Niemi, E. Kalso, P. Rauhala

Department of Pharmacology, Faculty of Medicine, University of Helsinki, Helsinki, Finland, Department of Clinical Pharmacology, Faculty of Medicine, University of Helsinki, Helsinki, Finland, HUSLAB, Helsinki, Finland, Department of Anaesthesia, Intensive Care Medicine, and Pain Medicine, Pain Clinic, Helsinki University Hospital, Helsinki, Finland

Aim of Investigation
Ketamine is an anesthetic that attenuates morphine tolerance in preclinical models of nociception when used at low doses. Its antidepressive properties are also under study. These effects have been thought to rely on the antagonism of N-methyl-D-aspartate (NMDA) receptors in the central nervous system (CNS). The antidepressive actions of ketamine may partly result from the actions of its metabolites. Norketamine, the main metabolite of ketamine, is also an NMDA receptor antagonist with less potency, whereas the effects of its NMDA receptor inactive metabolite hydroxynorketamine may result from the antagonism of alpha-7-nicotinic receptors and subsequent activation of mechanistic target of rapamycin (mTOR). We studied and compared the ability of ketamine, norketamine, and hydroxynorketamine to augment antinociception and to reverse tolerance in acute and chronic models of morphine administration.

Results
Norketamine (10 or 30 mg/kg) or hydroxynorketamine (30 mg/kg) did not enhance antinociception or cause locomotor deficiency in acute treatment either alone or combined with morphine (2.5 mg/kg). In morphine tolerant rats, 10 mg/kg ketamine abolished morphine tolerance for 120 minutes, whereas the effect of 30 mg/kg norketamine lasted for 150 minutes (P < 0.05 between the groups at 150 min). The antinociceptive AUCs of ketamine- and norketamine-treated groups over time (0–150 min) were similar. In morphine tolerant rats, acute ketamine caused marked psychomotor disturbance and locomotor deficiency up to 15 min after administration (P < 0.01), whereas norketamine had no acute locomotor effects. Acute hydroxynorketamine did not attenuate opioid tolerance.
**Conclusion**
The adverse CNS effects of ketamine may compromise drug compliance. Norketamine is interesting for further development as it did not produce locomotor disturbance at a dose that was effective in reversing morphine tolerance. This advantage may originate from the lower potency of norketamine as an NMDA antagonist. Hydroxynorketamine did not abolish morphine tolerance, which suggests that the inhibition of NMDA receptors is critical for the drug effect.
Title: Inhibition Of P2X4 Receptor Attenuates Mechanical Allodynia In Experimental Autoimmune Encephalomyelitis Rats

Poster Number PTH331

Authors

Nippon Chemiphar Co., Ltd, Misato, Saitama, Japan, Department of Life Innovation, Graduate School of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan, Kyusyu University, Fukuoka, Japan

Aim of Investigation
Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system. Many patients suffer from chronic pain induced by MS. P2X4 receptor (P2X4R) is an ATP-gated ion channel and known for the crucial role it plays in development of neuropathic pain following spinal nerve injury. Although the contribution of the P2X4R to MS is not clear, the increased expression of P2X4R in the spinal cord at the animal model of MS has been reported. In this study, we investigated the relation between P2X4R and the demyelinating neuropathic pain by utilizing experimental autoimmune encephalomyelitis (EAE) model.

Results
Mechanical allodynia was recorded as a significant reduction of paw withdrawal threshold in EAE rats compared to the control rats after day 12 post immunization. Repeated administration of P2X4R antagonist attenuated mechanical allodynia significantly without affect in the other EAE symptoms. The expression of P2X4R mRNA was markedly up-regulated at day 14 post immunization, and significant increase at day 14, 21 and 28 post immunization.

Conclusion
A time-dependent pattern of mechanical alldynia was similar to that of P2X4R expression. These results suggested that spinal P2X4R was involved in development of mechanical alldynia in a rat model of MS, and P2X4R antagonist could be a therapeutic agent for improvement of demyelinating neuropathic pain.
Aim of Investigation
Chronic opioid use is associated with down regulation of endogenous opioid pain-control mechanisms, leading to hypersensitivity to pain. It has been suggested that similar mechanisms may occur with chronic cannabis use, given the increasing understanding of the endogenous cannabinoid system in modulating pain, however there has been little investigation in humans. This project aimed to examine pain sensitivity in chronic cannabis users compared to age and gender-matched controls using the Cold Pressor Test (CPT), and to examine the response of the endocannabinoid system to pain stimuli. Specifically, stimuli such as fasting, exercise and stress-related ACTH increase plasma levels of THC in chronic users, and we hypothesized that pain stimuli may elicit similar responses.

Results
Twenty-four male participants were recruited to the study (cannabis using group, n = 13, non cannabis control group, n = 11) between November 2014 and December 2015. The cannabis users smoked an average of 6.3 grams cannabis per week and all gave negative saliva results for THC indicating abstinence from cannabis use for at least 12 hours prior to entering the experiment. Cannabis users were not in cannabis withdrawal at the time of the experiment (mean baseline Cannabis Withdrawal Scale scores = 0.97 (SD 0.99)). Cannabis users reported a longer time to first pain (pain sensitivity) than controls at both CPT-1 (Cannabis users = 16.9 s (SD 10.8), Controls = 12.6 s (SD 9.8)) and CPT 2 (Cannabis = 28.9 s (SD 38.5), Controls = 12.6 s (SD 9.8)) however these differences were not statistically significant (Time X group interaction: F1.69, P = 0.2). Cannabis users self reported time to first pain increased by 11.9 seconds between CPT-1 and 2, almost achieving statistical significance (Mean difference = 11.9 s, P = 0.07). Non cannabis using control participants did not show any decrease in their pain sensitivity between CPT1 and 2 (Mean difference = 0.48 s; P = 0.9). Cannabis users also had a greater pain tolerance than non cannabis using controls at both CPTs, again with cannabis users demonstrating
greater pain tolerance at CPT2 than at CPT1 (Cannabis CPT1 = 92.0 s (SD 67.6), Controls CPT1 = 58.6 s (SD 51.9); Cannabis CPT2 = 116.8 (SD 73.3), Controls CPT2 = 56.1 (SD = 44.39)). Whilst the interaction between time and group was not significant for pain tolerance (F1, 2.69, P = 0.1), post hoc pairwise analysis revealed that cannabis users pain tolerance significantly increased from CPT1 to CPT2 (Mean difference = 24.8 s; P = 0.03). Non cannabis using control participants did not increase their tolerance to pain between CPT1 and 2 (Mean difference = 2.54 s, P = 0.8). Plasma THC, 11-OH THC and endocannabinoid levels are pending.

**Conclusion**

Contrary to the original prediction, cannabis users had a lower pain sensitivity, and a greater pain tolerance, than control non cannabis users, although the findings did not reach significance – possibly due to the small sample size. Cannabis users became less sensitive and more tolerant to pain with successive CPTs. Non cannabis using controls did not alter their sensitivity or tolerance to pain with repeated CPTs. Pending blood analyses of endocannabinoid and THC response to the CPT may help to explain the apparent analgesia displayed in the cannabis users.
Title: Subunit-Specific Modulation Of Glycine Receptor Function By The Analgesic Alkaloid Gelsemine

Poster Number PTH333

Authors
G. Yevenes, P. Murath, A. Marileo, V. San Martin, B. Muñoz, C. Burgos, C. Lara

University of Concepcion, Concepcion, Chile

Aim of Investigation
Gelsemine is one of the principal alkaloids produced by the Gelsemium genus of plants. Recent studies have shown that gelsemine exerts analgesic effects on behavioral models, which are dependent on the activity of ionotropic glycine receptors (GlyRs). However, it is currently unknown whether gelsemine can modulate the glycine receptor function. In this study, we characterize the functional effects of gelsemine on recombinant and neuronal GlyRs.

Results
Our results show that gelsemine is a modulator of recombinant and native spinal GlyRs, which can exert conformation-specific and subunit-selective effects. The alkaloid potentiated homomeric α1 GlyRs and inhibited currents through α2 and α3 GlyRs. The gelsemine modulation occurs in a voltage-independent fashion and is associated with differential changes in the apparent affinity for glycine and in the open probability of the ion channel. In addition, the alkaloid modulates glycine receptors expressed in spinal neurons and shows minor effects on GABAA and AMPA receptors. At the synaptic level, gelsemine significantly diminished the frequency of miniature glycinergic synaptic events without altering the amplitude or the current kinetics. Likewise, the alkaloid also attenuated the frequency of glutamatergic synaptic events without changes in the amplitude.

Conclusion
Our results establish the pharmacological basis to explain, at least in part, the glycine receptor-dependent beneficial and toxic effects of gelsemine in animals and humans. In addition, the pharmacological profile of gelsemine may open new venues for future development of subunit-selective glycine receptor modulators.
Title: Chronic Pain Patients Followed In A Multidisciplinary Pain Center (MPC): Which Notifications In Addictovigilance?

Poster Number PTH334

Authors

University Hospital, Nantes, France, Nantes University Hospital, Nantes, France, Nantes University Hospital, Nantes, France, Nantes Hospital, Nantes, France

Aim of Investigation
Patients hospitalized in Multidisciplinary Pain Centers (MPC) often have multiple analgesic drugs, sometimes associated with drug dependence. The French addiction monitoring system (Addictovigilance) collects and analyzes notifications of problematic use of psychoactive substances, transmitted by healthcare professionals. The objective of this work was to assess cases of psychoactive substances' problematic use, collected among patients hospitalized in a MPC.

Results
During the study period, 108 notifications were received (for 433 patients hospitalized in the same period), comprising 162 substances identified as problematic. The subjects were mostly women (63.8%), mean age was 46.4 years. The main problematic substances were analgesics (45.7%, including oxycodone 13.6%, morphine 11.7%, tramadol 7.4%, acetaminophen 6.2%, fentanyl 3.1%) and benzodiazepines (34.0%). It was also found cannabis (8.6%), antidepressants (3.1%), buprenorphine (2.5%), alcohol (2.5%), gabapentine/pregabaline (1.2%) and hydroxyzine (1.2%). Of the 162 identified substances, an assessment of dependence criteria has been carried out for 134. The most frequent positive items were the withdrawal signs (78.6%), the desire or unsuccessful attempts to stop consumption (78.3%), the tolerance (70.6%) and long-term administration or higher doses that what was planned (61.7%). Health consequences were cited in 55.5%.

Conclusion
The problematic uses encountered in this particular population of chronic pain patients are characterized by physical and compulsive signs of dependence, with few harmful consequences.
excepted drugs side effects. These uses differ from the whole notifications received by the Addictovigilance system and are closer to analgesic-seeking behavior related to pseudo-addiction.
Title: Effectiveness Of The Active Back Programme - A Combined Physical And Psychological Programme - In Patients With Chronic Low Back Pain

Poster Number PTH335

Authors
J. Parry, L. Swift, D. Seegobin, A. Gilbert, H. Cohen, R. Berman

Royal National Orthopaedic Hospital, London, United Kingdom, Royal National Orthopaedic Hospital, Stanmore, United Kingdom, Royal National Orthopaedic Hospital, Stanmore, -- SELECT --

Aim of Investigation
Chronic back pain is one of the most disabling and costly long-term conditions in western society. In the United Kingdom, the estimated cost for back pain alone is £12.3 billion per year – equivalent to 22% of the annual NHS budget and it accounts for 4.1 million lost working days each year. The NHS Spinal Report of 2013 stated that commissioners should ensure a properly constructed Combined Physical and Psychological Programme (CPPP) be commissioned and given that such programmes are not available in most areas as yet, ‘this represents the single most serious gap in the provision of services for these patients at present’. The Active Back Programme (ABP) is a longstanding CPPP run by the Royal National Orthopaedic Hospital (RNOH). The aim of this study is to evaluate the effectiveness of the ABP across several domains including functional status, mental and physical health, pain and disability across patients with extreme back pain chronicity.

Results
We examined one hundred and thirty four patients across 18 programmes. Sixty five percent of participants had suffered back pain for more than 5 years prior to commencing the ABP. All data was analysed using SPSS v23. All data met parametric assumptions. Missing data was excluded list-wise. The paired t-test was used to assess the differences between outcomes at baseline and follow up. Across the cohort, patients demonstrated significant improvements in disability (ODI), walking (6MWT), confidence (PSFS) and mental health (SF-36) at six and eighteen week follow ups. Improvements were maintained at 1 year for ODI (mean difference = 10.79, p=<0.001, [95%CI 4.65-16.65]), 6MWT (mean difference = 62.78, p=<0.001, [95% CI 31.55-94.00]), PSFS (difference = 3.30, p=<0.001, [95%CI 2.33-4.28]) and SF-36 (mean difference = 15.88, p=0.009, [95% CI 4.24-27.52]). Although pain (NRS) was reduced this was not statistically significant. Scores were maintained at the 2 year mark however missing data resulted in not statistically significant comparisons to baseline. Attendance compliance at follow-ups exceeded
expectation with 91% attendance at 6 week and 18 week follow-ups. Attendance remained high at 83% for 1 year follow-up and 64% at 2 years.

Conclusion
A three week residential ABP at the RNOH shows a significant improvement of disability, physical status, confidence, mental health and pain reduction in patients with longstanding chronic back pain, which are sustained over a two year period. Follow-up compliance also remains high across this time period. Breaking through the Barrier’, Chief Medical Officer 2008 Annual Report, March 2009
www.backcare.org.uk BackCare Awareness Week: 'Work it out!' October 2009
Title: The Experience Of Brazilians Chronic Low Back Pain Patients Analyzed By The Fear-Avoidance Model

Poster Number PTH336

Authors
É. Vieira, C. Victor, J. Martins, J. Garcia, C. Mattos-Pimenta

São Paulo University, São Luís, Maranhão, Federal University of Maranhao, São Luís, Maranhão, Federal University of Maranhao, Sao Luis, BRAZIL, Nursing School of University of Sao Paulo, São Paulo, São Paulo

Aim of Investigation
To analyze thoughts, feelings, behaviors and consequences of avoidance movement in chronic low back pain patients as proposed by the Vicious Cycle of Fear-avoidance Model; and to describe the most feared movements of the PHODA´s pictures set.

Results
Bending the spine was the first cause of pain (48.2%, n=81); 71.4% of the patients had catastrophic thoughts ('This pain will kill me', 'I don't serve for anything more', 'I'll broke my back') and the most frequent behaviors related to pain episodes were staying at rest (27.4%), seek professional help (18.9%) and taking medicine (18.9%). High fear of movement and minor disability was stated by 44.4% of them, and intense fear and severe disability by 27.8%. The average fear in thermometer harm (score 0-100) above 50 was reported for 24 of 40 activities. The most threatening movements were 'working with the shovel' (33.3%), 'running' (33.3%), 'carrying shopping bags - one in each hand' (25.9%), 'mop the floor with squeegee' (25.9%) and 'abdominal hold down' (25.9%).

Conclusion
It was the first time it was performed the analysis of Vicious Cycle in Brazilian patients. Were observed the presence of exaggerated fear of movement, high level of disability and catastrophic thoughts occurred in more than two-thirds of the participants. These data showed the fear of the movement model is suitable for use in Brazilian patients.
Title: Development Of Inpatient Pain Management Program In Japan

Poster Number PTH337

Authors
N. Takahashi, S. Kasahara, S. Yabuki

Department of Pain Medicine and Orthopedic Surgery, Fukushima Medical University School of Medicine, Fukushima, Japan, Department of Pain Medicine, Fukushima Medical University School of Medicine, Fukushima, Japan

Aim of Investigation
Chronic pain states can develop during the period of tissue recovery following injury from a variety of causes, and may persist for a long time after tissue recovery. Because of its various manifestations, chronic pain is difficult to treat successfully. Patient management at a multidisciplinary pain clinic is one of the useful methods for the treatment for chronic pain, as has been demonstrated in the USA since 1960. A biopsychosocial model of well-being is a very important concept in the multidisciplinary pain clinic. This model is a general model or approach stating that biological, psychological, and social factors play a significant role in human functioning in the context of disease or illness. In Japan, we are implementing a multidisciplinary pain management program based on biopsychosocial factors guided by the IASP recommendations for such a program. Currently there are few facilities in Japan that administer a multidisciplinary pain clinic, especially an inpatient pain management program. The aim of this report is to describe our initial efforts in creating a Japanese inpatient pain management program using the biopsychosocial method of self-pain management.

Results
Three patients have been studied. The average change of outcomes among three patients before and after 3-week program were: 9.67 to 8.00 in numerical rating scale; 15.00 to 9.00, 13.33 to 10.33, 11.33 to 8.67 in each pain catastrophizing scale (rumination, magnification, and helplessness); 30.33 to 20.00 in the pain disability assessment scale; 11.00 to 6.67, 10.33 to 8.67 in the hospital anxiety and depression scale (anxiety and depression); 16.00 to 34.33 in the pain self-efficacy questionnaire; 9.00 to 5.67 in the Athens insomnia scale; 0.399 to 0.612 in the EQ-5D; 15.0° to 26.7° in extension trunk range of motion; 26.0 cm to 33.6 cm in the static flexibility test; and 7.5 cm to 0 cm in fingertip-to-floor. Thus, most outcomes were improved after the 3-week inpatient program. Trunk muscle flexibility was improved.
Conclusion
We have developed an inpatient pain management program and now report our first 3 cases. The results suggest that we may be able to improve the coping mechanisms of our patients for dealing with chronic pain, and that the program can improve their quality of life and flexibility. Our inpatient pain management program is being expanded to better serve chronic pain patients.
Title: Influence Of Physical Activity On Conditioned Pain Modulation

Poster Number PTH33

Authors
Y. Shiro, Y. Terasawa, Y. Ueda, K. Shimo, T. Matsubara
Nagoya Gakuin University, Aichi, Japan, Aichi Medical University, Aichi, Japan, Nihon Fukushi University, Aichi, Japan

Aim of Investigation
Physical inactivity is a perpetuating factor because of which pain can become chronic. Hence, guidelines for the treatment of musculoskeletal pain include recommendations of exercise to prevent progression to chronic pain. Pain relief, which is the overall beneficial effects of physical activity can be achieved through activation of endogenous pain inhibitory mechanisms. Furthermore, some studies suggest that engaging in physical activity of vigorous intensity may decrease the sensitivity to experimental pain stimulation in healthy adults. Conversely, a decrease of physical activity and dysfunction of endogenous pain modulation has been found in patients with chronic pain. However, the relationship between physical activity and the function of endogenous pain inhibitory mechanisms is still not well understood. Recent studies examined endogenous pain modulatory processing within the central nervous system by using an experimental test termed conditioned pain modulation (CPM). In this study, we investigated the relationship between intensity of physical activity and the CPM responses.

Results
There were no significant differences in age, height, weight, and baseline PPT among the three groups. PPT during increased significantly from before cold stimulation in the moderate and high groups (p <0.001, p <0.05), but did not significantly change in the low group. CPM response of the moderate group was significantly higher than that of the low group (p <0.05).

Conclusion
These results suggest that the low physical activity reduced the function of the endogenous pain inhibitory mechanisms. Furthermore, the moderate group exhibited comparable magnitudes of CPM response, and showed a greater magnitude of CPM response than the low group. Thus, moderate physical activity may be effective for improving endogenous pain inhibitory mechanisms.
Title: Effects Of An Ergonomic Adapted Training Of Workplace Conditions In Patients With Chronic Back Pain During A Three-Week Rehabilitative Medical Intervention.

Poster Number PTH339

Authors
T. Kunze, V. Henschke

MEDIAN Klinik Dahlener Heide, Schmannewitz, Germany, Rehabilitationsklinik Dahlener Heide, Dahlen, GERMANY

Aim of Investigation
Statutory retirement age in Germany has been raised to 67 years, at the same time increasing skills shortage is appearing due to demographic trend with a decline in the birth rate after 1970. The aim is to keep working people in the working process as long as possible, especially those in physically straining conditions by using measures of prevention and secondary prevention. Besides sufficient physical performance, ergonomic skills and function is necessary.

Results
Physical performance by means of PACT-questionnaire is rated significantly higher by male patients (142 points, equates light to medium capacity) compared to female patients (121 points, equates below light capacity). Patients achieved significantly better results with a load less than maximum regarding abilities for coordination, motor skills and strength. At the same time perceived exertion has been decreased significantly from 2.8 to 2.5 points (standing for light perceived exertion). The positive overall result of the multimodal pain-therapy program was proven by a significant reduction of pain level (NAS) from 4.8/10 to 2.9/10 and ODI-Score (21.8 to 17.6%, equates minimal disability through back pain).

Conclusion
Our study proved a positive effect of a three-week inpatient rehabilitative medical intervention regarding pain reduction, patient self-assessment of capability as well as improvement of abilities for coordination, motor skills and strength and additional decreased perceived exertion by conducting an ergonomic adapted training of workplace conditions. For this reason a rehabilitation measure contributes to improvement of the patient’s capability, which still have to remain in employment for more than 10 years on average.
Title: Impact Of Communication Style On Pain Related Variables -An Experimental Investigation

Poster Number PTH340

Authors
J. Söderstrand, S. Linton, M. Schrooten, K. Boersma

Örebro University, Örebro, Närke, Örebro University, Örebro, Sweden, Center for Health and Medical Psychology, Örebro University, Örebro, Sweden, Center for Health and Medical Psychology, Örebro, Sweden

Aim of Investigation
Though most treatments for pain – be it a medical, physiotherapeutic or psychological intervention- includes communication between health care providers and patients, research has not given enough attention to the role of communication. Good communication has shown to increase adherence (Butow & Sharpe, 2013; Pincus et al., 2013), patient satisfaction (Zachariae et al., 2003) and in some cases decrease symptom severity in pain patients (Pincus et al., 2013). Though there is ample evidence that good communication has positive effects, we still do not know enough to say what good communication really consists of or how communication exerts its influence on clinical outcome. Thus, there is a need to break down communication to manageable components, in order to assess their potential effect on pain related variables. The aim of this experiment is to test a component of communication (Validation/Invalidation) and see what impact it has on variables that are important in a health care setting such as pain catastrophizing and positive/negative affect.

Results
Results: Repeated measures ANOVA reveals no significant effects on any confounder or negative affect. Significance was reached on pain catastrophizing alone (p<.05).

Conclusion
Results indicate that pain catastrophizing does change over the course of the experiment, and that this change is attributable to interpersonal behaviors of the experimenters. These results underscore both the transactional aspect of pain catastrophizing as well as techniques aiming at emotion regulation when trying to affect pain catastrophizing.
Title: Effectiveness Of Primary Care Interventions Using A Biopsychosocial Approach In Chronic Low Back Pain: A Systematic Review

Poster Number PTH341

Authors
R. van Erp, I. Huijnen<sup>,2</sup><sup>,3</sup>, M. Jakobs<sup>,3</sup>, J. Kleijnen, R. Smeets<sup>,6</sup>

Department of Rehabilitation Medicine, CAPHRI, Maastricht University, Maastricht, Netherlands, Department of Rehabilitation Medicine, Maastricht UMC+, Maastricht, Netherlands, Adelante, Centre of Expertise in Rehabilitation and Audiology, Hoensbroek, Netherlands, Department of Occupational Therapy, Zuyd University of Applied Sciences, Heerlen, Netherlands, School for Public Health and Primary Care (CAPHRI), Maastricht University, Maastricht, Netherlands, Libra Rehabilitation, Eindhoven, Netherlands

Aim of Investigation
Recently performed systematic reviews show promising effects for multidisciplinary biopsychosocial rehabilitation interventions in reducing pain and disability in patients with chronic low back pain (CLBP). During the last years, more and more biopsychosocial interventions have been developed for primary care settings; however the evidence has not yet been systematically reviewed. The aim is to review the evidence for biopsychosocial primary care interventions as compared to waiting lists or other primary care treatments in reducing functional disability and pain, and improving work status in patients with CLBP. Secondly, as different biopsychosocial interventions exist varying in structure (e.g. duration, intensity) and more importantly in approach and practical implementation, this review aims to provide insight into the theoretical background, practical implementation and feasibility of biopsychosocial primary care interventions.

Results
Searches are conducted in November and December 2015 and resulted in 942 articles. After selection on Title and abstract, 41 articles remained. At this moment, researchers are selecting articles based on full text. Preliminary results will be available at the 16th World Congress of Pain.
Conclusion
This review is expected to be useful for future directions of biopsychosocial interventions in primary care for patients with CLBP.
Title: Integrated Psychosocial Interventions For Chronic Pain And Comorbid Psychiatric And Substance Use Disorders

Poster Number PTH342

Authors
V. Hruschak
University of Pittsburgh, Pittsburgh, PA

Aim of Investigation
To examine the direct relationship between evidence based treatment for concurrent disorders with simultaneous education of self-management for adults with chronic pain and comorbid psychiatric and substance use disorders in an outpatient group setting.

Results
Following completion of the MHSU Pain Management Group, a quantity of participants were able to either decrease or completely taper off analgesia and psychotropic medications with reported measures of pain relief. Some participants achieved early remission from substance use disorders while others noted a decrease in substance misuse. There were various participants on waitlists for mental health counsellors and following completion of group, withdrew themselves claiming improvement of mental status and adequate resources and skills acquired in order to manage their psychiatric illness. There was also one participant who discontinued regular appointments with his psychiatrist and returned to the care of his family physician. Another participant who was 'not ready' for the Occupational Rehabilitation 1 (OR 1) Program at Kelowna General Hospital was able to commence and complete OR 1 following his completion of the MHSU Pain Management Group.

Conclusion
The findings extrapolated from this study with adults in an outpatient setting, demonstrates correlation of improvement in prognosis, psychosocial functioning and other quality of life measures with the application of evidence based treatment of concurrent disorders and simultaneous education of self-managed care. Although rigorous research is still needed in this area, preliminary findings from the MHSU Pain Management Group are encouraging, thus this evidenced based approach should be promoted more extensively with this population.
Title: The Impact Of A Physiotherapy Led Pilates On Fear Avoidance Behaviour In Chronic Low Back Pain.

Poster Number PTH343

Authors
G. Kelly, S. Griffin, R. Galvin

University of Limerick, Limerick, Ireland

Aim of Investigation
Pilates is a commonly prescribed form of rehabilitative exercise for individuals with chronic low back pain (CLBP). Emphasis is placed on activation of deep abdominal muscles in order to promote spinal stability, where pain is explained in a biomedical manner and the spine is viewed as a weakened structure. This may evoke feelings of apprehension and negatively impact on beliefs and behaviours, including adoption of movement fear avoidance behaviour (FAB). This study aimed to determine the impact of Pilates on such FAB.

Results
30 individuals (female n=25, male n=5, mean age 43.0±9.2 years; mean duration of symptoms 8.1±7.5 years) participated. TSK scores increased significantly (p≤0.00) following Pilates indicating an increase FAB. Similarly SB scores increased significantly (p≤0.00) following Pilates indicating higher risk for further chronicity and the need for psychological interventions. No significant changes were noted in disability scores (RMDQ, p=1.02).

Conclusion
These findings indicate physiotherapy led Pilates exercises may not be an appropriate treatment option for all individuals with CLBP, as it may increase FAB and potentially result in further deterioration of the condition.
Title: Evaluation Of A Brain-Based Multimodal Rehabilitation Program For Chronic Pain

Poster Number PTH344

Authors
J. Saury, S. Hedström, M. Lövgren, M. Schult

Danderyd hospital, Stockholm, Sweden

Aim of Investigation
To evaluate the effects of a new rehabilitation method in a group of patients with chronic pain syndrome. The model is an adaptation of the brain-based therapy model from the field of psychotherapy. This model is characterized by the use of recent advances in the neuroscience to identify which elements of rehabilitation are relevant to enhance outcomes. It consists of the synthesis of evidence-based multimodal rehabilitation strategies and of interventions issued from a focus on specific brain structures thought to be involved in the pathogenesis to be treated. Applied to chronic pain, the focus is put on three brain areas thought to be involved in the emergence and perpetuation of pain: (i) the amygdala, which may contribute to the exacerbation of pain experiences by triggering the stress system through the HPA axis and the activation of conditioned responses in the presence of pain episodes; (ii) the prefrontal cortex, which is impaired by amygdala overactivity, provoking a loss of gray matter leading to cognitive impairment, and (iii) the hippocampus, whose function is impaired because of chronic amygdala overactivity, leading to memory and mood problems.

Results
A preliminary implementation of the program for a group of patients with chronic pain during 2015 showed promising results: in an interview by independent clinicians after the rehabilitation period, patients reported that they were satisfied with the program: it had help them understand how their brain contributes to their pain problems and they appreciated the opportunity to learn different strategies to handle these. As the asset of the program is its explanatory power, we expect to find that patients have increased their ability of handling their symptoms (self-efficacy), a better quality of life, lower pain levels and increased work capacity.

Conclusion
Our preliminary results concerning the implementation of a new rehabilitation method for chronic pain
related disability are promising as patients report positive reactions to the focus on brain processes and increased understanding of the neurobehavioral mechanisms perpetuating persistent pain symptoms.
Aim of Investigation
Our recent study investigated the heterogeneous stress responses associated with psychological characteristics in fibromyalgia (FM) patients. The largest subgroup is characterized by hypertensive stress response associated with the highest level of pain, physical impairment, catastrophising and anxiety. We assumed that this relationship between psychological and psychophysiological characteristics could be related to a diminished baroreflex sensitivity (BRS) as part of dorsal medial nucleus tractus solitarius (dmNTS) reflex arcs. Baroreceptors relay cardiovascular input to dmNTS that regulates pain, sleep, anxiety and blood pressure via projections to other areas in the brain stem and the pain network. We have previously shown that BRS in FM patients is diminished compared to healthy controls, but increases through systolic extinction training (SET), a combination of operant behavioral treatment and individualized peripheral electrical stimulation dependent on the cardiac cycle. After SET, FM patients show a long lasting remission of clinical pain in 82%. The present study investigates the relationships between psychophysiological (BRS, high frequency heart rate variability (HF)) and psychological (physical impairment, catastrophising, anxiety, physical activity) variables in the context of pain regulation.

Results
Only SET but not CVT shows a significant effect on clinical pain (p <.01) with a remission in 82% at T3. Both groups show increases in BRS and HF levels (all p's <.05), sensory, pain and tolerance thresholds to electrical stimuli (p <.01) at T3. After SET, patients show significantly reduced physical impairment, catastrophising and anxiety (all p's <.05) as well as increased physical activity. In contrast, CVT patients do not show any changes. BRS correlates significantly with catastrophising (r = -.394), anxiety (r = -.460), physical activity (r = .444) and impairment (r = .507, all p's <.05).

Conclusion
These data suggest that only SET, but not CVT alone succeeds in re-establishing intrinsic pain regulatory
mechanisms by affecting sensory, cognitive, affective and behavioral characteristics of pain processing whereas CVT seems to affect sensory characteristics only. This mechanistic analysis will assist scientific identification of systems-based pathways that contribute to autonomic and stress mechanisms that mediate chronic pain.
Title: Overcoming Geographic Barriers For Adolescents With Chronic Pain Living In Remote Locations

Poster Number: PTH346

Authors
B. Dick, K. Reid, M. Simmonds, S. Rashiq, M. Verrier

University of Alberta, Edmonton, Alberta, Stollery Children's Hospital, Edmonton, Alberta

Aim of Investigation
We sought to examine how teens and adults experiencing chronic pain respond to a best practice biopsychosocial treatment program when participating in treatment in person as compared to individuals who receive treatment in remote geographic locations via telehealth.

Results
Adolescents with chronic pain reported significant reductions in pain, pain-related disability, anxiety, and a significant improvement in sleep and quality of life following Pain 101. Only a trend toward reduction of depressive symptoms occurred immediately post-treatment. Significant improvement was maintained for pain, disability, and anxiety for an extended period (2 years) after Pain 101. Adults with chronic pain also showed significant reductions in pain, pain-related disability, anxiety, sleep, and quality of life but also showed significant reductions in depression. Further, these reductions were maintained for several of these factors at several post-treatment intervals. Of note, particular benefit was seen in adults who did not experience severe depression at baseline. No significant differences were found between subgroups of patients who attended via telehealth compared to those who attended in person. Estimates of cost savings to individual patients ranged from 1650–6600 Euro per program. Students missed two weeks less of school by attending Pain 101 through school teleconferencing equipment. Qualitatively, several patients reported that they would not have been able to attend without telehealth programming. The most common complaints regarding telehealth were occasional technical difficulties and not feeling as involved in the group social and supportive processes as they would have been had they attended in person.

Conclusion
Our findings strongly support the benefit of telehealth technology for individuals with complex chronic pain who live far from treatment centres. These benefits include the ability to participate in treatment
programs, significant cost savings, and less missed school for teens. Recommendations for effective use of this technology for providing chronic pain self-management programming will be discussed.
Title: Opiate Use By Chronic Pain Patients Referred To A Pain Management Program Remains A Problem But Initial Assessment Can Facilitate The Withdrawal Process.

Poster Number PTH347

Authors
L. Beeston, R. Martin, S. Jain, A. Asghari, C. Brooker, M. Nicholas

Pain management and Research Institute, St Leonards, Sydney, NSW, Pain mangement and Research Institute, St Leonards, Sydney, Australia, Pain mangment and Research Institute, Sydney, NSW, Pain management and Research Institute, Tehran, IRAN, Pain Management and Research Institute, Sydney, Australia, Pain Management Research Institute, Sydney, NSW

Aim of Investigation
This observational study sought to determine if there had been any change in opioid use by chronic pain patients referred to a pain management program at 3 time points over 15 years. Over this period changes have been made to the management of patients taking opioids at this pain centre and we were interested to see if these were reflected in the levels of opioid use at the start and end of the program.

Results
Data were available for over 100 patients at each occasion. On all three occasions, those taking opioids at admission and discharge from the program reported higher usual pain, worse depressive symptoms, higher disability, and more catastrophizing, stronger fear-avoidance beliefs, and lower pain self-efficacy. But what was noticeable was that the proportions taking opioids at admission had reduced over the 15 years from almost 70% to about 40%. About 10% on each occasion were still taking some opioid (usually less than before) by the end of the program. But the proportion on opioids at initial assessment/presentation at the pain centre was similar over the time period.

Conclusion
Opioid use remains very common amongst patients referred to a tertiary pain centre over the 15 year period studied. Similarly, over all time points, the use of opioids remains associated with higher pain, worse mood and disability, and more unhelpful cognitions. What has changed, however, is that withdrawal from opioids is happening more vigorously from initial assessment so that the proportion entering the program some weeks or months later is much less in 2015 than in 2001. This indicates that
it is worth pursuing measures to commence withdrawal well before such patients enter a program and this may help them to benefit more from the program than they might have otherwise.
Title: Relationship Among Conditioned Pain Modulation, Pain Sensitivity, And Autonomic Nervous System In Response To Aerobic Exercise-Induced Hypoalgesia In Healthy Subjects

Poster Number PTH348

Authors
T. Hattori, Y. Shiro, T. Matsubara
Maehara Orthopedics Rehabilitation Clinic, Obu, Aichi, Japan, Nagoya Gakuin University, Seto, Aichi, Japan, Nihon Fukushi University, Handa, Aichi, Japan

Aim of Investigation
Aerobic exercise is an effective treatment for chronic pain disorders. Exercise has been suggested to reduce pain sensitivity, a phenomenon known as exercise-induced hypoalgesia (EIH), and to prevent the development of autonomic dysregulation. EIH has been characterized by increased pain threshold as well as by decreases in pain intensity ratings during and following an exercise session. Recently, conditioned pain modulation (CPM) has been investigated as an indicator for central endogenous pain inhibitory mechanism, as the pain threshold primarily reflects the state of the peripheral nervous system. Currently, mechanisms responsible for EIH and the relationship among pain threshold, CPM, and autonomic nervous system in response to EIH are not clear. The aim of our study was to investigate the changes in CPM, pain sensitivity, and autonomic nervous system during and following aerobic exercise.

Results
PPT for the biceps and the quadriceps significantly increased immediately after and 15 min after exercise (P < 0.01). CPM for PPT significantly increased during the immersion of the hand in cold-water (P < 0.01), but CPM magnitude was not significantly different before, immediately after, and 15, 30, 45, and 60 min after the exercise. HR and LF/HF ratio significantly increased (P < 0.001) and HF significantly decreased (P < 0.01) during the exercise.

Conclusion
This study showed that EIH for the pain threshold prolonged up to 15 min after the aerobic exercise, but the magnitude of CPM was not found to be significantly different following the aerobic exercise. Therefore, aerobic exercise applied in this study could affect peripheral pain sensitivity, whereas it had little effect on the central endogenous pain inhibitory mechanism. Furthermore, sympathetic nerve activity increased and parasympathetic nerve activity decreased during the exercise, demonstrating
physiological responses to the exercise, but the relationship among autonomic nervous system, CPM, and pain sensitivity in response to EIH remains unclear.
Title: Opioid Use By Chronic Pain Patients Referred To A Pain Management Program Remains A Problem, But Initial Assessment Can Facilitate Withdrawal Process.

Poster Number PTH349

Authors
L. Beeston, R. Martin, S. Jain, A. Asghari, C. Brooker, M. Nicholas

Royal North Shore Hospital, Sydney, NSW, Pain mangement and Research Institute, St Leonards, Sydney, Australia, N/A, Tehran, IRAN, Pain Managment and Research Institute, Sydney, Australia, Pain Management Research Institute, Sydney, NSW

Aim of Investigation
This observational study sought to determine if there had been any change in opioid use by chronic pain patients referred to a pain management program at 3 time points over 15 years. Over this period changes have been made to the management of patients taking opioids at this pain centre and we were interested to see if these were reflected in the levels of opioid use at the start and end of the program.

Results
Data were available for over 100 patients at each occasion. On all three occasions, those taking opioids at admission and discharge from the program reported higher usual pain, worse depressive symptoms, higher disability, and more catastrophizing, stronger fear-avoidance beliefs, and lower pain self-efficacy. But what was noticeable was that the proportions taking opioids at admission had reduced over the 15 years from almost 70% to about 40%. About 10% on each occasion were still taking some opioid (usually less than before) by the end of the program. But the proportion on opioids at initial assessment/presentation at the pain centre was similar over the time period.

Conclusion
Opioid use remains very common amongst patients referred to a tertiary pain centre over the 15 year period studied. Similarly, over all time points, the use of opioids remains associated with higher pain, worse mood and disability, and more unhelpful cognitions. What has changed, however, is that withdrawal from opioids is happening more vigorously from initial assessment so that the proportion entering the program some weeks or months later is much less in 2015 than in 2001. This indicates that it is worth pursuing measures to commence withdrawal well before such patients enter a program and this may help them to benefit more from the program than they might have otherwise.
Title: Repetitive Pain Education With Exercise Improves Pain Catastrophizing In The Patients With Complex Chronic Pain.

Poster Number PTH350

Authors
K. Shimo, T. Ikemoto, T. Ushida

Institute of Physical Fitness, Sports Medicine and Rehabilitation. Aichi Medical University, Nagakute, Japan, Multidisciplinary Pain Center, Aichi Medical University, Nagakute, Japan

Aim of Investigation
Pain catastrophizing is a specific mindset with direct impact on the subject's behavior, functional ability and quality of life. In the patients with complex chronic pain, it is difficult to improve pain catastrophizing using a uniform therapeutic approach which seeks only to eliminate pain. Accordingly we developed a simple pain management program which consisted of both pain education based on cognitive-behavioral approach and exercise. We offer the programs once a week and patients can participate it as they want. In this study, we report effect of this program for pain catastrophizing in the patients with complex chronic pain.

Results
The mean PCS score at first participation was 40.1. In comparison with first participation, there were statistically significant changes in the PCS score at fifth (31.6, p<0.05), sixth (29.3, p<0.01), seventh (27.3, p<0.01) and eighth (25.8, p<0.01). On the other hand, regardless of participating many times, 3 patients still reported high pain catastrophizing (over 30 on the PCS).

Conclusion
This result indicated that repetitive participation to the programs consisting of pain education and exercise can improve pain catastrophizing thoughts in the patients with complex chronic pain. However, some patients didn't change their mindset in spite of voluntarily repeated participation. We need to figure out the reasons why pain catastrophizing thoughts won't be changed in those patients.
Title: Influence Of Mechanical Interventions On Evoked Perceptual Distortion In The Face Of Healthy Volunteers

Poster Number PTH351

Authors
L. Dagsdóttir, I. Skyt, L. Vase, L. Baad-Hansen, E. Castrillon, P. Svensson

Section of Orofacial Pain and Jaw Function, Department of Dentistry, Aarhus University, Aarhus, Denmark, Scandinavian Center of Orofacial Neurosciences, Aarhus, Denmark, Department of Psychology and Behavioral Sciences, Aarhus University, Aarhus, Denmark, Danish Pain Research Centre, Aarhus, Denmark, Section of Orofacial pain and Jaw Function, Department of Dentistry, Aarhus University, Aarhus, Denmark, Department of Dental Medicine, Karolinska Institute, Huddinge, Sweden

Aim of Investigation
Perceptual distortions (PD) can be defined as disturbances in the way a person perceives his or her body and is a well-known phenomenon following injections of local anesthetics (LA) in the dental practice. Persistent orofacial pain patients often perceive the painful face area as ‘swollen’, however, no clinical signs are present. These illusions may represent a PD and is known to have negative influences in regards to the psychosocial component of pain. The aim of this ongoing double-blinded, randomized, substance controlled study was to investigate, whether mechanical stimuli can affect experimentally evoked PD in the infraorbital region.

Results
The preliminary results showed significant main differences in the three groups regarding PD (ANOVA: p<0.001). A significant difference was found between group 1 (Mean±SEM) (28.5±1.4%) and group 3 (0.7±0.1%) (Tukey: p<0.001) as well as between group 2 (32.3±1.6%) and group 3 (Tukey: p<0.001) but not between group 1 and group 2 (Tukey: p = 0.735) after 10 min. ANOVAs showed that there was a significant difference in PD ratings over time (p < 0.001) following the LA injection, but no effects of the two types of mechanical stimuli (Pinprick or Brush) (p = 0.079). Reports regarding differences in PD before and after mechanical stimulation were close to significant (ANOVA: p = 0.058). A total of 30% of the participants in group 2 reported reduced PD scores when adding the pinprick stimulation and 65% reported increased PD scores by the brush strokes after 10 min. For group 1 with no mechanical stimulation only 5% reported increased PD scores when asked again. In the control group 3 none of the
participants reported changes in PD scores during the pinprick stimulation and only 5% reported changes in PD scores for the brush stimulation.

**Conclusion**
These preliminary findings may suggest that the phenomenon of perceptual distortion evoked consistently in healthy participants by an infraorbital nerve block can be manipulated by a simultaneous mechanical input to the affected area. This observation points to the need to further understand multisensory integration and the implications for chronic orofacial pains and their management.
Title: Investigating Sex Differences In Selective Attentional Biases Towards Facial Expressions Of Pain

Poster Number PTH352

Authors
E. Keogh, B. Bedford, S. Wang

University Of Bath, Bath, United Kingdom, University of Bath, Bath, United Kingdom

Aim of Investigation
It is currently unknown whether there are male-female differences in pain communication, and the few studies that have been conducted tend to produce inconsistent effects. Reasons for this could partly be because studies are not directly designed to consider sex differences, and/or they tend to rely on expression identification tasks. This study brings together two paradigms, from perception and attention respectively, to explore whether men and women differ in their selective attentional biases towards pain faces that are presented with different levels of perceptual information.

Results
No evidence was found for a selective attentional bias towards pain or fear faces at any level of the experiment. However, sex differences were found in the overall processing speeds towards the images. An interaction between spatial frequency and sex of participant (F(2, 74)=4.90, p<.05) revealed that men were faster in making a response when presented with high spatial frequency images, compared to intact or low spatial frequency images. An additional interaction was found between sex of face and emotion of face (F(1, 37)=4.38, p<.05). This indicated that participants were faster at making a response when stimuli contain images of males expressing pain.

Conclusion
Although no evidence was found for sex differences in attentional biases towards pain, other effects were found. This study found that both the sex of the observer and the person they are observing can effect attentional processing speed. Of particular interest is to consider why participants may be faster on this task when the expression being viewed is of a man in pain. This study highlights that designing studies to consider sex effects, as well as utilizing objective measures of cognitive bias are potentially useful directions to take in the future.
Title: Effects Of Repetitive Aerobic Exercise On Central Pain Modulation In Subjects With Chronic Neck Pain

Poster Number: PTH353

Authors

Nihon Fukushi University, Handa, Aichi, Japan, Nagoya Gakuin University, Seto, Aichi, Japan

Aim of Investigation
Acute aerobic exercise has typically reported to attenuate pain temporarily, a phenomenon termed exercise-induced hypoalgesia (EIH). EIH has generally been characterized by elevations in pain threshold as well as by reductions in pain intensity rating during and following an exercise session, but the central pain modulation mechanisms responsible for EIH are poorly understood. Recently, dynamic quantitative sensory testing such as temporal summation (TS) has been investigated as an indicator for the central pain modulatory mechanisms, as the pain threshold primarily reflects the state of the peripheral nervous system. The abnormally augmented TS is possibly responsible for the development of chronic pain conditions and the attenuation of EIH in subjects with chronic pain. However, the effect of aerobic exercise, especially the repetitive exercise, on TS in subjects with chronic pain remain unknown. The purpose of this study was to compare the changes in TS and pain sensitivity following aerobic exercise sessions once or 5 times a week in healthy controls and subjects with chronic neck pain.

Results
No significant differences were found for baseline PPT and TS magnitude of all muscles on the 1st day of the experiment in both groups. There were no significant differences on PPT and TS magnitude in response to the acute or repetitive exercise in the control group on the 3rd and 8th days. In the pain group, PPT of the biceps and the quadriceps significantly increased and TS magnitude of the trapezius and the biceps significantly decreased in response to the repetitive exercise on the 8th day, whereas there were no differences on those in response to the acute exercise on the 3rd and 8th days.

Conclusion
In the subjects with chronic neck pain, repetitive aerobic exercise for a week could reduce peripheral pain sensitivity at only non-painful sites and attenuate TS at painful and non-painful sites, although
there were no changes in those following acute aerobic exercise. Therefore, we consider that repetitive aerobic exercise performed 5 times a week could activate the central pain modulation system responsible for EIH, at least partially, in subjects with chronic neck pain.
Title: Assessment Of Pain During Epidural By The Sacral Hiatus

Poster Number PTH354

Authors
A. CHAHIDI, A. EL OUMRI, L. Leila BELAROUSSI

Moroccan Society of Neurophysiology, BENI MELLAL, Autre, University Hospital Mohamed VI Oujda
Morocco, Oujda, Morocco

Aim of Investigation
Epidural corticosteroid injections are used routinely in the treatment of discogenic sciatica. The objective of this study is to evaluate the pain felt by the patient undergoing epidural infiltration by the sacral hiatus, and in order to standardize an analgesia protocol during and after the act.

Results
- The study focused on a population of 100 patients, with a female preponderance of about 82%. The average age was 47.6 years [21-70] The hiatus was identified successfully in all patients. The average time for completion of the gesture was 28.8 minutes[1

Conclusion
- Epidural infiltration by the sacral hiatus is a quick gesture, but painful. Premedication is recommended, as well as support of the post-intervention pain. The use of ultrasound guidance is advantageous, to a reduce pain caused by reducing the durati
Date: 09/29/2016 03:15:00 PM

**Title:** Differential Expression Of Spinal Gaba And Opioid Receptors Modulates The Analgesic Effects Of Intrathecal Curcumin On Inflammatory Pain In Rats

**Poster Number** PTH355

**Authors**
M. Yoon, K. Park, J. CHOI, Y. Kim

Department of Anesthesiology and Pain Medicine, Chonnam National University, Medical School, Gwangju, Korea, Center for Creative Biomedical Scientists at Chonnam National University, Gwangju, Korea

**Aim of Investigation**
Curcumin is traditionally used as a herbal medicine. We explored the efficacy of intrathecal curcumin in relieving inflammatory pain and elucidated the mechanisms of action of curcumin interacting with GABA and opioid receptors at the spinal level.

**Results**
Intrathecal curcumin reduced the withdrawal threshold of carrageenan injection-induced nociception. Intrathecal GABA and opioid receptor antagonists reversed the curcumin-mediated antinociception. Carrageenan injection increased the levels of the opioid receptors mRNA, but not the GABA receptors mRNA levels. Intrathecal curcumin decreased the levels of opioid receptors mRNA in the spinal cords of carrageenan-injected rats.

**Conclusion**
Intrathecal curcumin was effective to inflammatory pain and such antinociception of curcumin was antagonized by both GABA and opioid receptor antagonists. Also, intrathecal curcumin increased the levels of opioid receptors, without affecting the levels of GABA receptors. Thus, spinal GABA and opioid receptors may, respectively, be directly or indirectly involved when curcumin alleviates inflammatory pain.
Title: Brain Activity In A Nonhuman Primate Model Of Oxaliplatin–Induced Neuropathic Cold Hypersensitivity

Poster Number PTH356

Authors

National Institute of Advanced Industrial Science and Technology (AIST), Human Informatics Research Institute, Tsukuba, Ibaraki, Japan, University of Tsukuba, Graduate School of Comprehensive Human Sciences, Tsukuba, Ibaraki, Japan, Hamamatsu Pharma Research, Inc. Pharmacology Group, Hamamatsu, Shizuoka, Japan

Aim of Investigation
Oxaliplatin, an anti–cancer chemotherapeutic used for the treatment of advanced colorectal cancer, has a distinctive neurotoxicity, inducing an acute peripheral neuropathy characterized by cold hypersensitivity. A preclinical nonhuman primate model of oxaliplatin–induced peripheral neuropathy using macaques was recently developed (Shidahara et al., 2016). The effect of clinical analgesics on cold hypersensitivity in this model parallel clinical findings; treatment with duloxetine ameliorated oxaliplatin–induced cold hypersensitivity, whereas pregabalin and tramadol did not. The results contrast to those obtained in oxaliplatin–treated rats, in which cold hypersensitivity was reduced by all analgesics. The pharmacological findings suggesting that macaques could be advantageous over rats in translating preclinical findings into clinically useful treatments for oxaliplatin–induced cold hypersensitivity. Brain activity is likely to be altered in the neuropathic state. Thus, brain activity was examined using functional magnetic resonance imaging (fMRI) in oxaliplatin–treated macaques and duloxetine was used to determine if its analgesic effect is due to changes in brain activity.

Results
Three days after oxaliplatin infusion, withdrawal latency to cold water was significantly decreased compared with the pre–infusion withdrawal latency, indicating cold hypersensitivity. Increased activity within a cluster located in the insular cortex, a brain region known show increased activity in patients with cold allodynia, was observed. The increased activity tended to be reduced following duloxetine treatment. The results suggest that reduction of insular cortex activity could in part underlie the analgesic effect of duloxetine on cold hypersensitivity.
Conclusion
Changes in brain activity as observed via fMRI in oxaliplatin–treated macaques parallel clinical findings in patients with neuropathic cold hypersensitivity. The current results also suggest that brain activity could be a useful quantitative method of assessing the effect of therapeutic interventions on oxaliplatin–induced neuropathic pain. The macaque model could be a useful approach in enhancing successful translating of preclinical findings to clinically useful treatments for oxaliplatin–induced neuropathic pain.
**Title:** Critical Role Of Transient Receptor Potential Vanilloid 1 In A Rodent Model Of Paclitaxel-Induced Acute Painful Syndrome

**Poster Number** PTH357

**Authors**

Federal University of Santa Catarina, Florianópolis, SC, Brazil, Universidade Federal de Minas Gerais, Santa Maria, BRAZIL, Universidade Federal de Santa Maria, Santa Maria, Brazil, Instituto de Ensino e Pesquisa da Santa Casa de Misericórdia de Belo Horizonte, Belo Horizonte, Brazil, Faculty of Medicine of Ribeirão Preto - USP, Ribeirão Preto, BRAZIL, University of Sao Paulo, Ribeirão Preto, Sao Paulo, Ribeirao Preto Medical School, University Of Sao Paulo, Ribeirao Preto/SP, BRAZIL, Instituto de Ensino e Pesquisa da Santa Casa de Belo Horizonte, Belo Horizonte, Brazil, University of the Extreme South of Santa Catarina, Criciúma, Brazil

**Aim of Investigation**
The clinical use of paclitaxel (PAC) as a chemotherapeutic agent is limited by its pain induction properties, notably neuropathic pain after repeated treatment. However, a single PAC injection may also cause an acute pain syndrome (P-APS) in at least 70-80% of patients, which is more prominent in the lower extremities and a relevant cause of morbidity. Despite there is no standard therapy to treat P-APS and its mechanisms are largely unknown, some evidence has pointed to a probable nociceptor sensitization and nerve pathology in this painful syndrome. Of note, the transient receptor potential vanilloid type 1 (TRPV1) is expressed mainly in nociceptors, where it plays a key role in the detection of several noxious painful stimuli. TRPV1 has been implicated with PAC-induced chronic neuropathic pain, but its role in PAC-related acute pain syndrome is unknown. Thus, the aim of this investigation was to elucidate the participation of TRPV1 in a model of acute pain syndrome induced by PAC in rodents.

**Results**
PAC produced mechanical and heat hyperalgesia as well as suppression of burrowing behaviors from 24 up to 48 hours after administration. The TRPV1 antagonism (SB-366791, 1 mg/kg, i.p.) reduced PAC-induced the mechanical and heat hyperalgesia, and burrowing supression. In addition, the TRPV1-positive sensory fiber ablation (resiniferatoxin, 200 µg/kg, s.c.) was able to largely reduce the mechanical and heat hypersensitivity induced by PAC. KO TRPV1 showed a pronounced reduction on mechanical allodynia to PAC acute injection, and did not develop heat hyperalgesia. Moreover, 24 hours
after its injection, PAC induced a chemical hypersensitivity to the TRPV1 agonist capsaicin (0.01 nmol/site) and increased TRPV1 immunoreactivity in dorsal root ganglion (DRG). Moreover, 24 hours of incubation with PAC (50 µM) in cultured DRG neurons increased not only the proportion of neurons responsible to capsaicin but also the amplitude of capsaicin-induced increase of calcium transients.

**Conclusion**

TRPV1 increased expression, sensitization and activation exerts a critical role in a model of P-APS in rodents, indicating that the TRPV1 receptor could be explored as a possible target for the treatment of P-APS. Acknowledgements CNPq, CAPES, FAPESP and FAPERGS (Brazil) are acknowledged by fellowships and financial support.
Title: Development Of A Novel Clinically Translatable Acute, Heat Pain Behavioral Model In Non-Human Primates

Poster Number PTH358

Authors

Merck & Co Inc, West Point, PA, Merck & Co Inc, Rahway, NJ

Aim of Investigation
To establish a clinically translatable acute heat pain behavioral model in Rhesus monkeys to evaluate effects of a selective Nav1.7 inhibitor.

Results
44°C produced very low levels of withdrawal response, whereas temperatures ≥46°C produced a temperature-dependent increase in the withdrawal response. Subcutaneous injection of morphine (0.3, 1 and 3 mg/kg), fentanyl (0.005 and 0.01 mg/kg), and tramadol (2.5 and 5 mg/kg) produced a significant dose-dependent inhibition of withdrawal responses from 46-50°C. Compound A (1-20 mg/kg), a selective inhibitor of the tetrodotoxin-sensitive voltage-gated sodium channel (Nav1.7) predominantly expressed in C-fibers, dose-dependently inhibited the withdrawal responses at 46°C and 48°C. In contrast, the GABAA receptor agonist diazepam (2 mg/kg, selected as a negative control to test whether reductions in arm withdrawal were related to sedation) had no effect on the response.

Conclusion
We describe a novel clinically translatable acute heat pain behavioral model in NHP with utility in screening analgesic compounds. The model was sensitive to opioid agonists and Nav1.7 blockade but not to diazepam, suggesting it is sensitive to clinically active and putative analgesics.
**Title:** Pain Management In The Mouse Osteotomy Model – Refinement Vs. Translation

**Poster Number** PTH359

**Authors**
A. Lang, P. Jirkof

Department for Rheumatology and Clinical immunology, Charité-Universitätsmedizin Berlin, Berlin, GERMANY, Division of Surgical Research, University Hospital Zurich, Zurich, SWITZERLAND

**Aim of Investigation**
Fracture healing disorders occur in approximately 10% of human patients and cause severe pain and reduced quality of life. The result of fractures is often severe pain. The efficient management of fracture pain is mandatory to ensure physiological bone healing. In addition, the selection of analgesics for fracture pain is restricted due to potential interfering properties of anti-inflammatory drugs. To develop and test new therapeutic strategies, the mouse is a frequently used laboratory animal in bone healing research. However, the identification and assessment of pain, stress and strain in the mouse is still challenging as well as the interpolation to the human. With this study, we aim at preparing standardized score sheets and recommendations for an evidence-based pain assessment procedure in bone-linked mice models, in order to identify or evaluate potential new anti-pain drugs.

**Results**
Results and the concluding score sheets for pain-assessment in bone-linked mice models will be presented.

**Conclusion**
Here, we will present preliminary results of our pain assessment study in the mouse osteotomy model and discuss the translational potential as well as interfering effects of the pain management on the bone healing. In order to enhance the knowledge on pain assessment in basic research studies and to effectively reduce lab animal usage, we conceived a refinement study embedded in a basic research study in the mouse osteotomy model to show the possibility to combine both studies and to reach a wider community with results in the field of refinement studies.
Title: A Nonhuman Primate Model Of Oxaliplatin-Induced Neuropathic Pain.

Poster Number PTH360

Authors

Hamamatsu Pharma Research, Inc., Hamamatsu, Japan, Hamamatsu University School of Medicine, Hamamatsu, Japan

Aim of Investigation
The platinum-based chemotherapeutic oxaliplatin is the standard treatment for advanced colorectal cancer. Unique to platinum-based chemotherapeutics is the induction of an acute cold hypersensitivity within hours or days of treatment in nearly all patients, which may lead to dose reduction or treatment termination. While there are a number of analgesics for neuropathic pain, there are currently no analgesics approved for specifically for oxaliplatin-induced neuropathic pain. A number of potential analgesics have been proposed for ameliorating oxaliplatin-induced neuropathic pain based on findings in rodent models, but few have shown clinical efficacy. This could be due in part to a lack of predictiveness of preclinical rodent models of oxaliplatin-induced peripheral neuropathy. Nonhuman primates (NHP) are phylogenetically closer to humans than rodents and may show drug responses that parallel those of humans. The current study pharmacologically characterized a NHP model of oxaliplatin-induced neuropathic pain and compared the effects of clinical analgesics to that of a rat model of oxaliplatin-induced neuropathic pain.

Results
All macaques demonstrated decreased tail withdrawal latency to 10°C water, or cold hypersensitivity, 3-5 days following one infusion of oxaliplatin. Withdrawal latencies gradually over time, fully recovering to pre-injection latencies two weeks after oxaliplatin infusion. Trends in decreased withdrawal latencies to 20°C and 42°C water in NHPs were observed. An acute cold hypersensitivity was observed following subsequent infusions of oxaliplatin. In rats, however, few demonstrated an early-onset cold hypersensitivity 3 days following two oxaliplatin injections. Thus, rats were treated with oxaliplatin twice weekly for 3 weeks. Sixteen days after the first injection of oxaliplatin, about 65% of all rats demonstrated acute cold hypersensitivity (hind paw responsiveness to acetone). Significant antinociception was obtained with duloxetine (30 mg/kg, p.o.) but not with pregabalin (30 mg/kg, p.o.)
and tramadol (30 mg/kg, p.o.) in NHP. However, duloxetine (30 mg/kg, p.o.), pregabalin (30 mg/kg, p.o.),
and tramadol (30 mg/kg, p.o.) significantly suppressed cold hypersensitivity in rats.

**Conclusion**
The current findings suggest behavioral and pharmacological distinctions between NHP and rat
responses to acute oxaliplatin treatment. The antinociceptive effect of duloxetine, and no other drug, in
the NHP model parallels clinical findings, wherein duloxetine showed significant analgesia in a phase III
clinical trial. While duloxetine also demonstrated efficacy in the rodent model, pregabalin, which has not
demonstrated efficacy in oxaliplatin-induced neuropathic pain, also showed efficacy. The current NHP
model could be useful in testing novel treatments for oxaliplatin-induced peripheral neuropathy as well
as elucidating mechanism.
Title: Influence Of Stage Of Estrous On Pain Control And Assessment In A Murine Model Of Sepsis

Poster Number PTH361

Authors
J. Nemzek, L. Kennedy
University of Michigan, Ann Arbor, MI, Case Western Reserve University, Cleveland, OH

Aim of Investigation
Animal models used in biomedical research often employ surgery or other methods that could result in pain and/or distress. For surgical models of sepsis, the use of analgesics has been controversial. Unrelieved pain may alter the model but the use of an analgesic such as buprenorphine may also change outcomes. Previously, we have shown that sepsis outcomes in a murine surgical model may be influenced by the use of buprenorphine in male mice of some strains and in female mice at certain stages in the estrous cycle. However, we have not investigated how the relative effectiveness of buprenorphine may be influenced by stage of estrous in that model. Therefore, the aim of this study was to compare behavioral and grimace pain scores obtained after surgery and buprenorphine administration when the manipulations occurred at different stages of estrous.

Results
The highest average behavioral pain scores from the two observers (3.5 ± 0.3 and 3.7 ± 0.3) were observed in the mice given buprenorphine and surgery during metestrus. These scores were significantly different than those seen during estrus for one observer (2.4 ± 0.4; p=0.03) and proestrus for the other observer (2.6 ± 0.3; p=0.02). Likewise, the grimace scores from the two observers were highest in the metestrus mice (1.6 ± 0.3 and 2.3 ±0.4) and lowest in proestrus (1.0 ± 0.3; p=0.054 and 1.2± 0.3; p=0.04). Scores were consistently higher in the stages of estrous that are defined by low estrogen levels (metestrus and diestrus) as compared to those defined by high estrogen levels (proestrus and estrus).

Conclusion
In this study, the influence of a standard dose of buprenorphine in mice in a surgical sepsis model was assessed by two pain scoring methods. Pain scores were highest in the stages of estrous associated with lower estrogen levels. This parallels our previous findings of poorer sepsis outcomes in metestrus mice. This suggests that either the control of pain or the assessment of pain may be influenced by the stage of estrous. Further studies are needed to discern the interrelationships of pain assessment, pain control...
and estrous cycle in animal models of disease. This study was funded by a grant from the American College of Laboratory Animal Medicine (ACLAM) Foundation.
Title: Unknown Transcripts Regulated By Capsaicin Application In Rat Trigeminal Ganglion.

Poster Number PTH362

Authors
E. Ohki, M. Okumura, O. Tadokoro, E. Kondo

Matsumoto Dental University Hospital, Shiojiri, Nagano, Japan, Department of Oral Anatomy, Matsumoto Dental University, Shiojiri, Nagano, Japan

Aim of Investigation
Capsaicin application is a nociceptive stimulus for sensory neurons, and the activation of neurons can alter gene expression. The transcripts influenced by capsaicin stimulus are not only from well identified genes, but also from unidentified regions which may include unidentified genes, unidentified alternative splicing products, or untranslated functional RNA. The aim of this investigation is to examine the relationship between capsaicin stimulus and such unknown transcripts.

Results
Microarray analysis showed 48 up-regulated transcripts (>1.7, vs saline), after capsaicin application, with 24 transcripts from the intron region of identified genes, and the other 24 transcripts from the long inter-gene region where no functional gene was located. Only 1 transcript was down-regulated (<1/1.7, vs saline), after capsaicin application. PCR analysis indicated that all of the 24 transcripts from intron regions were existed in RNA extracted from trigeminal ganglia. However, the expression levels were very low and difficult to detect, and because of their low level expressions, 13 transcripts could not be tested by real-time PCR. Of the other 11 transcripts, 6 were confirmed by real-time PCR to be up-regulated after capsaicin stimulus. These up-regulated transcripts were transcribed from the intron regions of rat Tra2a, Cadm1, LOC685917, Gnas, RBm39, Ccln1, respectively.

Conclusion
Gene expression alterations induced by capsaicin application included many transcripts from the intron region or inter-gene region. The fact that almost of them were up-regulated, with only 1 down-regulated one included, may indicate the importance of these up-regulations, even though their expression levels were very low. We confirmed the up-regulation of 6 transcripts derived from intron regions. However, the precise description for full length image, function, and significance of these transcripts needs further investigation.
Title: Reduced Local Recruitment Of Neutrophil Affected The Attenuation Of Pain Behavior Following Hind Paw Incision In Blt1 Deficiency Mice

Poster Number PTH363

Authors
M. Asahara, N. Ito, Y. Yamada, M. Nakamura, T. Yokomizo, T. Shimizu

Department of Anesthesiology, Faculty of Medicine, The University of Tokyo, Tokyo, Japan, Department of Life Science, Faculty of Science, Okayama University of Science, Okayama, Japan, Department of Biochemistry, Juntendo University School of Medicine, Tokyo, Japan, Department of Lipid Signaling Project, Research Institute, National Center for Global Health and Med, Tokyo, Japan

Aim of Investigation
Leukotriene B4 (LTB4) is a lipid mediator enhancing recruitment and activation of neutrophils, which is a common feature of inflammation and tissue injury. BLT1 is a high affinity receptor of LTB4, and BLT1KO mice exhibited reduced acute inflammatory pain responses following intraplantar injection of formalin (Asahara et al.). To elucidate the role of LTB4-BLT1 signaling in incisional pain model, we have studied pain behavior and local infiltration of neutrophils using BLT1 KO mice and wild-type mice.

Results
BLT1KO mice showed significantly reduced mechanical thresholds of ipsilateral side of hind paw, on 2hrs, 1 day, 2 days, 3 days, and 4 days after incision compared with the wild type mice. The numbers of infiltrated neutrophil was peaked on 1 day after incision in both wild type and BLT1KO mice and increased significantly in wild type mice compared with the BLT1KO mice. In the wild type mice, a greater numbers of infiltrated neutrophil was observed than BLT1KO mice on 1 day, 2 days, and 3 days after incision.

Conclusion
These results substantiated that reduced local infiltration of neutrophil may affect the attenuation of pain behavior on early phase of incisional pain in BLT1KO mice. Blocking of BLT1 on local wound site might be effective to control the neutrophil recruitment and reduce pain from surgical incision.
Title: Testosterone Influence On Pain Behavior During Postoperative Period: A Pilot Study

Poster Number PTH364

Authors
J. Barbosa Neto, B. Bonfim, T. RODRIGUES, C. Palmeira, M. Cartagenes, J. Garcia, H. Ashmawi

Sao Paulo University, Sao Paulo, Brazil, Federal University of Maranhao, Sao Luis, Brazil

Aim of Investigation
It is well established that female subjects experience more pain than male after inflammatory or neuropathic pain stimuli. However, the basis for this sex difference is still unknown, although variables including biological, psychological, and cultural differences have been hypothesized as possible explanatory factors for these differences. The influence that gonadal hormones have on how male and female express pain behavior has been a subject of research for almost two decades, and a direct link between gonadal hormone and difference in pain sensitivity is still controversial. In male subjects, research indicates that testosterone might have anti-nociceptive action, even though physiological basis is still unknown. In order to understand the influence that testosterone would have on pain behavior with male subjects, we conducted a postoperative pain model comparing normal versus pharmacologically castrated rats.

Results
At the 2 hour evaluation, there was statistically significant difference found in Von Frey test, with higher withdrawal thresholds in testosterone group (T= 16.7 vs. F=12.1, p=0.01), suggesting more pain in group F, but no difference was found by other tests. In 1stPO, guarding pain showed higher scores in testosterone group (T=13.7 vs F=9.3, p<0.0001). In 2ndPO and 3rdPO only WB showed statistical difference between groups (T=34.55 vs. F=24.08, p=0.0215; T=35.97 vs. F=27.75, p= 0.048). At the 7thPO, all tests presented statistical difference between groups, (GP: T=3.7 vs. F=8.8, p=0.001; VF: T=44.19 vs. F=50.37, p=0.025; WB:T=45.84 vs. F=29.13, p<0.001).

Conclusion
This preliminarily results did not conclusively demonstrate a protective action of testosterone for postoperative pain after plantar incision, as tests presented conflicting data.
Title: Ngf Increased In Skeletal Muscle Has A Role In Muscular Mechanical Hyperalgesia In Inactivity Model.

Poster Number PTH365

Authors

Department of Functional Anatomy, Kanazawa University Graduate School of Medical Sciences, Kanazawa, Japan, Nagoya Gakuin University, Seto, Japan, Department of Histology and Embryology, Kanazawa University Graduate School of Medical Sciences, Kanazawa, Japan

Aim of Investigation
Physical inactivity has been reported as one of the factors of developing muscular disorders or chronic pain. Inactivity such as prolonged bed rest causes muscle atrophy and joint contracture. Recently, nerve growth factor (NGF) is known to be involved in muscle hyperalgesia in both human and animal models, and is produced in injured and inflammatory tissues. However, it is unclear whether the inactivity directly causes muscular pain, and NGF has crucial role on pain caused by the inactivity. The aim of the present study is to confirm the involvement of NGF in muscular pain associated with the inactivity.

Results
The mechanical withdrawal threshold on the gastrocnemius muscle in the inactivity model was significantly decreased along with the inactivity periods. The range of motion in dorsiflexion of the ankle joint was also limited in this model, and muscle wet weight and relative muscle wet weight decreased. After the inactivity for 4 weeks, the expression of NGF mRNA and protein were increased in the muscle. The immunoreactivity of NGF in the muscle tissues was observed in muscle cells. However, the apparent damages of muscular tissue were not observed, and there were also no remarkable changes such as infiltration of inflammatory cells. The mechanical withdrawal threshold was completely improved by intramuscular injection of anti-NGF antibodies. In addition, the NGF positive cells also increased in the muscle sensory neurons.

Conclusion
We could develop an animal model of muscular hyperalgesia induced by physical inactivity. This model would be useful to understand the mechanisms of muscular pain induced by the inactivity. After the inactivity, the skeletal muscle cells under non-inflammatory condition produced NGF, which may
contribute to the muscular mechanical hyperalgesia through the sensitization of primary afferent neurons innervating the muscle.
Date: 09/29/2016 09:30:00 AM

**Title:** Muscle Injury With Prolonged Infiltration Of Inflammatory Cells Induces Persistent Postsurgical Pain And Spinal Microglial Activation

**Poster Number** PTH366

**Authors**
Y. Yoshiyama, Y. Sugiyama, S. Tanaka, D. Sugiyama, S. Fuseya, M. Kawamata

Shinshu University School of Medicine, Matsumoto, Japan

**Aim of Investigation**
Local chronic inflammation has been suggested as one of the causes of persistent postsurgical pain (PPSP); however, no model reflecting the pathology of PPSP has been established. Recently, it was reported that subcutaneous muscle incision rather than skin incision was a factor associated with hyperalgesia. Based on the above, we hypothesized that muscle injury with persistent inflammation would induce PPSP. The aims of this study were to develop a new model of PPSP with persistent inflammation in muscle, and to investigate the mechanism of PPSP.

**Results**
Plantar muscle cryoinjury induced greater mechanical hyperalgesia from day 5 to 8 and spontaneous pain from day 3 to 7 compared with plantar muscle incision. In plantar muscle cryoinjury, the number of inflammatory cells in injured muscle and spinal Iba-1 expression were significantly higher compared with those in plantar muscle incision. Taken together, plantar muscle cryoinjury is a more appropriate model of PPSP compared with plantar muscle incision.

**Conclusion**
Our new model involving plantar muscle cryoinjury of plantar muscle induced persistent inflammation at the postsurgical wound site and persistent inflammatory pain. This model effectively reflected the characteristics of PPSP. In addition, the results of this study suggest that spinal microglial activation is involved in the pathogenic mechanism of PPSP.
Title: Maternal Social Separation During The Stress Hyporesponsive Period Attenuated The Fear-Related Behavior

Poster Number PTH367

Authors
N. Koyama, K. Daun, S. Hitoshi

Shiga University of Medical Science, Otsu, Japan

Aim of Investigation
Fear avoidance theory is a model that describes how individuals develop chronic pain as a result of avoidant behavior based on fear, but the mechanism are not well defined. The person who does not exhibit exaggerated fear-related behavior may not develop chronic pain. Meanwhile, postnatal stress increased the number of neural stem cell and reversed the effect of prenatal stress (Kippin et al., JNeurosci 2004). During postnatal development, the newborn mice undergo a period of reduced responsiveness of the pituitary adrenal axis so called the stress hyporesponsive period (SHRP). The SHRP is hypothesized to be neuroprotective against the stress-induced excessive release of corticosterone during postnatal development. Therefore, we are aiming to investigate the effect of maternal social separation during SHRP on fear-related behavior and proliferation.

Results
The level of corticosterone was significantly lower in early-MSS mice compared to late-MSS mice. A significant increase in numbers of BrdU immunoreactive cells in the dentate gyrus and subventricular zone in early-MSS. In open field test, the late-MSS showed hyperactivity, although there was no significant difference among control and early-MS on the time spent in the center area, which is not indicative of a reduction in anxiety-like behavior. The fear-conditioning test is a Pavlovian associative learning. In conditioning training, conditioning stimulus (context/cue) was given pairing with an aversive unconditioning stimulus: US. Contextual test was performed without US in same context as training chamber, and cued test was performed in altered context without cued period followed by with cued period. Early-MSS/late-MSS mice immobilized lesser on contextual and cued test compared to control. Especially in late-MSS mice, immobilizing level during cued stimulus was significant attenuated. But there was no significant difference on the startle response and the threshold of foot shock. Both fear memory and fear-extinction learning was not impaired in early-MSS/late-MSS mice.
Conclusion
Maternal social separation during/after SHRP promoted the hippocampal neurogenesis attenuating the fear-related behavior, without impairing the anxiety, startle response and fear learning. There is the possibility that clarification of a molecular mechanism underlying proliferating effect of maternal social separation contribute the new treatment for chronic pain.
Date: 09/29/2016 09:30:00 AM

**Title:** Study Of Antinociceptive Effect Of Solidago Chilensis Meyen (Arnica) In Animals Submitted To Behavioral Model Of Inflammatory Pain

**Poster Number** PTH368

**Authors**
L. FERRACINE, C. Rego, A. GUIMARAES
FACULDADE DE MEDICINA DE MARILIA- FAMEMA, SALES OLIVEIRA, Brazil, Famema, Marilia, Sao paulo, FAMEMA, sao paulo, SP

**Aim of Investigation**
Aim of Investigation: Pain sensation corresponds to one of the main causes of individual disability. Currently, pain sensation can be treated by several drugs, including nonsteroidal anti-inflammatory drugs, opioids, anticonvulsivants, antinflammatories, and others. However, since the beginning, man uses nature plants in the search for new therapeutic tools. From scientific point of view, the research of medicinal plants is not well studied and disseminated in Brazil, in spite of the wealth of the Brazilian flora. Among the species used therapeutically, on Brazilian popular medicine, a plant from Asteracea family, Solidago chilensis Meyen (arnica), with analgesic properties has been much studied in Brazil. However, little is known about its effects on the pain sensation. Therefore, the objective of this work is to evaluate antinociceptive effect of this plant in animals submitted to behavioral model of inflammatory pain, by comparing its antinociceptive effects with the analgesic effect of known drugs as weak (tramadol) and powerful opioid agents (morphine).

**Results**
Results: According to obtained data we can suggest that oral administration of arnica 6CH homeopathic solution, in PLUS solution, administrated 2 hours before test, induced significant antinociceptive effect on rats submitted to formalin test, as compared to control and tramadol groups. The antinociceptive effect of arnica was observed during the whole test. As comparing to morphine group, we can suggest that the Antinociceptive effects of arnica did not differ in significant way.

**Conclusion**
Conclusions: It was concluded that homeopathic solutions of Solidago chilensis Meyen 6CH in PLUS Solution treatment showed a potent antinociceptive effect on rats submitted to inflammatory process by intraplantar injection of formalin solution into the right hind paw of rats – Formalin test. The
obtained data demonstrated that the antinociceptive effect of arnica, observed along all the test time was effective on both irritating and inflammatory phases of formalin solution. These results can support the use of Arnica as analgesic medicinal folk in Brazil. Keywords: Solidago chilensis Meyen, arnica, antinociceptive effects, inflammatory pain
**Title:** Sex Dependent Role Of Tlr4 And Microglia In Collagen Antibody-Induced Mechanical Hypersensitivity

**Poster Number** PTH369

**Authors**

Department of Physiology, Stockholm, Sweden, Department of medicine, Stockholm, Sweden

**Aim of Investigation**
We have previously shown that intrathecal injection of the high-mobility group box-1 protein (HMGB1) in its TLR4 preferring redox state induce pain-like behavior in both male and female mice. Further, blocking spinal HMGB1 reverses collagen antibody induced arthritis (CAIA) induced mechanical hypersensitivity in both male and female mice. However, it has been suggested that TLR4 and spinal microglia play an essential role in pain signaling only in male mice. Thus the aim of the current study was to further investigate if there is a sex-dependent role of TLR4 and spinal glial cells in nociceptive signal transmission in the CAIA model.

**Results**
Intravenous injection of collagen antibody cocktail induced transient inflammation with persistent mechanical hypersensitivity. In BALB/c mice mRNA levels of the glia-associated factors Cd11b (microglia) and Gfap (astrocyte) were elevated in late phase, but not in the inflammatory phase, in male mice. Cd11b and Gfap levels were not altered in spinal cords at any time point subsequent to induction of CAIA in female mice. A significant increase in the light intensity for Iba1 (microglia) and GFAP immunoreactivity in late phase of the CAIA model was observed in male but not in female mice, in accordance with the mRNA findings. In contrast, in CBA mice no change in spinal Cd11b or GFAP mRNA levels were detected during the inflammatory and post-inflammatory phase. Still, an increased Iba1 and GFAP immunoreactivity was detected in lumbar spinal cords from both male and female mice collected in the late phase. While effective in male mice, i.t. injection of minocycline and s.c. injection of amitriptyline did not reverse CAIA-induced mechanical hypersensitivity in female mice. Intrathecal injection of LPS-RS in the late phase did not attenuate pain-like behavior in either sex while i.t injection of HMGB1 neutralizing antibody reversed pain-like behavior in both male and female mice.
Conclusion
Our data suggest that biochemical and morphological signs of altered spinal microglia and astrocyte reactivity in response to CAIA is both a sex and strain dependent. Interestingly, while inhibiting microglia activity (using minocycline) only reversed mechanical hypersensitivity in male mice, differential effects was achieved using various means of interfering with TLR4. Thus future studies are warranted in order to decipher the role of glial cells and TLR4 in arthritis-induced pain-like behavior.
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**Title:** Firing Activity In The Sensorimotor Cortex In A Mouse Model Of Neuropathic Pain

**Poster Number** PTH370

**Authors**
C. Ohsugi, M. Ohsawa, M. Murayama
Tokyo Institute of Technology, Tokyo, Japan, RIKEN BSI, Saitama, Japan, UnivDept. Neuropharm., Grad. Sch. Pharmceu. Sci., Nagoya city Univ, Nagoya, Japan

**Aim of Investigation**
The role of cortico-cortical circuits in nociception is not clear. We previously reported that a reciprocal projection exists between the secondary motor cortex (M2) and the somatosensory cortex (S1), and that this projection is essential for accurate sensory perception (Manita et al., Neuron 2015). To understand the physiological roles of this circuit in neuropathic pain, we recorded multiunit activity from S1 and M2 of a mouse model of neuropathic pain induced by partial sciatic nerve ligation (PSNL) of the left hindpaw. Thus, we determined whether these regions are engaged in neuropathic pain and monitored their changes.

**Results**
We found differences in the firing rate of S1 and M2 neurons between the Sham and PSNL groups.

**Conclusion**
Further experiments on the cortico-cortical circuit in this mouse model are needed to elucidate the neural mechanisms of neuropathic pain. The authors have no financial relationships to disclose.
Title: Pharmacological Studies Of Spinal Alpha 2 Adrenoceptor Subtypes In A Rat Model Of Trigeminal Neuropathic Pain

Poster Number PTH371

Authors
K. Nakai, A. Nakae, T. Kubo, Y. Minegishi, Y. Fujino, K. Hosokawa

Department of Plastic and Reconstructive Surgery, University of Fukui Hospital, Eiheiji, Japan, Immunology Frontier Research Center, Osaka University, Laboratory of Brain-Immune Interaction, Suita, Osaka, Department of Plastic Surgery, Osaka University Graduate School of Medicine, Suita, Japan, Department of Anesthesiology and Intensive Care Medicine, Osaka University Graduate School of Medici, Suita, Osaka, Japan

Aim of Investigation
Substantial evidences revealed that descending spinal adrenergic transmission had an important role in the process of pain modulation. Spinal administration of the alpha 2 adrenergic receptor agonists has been shown to produce antinociception. The contribution of spinal alpha 2 adrenergic receptor subtypes in inhibiting the trigeminal neuropathic pain remained unclear. Chronic constriction injury to the infraorbital nerve (ION-CCI) has proven a useful model for trigeminal neuropathic pain. The present study evaluated the possible role of spinal alpha 2A and alpha 2C adrenergic receptors in ION-CCI rat model.

Results
Intrathecal administration of guanfacine and nitrobiphenyline increased mechanical thresholds in a dose dependent manner (P <0.05). BRL 44408 significantly reduced the anti-allodynic effect of guanfacine. JP 1302 significantly reduced the anti-allodynic effect of nitrobiphenyline.

Conclusion
The results indicated that descending pain inhibitory system in the spinal cord may be activated via spinal alpha2A and alpha2C adrenergic receptors in a rat model of trigeminal neuropathic pain.
Aim of Investigation

Pain is a global affliction that affects people of every age, gender, and ethnicity. Peroxynitrite (PN) and its reactive precursors, superoxide (SO) and nitric oxide (NO), are involved in the development and maintenance of pain via post-translational nitration and modification of various proteins. Because SO, NO and PN contribute to the development and maintenance of both peripheral and central sensitization, they are attractive targets for pain management strategies. Indeed, current studies have shown that therapeutic strategies targeting SO, NO and PN are able to both prevent and reverse the pathologies associated with pain of various etiologies. Nitric oxide can also concur to modulate signal transduction upon certain stimuli by means of other mechanisms that lead to transient protein modification. The main chemical reaction underlying this mechanisms is the S-nitrosylation of cysteine residues. It consists on the covalent addition of an NO moiety to a reactive sulphydryl, which results in the formation of an S-nitrosothiol derivative (SNO). The reaction is catalyzed by denitrosylating enzymes, the most important of which is the NADH-dependent S-nitrosoglutathione (GSNO) reductase (GSNOR), that decreases indirectly the concentration of protein SNOs (PSNOs).

Results

For the first time, we show that GSNOR-KO mice develop mechanical allodynia and thermal hyperalgesia. We also demonstrate that mechanical allodynia and thermal hyperalgesia are associated
with protein S-nitrosylation in L4-L5 tract of the spinal cord and that antioxidant administration is able to block these events.

**Conclusion**

In this work, we propose that protein S-nitrosylation is also critical in the pain pathway and could represent a post-translational modification implicated in the central sensitization leading to pain sensibility. These findings could provide novel insight into the involvement of GSNOR and S-nitrosylation in pain identifying a new target for the development of pain therapies. This work has been supported by funds from PON03PE_00078_2, PON03PE_00078_1/F1, PON03PE_00078_2/F1 and IBSA Foundation.
Title: Loss Of Inhibitory Tone On Spinal Cord Dorsal Horn Neurons In A Mouse Model Of Neuropathic Pain

Poster Number PTH373

Authors
M. Cordero-Erausquin, M. Medrano, D. Dhanasobhon, I. Yalcin, R. Schlichter

Institut Des Neurosciences Cellulaires Et Integratives UPR3212 CNRS, Strasbourg, France

Aim of Investigation
Plasticity of inhibitory transmission in the spinal dorsal horn (SDH) is thought to be a key mechanism responsible for pain hypersensitivity in neuropathic pain syndromes. However in vivo recordings performed in rats have provided controversial data concerning the plasticity of inhibitory transmission in neuropathic models, arguing for either a decrease or an increase of GABAergic tone. Most studies so far have focused on SDH neurons responding to natural peripheral stimulations but showing no spontaneous ongoing activity between stimuli (non-spontaneously active or NSA neurons). However, some SDH neurons display considerable ongoing activity in the absence of experimentally-applied stimuli (spontaneously active or SA neurons). In the present study, we systematic analyzed both SA and NSA neurons to provide an exhaustive characterization of the neurons involved in sensory processing of mechanical information and their plasticity after nerve injury in mice. With this approach, we aimed at assessing whether an inhibitory tone can be detected in the mouse SDH, whether this tone undergoes plasticity in a model of neuropathy, and what could be the underlying mechanism of this plasticity.

Results
SA and NSA neurons represented respectively 59% and 41% of recorded neurons, and were predominantly wide dynamic range (WDR) in naïve mice. Nerve-injured mice displayed a marked decrease in mechanical threshold of the injured paw. After nerve injury, the proportion of SA neurons was increased to 78%, suggesting that some NSA neurons became spontaneously active. In addition, the response to touch (but not pinch) was dramatically increased in SA neurons, and high-threshold (nociceptive specific) neurons were no longer observed. Application of bicuculine and strychnine significantly increased responses to innocuous mechanical stimuli in SA and NSA- neurons from sham animals, but had no effect in sciatic nerve-injured animals. Moreover, in nerve-injured mice, local spinal administration of acetazolamide restored responses to touch similar to those observed in naïve or sham mice.
**Conclusion**

Our study reveals a dramatic loss of spinal inhibitory tone in neuropathic conditions. In addition, it suggests that a shift in the reversal potential for anions is an important component of the abnormal mechanical responses and of the loss of inhibitory tone recorded in this model of nerve injury-induced neuropathic pain.
Title: Cell And Molecular Basis Of Deep Pain Chronification

Poster Number PTH374

Authors
S. Sikandar, S. Santana-Varela, Q. Millet, J. Wood

WIBR, University College London, London, United Kingdom

Aim of Investigation
We are exploring the molecular contributions underlying the transition of acute to chronic deep tissue pain. We first established a mouse model of musculoskeletal pain using repeated intramuscular inflammatory injections in order to reproduce the temporal and widespread sensory changes observed clinically. We assessed these changes in nociceptive processing during the course of the model using behavioural assessments and in vivo electrophysiological characterisation of spinal cord excitability. We also correlated these findings with the degree of peripheral damage in muscle tissue and the time following inflammatory injections. We then assessed the contribution of the DRG nociceptor population to the induction and maintenance of ongoing pain in this model using a genetic approach to ablate DRG neurones that are Nav1.8 positive. In order to further explore the subsets of primary afferents that are likely to underlie deep tissue nociception, we first created a chemical expression profile of muscle afferents using retrograde labeling and immunohistochemical staining with known primary afferent markers. This approach also paves way for genetic profiling of muscle afferents using the unbiased approach of single cell RNA sequencing of DRG neurones innervating muscle.

Results
We used a mouse model of muscle priming in order to explore the molecular and cellular contributions to the transition of acute to chronic pain. This model of muscle priming selectively produces secondary mechanical, but not thermal, hypersensitivity with no changes in motor function. Contralateral changes in secondary mechanical hypersensitivity develop around two weeks following the initial injection. Importantly, both ipsilateral and contralateral hypersensitivity are maintained for the duration of at least 4 weeks in the absence of peripheral damage caused by injection of inflammatory substances, suggesting an important role for central nociceptive processing in the maintenance of chronic pain. We report novel findings of the contribution of the DRG Nav1.8 positive nociceptor population in the maintenance, but not initiation, of chronic pain. In contrast to earlier findings for cutaneous inflammatory pain, these neurones are not necessary for acute deep tissue pain. However, our
behavioural results demonstrate that Nav1.8 positive neurones are important for the transition of acute to chronic musculoskeletal pain as (1) bilateral hypersensitivity and (2) prolonged chronic pain do not develop in Nav1.8DTA mice in our model of muscle priming. Electrophysiology results parallel our behavioural findings as primed littermate controls with two successive inflammatory injections show both ipsilateral and temporally-dependent contralateral hypersensitivity of dorsal horn neurones to mechanical stimulation, with no changes in thermal sensitivity. In contrast, spinal excitability of Nav1.8DTA primed mice that received two consecutive inflammatory injections is not significantly different to Nav1.8DTA control mice that only received one inflammatory injection. Our chemical expression profile of muscle primary afferents using retrograde labeling of muscle neurones alongside immunohistochemical co-labeling of primary afferent markers demonstrate the existence of unique primary afferent populations distinguishing muscle sensory neurones. This muscle afferent population includes a proportion of Nav1.8 expressing cells in the DRG, substantiating our behavioural and electrophysiology findings using the Nav1.8DTA mice. These findings are likely to be reproduced by subgroups of primary afferents that will be genetically defined using single cell RNA sequencing.

Conclusion
We have established a paradigm for muscle priming in mice that models the transition of acute to chronic pain. Importantly, we observe the clinical phenomena of prolonged pain, as well as accompanied temporal and spatial sensory changes as observed in many musculoskeletal pain syndromes. In contrast to earlier findings exploring the functional role of the Nav1.8 positive nociceptor population in cutaneous pain, we found that these neurones are not necessary for acute inflammatory muscle pain. However, our findings support a role of these neurones in the maintenance of the 'primed' state, and therefore indicate that this nociceptor population is crucial for the transition of acute to chronic pain. We also demonstrate findings of novel chemical and genetic expression profiles distinguishing subsets of muscle primary afferents.
Title: Augmented Pain Response To Intra-Articular Injection Of Brain Derived Neurotrophic Factor In Rats With Monosodium Iodoacetate Induced Osteoarthritis.

Poster Number PTH375

Authors
P. Gowler, R. Suzuki, D. Walsh, V. Chapman

Arthritis Research UK Pain Centre, University of Nottingham, Nottingham, United Kingdom, Pfizer Neusentis, Cambridge, United Kingdom

Aim of Investigation
Previous studies have explored the contribution of brain derived neurotrophic factor (BDNF) to chronic pain states (1,2). BDNF, and its receptors trkB and p75<sup>NTR</sup>, are expressed in the synovial fluid of mice with collagen induced rheumatoid arthritis (3). In human osteoarthritis (OA), plasma levels of BDNF are increased compared to controls, and this was found to correlate with reported pain (4). These findings suggest BDNF may have a role in the inflammatory processes associated with osteoarthritis. Previous work by our group has shown that rats with monosodium iodoacetate (MIA) induced OA exhibit increased pain behaviour following intra-articular injection of nerve growth factor (NGF), compared to controls (5). Here we investigated if peripheral BDNF can drive pain behaviour in naïve rats and whether this response was augmented in rats with MIA induced OA.

Results
Intra-articular injection of 10µg BDNF in naïve rats did not alter weight-bearing asymmetry (4.25% ± 0.3) or hindpaw withdrawal thresholds (18.1g ± 1), compared to the saline control (2.25% ± 0.4, 19.2g ± 0.9, respectively). In rats with established MIA induced joint pathology and pain behaviour, intra-articular injection of 10µg BDNF significantly increased weight-bearing asymmetry (30.6% ± 1.9) and decreased hindpaw withdrawal thresholds (7.1g ± 0.4) at 4 days post-BDNF injection, compared to MIA saline treated rats. (10.9% ± 2.5, 14.5g ± 1.1, respectively). Consistent with our previous work, intra-articular injection of 10µg NGF significantly increased weight-bearing asymmetry in MIA treated rats (21.5% ± 0.6), but did not alter hindpaw withdrawal thresholds (11.6g ± 1).

Conclusion
Rats with MIA induced joint pathology exhibited a greater behavioural response to intra-articular injection of BDNF than naïve or saline treated rats. The basis for this up-regulation may be an increased
expression, or coupling of TrkB or p75 NTR, the receptor targets for BDNF, which will be investigated in the future. The ability of an anti-BDNF treatment to modify MIA-induced joint pain will also be the focus of future work.


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Title: Neonatal Cisplatin Treatment Induces Long Lasting Pain Into Adulthood

Poster Number PTH376

Authors
R. Hulse, E. Murphy, J. Lloyd, G. Hathway
School of Medicine, University of Nottingham, Nottingham, United Kingdom, School of Life Sciences, University of Nottingham, Nottingham, United Kingdom

Aim of Investigation
Cisplatin is a cytotoxic agent that is used as an anti-cancer treatment. In adults cisplatin causes significant sensory neuropathy. It is also used extensively as an anti-cancer treatment in children and has been documented that many children suffer from neurological complications, in particular pain.

Results
Cisplatin treatment led to a prominent but delayed mechanical and thermal hyperalgesia, with an onset at P22 when compared to sham controls. Cisplatin led to a significant peripheral sensory neurodegeneration at P16-20, highlighted by a reduction in PGP9.5+ve and CGRP+ve intraepidermal nerve fibre density in the plantar skin versus controls. At P45 there was an increase in PGP9.5+ve and CGRP+ve intraepidermal nerve fibre density in the plantar skin of cisplatin treated animals versus controls. Furthermore, at P45 there was no difference in total DRG sensory neuron (NeuN+ve and PGP9.5+ve) number. The % of IB4+ve, CGRP+ve and NF200+ve DRG neurons was not different between groups at P45, however there was an increase in the % of TrkA+ve DRG sensory neurons in the cisplatin group when compared to controls.

Conclusion
Cisplatin impacts upon the peripheral sensory nervous system leading to exaggerated pain perception later life. This is a significant factor in the decline in the quality of life in childhood cancer survivors.
Title: Characterization Of The Immune Cell Infiltrate And Pain In The Progression Of 4Nqo-Induced Oral Carcinogenesis In Mice

Poster Number PTH377

Authors
N. Scheff, J. MacRae, Z. Conley, B. Schmidt

New York University, New York, NY, NYU Bluestone Center for Clinical Research, New York, NY

Aim of Investigation
Oral cancer patients report severe pain during function. Oral cancer pain is hypothesized to be due to tumor proliferation, perineural invasion, secretion of pro-nociceptive mediators and infiltration of the immune cells into the cancer microenvironment. Of those possible mechanisms, immune cell infiltration into the cancer microenvironment, which is a hallmark of cancer, is the least studied. Cancers attract immune cells into the cancer microenvironment by secreting cytokines and chemokines. Our understanding of the role of immune cells in cancer pain is obstructed because current human xenograft models used to study oral cancer pain fall short in terms of assessing inflammation, as they require immunosuppressed mice. Moreover, the xenograft model does not provide the opportunity to study precancerous stages. To overcome this barrier we have utilized a carcinogen-induced murine model of oral squamous cell carcinoma (SCC) to study changes in the immune cell infiltrate and pain during oral carcinogenesis.

Results
Female and male mice differed in pain behavior and inflammatory infiltrate. Consistent with clinical reporting, females showed significantly greater pain (increase in gnaw time) with tongue SCC compared to males. Furthermore, females with moderate and severe dysplasia demonstrated greater pain behavior than males at these precancerous stages. Female tongue SCC had higher immune cell infiltrate (CD45+ tongue cells) compared to dysplasia. In contrast, immune cell infiltrate peaked in severe dysplasia stage compared to tongue SCC and earlier precancerous stages in males. The changes in immune cell infiltrate for both sexes were comprised of increases in macrophages/mast cells (CD11b+CD11c- tongue cells), granulocytes (CD11b+GR1+ tongue cells) and T cells (CD3+ tongue cells).

Conclusion
Using a carcinogen-induced oral cancer mouse model, we show that oral precancers are painful during
function and that there is a sexual dichotomy, which is also reflected in the immune cell infiltrate. Analysis of the correlation between pain and immune cell infiltrate demonstrates a reverse correlation and suggests potential immune cell infiltrate-induced endogenous analgesia. Pending results will allow us to understand the change in pain and immune cell infiltrate in females and males as precancers progress to cancer.
Title: Does Diabetes Mellitus Cause Altered Sensory Processing In Cats?

Poster Number: PTH378

Authors:
J. Murrell, F. Holmes, A. Hibbert, T. Knowles

University of Bristol, Langford, United Kingdom, University of Bristol, Bristol, United Kingdom

Aim of Investigation
Diabetic peripheral neuropathy (DPN) affects up to 50% of human patients with Type 1 and 2 diabetes mellitus, manifest clinically as painful neuropathic symptoms such as alldynia and insensitivity to sensory stimuli, which increases the risks of peripheral tissue injury. Feline diabetes mellitus (FDM) closely resembles human diabetes in many features and has been proposed as a spontaneous translational model for human diabetes mellitus. Similar to human diabetes, FDM can also be associated with diabetic neuropathy, the functional and histopathological features of which have been described in clinical diabetic feline patients. However, concurrent changes in sensory processing or the presence of neuropathic pain or paraesthesia have not been investigated. If FDM is associated with pain or paraesthesias it represents an important welfare concern and indicates that sensory disturbances should be evaluated as part of the clinical ongoing assessment of feline diabetic patients. The aim of this study was to investigate whether cats with FDM show altered responses to thermal and mechanical stimuli compared to healthy control cats.

Results
When all cats, paws and occasions (test 1 or test 2) were considered in a single model, disease status (diabetic or control) did not significantly affect mechanical threshold or latency to withdraw from the cool stimulus. When data from all cats were combined, there was a significant difference in mechanical thresholds between fore and hind paws (P<0.01) with average median (range) withdrawal threshold for the fore paws being 26.69 (0.057-986) g and average median (range) withdrawal threshold for the hind paws being 70.84 (0.92-986) g. When the presence or absence of diabetic neuropathy was added to the statistical model, there was a difference between fore and hind limbs with an interaction with the presence of neuropathy (P=0.046); diabetic neuropathy in the hind limbs was related to a decrease in the sensitivity of the fore paws to punctate mechanical stimuli. The presence of diabetic neuropathy did not affect withdrawal latency from the cool stimulus and there were no differences in withdrawal latency between fore and hind paws.
**Conclusion**

Diabetic neuropathy decreases the sensitivity of all four paws to mechanical stimuli whereas sensitivity to cool stimuli is unchanged. This should be considered during the ongoing management of cats with FDM.
Title: The Src Family Kinase Inhibitor Dasatinib Delays Pain-Related Behavior And Conserves Bone In A Rat Model Of Cancer-Induced Bone Pain

Poster Number PTH379

Authors
C. Appel, S. Gallego-Pedersen, L. Andersen, S. Falk, M. Ding, A. Heegaard

University of Copenhagen, Copenhagen, DENMARK, University of Southern Denmark, Odense, DENMARK

Aim of Investigation
Cancer-induced bone pain most often arises when cancerous cells metastasize to bone, leading to a severe and unique type of pain known to significantly compromise patients' quality of life. Src family protein tyrosine kinases, and especially the member Src, are implicated in processes involved in cancer-induced bone pain, including cancer growth, bone degradation and nociceptive signaling. Uncoupling Src from the NMDA receptor complex has proven successful in ameliorating inflammatory and neuropathic pain. Here we investigate the role of the Src in cancer-induced bone pain and if inhibition of Src by a multi-targeted tyrosine kinase inhibitor, dasatinib, can decrease tumor burden, bone degradation, spinal sensitization, and thereby reduce pain-related behavior.

Results
Treatment with high dose dasatinib delayed pain-related behavior in cancer-induced bone pain. X-ray images and µCT showed that dasatinib was able to preserve bone mass, which was supported by a significant reduction of TRAP5b in the high dose dasatinib group. There was no difference in bioluminescent tumor signal between groups. Western blot analyses of the spinal cord segments showed no difference between the ipsilateral and contralateral side in Src or pSrc expression; pSrc expression was not increased in the cancer vehicle group compared to the sham vehicle group, but dasatinib decreased the expression of pSrc in a dose-dependent manner.

Conclusion
Daily oral administration of the multi-targeted, non-receptor tyrosine kinase inhibitor, dasatinib, starting from day 7 post inoculation, delayed pain-related behavior. Daily administration of both doses of dasatinib prevented bone degradation and Src phosphorylation, but did not have a significant effect on bioluminescent tumor signal in the rat tibia.
**Title:** Investigation Of Macrophage Targeted Analgesic Nanoparticles In An LPS Mouse Model

**Poster Number** PTH380

**Authors**
T. Komatsu, L. Liu, J. Janjic

Daiichi University of Pharmacy, Fukuoka, Japan, Graduate School of Pharmaceutical Sciences, Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA

**Aim of Investigation**
In this study we investigated the effect of macrophage-targeted nanoparticles with anti-inflammatory properties on inflammatory signaling pathways in cells and inflammation and pain behavior in an LPS mouse model. Our earlier work and the current study tested the hypothesis that nanoparticles are suitable therapeutic and imaging strategies for inflammatory diseases and pain. In previous studies we demonstrated that anti-inflammatory nanoparticles formulated as nanoemulsions carrying Celecoxib (CXB/NE) are internalized by macrophages and show greater accumulation in the inflamed paw injected with Complete Freund's Adjuvant (CFA). (Patel, Beano, Anderson and Janjic, 2015 Clinical Immunology). We also showed that COX-2-inhibiting nanoparticles reduce macrophage infiltration in the CFA-treated mouse paws. Based on these results, we hypothesized that COX-2-inhibiting nanoparticles lead to anti-inflammatory and anti-nociceptive effects in the LPS pro-inflammatory mouse model. In the present study, we examined inflammation-associated cell-signaling pathways in LPS-activated macrophages exposed to escalating doses of COX-2-inhibiting nanoparticles. Further, we investigated the efficacy of nanoparticles in LPS-induced inflammation using near-infrared optical imaging of macrophage infiltration. These imaging studies were run in parallel with pain behavior testing in LPS-treated animals.

**Results**
LPS dose-dependently induced the expression of COX-2 and MCP-1 and the production of PGE2 in macrophage cells. The CXB/NE was internalized by macrophage cells and attenuated LPS-induced release of PGE2 and expression of MCP-1 in macrophage cells. These results suggest that CXB/NE suppresses inflammatory cytokines and chemokines such as MCP-1 induced through PGE2 in LPS-stimulated macrophage cells and may reduce macrophage infiltration. Detailed pharmacological investigations of nanoparticle effects on inflammatory pathways will be investigated in dose-response and temporal kinetic studies. Imaging and pain behavior studies will also be investigated.
Conclusion
CXB/NE is internalized by macrophages and exhibits greater accumulation at the site of inflammation. CXB/NE showed a strong and prolonged antinociceptive effect on inflammatory pain, perhaps by inhibiting production of key pro-inflammatory mediators. We will test the hypothesis that the antinociceptive effects of NE/CXB on LPS-induced hyperalgesia in mice is dependent on anti-inflammatory effects of nanoparticles on infiltrating macrophages at the site of inflammation. The presented work seeks to demonstrate the value of nanomedicine to pain research and lead to development of new inflammatory pain treatments.
Aim of Investigation
Obesity and chronic pain are often co-morbid conditions that affect the lives of millions worldwide. The American diet is typically high in saturated fats, refined sugars and carbohydrates and contributes to a pro-inflammatory state that may underlie other disorders. We have shown that an American diet is not only pro-inflammatory, but prolongs recovery from injury in rodents. Here, we extend those findings with a novel Standard American Diet (SAD) tested in rats.

Results
SAD-fed rats showed significant increases in weight, blood glucose levels and fat mass compared to REG-fed rats. Following chronic inflammatory pain induction, SAD-fed male rats showed prolonged recovery, whereas there was no diet-mediated effect on recovery in female rats. Male SAD-fed rats showed increased pro-inflammatory cytokines typical of microglia (IL-1β, IL-6, TNFα) as a result of diet consumption. On the other hand, female SAD-fed rats showed increases in cytokines and chemokines related to T cell activation (CXCL12, IFN-γ, IL-4, IL-13), suggesting that different cellular system were activated by the SAD in male and female animals. Finally, we expect that the underlying mechanism for the pro-inflammatory state and the prolonged recovery as a result of the SAD was due to SAD-induced microglial activation. To that end, we have found that the SAD caused a significant increase in microglial activation in the dorsal horn, perhaps the basis for the behavioral effects seen. Current experiments are characterizing microglial activation in central brain sites that include the hypothalamus, periaqueductal gray, ventral tegmental area and prefrontal cortex.

Conclusion
Together, these data suggest that the American diet is pro-inflammatory, results in significant immune system activation and that this activation may result in persistent pain following injury. Blockade of the
pro-inflammatory effects of the American diet are likely to improve health outcomes related to recovery from injury/surgery.
Title: Investigating Diffuse Noxious Inhibitory Controls (Dnic) In A Monoiodoacetate (Mia) Rat Model Of Osteoarthritis.

Poster Number PTH382

Authors
S. Lockwood, L. Gonçalves, K. Bannister, A. Dickenson

University College London, London, United Kingdom

Aim of Investigation
The chronic pain associated with the degenerative joint disease osteoarthritis (OA) was often referred to as being generated in the periphery only, with the main focus being on the generation of inflammatory mediators at the location of the injured joint. However the presence of secondary hyperalgesia and referred pain in patients suggests that a central component must contribute to the pain experience. Diffuse noxious inhibitory controls (DNIC) are an endogenous descending inhibitory control pathway whereby a conditioning (noxious) stimulus in one remote body region inhibits pain felt in another discreet body region. I aimed to investigate changes in this endogenous inhibitory system (DNIC) in both early inflammatory phase (days 2-6 post injection) and late chronic phase (14 days post injection) MIA animals.

Results
I show that WDR neuronal responses to conditioning stimulus (noxious ear pinch) were inhibited in early phase MIA animals and control animal groups. However in the late phase MIA animals WDR neuronal responses were no longer inhibited in the presence of the conditioning stimulus. As it is believed that the integrity of DNIC pathways relies on a balance between descending inhibitory and facilitatory pathways, I have successfully used pharmacological manipulation at the level of the spinal cord to restore this balance in late phase MIA animals and thus reinstate the level of inhibition seen with conditioning stimulus to those levels observed in control animal groups.

Conclusion
The results suggest an abnormality in this particular endogenous inhibitory system in late phase MIA animals. This provides further evidence for a central contribution, involving an imbalance in descending facilitatory and inhibitory pathways, to the chronic pain associated with OA.
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**Title:** Chemogenetic Sensitization Of Pain Pathwaysperipheral Nociceptors In Freely Moving Animals

**Poster Number** PTH383

**Authors**

H. Alkhani, A. Ase, P. Séguéla

Montreal Neurological Institute, McGill University, Montréal, Québec, Canada, Alan Edwards Centre for Research on Pain, Montréal, Québec, Canada

**Aim of Investigation**

Pain is an unpleasant acute or chronic sensation experienced following peripheral injury, inflammation or ischemia. Current models used to investigate pain behaviors in rodents are plagued with pitfalls ranging from lack of spatiotemporal specificity to mandatory invasiveness. Our aim was to generate a spatially specific, non-invasive pain model in rodents for the investigation of nociceptive signaling pathways based on designer receptors exclusively activated by designed drugs (DREADDs), in this case the mutated Gq-coupled muscarinic receptor M3 (hM3D) sensitive to the biologically inert ligand clozapine-N-oxide (CNO) and insensitive to its native agonist acetylcholine.

**Results**

We report a novel transgenic mouse model based on metabotropic hM3D (Gq-coupled DREADD)-mediated sensitization of peripheral nociceptive pathways in virally-transduced Nav1.8(+) nociceptors, without administration of any external noxious stimuli or injury. Systemic activation of hM3D induced by intraperitoneal CNO injections evoked strong nocifensive behavior with reduced locomotion, squinting of the eyes and ruffled fur. Intradermal paw injections of CNO resulted in robust acute thermal hyperalgesia and mechanical allodynia as measured in Hargreaves and Von Frey tests. Moreover, CNO induced edema and redness in the injected paws, indicating the activation of neurogenic inflammatory mechanisms similarly observed in sensitization protocols with local capsaicin injection. The observed nocifensive behaviors appear to be specifically due to the contribution of small and medium diameter Nav1.8(+) DRG neurons, as indicated by our histology data, with central projections limited to lamina I and II of the dorsal horn of spinal cord. The selective TRPV1 antagonist AMG9810 strongly reduced CNO-induced hyperalgesia in our mouse model, indicating a critical role of calcium-permeable TRPV1 channels in both thermal and mechanical sensitization.
Conclusion
These findings demonstrate for the first time the chemogenetic control of peripheral sensitization in behaving mammals, enabling selective metabotropic activation of peripheral afferents in vivo. Our results provide a proof-of-concept demonstration that chemogenetic interrogation of the contribution of specific classes of genetically-identified primary afferents to peripheral sensitization is possible. Non-invasive chemogenetic rodent pain models combining effective spatial penetrance with neuronal specificity, complementary to optogenetic models, have the potential to facilitate drug development and target validation for migraine or chronic pain relief.
Title: Establishment Of An Optimised Rat Model Of Stavudine-Induced Antiretroviral Toxic Polyneuropathy (AtN)

Poster Number PTH384

Authors
A. Kuo, M. Smith

Centre for Integrated Preclinical Drug Development, The University of Queensland, Brisbane, QLD, Australia, School of Pharmacy, The University of Queensland, Brisbane, Australia

Aim of Investigation
Stavudine is an anti-retroviral drug listed on the World Health Organisation's List of Essential Medicines (19th Ed). Stavudine is widely used to prevent and treat HIV/AIDS in resource-limited clinical settings. Usage of stavudine (d4T) is often associated with development of ATN, necessitating a reduction in the d4T dose with the associated risks and/or administration of a 2nd drug to treat the ATN-associated neuropathic pain. The aim of this study was to establish an optimised rat model of d4T-induced ATN in the Wistar Hannover (WH) rat as a means to gain insight into the pathobiology of this distressing neuropathic pain condition.

Results
For groups of rats administered 2 x IV injections of d4T at 25 mg/kg, 2, 3, 4 and 5 x IV injections of d4T at 50 mg/kg (n=6 per dosing regimen), or 2, 3, 4 and 5 x IV injections of saline (n=3 per treatment regimen), body weights did not differ significantly (p>0.05) between the treatment groups. Similarly, adverse effects were not observed in any treatment group. Mechanical allodynia did not fully develop in the hindpaws of rats given 2 x IV doses of d4T at 25 mg/kg. However, for rats administered 2 x IV doses of d4T at 50 mg/kg, mechanical allodynia was fully developed in the bilateral hindpaws on day 7 of the d4T treatment regime. The optimal dosing regimen was found to be five doses of d4T (50 mg/kg) with mechanical allodynia fully developed in the bilateral hindpaws from day 17 until at least day 38. Thermal hyperalgesia developed in the bilateral hindpaws of rats administered either four or five doses of d4T at 50 mg/kg, and it remained stable from days 11 to 25 and days 10 to 42 respectively.

Conclusion
We have established an optimised d4T induced WH rat model of ATN involving administration of 5 x IV
doses of d4T at 50 mg/kg at twice-weekly intervals. Our model has considerable potential for investigation of the pathobiology of this condition.
Title: Pacap/Vip System Dysregulation In The Hypothalamus Of Nerve Injured Rats

Poster Number PTH385

Authors
A. Castorina, M. Vogiatzis, J. Kang, K. Keay

The University of Sydney, Sydney, NSW

Aim of Investigation
Neuropathic pain (NP) is a multi-factorial disorder affecting both physical and psychological/emotional states. In a rat model of NP, potentially maladaptive psychosocial behaviours are evoked by sciatic nerve chronic constriction injury (CCI) in a subset (~30%) of animals. In these rats, social behaviours are disrupted, the sleep-wake cycle is disturbed and hypothalamic regulation of both adrenal cortical and thyroid activity is altered. Pituitary adenylate cyclase activating polypeptide (PACAP) and vasoactive intestinal peptide (VIP) are two homologous neuropeptides whose neurobiological activities in the hypothalamus include circadian rhythm regulation. VIP-expressing neurons in this brain area receive photonic input from the retino-hypothalamic tract. In addition, VIP/VPAC2 knockout and VPAC2 overexpressing mice each display disrupted sleep-wake cycles, suggesting that a tight regulation of the VIP/VPAC2 axis might play a key role in the functionality of circadian rhythmicity. We hypothesised therefore that changes in PACAP/VIP relations in the hypothalamus might contribute to maladaptive behavioural changes shown by the subgroup of rats with sciatic nerve CCI, whose psychosocial disturbances are remarkably similar to human NP patients. This study aimed to investigate the expression profiles of PACAP/VIP and related receptors in the hypothalamus of sciatic nerve CCI rats.

Results
PACAP mRNA levels were down regulated bilaterally in both sham-operated controls and CCI rats by similar extents (p<0.05), and VIP transcript levels were increased bilaterally in CCI rats (p<0.001). At the receptor level, PAC1 levels were unaffected by CCI, whereas VPAC1 mRNAs were reduced bilaterally in sham-operated controls when compared to CCI rats (p<0.05). We also revealed a bilateral up-regulation in hypothalamic VPAC2 mRNA in CCI rats (p<0.01). Our gene expression findings are supported by Western blot data, demonstrating that both VIP and VPAC2 proteins were bilaterally up-regulated in the hypothalamus of CCI rats.
Conclusion
The present data shows that the endogenous hypothalamic PACAP/VIP system undergoes perturbation following sciatic nerve CCI. The VIP/VPAC2 axis is specifically enhanced by the experimental nerve injury. In contrast, PACAP and VPAC1 receptor expression demonstrates sensitivity to additional features of the experimental methodology. Sleep disturbances have been reported following over-expression of VIP and its binding receptor VPAC2. Therefore our evidence may support a role for enhanced hypothalamic VIP/VPAC2 in the sleep disturbances associated with NP. That both people and animals with NP show significantly interrupted sleep highlights the potential clinical importance of this finding. We Acknowledgement Funding from the NGW Macintosh Memorial Fund.
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**Title:** Peripheral And Central Neuroimmune Changes Associated With Pain Behaviours In An Animal Model Of Multiple Sclerosis

**Poster Number** PTH386

**Authors**

University of New South Wales, Sydney, NSW, University of New South Wales, Sydney, New South Wales, University of New South Wales, Sydney, -- SELECT --

**Aim of Investigation**
Pain is a widespread and debilitating symptom of multiple sclerosis (MS), a chronic inflammatory demyelinating disease of the central nervous system. Although central neuroinflammation and demyelination have been implicated in MS-related pain, the contribution of peripheral and central mechanisms during different phases of the disease remains unclear. In this study, we used the animal model experimental autoimmune encephalomyelitis (EAE) to examine both stimulus-evoked and spontaneous pain behaviours over the course of chronic disease, and assessed potential underlying pathological mechanisms.

**Results**
We found that mechanical allodynia of the hind paw preceded the onset of clinical EAE, but was unmeasurable at clinical peak. This mechanical hypersensitivity coincided with an increased microglial activation confined to the dorsal horn of the spinal cord. The development of facial mechanical allodynia also emerged in pre-clinical EAE, persisted at the clinical peak, and corresponded with pathology of the peripheral trigeminal afferent pathway. This included T cell infiltration and specific damage to myelinated neurons, both of which arose prior to overt central lesion formation. Measurement of spontaneous pain using the mouse grimace scale showed significantly increased facial grimacing in mice with EAE during clinical disease. This was associated with multiple peripheral and central neuroimmune changes including a decrease in myelinating oligodendrocytes, increased T cell infiltration and macrophage/microglia and astrocyte activation.

**Conclusion**
Overall, these findings suggest that different pathological mechanisms underlie stimulus-evoked and spontaneous pain in EAE, and that these behaviours predominate in unique stages of the disease.
Title: Transplant-Mediated Enhancement Of Inhibitory Controls In The Rostral Anterior Cingulate Cortex Ameliorates Ongoing Pain Provoked By Nerve Injury.

Poster Number PTH387

Authors
D. JUAREZ-SALINAS, J. Braz, A. Basbaum

University of California, San Francisco, san francisco, CA, University of California San Francisco, San Francisco, CA, Univ of California - San Francisco, San Francisco, CA

Aim of Investigation
The rostral anterior cingulate cortex (rACC) is a major contributor to the affective, but not the sensory discriminative component of chronic pain in both rodents and humans. After ablation of the rACC, patients with chronic pain no longer perceive painful stimuli as bothersome and ongoing pain is reduced. It follows that prolonged inhibition of the rACC should also be therapeutic. Unfortunately, not only are lesions very invasive, they are rarely restricted as fibers passing through this region are also destroyed. Here, we developed a novel approach to enhance inhibition of the rACC in a targeted and long-lasting manner.

Results
Control animals that received medium, but no cells, in the rACC had a large preference for the gabapentin-paired side of the box, indicating that they still experienced ongoing pain. In contrast, mice transplanted with MGE cells in the rACC (30 days post-transplant) did not have a preference for the analgesic, indicating that they no longer experienced ongoing pain. Importantly, MGE transplantation in the rACC did not reduce paclitaxel-induced mechanical hypersensitivity. Thus, the transplants had no effect on the sensory discriminative features that characterize the paclitaxel model. Interestingly, mice in which MGE cells were detected in both the rostral and posterior ACC (pACC) had a preference for the analgesic side of the box, suggesting that inhibition of the pACC is pro-nociceptive and can block the behavioral effects of MGE transplantation in the rACC.

Conclusion
Based on previous studies, it is likely that the transplanted neurons induce a relatively non-selective inhibition of rACC neurons. We conclude, therefore, that transplant-mediated prolonged inhibition of the rACC MGE, as for surgical ablation, can successfully relieve ongoing pain in this chemotherapy
model. This preclinical study supports the idea that selective and long lasting inhibition of the rACC is a viable non-ablative therapeutic strategy for the treatment of chronic pain.
Title: Nerve Injury Produces Differing Phenotypes Of Exploratory Behaviour In Rats

Poster Number PTH388

Authors
N. Fiore, P. Austin

University of Sydney, Sydney, NSW

Aim of Investigation
Chronic constriction injury (CCI) evokes sensory 'pain' (allodynia) in all rats, and evokes disturbances in complex behaviours in a sub-population. Furthermore, spared nerve injury impairs short-term spatial memory when learning the radial maze task. Here we examined whether pre-established spatial memory and exploratory behaviour on the radial maze task were altered after CCI.

Results
Sham injury had no effect on exploratory behaviour, rota-rod performance or short-term memory. Following CCI, exploratory behaviour, rota-rod performance and short-term memory were all unaltered in one subgroup of rats (n=10), termed 'Unaffected exploration'. Another subgroup of rats (n=6) displayed impairments in their exploratory behaviour post-injury, showing both a 2-fold increase in their time in the central atrium per entry and a 30% decrease in their activity within the central atrium on at least 7 days post-CCI. This subgroup of rats is termed 'Impaired exploration' as these changes indicate a withdrawal from pellet seeking. In a third subgroup (n=6), rats displayed similar changes to Impaired exploration rats on at least 3 of the first 5 days post-CCI, but not thereafter. This subgroup of rats also displayed a decrease in working memory errors compared to both their pre-injury baseline (p<0.05) and Unaffected exploration rats post-injury (p<0.05). This subgroup of rats is termed 'Strategic exploration' as these changes in exploratory behaviour lead to improved short-term memory following nerve injury. Impaired exploration and strategic exploration rats both showed a decrease in rota-rod performance on the initial two post-CCI trials (p<0.001), and all subgroups displayed equivalent mechanical allodynia across the post-CCI von Frey tests.

Conclusion
These data highlight that nerve injury drives neural adaptations that characterise three differing phenotypes of exploratory behaviour and short-term memory performance on the radial maze task. Furthermore, testing only for allodynia or motor activity is not sufficient to detect these individual
differences in pellet-seeking strategies, which fits with clinical studies that show sensory 'pain' resulting from surgical nerve damage does not predict the development of behavioural disturbances. Therefore, these nerve-injury driven phenotypes of exploratory behaviour provide a novel paradigm to investigate the neural adaptions responsible.
Title: Pharmacologic Characterization Of Pain Medications In Spared Nerve Injury Model Of Neuropathic Pain In Rats

Poster Number: PTH389

Authors: J. Li, R. Lopez, D. Cho, S. Wang

HARBOR-UCLA MEDICAL CENTER, TORRANCE, CA

Aim of Investigation
Neuropathic pain is characterized by sensory abnormalities such as hyperalgesia, or allodynia. Peripheral neuropathic pain is frequently observed in patients with diabetes, herpes infection, and so on. The pharmacotherapy for neuropathic pain has had a limited success. Evaluation of neuropathic pain in humans is very difficult. Therefore, there is a need of easily reproducible animal models to broaden the knowledge of neuropathic pain. Recently, a spared Nerve injury animal model of neuropathic pain was developed to study its pathophysiology. In this model, the mechanical allodynia is persistent, and mimics many features of clinical neuropathic pain. This study used sciatic spared nerve injury neuropathic pain animal model to investigate the pharmacologic characterization of pain medications.

Results
The threshold for mechanical stimulus in the ipsilateral hind paw of sural region significantly reduced within 2 days of post injury, and persisted for up to 2 months in rats. Gabapentin (160 mg/kg, i.p.) significantly alleviated mechanical allodynia for at least 3h, while no significant effects were observed for ketorolac (30mg/kg, i.p.); Injection of morphine (10 mg/kg, i.p.) significantly attenuated mechanical hypersensitivity in response to von Frey filaments for over 5 hours. Ketamine (10mg/kg, i.p.) also markedly increased the threshold, however it only lasted less than 2 hours.

Conclusion
Our study has shown the spared Nerve injury animal model has an increased responsiveness to nonnoxious stimuli in the ipsilateral sural region. Each type of pain medication exhibits its own analgesic profile on mechanical allodynia in rats, may suggest their different roles in neuropathic pain management.
Aim of Investigation
The high incidence of osteoarthritis (OA) in the elderly population together with the increasing age of the general population means that a growing number of individuals will suffer from OA pain in the decades to come. This situation emphasizes the need to optimise preclinical models of OA for investigation of the pathobiology of this condition and to assess the disease-modifying effects of potential novel therapeutics. Hence, our aim was to establish and pharmacologically characterise an optimised rat model of monoiodoacetate (MIA)-induced OA as means for assessment of the analgesic efficacy of new molecules from drug discovery in order to identify those with potential as novel and well-tolerated analgesics for relief of OA pain.

Results
There was rapid development of altered gait that was sustained throughout the experimental period following intra-articular injection of MIA in rats. By contrast, for rats administered intra-articular saline, gait parameters remained unaltered for the 28-day study period. However, there were no significant differences (p>0.05) between the 3 MIA-groups. Mechanical allodynia was fully developed in the ipsilateral hindpaws from day 12 to day 28 post-MIA injection. In rats with PWTs ≤6g in the ipsilateral hindpaws, single bolus doses of gabapentin and morphine produced dose-dependent relief of mechanical allodynia whereas meloxicam and amitriptyline lacked efficacy in the doses tested. Each of the doses of intra-articular MIA assessed induced a significant difference (p<0.05) in weight bearing between the ipsilateral and contralateral hindlimbs.

Conclusion
We have established and pharmacologically characterized an MIA-induced rat model of OA. Intra-articular injection of MIA at 2, 2.5 or 3 mg (but not saline) induced sustained mechanical alldynia and
altered gait parameters for at least 28-days. MIA-induced changes in pain behavioural endpoints were biphasic, with the initial phase lasting approximately 8 days and the chronic phase beginning at day 12-14 and persisting for ≥35 days. The MIA-rat model of OA-induced pain is suitable for investigation of the pathobiology of OA and for identification of new molecules with potential to alleviate this condition.
Title: Relationship Between Pain-Related Behavior And Bdnf Expression In A Rat Nucleus Pulposus Applied Model

Poster Number PTH391

Authors
S. Seki, M. Sekiguchi, S. Konno

Fukushima Medical University School of Medicine, Fukushima, Japan, Dept. of Orthopaedic Surgery, School of Medicine, Fukushima Medical Univ., Fukushima, Japan, Department of Orthopedic Surgery, Fukushima Medical University School of Medicine, Fukushima, Japan

Aim of Investigation
Lumbar disc herniation causes neuropathic pain. It has emerged that brain-derived neurotrophic factor (BDNF) may play an important neuromodulatory role in the dorsal horn of the spinal cord. And current findings suggest that the activation of p38 mitogen-activated protein kinases (p38 MAPK) contributes to inflammatory and neuropathic pain by regulating BDNF expression. However, contribution to pain-related behavior between BDNF and p38 has been unclear. The aim of this study was assessed a relationship between pain-related behavior, BDNF, and p38 expression induced by nucleus pulposus (NP) applied to nerve roots in rats.

Results
The mechanical withdrawal threshold in the NP group was significantly decreased for 35 days compared with that in the sham group (p<0.05). Both p-p38 and BDNF positive cells were localized with microglia and neurons in the dorsal horn of spinal cord. In the NP group, the expression of p-p38-IR and BDNF-IR cells increased from day 2 to 21 compared with the sham group (p<0.05).

Conclusion
The rat nucleus pulposus applied model using this study has known to induce inflammation and neural damage in dorsal root ganglion. According to the results of this study, from 2days after surgery reduction of the mechanical threshold was observed, and BDNF and p38 were expressed in both activated microglia and neurons in dorsal horn. Therefore, BDNF might be a target for the development of novel analgesics to treat for neuropathic pain.
Title: Dissociating Analgesic And Sedative Actions Of Anaesthetic Drugs With Magnetoencephalography (Meg); Initial Results

Poster Number PTH392

Authors
N. Saxena, A. Forsyth, A. Babic, S. Dasari, L. Richmond, S. Worthen, J. Hall, S. Muthukumaraswamy

Cardiff University, Cardiff, United Kingdom, University of Auckland, Auckland, New Zealand, Wellcome Trust Laboratory for MEG Studies., Birmingham, United Kingdom

Aim of Investigation
Most analgesic drugs have sedative side effect while most anaesthetic drugs have some analgesic activity. The mechanism of action of anaesthetic-induced analgesia is poorly understood, and being able to dissociate the mechanisms of sedation and analgesia would greatly aid in the development of "cleaner" analgesic compounds. Previous literature shows that pain decreases alpha (α; 8-12 hz) and beta (β; 12-20Hz) activity in the somatosensory cortices which corresponds with increases in fMRI BOLD activity. Dexmedetomidine (an α-2 adrenergic agonist sedative) produces spatially broad increases in α and low β with suppression of upper beta and higher frequencies. Propofol (GABAergic sedative) produces spatially broad increases in beta band activity and increases in α at high doses with suppression in α at low doses. Aim: To assess whether MEG can reliably demonstrate the properties of the analgesic effect of common anaesthetics.

Results
It was found that both propofol and dexmedetomidine administration resulted in a significant lessening of the decrease in low alpha (8-10 Hz) and beta (13-30Hz) oscillatory activity seen during pain, in occipital, temporal, and parietal areas, as compared to placebo. There were no significant differences found between the two drugs.

Conclusion
To our knowledge this is the first study exploring neurophysiology of pain in sedated humans using MEG. This study shows the potential of MEG in providing an objective marker of analgesic effects and holds promise for evaluation of pain models and analgesic drug development.
**Title:** Electrophysiological Property Of Spinally Projecting Serotonergic Neurons In The Rostral Ventromedial Medulla In Bac Transgenic Mice.

**Poster Number** PTH393

**Authors**
T. Fukushima, Y. Hori

Department of Physiology and Biological Information, Dokkyo Medical University, Mibu, Toshigi, N/A, Tochigi, JAPAN

**Aim of Investigation**
Serotonergic neurons in the rostral ventromedial medulla (RVM) in the brain stem play an important role in the modulation of nociceptive information. The aim of this study is to characterize spinally projecting serotonergic neurons in the RVM.

**Results**
Substitution of the internal K⁺ with Cs⁺ inhibited the K⁺ currents and evoked a increase in a plateau component of an action potential. A depolarizing voltage pulse also induced an action current with a plateau component. The plateau component was obviously reduced in the external solution without Ca²⁺ or was blocked with external Cd²⁺, indicating that the component was dependent on Ca²⁺ entry. By contrast, in Dil labeled neurons without GFP fluorescence, the substitution of the internal K⁺ with Cs⁺ did not induce the plateau component.

**Conclusion**
These results suggest that functional expression of voltage-sensitive Ca²⁺ channels in serotonergic neurons may be different from that in neurons of other phenotypes. To identify which type of Ca²⁺ channels are involved in the plateau components, we are currently investigating effects of several types of Ca²⁺ channel selective antagonists on the action potentials recorded from the serotonergic neurons in the RVM. This work was supported by JSPS KAKENHI Grant Number 23790648.
Title: Cognitive Modulation Of Protective Reflexes – Hard Wired Or Learnt Early? Preliminary Investigation Of The Hand-Blink Reflex In Blind People.

Poster Number PTH394

Authors
S. Wallwork, G. Iannetti, R. Bufacchi, L. Moseley

University of South Australia, Adelaide, Australia, University College London, London, UNITED KINGDOM

Aim of Investigation
Pain is perhaps the most sophisticated protective response – it is modulated by innumerable factors and compels us to behave in a way that protects our body. The hand-blink reflex (HBR) has long been thought of as one of the least sophisticated protective responses – a non-noxious stimulus to the median nerve at the wrist causes an eye blink. The HBR provides a potentially powerful experimental paradigm for investigating fundamental processes involved with the modulation of perceived threat. In sighted people, when the stimulated hand is close to the face the HBR is augmented. Modulation of the HBR is finely adjusted seemingly according to the implicitly evaluated risk of damage to the eye. Is the HBR and its modulation hard-wired or learnt? We investigated (1) whether people who are totally blind have an intact HBR and (2) whether modulation of the HBR is present in people with total blindness.

Results
Five of the blind participants demonstrated an intact HBR. Of those, four had 'late-onset blindness' (acquired after 3 years of age) and one had 'early-onset blindness' (acquired before 3 years of age). The four with 'late-onset blindness' had a HBR that was facilitated when the stimulated hand was close to the face, similar to what was observed in the sighted participants. The participant with 'early-onset blindness' had a HBR that was not affected by the position of the stimulated hand in relation to the face.

Conclusion
The HBR is present in some people with blindness. Our results suggest that modulation of the HBR is established early in life and does not extinguish despite years of total blindness.
Title: How Attention Modulates Pain Habituation

Poster Number PTH395

Authors
Y. Lin, T. Wu, S. Yang, Z. Lu, C. Huang, Y. Shih, M. Tseng

Graduate Institute of Brain and Mind Sciences, National Taiwan University College of Medicine, Taipei, Taiwan, Department of Computer Science and Information Engineering, National Taiwan University, Taipei, Taiwan

Aim of Investigation
The cognitive modulation of pain substantially affects pain experience in humans. Decreased sensitivity to repetitive painful stimulation, i.e., pain habituation, is a natural phenomenon in acute pain, which not only provides immediate pain relief in healthy subjects but possible contributes to pathological pain conditions when the extent of habituation is reduced. Evidence suggests a modulatory effect of attention on pain habituation. However, few studies so far have explored the effect of interaction of two cognitive factors on the experience of pain. The current study investigates whether distraction affects pain habituation.

Results
The reaction time of Stroop tasks between the early and the late series of Stroop tasks was comparable, indicating no practice effects. Intriguingly, compared with the neutral group, incongruent group demonstrated a significantly larger extent of pain habituation.

Conclusion
The most important finding in the current study is that we successfully display the impact of attention on the habituation to pain. Results obtained from this study provide an example of how different cognitive factors (habituation and attention) interact to modulate human experiences of pain.
Title: Effect Of Morphine Microinjection Into The Insular Cortex On Mechanical Allodynia And Thermal Place Preference/Avoidance Following Tibial Nerve Transection In Rats

Poster Number PTH396

Authors
R. Hazrati, S. Farajinejad, G. Vafaei Saiah, E. Khalilzadeh

University of Tabriz, Tabriz, Iran, University of Tabriz, Tabriz, -- Iran --, University of Tabriz, Tabriz, -- Iran--

Aim of Investigation
The insular cortex is often bilaterally activated following inflammation, acute and chronic pain, neuropathic pain and noxious somatosensory stimulation which has been suggested that insular cortex play an important role in pain processing. In the present study, we investigated the effect µ opioid receptor activation in the insular cortex on mechanical allodynia and thermal place preference/avoidance following tibial nerve transection (TNT) in rats.

Results
Sham animals did not show any cold allodynia and mechanical hypersensitivity in comparison with naïve animals. In the saline treated group, tibial nerve transection significantly increased mechanical sensitivity. Microinjection of morphine at doses of 2, 4 and 8 µg/0.5 µl significantly increased mechanical threshold. Administration of naltrexone (5 µg/0.5 µl/site) alone had no effect on mechanical threshold, but pretreatment of animals with naltrexone inhibited the anti-allodynic effect of morphine (8 µg/0.5 µl/site) in the Von Frey test in comparison with the morphine 8 µg group. In the double plate test tibial nerve transection significantly decreased animal activity, time spent in cold plate and increased escape index from the cold plate (E.I) in comparison with intact animals. Microinjection of morphine (2, 4 and 8 µg/site) into the insular cortex significantly prevented from cold aversion, increased animal activity and decreased E.I, 28 days after TNT surgery, also pretreatment of animals with naltrexone reversed morphine effects in thermal place preference/aversion test.

Conclusion
Microinjection of morphine into the insular cortex improved mechanical hypersensitivity as well as cold aversion behaviors in this model of neuropathic pain. Antinociceptive effects of morphine were blocked by the opioid antagonist naltrexone in this study.
Title: Acc-Dpag Projection Neurons Modulate Pain Behaviors In Mice

Poster Number PTH397

Authors
J. Dickinson, G. Corder, C. Sotoudeh, G. Scherrer

Stanford University, Menlo Park, CA, Stanford University, Palo Alto, CA

Aim of Investigation
Pain is a both a sensory and emotional experience in which noxious stimuli trigger intense aversion. The unpleasantness of pain usefully motivates one to escape from threats, but this aversion can exist in the absence of real threats or when escape is impossible. Given the substantial ability of aversive emotions to enhance pain sensitivity and increase the risk of comorbid disorders such as depression and anxiety, a potentially useful strategy to treat pain is to bypass sensory blockade and instead target the aversion pain evokes. However, we currently lack comprehensive understanding of what specific circuits are engaged during pain aversion and how changing the neural activity in these circuits impacts pain perception. Multiple human and rodent studies have shown a tight link between activity in the Anterior Cingulate Cortex (ACC), a high-order, non-sensory neocortical structure, and pain aversion. Human imaging studies show increased ACC activity in response to painful stimuli, and positive correlations between ACC excitation and aversion intensity. In rodents, ACC lesions reduce pain aversion and in some cases reduce sensation, while increased ACC excitation both generates aversion and increases nociceptive sensitivity. Of its many projections, the ACC connects with the Periaqueductal Gray (PAG), a midbrain structure with functions linked to both expression of aversive behaviors and descending control of nociception at the level of the spinal cord. We aim to test the hypothesis that the ACC-PAG projection neurons encode an aversive signal that also modulates pain sensation.

Results
Our results suggest that this subpopulation of ACC neurons have the ability to alter 1) the animal's sensitivity threshold to detect noxious mechanical and heat stimuli, 2) the amount of time the animal spends in the noxious side of a thermal place-preference test, and 3) the duration of nocifensive behaviors in response to the stimuli. Gross motor behaviors during this circuit manipulation, such as distance and velocity traveled, remain normal.
Conclusion
We have identified a subpopulation of ACC neurons that modulate multiple dimensions of pain behavior. The identification of a specific ACC circuit could guide the development of more selective therapies that target pain pathology while leaving other sensory, emotional, and cognitive facilities intact.
**Title:** Neuronal Hyperexcitability In The Ventrobasal Thalamic Complex Of Neuropathic Rats Is Partially Reversed By Pregabalin

**Poster Number** PTH398

**Authors**
R. Patel, A. Dickenson

University College London, London, United Kingdom

**Aim of Investigation**
Neuropathic pain represents a substantial clinical challenge, and understanding the underlying neural mechanisms and back-translation of therapeutics could aid targeting of treatments more effectively. The ventrobasal complex is the major termination site for the spinothalamic tract and relays nociceptive activity to the somatosensory cortex, however under neuropathic conditions, it is unclear how hyperexcitability of spinal neurones converges onto thalamic relays. This study aims to identify neural substrates of hypersensitivity, and the influence of pregabalin on central processing.

**Results**
In neuropathic rats, WDR neurones have elevated evoked responses to low and high intensity punctate mechanical stimuli, dynamic brushing, innocuous and noxious cooling, but less so to heat stimulation of the receptive field. NS neurones in SNL rats also display increased responses to noxious punctate mechanical stimulation, dynamic brushing, noxious cooling and noxious heat. In addition, WDR, but not NS, neurones in SNL rats exhibit substantially higher rates of spontaneous firing, which may correlate with ongoing pain. The ratio of WDR:NS neurones is comparable between SNL and naïve/sham groups suggesting relatively few NS neurones gain sensitivity to low intensity stimuli leading to a 'WDR phenotype'. After neuropathy, the proportion of cold sensitive WDR and NS neurones increases, supporting that changes in frequency dependent firing and population coding underlie cold hypersensitivity. In SNL rats, pregabalin reduced evoked neuronal responses but not elevated spontaneous activity.

**Conclusion**
These data provide evidence of phenotypic changes in neuronal sensitivity that may in part underlie cold and brush hypersensitivity and that WDR neurones, and not NS, encode hypersensitivity to low intensity stimuli. In addition, pregabalin normalises neuronal hyperexcitability to mechanical and heat stimuli in
neuropathic rats whilst having no effect on elevated spontaneous activity or normal neuronal coding. These findings correlate with clinical observations that gabapentinoids have a high 'number needed to treat' when ongoing pain is used as a primary endpoint, but is efficacious in neuropathic conditions where mechanical hypersensitivity is prominent.
Title: Neural Ensemble Coding Of Nociceptive Information In The Amygdala Drives Pain Affect

Poster Number PTH399

Authors
G. Corder, B. Ahanonu, B. Grewe, M. Schnitzer, G. Scherrer
Stanford University, Palo Alto, CA

Aim of Investigation
Pain is a cohesive multidimensional experience comprising sensory and emotional modules, but it remains unclear how nociceptive sensory signals are imbued with negative affect. The basolateral amygdala (BLA) is necessary for emotional learning, and links sensory-driven neural inputs (e.g. nociception) to output brain regions controlling perception (e.g. aversion) and behavior-selection (e.g. avoidance). Prior work has uncovered molecular, synaptic and cellular substrates of nociceptive processing in the BLA, but high-dimensional neural ensemble mechanisms underlying the generation of pain affect remain unexplored. Furthermore, chronic pain states can be viewed as a neurological disease in which injury-induced neuroplasticity leads to miscoding of sensory information (e.g. spontaneous pain and allodynia). Such chronic sensory dysfunctions are associated with persistent negative affect, which often results in comorbid disorders such as anxiety and depression. Thus, we aim to uncover the crucial BLA ensemble underpinnings facilitating the misrepresentation of sensory stimuli and the generation of the negative affective component of chronic neuropathic pain.

Results
In normal mice, prior to nerve injury, neuronal ensemble responses, time-locked to natural and optogenetic-evoked pain behaviors, revealed small (5-8% of all imaged neurons) and unique (>10% overlap between modality-specific representations) patterns of activity for thermal and mechanical, and innocuous and noxious stimuli. Strikingly, after the establishment of neuropathic pain the ensemble responses evoked by prior innocuous stimuli transformed such that the network representation was more similar to activity patterns evoked by frankly noxious stimuli. Chemogenetic silencing of the BLA pain ensemble in mice with neuropathic pain did not alter reflexive responses to noxious stimuli. By contrast, time spent attending to the injured paw following noxious stimulation, as well as motivated escape away from the noxious stimulus, were dramatically reduced.
Conclusion
We have identified unique neural ensemble representations of noxious information in the BLA that facilitate the innate, negative affective qualities of the pain experience, and drive appropriate motivated behaviors such as escape and attending to the injury. Additionally, our findings establish how BLA neural activity evolves under chronic pain states to assign negative valence to previously innocuous stimuli, possibly contributing to pathological sensory dysfunctions like allodynia, and psychological comorbidities like depression. Together, our long-term goal it to more fully uncover how neural coding in the amygdala shapes our perception of pain.
Date: 09/29/2016 09:30:00 AM

Title: Effects Of Histamine H1 And H2 Receptor Antagonists Microinjection Into The Insular Cortex On Thermal Place Preference/Avoidance Following Tibial Nerve Transection In The Rats

Poster Number PTH400

Authors
F. Azarpey, R. Hazrati, E. Khalilzadeh

University of Tabriz, East Azarbayjan / Tabriz, - Please Select -, University of Tabriz, Tabriz, Iran, University of Tabriz, Tabriz, -- SELECT --

Aim of Investigation
Tibial nerve transection (TNT) induces disabling severe neuropathic pain in the form of allodynia (a painful response to normally non-noxious stimuli). In the present study, we have evaluated the effect of pharmacological inhibition of histamine H1 and H2 receptors in the insular cortex on non-noxious cold aversion and thermal place preference behaviors in the neuropathic rats using the modified double plate technique.

Results
Tibial nerve transection significantly (P <0.05) reduced distance traveled and time spent on cold plate (as the result of cold allodynia) and increased E.I in comparison with sham and normal animals. Intra-insular microinjection of all doses of chlorpheniramine (2.5, 5 and 10 µg/site) significantly increased time spent on cold plate and decreased E.I in comparison with the TNT group. Microinjection of ranitidine at doses of 2.5 and 5 µg/site did not produce significant effects, but at a dose of 10 µg/site significantly increased time spent on cold plate and decreased E.I in comparison with the TNT group that received normal saline. Both chlorpheniramine and ranitidine did not alter locomotor activity of animals in comparison with the neuropathic animal that received normal saline.

Conclusion
Pharmacological inhibition of insular cortex histamine H1 and H2 receptors significantly reduced cold allodynia and cold aversion behaviors in the double plate test and also have no significant effect on locomotor activity of neuropathic rats.
**Title:** Pre-Injury Periaqueductal Grey Functional Connectivity Is Implicated In Pain Vulnerability Of Healthy Individuals

**Poster Number** PTH401

**Authors**
M. Mezue, V. Wanigasekera, Y. Kong, I. Tracey

University of Oxford, Oxford, United Kingdom, FMRIB Centre, University of Oxford, Oxford, United Kingdom

**Aim of Investigation**
A critical role for the periaqueductal grey (PAG) in facilitatory/inhibitory descending pain modulation has been suggested both in animal models and human studies. Previous neuroimaging studies have underlined the importance of PAG connectivity with the brainstem and forebrain in the perception of phasic pain stimuli. More recent work has enabled better understanding of structural and functional models of connectivity between different segments of the PAG and the rest of the human brain. We have previously presented work that highlights a relationship between metabolic activity in the PAG (measured using arterial spin labelling (ASL) and magnetic resonance spectroscopy), and human vulnerability to persistent experimental pain. Following from this, we here assess the role of pre-injury functional connectivity of the PAG to cortical and subcortical structures on the perception of persistent pain and other correlates of central sensitisation.

**Results**
Following capsaicin application, subjects developed (mean±SD) punctate unpleasantness hyperalgesia of 27.9 ±16.9 and ongoing pain of 13.7 ±18.6. Baseline PAG connectivity with brain regions including the posterior and mid insula, secondary somatosensory cortex (SII) and dorsolateral prefrontal cortex (DLPFC) was negatively correlated with subsequently developed punctate hyperalgesia scores (whole-brain cluster corrected: Z>2.3, p<0.05). There was also a negative correlation between baseline PAG CBF values and PAG connectivity with the mid and posterior insula, SII, mid anterior cingulate cortex and the DLPFC (whole-brain cluster corrected: Z>2.3, p<0.05).

**Conclusion**
Our previous work suggests a positive relationship between pre-injury PAG activity, as measured by CBF, and persistent pain. Here we show that such a relationship may be explained by pre-existing functional
connectivity profiles between the PAG and cortical areas important in pain perception. Along these lines, individuals who are more susceptible to pain have high baseline PAG activity but low baseline connectivity with several pain related and pain modulatory related (e.g. DLPFC) brain regions. This might imply that such subjects have poorer descending inhibitory capability.
Title: Effects Of Uncertain Expectation On The Experience Of Pain

Poster Number PTH402

Authors
Y. Shih, S. Yang, T. Wu, Z. Lu, C. Huang, Y. Lin, M. Tseng

Graduate Institute of Brain and Mind Sciences, National Taiwan University College of Medicine, Taipei, Taiwan, Department of Computer Science and Information Engineering, National Taiwan University, Taipei, Taiwan

Aim of Investigation
Human experiences of pain are robustly shaped by the expectation of incoming noxious stimuli. So far, neural substrates underlying the expectation of certain pain intensity have been investigated by several studies. Given that little research examines the difference between the expectation of certain vs. uncertain pain intensity, the current study recruits healthy adults to receive painful stimulation under different expectancy conditions. We hypothesize that uncertain expectation of incoming noxious stimuli will enhance pain experience.

Results
Consistent with previous studies, certain expectations of an increase and a decrease in pain markedly enhanced and reduced pain ratings, respectively. Of note, uncertain expectations of pain also increased pain ratings. For painful stimulus intensity with a VAS score of 5, ratings following the uncertain cue were significantly higher than those following certain cues.

Conclusion
For the first time, we provide evidence that uncertain expectations enhance the experience of pain. This novel finding serves as the behavior basis for how uncertain anticipations influence pain. We will collect fMRI data to disclose the underlying neural mechanisms.
Aim of Investigation
Itch and pain are closely related but distinct sensations. Intradermal injection of acid generates pain in both rodents and human; however, few studies address the intriguing issue whether proton can be a pruritogen as well.

Results
We report here three lines of evidence to show that protons act on dorsal root ganglion (DRG) pruriceptors and generate itch sensation in mice. First, Citric acid (0.2M) pH-dependently induces scratching response in mice when applied intradermally to the nape skin. Second, acidified buffer at pH3.0 elevates intracellular calcium in DRG pruriceptors. Third, intradermal citric acid (pH=3.0) injection in the nape skin model induces a pruritogen-like, but not algogen-like c-Fos immunoreactivity pattern in the cervical spinal cord. To identify the possible acid-sensing channels/receptors that are involved in the proton-evoked itch, we screened: 1) pharmacologically the itch response when intradermal acid solution is injected in combination with specific antagonist targeting to ASIC3, TRPV1, or TRPA1; 2) genetically in mutant mouse lines lacking ASIC3, TRPV1, or TRPA1 in the nape skin model. Results indicate TRPV1, but neither ASIC3 nor TRPA1, is involved in the acid-induced scratching response.

Conclusion
Together, we conclude that proton is a potent pruritogen and could act on TRPV1 for the acid-induced pruriception.
Title: Anoctamin 1 Mediates Histamine-Independent Itch Signaling In Sensory Neurons

Poster Number PTH404

Authors
U. Oh
Seoul National University, Seoul, Korea

Aim of Investigation
ANO1 is highly expressed in subset of TRPV1 positive small sensory neurons and activated by several inflammatory mediators, for instance endothelin, carbachol or bradykinin via activation of each GPCRs. Because many itch producing agents such as histamine, CQ, SLIGRL induce itch responses by activation of GPCRs, these data raise possibility that ANO1 is likely a functional roles as a downstream molecules for itch. Therefore, we tested whether ANO1 could be activated by CQ or SLIGRL through Mrgpr-mediated signaling.

Results
We found that ANO1 is the primary transduction channel mediating chloroquine and SLIGRL-induced itch signaling in sensory neurons and heterologous cells. Compared to control mice, Adv-ano1fl/fl mice which is deficient of Ano1 specifically in DRG neurons displayed a significant reduction in scratching behaviors to chloroquine or SLIGRL injection, but not histamin injection.

Conclusion
ANO1 appears to be an essential component of transduction channel downstream of histamine-independent and Mrgpr-dependent itch.
Title: Pharmacological (Gaba-A/B) And Transplant-Mediated Enhancement Of Gabaergic Controls Ameliorate Chronic, Inflammatory Itch

Poster Number PTH405

Authors
J. Braz, F. Cevikbas, C. Solorzano, D. Villafuerte, M. Sulk, T. Buhl, M. Steinhoff, A. Basbaum

University of California San Francisco, San Francisco, CA, Univeristy Medical Center Goettingen, Goettingen, Germany, University College Dublin (UCD) and Charles Institute of Dermatology, Dublin, Ireland

Aim of Investigation
Chronic itch remains a major intractable clinical condition that negatively impacts the quality of life of millions of patients. Recent studies have emphasized the presence of GABAergic inhibitory controls that regulate the processing of pain and itch messages at the level of the spinal cord dorsal horn. Despite these findings, pharmacological regulation of pain processing by GABAergic agonists has been disappointing (e.g. with the GABA-B agonist, baclofen) and to our knowledge there are no clinical reports using these agonists in the management of chronic itch. Conceivably, a relatively narrow therapeutic window limits use of GABAergic agonists. Here, we used two different approaches to reexamine the impact of GABAergic neurons against itch. We demonstrate that increasing GABAergic inhibitory controls, either by transplant of GABAergic progenitor cells or with synergistic low-dose combinations of GABA receptor agonists is in fact very effective against itch provoked by a wide variety of pruritogens. Both approaches are also remarkably therapeutic in the IL31-overexpressing transgenic mouse (IL31OE), a model of atopic dermatitis (AD), an inflammatory, relapsing pruritic skin disease that is particularly difficult to manage.

Results
Intraspinal transplantation of GABAergic precursor cells not only decreased spontaneous scratching in the IL31OE mice, but also reduced the incidence and severity of the associated skin eczematous lesions. Pharmacological activation of endogenous GABA receptors by non-sedating doses of either muscimol or baclofen was also effective in the IL31OE mice. Moreover, a combination of low doses of muscimol and baclofen had broad, indeed synergistic, anti-pruritic effects against a variety of histaminergic and non-histaminergic pruritogens. Remarkably, the synergistic combination against pruritus occurred without concomitant increases in sedation.
Conclusion
Here, we demonstrate that increasing GABAergic inhibition, particularly at the level of the spinal cord, has significant utility in the management of a chronic, inflammatory itch (AD) model, indicating that this approach may be beneficial in the management of intractable itch in patients. Our results also highlight the broad therapeutic value of the GABAergic precursor cell transplantation approach for the management of both chronic pain and itch.
Title: Expression Of Dynorphin By Heterogeneous Populations Of Dorsal Horn Inhibitory Interneurons

Poster Number PTH406

Authors
E. Polgar, M. Gutierrez-Mecinas, N. Mooney, E. O'Connor, K. Robertson, A. Todd

University of Glasgow, Glasgow, United Kingdom

Aim of Investigation
Chronic itch and pain are often difficult to treat and represent major unmet clinical needs. Although there has been extensive study of the neuronal circuits that process nociceptive information, interest in itch mechanisms emerged more recently and we know relatively little about the circuitry responsible for transmitting and modulating pruriceptive input. To understand how different types of sensory information are processed in the spinal dorsal horn we need to unravel the complex synaptic circuits involving interneurons, which form the vast majority of the neurons in the superficial laminae. We have identified four largely non-overlapping classes of inhibitory interneurons in laminae I-III, defined by expression of specific neurochemical markers: (1) dynorphin and galanin, (2) neuronal nitric oxide synthesise (nNOS), (3) neuropeptide Y and (4) parvalbumin. We subsequently reported that the dynorphin/galanin and nNOS populations were specifically lost in mice lacking the transcription factor Bhlhb5, a model of chronic itch. This suggested a role for one or both of these populations in suppressing itch. However, a recent study reported that ablation of cells that expressed Cre recombinase in a preprodynorphin-Cre (PPD-Cre) knock-in mouse prevented mechanical pain, but had no effect on itch. In the present study we aimed to gain a better insight into the role of the dynorphin-expressing neurons by identifying the cells that expressed Cre in the PPD-Cre mouse.

Results
We found that in laminae I-II of the PPD-Cre;Ai9 mouse ~15% of all neurons were tdTom+, and the great majority of these (~80%) were inhibitory interneurons, as defined by expression of the transcription factor Pax2. We confirmed that there was extensive overlap of PPD and galanin in inhibitory interneurons, and found that all of these cells were tdTom+. The PPD/galanin cells accounted for the majority of tdTom+ inhibitory interneurons, but we also found that nNOS-, parvalbumin and NPY-expressing cells were included among the tdTom+ neurons. In mice that received intraspinal injection of AAV.flex.eGFP, as expected, all of the eGFP-labelled cells were tdTom+. These accounted for ~80% of the tdTom cells near the injection site, and included both inhibitory (Pax2+) and excitatory (Pax2-) cells.
Most (85%) of the eGFP+ cells were PPD-immunoreactive. However, all of the parvalbumin- and many of the nNOS-containing tdTom+ cells did not express eGFP. Although cells with tdTom but not eGFP could have failed to take up the AAV.flex.eGFP, the fact that these had specific neurochemical phenotypes (often nNOS- or parvalbumin-immunoreactive) implies that this was not the case, but rather that these are cells that transiently expressed dynorphin during development.

Conclusion
These results suggest that although most tdTom+ cells in the PPD-Cre;Ai9 mouse continue to express dynorphin, there is also transient expression of Cre (and presumably dynorphin) among other populations of inhibitory interneurons, including some belonging to the nNOS and parvalbumin populations. This indicates that care is needed in interpreting the results of experiments in which Cre is used to switch on transgene expression in specific neuronal populations, because this approach may capture transient expression of the gene of interest. Alternative methods are to use inducible recombinases (e.g. Cre-ERT2) or injection of viral vectors that express cre-dependent transgenes in adult animals.
Title: Reversing Nocebo Effects By Conditioning With Verbal Suggestion

Poster Number PTH407

Authors
D. Bartels, A. van Laarhoven, M. Stroo, K. Hijne, K. Peerdeman, R. Donders, P. van de Kerkhof, A. Evers
Leiden University, Leiden, Netherlands, Radboud University Medical Center, Nijmegen, Netherlands

Aim of Investigation
Nocebo effects are negative treatment effects, unrelated to the treatment mechanism, which are induced by patients' expectations of worsening. Nocebo effects are known to contribute to the experience of physical symptoms such as pain and also itch, however it is not known how to minimize or reduce nocebo effects. In this study, we examined whether nocebo effects can be reduced by positive expectation induction with respect to electrical itch stimuli in healthy subjects.

Results
Positive expectation induction resulted in a significantly smaller nocebo effect in comparison with both control groups. Mean change itch NRS scores showed that the nocebo effect was even reversed, signifying a placebo effect.

Conclusion
The current study is the first to demonstrate that nocebo effects can be reversed by conditioning with verbal suggestion. A better understanding how to diminish and reverse nocebo responses might eventually contribute to increased treatment effectiveness and improved quality of life for patients suffering from chronic itch conditions and potentially also pain.
**Title:** Can A Single Pulse Transcranial Magnetic Stimulation Targeted To The Motor Cortex Interrupt Pain Processing?

**Poster Number** PTH408

**Authors**
L. Kisler, I. Gurion, A. Sinai, Y. Granovsky, S. Shamay-Tsoory, D. Yarnitsky, I. Weissman-Fogel

Department of Psychology, University of Haifa, Technion Faculty of Medicine, Nahariya, Israel, Department of Psychology, University of Haifa, Haifa, Israel, Department of Neurosurgery and Neurology, Rambam Health Care Campus, Haifa, Israel, Rambam Health Care Campus And Technion Medical School, Haifa, ISRAEL, Rambam Helath Care Campus, Technion Faculty of Medicine, Haifa, Israel, Department of Physical Therapy, Faculty of Social Welfare and Health Sciences, University of Haifa, Haifa, Israel

**Aim of Investigation**
The primary motor cortex (M1) is suggested to be involved in pain modulation. Stimulation of M1 has an inhibitory effect on clinical and experimental pain. Previous studies show that single pulse Transcranial Magnetic Stimulation (TMS) can elicit a brief disruption in cortical activity, which results in an interruption of the targeted behavioral function. Using this technique, known as virtual lesion (VL), we aimed to investigate the contribution of M1 to pain processing. We hypothesized that TMS-VL will induce an increase in pain ratings of experimental noxious stimuli as compared to stimuli with no TMS, or sham conditions.

**Results**
Pain-related M1 peak activation was found in 251.82±16.45 msec. In the VLM1 protocol, pain ratings were 50.8±12.9 in the pain-alone condition, 54.9±13 for TMS-VL, and 52.8±13.4 for SHAM-VL with no significant difference between these conditions. Pain ratings in VL-50 (51.9±21.8) and SHAM-50 (51.8±22) conditions were significantly higher (two tailed t-test: P=0.040 and P=0.042, respectively) than pain ratings in the pain-alone condition (46±17.6). No differences in pain ratings were found for the VL+150 (50.5±23.9) and SHAM+150 (49.5±22.8) conditions as compared to the pain-alone condition. In both VL-50 and VL+150 protocols, no significant differences in pain ratings were found between TMS-VL and SHAM-VL conditions.
Conclusion
The current results suggest that a single pulse TMS administered either 50ms prior or 150ms following painful stimulus, or time locked to the individual pain-related M1 activation, failed to interrupt experimental pain processing more than sham. Small number of subjects and large inter-subject variability in pain perception, pain related psychological factors and cortical excitability may contribute to the lack of VL effect on experimental pain perception. Taken in consideration that the pain neuromatrix comprised of many brain areas that are involved in pain processing, it is assumed that interrupting the neural activity of a single brain area will not necessarily influence the complex, multi-dimensional and subjective experience of pain. Perhaps, single pulses TMS applied to multiple brain areas may have a better chance to successfully interrupt pain processing.
Title: Impact Of Experimental Medial Knee Pain On Deep Tissue Hyperalgesia And Muscle Strength.

Poster Number PTH409

Authors
S. Oda, M. Izumi, K. Aso, M. Ikeuchi

Department of Rehabilitation Center, Kochi Medical School Hospital, Nankoku, Japan, Department of Orthopedic Surgery, Kochi Medical School, Kochi University, Nankoku, Japan

Aim of Investigation
Clinically localized medial knee pain is the most frequent observations in patients with knee disorders. However it has not been investigated why many patients tend to feel knee pain in the medial side and how it affects their treatment outcome. The aim of this experimental study is to clarify characteristics of medial knee pain and its potential for modulating sensory and motor function in humans.

Results
MP demonstrated higher VAS scores than LP and compared with isotonic saline (P<0.05). Localized medial knee pain was observed in MP while referred pain areas to lateral parts of the lower leg were found in LP. PPTs were decreased on medial and lateral part of the knee in MP but only on the lateral knee in LP (P<0.05). Bilateral reduction in muscle strength of the quadriceps and grip power was observed although MP caused significantly larger reduction of ipsilateral quadriceps strength compared with LP (P<0.05).

Conclusion
Medial knee structures were possibly vulnerable to nociceptive input that caused spreading hyperalgesia and higher reduction of the muscle strength compared with lateral knee structures. This novel model may open for a better understanding of the pain mechanisms in knee disorders.
Aim of Investigation
Minocycline prevents behavioural hypersensitivities in animal models of peripheral nerve injury but translational efficacy in human studies is lacking. This study was aimed at pursuing two questions: (1) Do repeated injections of hypertonic saline in human subjects induce an ongoing hypersensitivity that outlasts the acute response? (2) Can pre-treatment with minocycline alleviate the altered behavioural hypersensitivity?

Results
On day 1 prior to HS injection, all subjects were healthy, possessing a few sore spots on palpation (3.1 ± 0.9 bilaterally) and subjects reported no cold allodynia. By day 9, however, subjects receiving no treatment experienced an intense bilateral increase (P=0.0013) in the number of sore spots on the TA (ipsilateral 14.6 ± 6, contralateral 9.4 ± 4.1). Subjects treated with placebo experienced a statistically similar number of sore spots (ipsilateral 9.2 ± 3.2, contralateral 7.3 ± 2.4), whereas this muscle soreness was not observed in the minocycline group (ipsilateral 1.8 ± 0.9, contralateral 2.8 ± 1.3). Additionally, only 10% of subjects treated with minocycline demonstrated cold allodynia on day 9, compared to 40% of subjects in the placebo group and 60% of subjects in the no treatment group. Minocycline had no effect on the intensity, duration or location of the acute pain response to HS injection.

Conclusion
In this study we established a human experimental model of hypersensitivity causing intense bilateral muscle soreness and cutaneous cold allodynia. Both effects outlasted the acute response to HS injection. These sensory perturbations were prevented when subjects were treated with minocycline. It is likely that the neuro-anti-inflammatory properties of minocycline are responsible for the alleviation of the hypersensitivity. However the exact mechanisms involved remain unclear. Results from this study
suggest that minocycline pre-treatment may provide subjects with an improved quality of life by diminishing both deep and cutaneous hypersensitivity. Further studies will focus on the fundamental mechanism behind minocycline's efficacy as an anti-neuropathic treatment.
Aim of Investigation
Pain is the most frequently cited symptom associated with rotator cuff tear (RCT) and surgery is often indicated for patients with severe pain. On the other hand, it is well known that many people in the general population have an asymptomatic RCT. These facts indicate that etiology and mechanism of rotator cuff pain is not fully known. The aim of this experimental study is to investigate characteristics of rotator cuff pain and its potential for modulating muscle strength around the shoulder.

Results
Rotator cuff pain demonstrated significantly higher VAS scores than trapezius pain and compared with isotonic saline (P<0.05). Extensive pain referral patterns to areas including the upper arm and forearm were observed in rotator cuff pain while trapezius pain showed localized distribution around the injection site (P<0.05). Maximal isometric muscle strength decreased by approximately 40% at abduction, external rotation, and internal rotation of the shoulder in rotator cuff pain (P<0.05), which was within 10% and not significant in trapezius pain and isotonic saline injections.

Conclusion
This is the first human rotator cuff pain model targeting the tendon in the most common area of RCT. Rotator cuff was possibly vulnerable to nociceptive input, which caused extensive pain referral and higher reduction of the muscle strength compared with trapezius pain. This novel model provides the specific pain patterns originating from rotator cuff, which may open a better understanding of the pain mechanisms in patients with RCT.
Title: An In Vitro Model To Study The Pathogenesis Of Congenital Insensitivity To Pain

Poster Number PTH412

Authors
L. McDermott, G. Weir, A. Clark, D. Bennett

University of Oxford, United Kingdom, University of Oxford, United Kingdom

Aim of Investigation
Loss-of-function mutations in SCN9A, the gene encoding the α-subunit of the voltage-gated sodium channel Nav1.7, cause congenital insensitivity to pain in humans. Mutant channel function has previously only been investigated in heterologous expression systems owing to the inherent difficulties in obtaining primary tissue. Induced pluripotent stem cell (iPS) technology circumvents this issue, enabling the condition to be studied in a disease relevant cell type. Here we describe the production of functional sensory iPS-derived neurons from patients with loss of function mutations in Nav1.7.

Results
Differentiation of patient iPSCs revealed no deficits in cell viability or axonal outgrowth. Cells expressed the canonical sensory neuron markers Brn3a and Islet-1, and no difference in gross morphology between patient and control lines was observed. Endogenous channel function was assessed using whole cell patch clamp. Significant changes in intrinsic excitability were seen relative to control lines, marked by significant (p<0.05) increase in rheobase, the minimum depolarising current required to evoke an action potential (ΔSCN9A 150 pA, n=49, vs. Control 98 pA, n=47). The ability of the neurons to repetitively fire also differed; diseased lines fired significantly (p<0.01) fewer action potentials over a range of stimulation levels. Results were in agreement with a reduction in intrinsic excitability. Ongoing work using CRISPR/Cas9 seeks to genetically correct the affected iPS cells and permits the de novo introduction of SCN9A mutations in healthy controls.

Conclusion
The amenability of this in vitro model enables further study of the cellular pathology of CIP and research into novel functions of the Nav1.7 channel.
Title: Electrophysiological Correlates Of Spatial Summation To Noxious Heat: The Possible Role Of A-Delta Fibers

Poster Number PTH413

Authors
Y. Granovsky, N. Raz, R. Defrin

Rambam Health Care Campus And Technion Medical School, Haifa, Israel, Department of Physical Therapy, Sackler Faculty of Medicine. Sagol School of Neuroscience, Tel Aviv, Israel, Tel-Aviv University, Tel Aviv, Israel

Aim of Investigation
Although spatial summation of pain (SSP) is central to the processing of pain intensity and quality; its mechanism is not understood. We previously found greater heat SSP in hairy than glabrous skin, suggesting that perhaps A-mechano-heat II (AMH-II) nociceptors are the dominant subserving system. In order to further explore the role of A-delta fibers in SSP, we analyzed the electrophysiological correlates of SSP under conditions that minimize the influence of different skin thicknesses.

Results
Both N2 and P2 amplitudes were larger in hairy than glabrous skin, but a differential effect of SSP was found on the CHEPs. Despite similar psychophysical SSP, the electrophysiological SSP reflected in N2, but not P2 amplitude (subtracting N2 amplitude of the small from the large probe), was larger in hairy than glabrous skin. Nevertheless, regardless of skin type, P2 amplitudes of the large probe were higher than those of the small probe.

Conclusion
Considering the fast rate stimuli and the lack of AMH-II in glabrous skin, a greater SSP effect in hairy than glabrous skin, manifested by N2 amplitude, may suggest that SSP is mainly subserved by AMH nociceptors. The fact that overall SSP is primarily manifested in P2 amplitude suggests the role of the cingulate cortex in determining SSP.
Title: Exploring The Effect Of Friendship On Pain: Do Sex And Competitiveness Have An Impact On Pain Experiences?

Poster Number PTH414

Authors
R. Edwards, C. Eccleston, E. Keogh

University of Bath, Bath, United Kingdom

Aim of Investigation
In recent years, our understanding of the various social influences that effect the communication of pain has improved. We know that the presence of an observer can influence pain experiences and how it is reported. The nature of the relationship between individuals experiencing pain and observers can also impact on pain. For example, Edwards et al. (in prep) found that individuals are less sensitive to pain in the presence of a friend, when compared to a stranger or romantic partner – especially in males. Drawing on theories of friendship, it seems that competitiveness and cooperativeness towards common goals can impact on social interactions between friends. We therefore investigated the role of competitiveness and cooperativeness on the reporting of pain between same-sex and opposite-sex friends. We hypothesised that pain threshold and tolerance levels would be higher when placed in a competitive condition, and that this would be most pronounced within males.

Results
Analysis of the competitive VAS scales indicated that participants rated themselves as more competitive following both the cooperative and competitive conditions. Interestingly, VAS cooperativeness scores were similar following each of the two tennis conditions. This suggests that whilst we were able to induce competitiveness, the manipulation did not produce differences in cooperation. When we looked at the effects of sex and the tennis condition on cold pressor pain scores, no significant main or interaction effects were found.

Conclusion
These results of the current study mean that it is not yet possible to say whether there are sex differences in the effects that cooperative/competitive interactions between dyads have on pain scores. Interestingly, and in contrast to our previous study, no effect of the sex of observer was found on pain. Furthermore, whilst we were able to increase competitiveness through our task manipulation, the
experimental manipulation of cooperation was difficult to achieve. One possibility for these effects could be that the heightened competitiveness induced in all participants overrode any more subtle observer effects, and whether they were male or female. It would be interesting to consider what would have been found if a highly cooperative task had been used. This is just the start of an interesting line of research, and points to the needs to have better ecologically and contextually relevant paradigms which may better evoke the experiences of competitiveness and cooperativeness in relation to the experience of pain.
**Title:** Motor Cortex Excitability: A Novel Facet Of Pain Modulation?

**Poster Number** PTH415

**Authors**
Y. Granovsky, A. Sinai, D. Yarnitsky

Rambam Health Care Campus And Technion Medical School, Haifa, Israel, Rambam Health Care Campus, Haifa, Israel, Nahariya, None, Rambam Health Care Campus, Technion Faculty of Medicine, Haifa, Israel

**Aim of Investigation**
Motor cortex excitability represents a balance between the activity of excitatory pyramidal neurons and inhibitory inter-neurons. Experimental painful stimuli inhibit excitability of primary motor cortex (M1), and, in turn, activation of M1 (via high-frequency repeated transcranial magnetic stimulation, TMS) reduces pain. TMs is therefore used in chronic pain therapy. However, the relationship between the baseline M1 excitability and pain sensitivity in pain free subjects has not been yet elucidated. We hypothesized that motor cortex excitability is inversely correlated with pain sensitivity.

**Results**
Among all psychophysical parameters, the measures of M1 excitability correlated only with CPM efficiency and with TS magnitude to electrical stimuli; efficient CPM was associated with longer MEP duration (r=-0.535, p<0.001), higher MEP amplitude (r=-0.436, p=0.003) and larger area under the curve (AUC) of the MEP (r=-0.480, p=0.002). In line, high TS magnitude (reflects pain facilitation) was associated with shorter MEP duration (r=-0.421, p=0.007), and with lower AUC of the MEP (r=-0.327; p=0.039). In addition, high TS magnitude was associated with smaller increase of CSP (r=-0.384; p=0.023). Further, using regression analysis, we revealed that between two facets of pain modulation, CPM and TS, efficient CPM but not low TS was the major contributor for high cortical excitability. This was shown for the measures MEP AUC (p=0.006; regression model p=0.004) and MEP duration (p<0.001; regression model p=0.001). In addition we divided our subjects to those with anti-nociceptive profile of pain modulation (efficient CPM and low TS magnitude, N=12) and pro-nociceptive profile (less-efficient CPM and high TS magnitude, N=12). T-test analysis indicated that the subjects with anti-nociceptive profile were characterized by higher M1 excitability: early onset of MEPs, longer MEPs duration, larger amplitudes and AUCs.
Conclusion
Overall, our findings show that the excitability of the primary motor cortex is positively associated with pain inhibition, and inversely associated with pain facilitatory mechanisms. Higher excitability of the primary motor cortex is associated with anti-nociceptive characteristics of pain modulation in healthy subjects and vice versa. In the search of clinically relevant measures of pain modulation that can serve in the characterization of pain phenotypes and prospective response to pain therapy, TMS based assessment of cortical excitability stands out as an objective and easy to obtain parameter.
Title: Spatial Changes In Mechanical Pain Sensitivity After A Standardized Incision

Authors
M. Pereira, M. Mühlenhoff, T. Klein, P. Zahn, E. Pogatzki-Zahn

University Hospital Muenster, Muenster, Germany, Mundipharma Research GmbH & Co. KG, Limburg (Lahn), Limburg (Lahn), Germany, Ruhr University of Bochum (RUB), Bochum, Germany

Aim of Investigation
Central sensitization plays a major role in the development of chronic pain caused by tissue injuries; it is, however, basically unclear, how different measures of central sensitization relate to each other. Using an experimental incision in human volunteers, we therefore studied the spatial pattern of mechanical pain sensitivity surrounding an incision and how it relates to the area of secondary hyperalgesia within and outside its border at different times after incision.

Results
All volunteers developed areas of secondary hyperalgesia surrounding the incision, which were maximal 1h post-incision (median [interquartile range]: 1578 mm² [835;2367], n=18) and decreased over time (Friedman's test on time course: p<0.001). MPS assessed on the rings inside the secondary hyperalgesia area was generally higher compared to the rings outside the secondary hyperalgesia area. On Day 1 (1-9h), MPS was maximal on the ring closest to the incision and decreased log-linearly with increasing distance to the incision (r=-0.97). Over time, MPS was highest 1h after the incision and decreased log-linearly thereafter (r=-0.99). Secondary hyperalgesia at 1h, but not at the remaining time-points, correlated with MPS surrounding the incision (p=0.05; r=0.47). The incision induced a trend of a decrease in heat pain thresholds (p=0.05), while other thermal thresholds were not affected.

Conclusion
Mechanical pain sensitivity decreases log-linearly with increasing distance to the incision, and, an additional sharp decrease occurs beyond the border of secondary hyperalgesia. Mechanisms responsible for these central effects and their role for prolonged chronic pain after injury need further investigation.
Title: When And Who Feels The Pain? An Eeg Study On The Expectation Of Painful Stimulation On Others

Poster Number PTH417

Authors
A. Piedimonte, G. Guerra, S. Vighetti, M. Molo, F. Benedetti, E. Carlino

University of Turin, Department of Neuroscience, Turin, Italy, Fondazione Carlo Molo, Turin, Italy, University of Turin Medical School, Turin, Italy

Aim of Investigation
Pain is a complex experience that involves different factors. In particular, the context in which a painful stimulation is delivered is crucial. The aim of the present study is to investigate how physical, social and temporal cues modulate pain perception using contingent negative variation (CNV), a well-known electrophysiological measure related to the expectation of an imperative stimulus after the presentation of a warning stimulus. In our study, physical context is represented simply by the difference between high intensity and low intensity electrical stimulation delivered to participants. Social context is represented by the fact that participants not only did receive the stimulation but also observed another participant receiving it. Finally, temporal context is represented by the order in which participants received or observed the painful stimulation.

Results
Results of the study showed a decrease in pain perception, a decrease in CNV mean amplitude (i.e. a smaller CNV) and an increase in RT when electrical stimuli followed the presentation of the green light compared to the red light (physical context). This result was confirmed not only in participants who received the stimulation (T group) but also in participants who observed (O group) the stimulation (social context). Moreover participants who first observed the stimulation and then received it (OT group) presented a significant increase of CNV mean amplitude in comparison with participants who first received the stimulation (TO group) and a positive correlation between their NRS and empathy scores (temporal context).

Conclusion
The data collected in this study show that both physical and temporal aspects of the context, as well as social constraints modulate the experience of pain at the behavioral as well as at the electrophysiological level.
Title: Cold Water Test And Analgesia Nociception Index In Women Operated For Breast Cancer

Poster Number PTH418

Authors
H. Harno, L. Haasio, R. Sipilä, E. Ruoppa, E. Kalso

Helsinki University Hospital, Division of Pain Medicine, Department of Anesthesiology, Espoo, Finland, University of Helsinki, Department of Statistics, HUS/Helsinki, Finland, Helsinki University Hospital and University of Helsinki, Vantaa, Finland, Helsinki University Hospital, Division of Pain Medicine, Department of Anesthesiology, HUS/Helsinki, Finland, Helsinki University Hospital and University of Helsinki, Division of Pain Medicine, Helsinki, Finland

Aim of Investigation
Previously we have studied 1000 women who underwent treatment for breast cancer. At the 1-year follow-up 16% or the patients reported at least moderate post surgery pain. In the NeuroPain project we will assess factors that are associated with persistent neuropathic pain following breast cancer surgery in this patient cohort. Analgesia Nociception Index (ANI) is a new pain monitor based on heart rate variability. It has recently been approved for intraoperative nociception monitoring. In this project we wanted to repeat the cold-water test in the patients after a 5-year follow-up and to assess the autonomic system function using the ANI-monitor during the cold-water test.

Results
So far we have studied 146 patients. The distribution of pain intensities and the times the patients tolerated the cold water showed significant interindividual variation (Figure 2). The pain values measured at this follow-up visit and the original presurgery visit correlated well (r=0.39 at 15 seconds, r=0.29 at 30 seconds) (Figure 3). The time patients tolerated the cold water at this follow-up and original visit also showed strong correlation (r=0.60). The connection between the pain intensity values during the cold-water test and the ANI-measures reflecting the parasympathetic tone was estimated with a linear mixed model with a random intercept and slope varying between patients. The mean effect plot for parasympathetic tone is shown in Figure 4.

Conclusion
The ANI-monitor shows a nice correlation with the patient-reported pain intensity values. Next we will
study the individual differences in the autonomic responses and any associations with other phenogenotypes.
Title: Pain-Related Gamma-Band Oscillations Elicited In The Human Insula Are Modulated By Epileptic Activity

Poster Number PTH419

Authors

Saint-Luc University Hospital, Brussels, Belgium, Université Catholique de Louvain, Brussels, Belgium, Université catholique de Louvain, Brussels, Belgium, Université Libre de Bruxelles, Brussels, Belgium

Aim of Investigation
Insular epilepsy is rare and difficult to diagnose. Surface electroencephalography (EEG) is not modified by specific insular epileptic activity (EA), and there are few clinical features pointing specifically to an insular ictal onset zone (IOZ). Functions attributed to the insula include autonomic regulation and somesthesic integration. Furthermore, the insula is thought to play a major role in the perception of pain, a multi-dimensional experience that comprises sensory, affective, and cognitive components. We recently found that nociceptive stimuli elicit consistent gamma-band oscillations (GBOs, 40-90 Hz) in the human insula (Pain-related gamma-band oscillation in the human insula. Same authors, under review). Because non-nociceptive stimuli do not elicit a similar response, these high frequency oscillations could reflect activity specific for nociception and pain. Here we analysed how EA affects GBOs within the insular cortex.

Results
In all patients, thermonociceptive stimuli consistently elicited a clear enhancement of GBO power at most insular contacts, peaking 245 ms ± 12 ms after stimulus onset, but not at other intracerebral contacts. A linear mixed model (LMM) analysis performed on GBO magnitudes using 'modality' (thermonociceptive, vibrotactile, auditory, and visual), 'EA' (present, absent), and 'IOZ' (present, absent) as fixed factors, and 'subject' as a contextual variable, showed a main effect of 'modality': the magnitude of the GBOs elicited by nociceptive stimuli was significantly greater than the magnitude of GBOs elicited by vibrotactile, auditory, and visual stimuli (F=20.29, p<.001). The presence of EA significantly decreased the magnitude of GBOs elicited by nociceptive stimuli (significant interaction between 'modality' and 'EA': F=5.74, p=.001). Finally, insular contacts involved in the IOZ displayed significantly greater GBO
magnitudes after nociceptive stimulation (significant interaction between 'modality' and 'IOZ': F=4.69, p<.001).

**Conclusion**
Nociceptive stimuli elicit consistent GBOs in the insular cortex. Our results show that epileptic activity modulates the magnitude of pain-specific GBOs in a bimodal manner: insular contacts involved in the ictal onset zone show enhanced nociceptive-evoked GBOs, whereas contacts involved in interictal activity show decreased GBOs. Further research is needed to investigate how changes in connectivity resulting from epileptogenic processes might account for these observations.
Title: The Test-Retest Reliability And Agreement Of Eye Tracking To Measure Attentional Bias To Threat Words

Poster Number PTH420

Authors
I. Skinner<sup>,2</sup>, M. Huebscher<sup>,2</sup>, L. Moseley, H. Lee<sup>,2</sup>, A. Traeger<sup>,2</sup>, B. Wand, S. Gustin<sup>,5</sup>, J. McAuley<sup>1</sup>

Neuroscience Research Australia, Sydney, NSW, Australia, Prince of Wales Clinical School, University of New South Wales, Sydney, NSW, Australia, University of South Australia, Adelaide, SA, Australia, School of Physiotherapy, The University of Notre Dame Australia, Fremantle, WA, Australia, School of Psychology, University of New South Wales, Sydney, NSW, Australia

Aim of Investigation
Evidence for attentional bias in pain is mixed. Recently eye tracking has been suggested as a method of measuring attentional bias, but its test-retest reliability has not been investigated. Attentional bias is inferred when preferential viewing of threat-related words is recorded from an eye tracker. We aimed to determine the test-retest reliability and level of agreement of eye tracking to detect attentional bias to threat-related words in healthy participants.

Results
50 healthy participants (23 males; age 27±10 years) were tested. The mean bias scores varied from 47.2% to 51.2% across the 12 outcome measures. The highest ICC was the total dwell time 1000-4000ms when viewing the general threat words: ICC = .73. The lowest ICC was the first fixation duration when viewing the sensory pain words: ICC = - .16. The sensory pain words consistently demonstrated lower ICCs than the affective and general threat words. The lowest SEM was the first fixation latency when viewing affective pain words: SEM = 2.35%. The highest SEM was the second run dwell time when viewing sensory pain words: SEM = 15.07%.

Conclusion
There is considerable variation in the test-retest reliability and level of agreement when using eye tracking to assess attentional bias to threat related words in healthy participants. The outcome measure selected and category of threat words affect both the test-retest reliability and level of agreement. Consideration should be given to selection of stimuli and outcome measures, and their effect on...
reliability, when designing eye tracking studies to assess attentional bias. These results support the use of some parameters for the investigation of attentional bias using eye tracking, but also call into doubt the utility of many eye tracking parameters that are commonly used.
Title: Muscular Hypersensitivity Induced By Hypertonic Saline Infusion In Adjacent Muscles: A Bi-Directional Interaction

Poster Number PTH421

Authors
J. Dunn, S. Nagi, S. Mavromihalis, D. Mahns

Western Sydney University, Penrith, NSW, Linköping University, Linköping, Sweden, University of Western Sydney, Penrith, NSW

Aim of Investigation
It has long been well established, in both literature and the work of this study group, that the infusion of hypertonic saline (HS) into muscle groups can result in the development of hypersensitivity in adjacent skin regions. However, whilst interactions in adjacent body regions have been observed in cutaneous tissue it remains ambiguous as to whether hypersensitivity can develop within neighbouring muscles in addition to this cutaneous allodynia. This project aimed to quantify the capacity of pain in one muscle to induce allodynic responses in adjacent muscles.

Results
In all experiments an NS infusion was administered into muscles at the start of the procedure to ensure that an NS infusion was innocuous under control conditions. During HS infusion in FCU, the infusion of NS into the ADM developed pain character with subjects reporting an increase in overall pain. The same is true in the reverse experiments with hypersensitivity evoked across the FCU in the context of a HS infusion into ADM. The emergence of a painful response to the NS stimulus during infusion of HS into an adjacent muscle is indicative of hypersensitivity/allodynia. The results from the myelinated-fibre block component of this study will be presented at the conference.

Conclusion
The results from this study show that in the context of background pain from infusion of HS into a muscle, a degree of muscular allodynia is also seen in adjacent muscles. The repeatability of this interaction when the muscle groups (FCU and ADM) are reversed indicates that this is a bi-directional phenomenon and not dependent upon proximal-distal location of the pain source. Furthermore, the lack of pain seen to infusion of NS into the ADM is evidence that this result is independent of local muscle distention and is most likely due to the context of background muscle pain.
Title: Expectation And Attention To Pain Jointly Modulate Neural Gain In Somatosensory Cortex

Poster Number PTH422

Authors
F. Fardo, R. Aukstulewicz, M. Allen, M. Dietz, A. Roepstorff, K. Friston

Aarhus University, Aarhus, Denmark, University of Oxford, Oxford, United Kingdom, University College London, London, United Kingdom

Aim of Investigation
Top-down influences such as expectation and attention strongly shape the amplitude of evoked neural activity and the intensity of felt pain in response to noxious events. Although violations of expectation (deviance) and attention exert similar effects on pain processing, the extent to which they rely on similar neural mechanisms is unknown. Here, we investigated how deviance and attention influence effective connectivity within and between regions of the somatosensory pain-related hierarchy. By using dynamic causal modelling (DCM) for magnetoencephalography (MEG), we assessed how these factors shape the cortical dynamics governing network connectivity in pain processing, identifying the role of intrinsic connectivity in superficial pyramidal cells, and extrinsic connectivity between different neuronal populations defined according to a canonical microcircuit model. Our results suggest that a predictive coding mechanism governs the influence of both attention and expectancy effects on pain.

Results
We found evidence for a somatosensory network comprising bilateral primary and secondary somatosensory cortex (S1 and S2), inferior frontal gyrus (IFG) and inferior parietal lobe (IPL). Within this network, sensory deviance and attention to pain jointly increased the gain of superficial pyramidal cells in S1 and S2. In the predictive coding scheme, gain modulation of superficial pyramidal cells corresponds to increased precision (inverse variance or certainty) of ascending prediction errors. Further, sensory deviance enhanced recurrent (forward and backward) connectivity between somatosensory and fronto-parietal regions. This increased recurrent connectivity is linked to prediction error minimization, as violations of sensory expectation generate prediction error signal conveyed by feed-forward connections, while predictions are mediated by backward connections from higher order regions to sensory areas.
Conclusion
The computational theory of predictive coding provides a compelling explanation of the mechanisms underlying deviance detection and attention to pain in modulating the magnitude of pain-related evoked responses. Neurobiologically, this modulation reflects coupling changes in connection strength within and between regions of a somatosensory network, linked to precision-encoding and prediction error minimization.
Title: Interaction Between Conditioned Pain Modulation (Cpm) And Temporal Summation: A Comparison Of Two Different Stimulus Modalities

Poster Number PTH423

Authors
C. Horn-Hofmann, E. Schnabel, M. Kunz, M. Madden, S. Lautenbacher

University of Bamberg, Bamberg, Germany, Faculty of Medical Sciences, General Practice-Department, University of Groningen, Groningen, Netherlands

Aim of Investigation
Conditioned pain modulation (CPM) and temporal summation are two experimental paradigms capturing endogenous pain modulation which have recently gained importance due to their association with clinical pain. CPM describes the inhibition of the pain response to a test stimulus (TS) by the concurrent application of a second noxious stimulus, the conditioning stimulus (CS). Temporal summation describes the enhanced pain response to repetitively presented noxious stimuli compared to single stimuli despite identical stimulus intensity. A possible interaction between inhibitory (CPM) and excitatory (temporal summation) mechanisms might be of clinical relevance, but previous research has yielded inconsistent results. The present study aimed at testing the interaction between CPM and temporal summation effects using two different stimulus modalities, heat and pressure.

Results
For both pressure and heat TS, CPM was induced successfully by both CS intensities (hot and painful temperature). In addition, temporal summation was observed for both modalities, i.e. train stimuli were rated as more intense compared to single stimuli. Interestingly, an interaction between CPM and temporal summation was observed only for heat stimuli: Here, CPM was more effective in reducing the sensation elicited by the train stimulus than that elicited by the single stimulus when the painful CS was applied. Hence, the temporal summation effect, i.e. the difference between train stimulus and single stimulus, disappeared in this condition.

Conclusion
Equivocal results concerning interactions between CPM and temporal summation might be explained by a modality-dependence of such effects. In our study, CPM was more pronounced for train stimuli compared to single stimuli only for heat but not for pressure stimulation. These results indicate that for
heat stimuli, CPM might be more efficient when the pain system is in a sensitized state. Future research
should aim at further clarifying the role of stimulus modality for the interplay of CPM and temporal
summation.
Title: Spinal And Supraspinal Pain-Motor Interactions Triggered By A Transient Noxious Stimulus

Poster Number PTH424

Authors
M. Algoet, D. Julie, G. Iannetti, A. Mouraux

Université Catholique de Louvain, Brussels, Belgium, University College London, London, UNITED KINGDOM

Aim of Investigation
Our aim was to characterize, in healthy volunteers, the time course of the effects of a transient nociceptive stimulus delivered to a limb on motor function at spinal and supraspinal levels, and to explore the pattern of limb muscles affected by this modulation. We hypothesized that, because of its threatening nature, the occurrence of a short-lasting nociceptive stimulus should facilitate a defensive movement of the stimulated limb, which would translate in a specific and time-dependent modulation of motor excitability within the muscles involved in the withdrawal of the stimulated limb.

Results
We observed three main findings. First, nociceptive stimuli induced an early-latency (100 ms) enhancement of spinal motor excitability in hand flexor muscles of the stimulated hand. This early and lateralized facilitation was followed by a later (150-400 ms) decrease of motor excitability in extensor muscle and flexor hand muscles, which was maximal at the stimulated limb. Finally, we observed a long lasting (350-2000 ms) enhancement of MEPs in all muscles of the hand contralateral to the laser stimulus, extending 350 ms onwards after nociceptive stimulation. This later effect was attributed to nociceptive-motor interactions occurring at cortical level.

Conclusion
In the present study, we show that a transient nociceptive stimulus delivered to the hand dorsum induces a modulation of motor excitability in a limb specific manner and with a time-specific profile reflecting the relative contribution of spinal and supraspinal mechanisms. Previous studies have shown that non-nociceptive stimulation of the median nerve exerts a similar early latency enhancement and late latency reduction of motor excitability in the flexor muscles of the ipsilateral hand. In contrast, only nociceptive stimuli appear to induce a very long lasting asymmetry of motor excitability in the ipsilateral vs. contralateral limb, suggesting that the latter effect could be specific for nociception.
Title: Vocalizations During Pain And Their Phonetic Characteristics

Poster Number PTH425

Authors
S. Lautenbacher, M. Salinas-Ranneberg, M. Kunz, O. Niebuhr

University of Bamberg, Bamberg, Germany, Faculty of Medical Sciences, General Practice-Department, University of Groningen, Groningen, Netherlands, University of Southern Denmark, Sønderbor, Denmark

Aim of Investigation
The understanding of non-verbal indicators of pain is pressing and not far advanced. There are three behavioral domains with pain communicative function: facial expression, body posture and movement, and vocalization. Vocalization, although an omnipresent accompaniment of pain, is clearly understudied. Objective phonetic characterizations of pain vocalization are definitely missing. The present study aims to provide first insights.

Results
For phonetic characterization we used (as a first approach) mean and range of the fundamental frequency (F0) and the pitch of the vocalizations. There was an increase of mean F0 restricted to the highest temperature, which was clearly painful. This increase varied dependent on the vowel produced (strongest in 'u' and 'schwa', weaker in 'a' and 'i'). The other two phonetic parameters did not show any pain indicative changes.

Conclusion
There was a pain-associated change in the fundamental frequency, preferentially in those vowels with most subjective similarity to vocalizations that might be described as pain groaning. There are hints from the literature suggesting that other forms of distress might also be encoded in an increase of the fundamental frequency. The collected database also allows for more sophisticated phonetic analyses to comprehensively and objectively describe pain vocalizations.
Date: 09/29/2016 09:30:00 AM

**Title:** Faces Of Pain: Facial Activity Patterns In Chronic Pain Patients

**Poster Number** PTH426

**Authors**
M. Kunz, K. Prkachin, S. Lautenbacher

Faculty of Medical Sciences, General Practice-Department, University of Groningen, Groningen, Netherlands, University of Northern BC, Prince George, BC, University of Bamberg, Bamberg, Germany

**Aim of Investigation**
Facial activity during pain is not unspecific grimacing but conveys pain specific information to the social environment. Nevertheless, there is also substantial inter-individual variations in facial expressions of pain, suggesting that there might be various 'faces of pain'. Using experimental pain induction, we could recently show that variations in facial expressions can indeed be clustered into distinct facial activity patterns. With the present study, we wanted to investigate whether these facial activity patterns can also be found in chronic pain patients who are experiencing clinical pain conditions.

**Results**
Cluster analyses revealed distinct activity patterns during pain, which stably occurred across range-of-motion tests. Each cluster was composed of different combinations of single facial responses that have been previously shown to be indicative of pain, with most clusters involving the contraction of the muscles surrounding the eyes. Moreover, the distinct faces of pain were also comparable to the facial activity patterns found using experimental pain.

**Conclusion**
Cluster analyses revealed distinct activity patterns during pain, which stably occurred across range-of-motion tests. Each cluster was composed of different combinations of single facial responses that have been previously shown to be indicative of pain, with most clusters involving the contraction of the muscles surrounding the eyes. Moreover, the distinct faces of pain were also comparable to the facial activity patterns found using experimental pain.
Title: Effects Of A Painful Jaw Clenching Task And Visual, Auditory, And Gustatory Conditioning Stimuli In Healthy Participants

Poster Number PTH427

Authors

Section of Orofacial Pain and Jaw Function, Department of Dentistry, Aarhus University, Aarhus, Denmark, Graduate School of Dental Medicine, Hokkaido University, Sapporo, Japan, Sapporo, Japan, Division of International Affairs, Graduate School of Dental Medicine, Hokkaido University, Sapporo, Japan, Danish Pain Research Center and Dept. of Neurology, Aarhus University Hospital, Aarhus, Denmark, Dept. of Health Science and Technology, Aalborg University, Aalborg, Denmark, Department of Orofacial Pain and Jaw Function, Faculty of Odontology, Malmö University, Malmö, Sweden, Dept. of Crown and Bridge Prosthodontics, Graduate School of Dental Medicine, Hokkaido University, Sapporo, Japan, Malmo University, Malmo, SWEDEN, Aarhus University, Section of Orofacial Pain and Jaw Function Dept of Dentistry, Aarhus, DENMARK

Aim of Investigation
To investigate, in a randomized, controlled, crossover study, the effects of stressful conditioning stimuli, i.e. visual, auditory, and gustatory on pain sensitivity and affective states during experimental jaw clenching in healthy participants.

Results
The experimental clenching task evoked low levels of pain (peak NRS = 2.6 ± 1.5), unpleasantness (peak NRS = 3.7 ± 1.9), fatigue (peak NRS = 3.7 ± 1.8), and stress (peak NRS = 3.3 ± 1.8) (ANOVA: P < .001); however, there were no differences between sessions (ANOVA: P > .670). The unpleasantness scores were significantly higher during the visual, auditory, and gustatory stimuli at initial stimulation compared with control (students t-test: P < .050). The total PRI score (peak PRI = 7.7 ± 5.4) and the pain drawing area showed also significant effects of time (ANOVA: P < .014), but no differences were found between sessions (ANOVA: P > .592).

Conclusion
In this study, the experimental jaw clenching task in healthy participants resulted in low levels of pain, unpleasantness, fatigue, and stress, and this effect was only marginally influenced by the conditioning
sensory stimuli suggesting the capability in healthy individuals to inhibit noise from multisensory integration. Further studies of multisensory integration in patients with chronic orofacial pain are warranted.
Title: Interaction Of Nerve Growth Factor (Ngf) And Glial Cell Line-Derived Neurotrophic Factor (Gdnf) In Inducing Muscular Mechanical Hyperalgesia In Rats

Poster Number: PTH428

Authors
K. Mizumura, S. Murase, C. Kihara, T. Nasu
Chubu University, College of Life and Health Sciences, Kasugai, Japan, Nihon Bioresearch Inc., Hashima, Japan, Mejiro University, Saitama, Japan

Aim of Investigation
We have previously shown that NGF and GDNF are upregulated through activation B2 bradykinin receptor and COX-2, respectively, in the muscle after lengthening contraction (LC). They sensitize muscle nociceptors to mechanical stimulation (Murase et al, J.Neurosci. 2010; Eur.J.Pain 2014). After blocking one of these pathways, delayed mechanical hyperalgesia after LC (delayed onset muscle soreness, DOMS) does not develop, indicating there must be interaction between NGF and GDNF pathways. To address this point we examined whether intramuscular injection of mixture of low dose NGF and GDNF, which by itself alone induces no muscular mechanical hyperalgesia, induces hyperalgesia. To know whether this interaction occurs at the primary afferent level, we performed pERK immunohistochemistry of DRG neurons.

Results
Exp 1) Intramuscular injection of low dose of NGF (0.1 µM) and GDNF (0.008 µM) did not induce mechanical hyperalgesia, yet the mixture of them (volume 20 µL) induced pronounced muscular mechanical hyperalgesia. Exp 2) The number of pERK (+) DRG neurons (L4 - L6) observed after the injection of low dose NGF or GDNF was almost the same as that after injection of PBS, in contrast, injection of their mixture clearly increased the number of pERK(+) neurons. The cell size distribution of the mixture of low dose NGF and GDNF was different from neither that of high dose of NGF (0.8 µM) nor that of GDNF (0.03 µM). Exp 3) Capsazepine 50 µM almost completely reversed the mechanical hyperalgesia induced by the low dose mixture of NGF and GDNF, amiloride 50 mM partially reversed it. On the other hand none of CGRP antagonist CGRP(8-37) (20, 100 µM), NK1 receptor antagonist L-703606 (0.1,1 mM), or NMDA receptor antagonist DL-AP5 (0.5 mM, 5 mM) reversed the mechanical hyperalgesia induced by the mixture of low dose NGF and GDNF.
Conclusion
These results demonstrate that NGF and GDNF interact at the primary afferent level. Previous report suggests that DRG neurons sensitive to NGF and those sensitive GDNF belong to different subsets, and overlap between two groups is small. However, present pERK study suggests that NGF, GDNF and the mixture of their low doses sensitize the same neuron group. This may suggest that interaction may occur through substances that afferent neurons release, and that neither substance P, CGRP nor glutamate is responsible for this. Alternatively some cells in the muscle other than afferents may play a role in this interaction.
Title: In Vitro Cellular Model Of Non-Canonical Signaling Linked To Hyperalgesic Priming: Potentiation Of Camp-Erk Responses Downstream Of Pka, Pkc And Rapgef2

Poster Number PTH429

Authors

University Hospital of Cologne, Cologne, Germany, NIH Pain Center (UCSF), San Francisco, CA

Aim of Investigation
In vitro characterization of the signaling alterations imposed on the cAMP signaling cascade by the IL-6 family member Oncostatin M.

Results
We characterized the signaling effects of the cytokine oncostatin M (OSM) onto subgroups of nociceptive neurons in culture. We used phospho-PKA-RII and phospho-ERK to monitor the responses in the canonical (cAMP/PKA) and alternative (cAMP to ERK) pathways downstream of GPCR activation. OSM pretreatment strongly potentiated GPCR-induced ERK response amplitudes as well as response duration. As switching of GPCR/cAMP signaling to other pathways than PKA as well as the prolongation to GPCR-ligands of the cellular results resemble the classical aspects of in vivo priming, we tested, if OSM induces priming in male adult rats. Indeed, similar to well established priming agents OSM resulted in a strongly prolonged PGE2-induced hyperalgesia if tested 1 week after a single intradermal injection. Next, we analyzed in depth which cellular changes underlie OSM-based priming. Neither forskolin dose response nor PKA-RII amplitudes nor PKA-RII kinetics were altered by OSM pretreatment. We found OSM-priming to be specific to the cAMP pathway, as GDNF-induced pERK responses were not affected by OSM exposure. cAMP activation of the ERK cascade was mediated by both PKA and RapGEF2, with OSM modulating the signaling downstream of both components. OSM effects in vitro were resistant to the wash-out of the cytokine, required hours as well as de novo protein expression to manifest, and were specific to IB4(+)/CaMKIIa(+) neurons. Finally, we tested if the effects observed with OSM in vitro are also observed with other priming agents as GDNF or NGF. Interestingly, only GDNF had similar effects to OSM on the cAMP-ERK crosstalk.
Conclusion

Switching of intracellular signaling cascades and strong enhancement of PGE2-induced hyperalgesia over long periods of time are hallmarks of priming. The detailed cellular signaling analysis allowed us to identify a novel priming agent, OSM. In addition to the previously identified mechanisms based on G-protein switch and EPAC signaling, our results on OSM-induced priming suggest a third mechanism based on potentiation of the ERK activity via the pathways normally linking cAMP production with ERK activity. We propose this cellular model of OSM-induced signaling switch as a novel tool to study in detail non-canonical signaling induced by priming agents.
Title: Cxcl12 Regulates The Axon Morphogenesis Of Sympathetic Neuron In Vitro

Poster Number PTH430

Authors
J. Xu, X. Liu, B. Ma, K. Ma

Pain management Center, Xinhua Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

Aim of Investigation
Sympathetic fiber innervation changes in various pathologic situations. Abnormal sympathetic sprouting in skin and dorsal root ganglions has been found in animal models and human cadavers of chronic pain. The roles of cytokines and neurotrophins are responsible for the sprouting. Systemic anti-inflammatory corticosteroid can reduce sympathetic sprouting as well as pain behaviors suggests that inflammation may contribute to the abnormal innervation, too. Chemokines are small cytokines induced by proinflammatory stimuli. Emerging evidences indicate that CXCL12, a CXC subfamily chemokine, contributes to the initiation and maintenance of chronic pain. Previous studies also show that CXCL12 can affect axon outgrowth. So we proposed that, CXCL12 could regulate the sympathetic fiber morphogenesis in vitro, which might suggest a new way of CXCL12 to participate in chronic pain.

Results
1. CXCR4 and CXCR7 were co-expressed with mouse sympathetic neurons after 24 hours after plated. (Fig.2)
2. Rat sympathetic neurons treated with CXCL12 for 12 hours showed more complexed axonal Sholl morphology (P<0.001) and more branch points (P<0.05), but no significant total cable length of axons (P>0.05). However, when we focused on the root (first process) of the exposed axons, Sholl plots showed less complexity compared with the control group (P<0.0001). (Fig.3)
3. CXCL12 might reduce the axon repellent effects of semaphorin3C on cultured mouse sympathetic neurons. (Fig.4)

Conclusion
1. CXCR4 and CXCR7 were expressed on the primary cultured sympathetic neurons. 2. Sympathetic neurons treated with CXCL12 showed more complex axon morphogenesis, but the complexity of the first process axons were significantly lower. 3. CXCL12 might change cultured sympathetic axon
morphogenesis by both promoting axon terminal branching and reducing the effectiveness of repellent Semaphorin3C.
Title: Upregulation Of Ih Expressed In Ib4-Negative Aδ Nociceptive Drg Neurons Contributes To Mechanical Hypersensitivity Associated With Cervical Radiculopathic Pain

Poster Number PTH431

Authors
C. Luo, D. Liu, N. Lu, W. Han, R. Xie, S. Hu

Department of Neurobiology, Fourth Military Medical University, Xi'an, China

Aim of Investigation
Some patients with cervical radiculopathy develop severe pain, which can be extremely difficult to treat and severely limit patients' daily functions. Cervical radiculopathic pain (CRP) often associates with aberrant mechanical hypersensitivity (hyperalgesia and allodynia). Primary sensory neuron's ability to sense mechanical force forms mechanotransduction. However, whether this property undergoes activity-dependent plastic changes and underlies mechanical hypersensitivity associated with CRP are poorly understood.

Results
Given the prominent contradiction between highly-increasing incidence of cervical radiculopathy and the serious lacking of animal models reflecting actual pathophysiological processes of CRP, here we first present a new CRP model producing a chronic compression of C7/C8 DRGs in rats by inserting a fine stainless steel rod into corresponding intervertebral foramen and thereby producing a stenosis of the intervertebral foramen. The operated rats displayed a pronounced, long-lasting behavioral phenotype characterized by intense mechanical hypersensitivity in the ipsilateral forepaw that mimics the pain symptoms observed clinically. In addition, significant thermal hyperalgesia and frequent spontaneous pain behaviors were observed as well. Binding to isolectin-B4 (IB4) have been used to define different subgroups of nociceptive DRG neurons. Following chronic compression of C7/C8 DRGs, IB4 negative Aδ-type (IB4- Aδ) nociceptive DRG neurons, but not IB4-positive (IB4+) or IB4- C-type nociceptive neurons exhibited frequent spontaneous activity together with robust increase of excitability. Furthermore, focal mechanical stimulation on the somata of IB4- Aδ neurons derived from CRP rats elicited exaggerated high-frequency firing and long-lasting afterdischarge, indicative of abnormal neuronal mechanical hypersensitivity. Upregulated HCN1 and HCN3 channels and increased Ih current on this subset of primary nociceptors underlies the spontaneous activity together with neuronal mechanical
hypersensitivity, which further contributes to the behavioral mechanical hypersensitivity associated with CRP.

Conclusion
This study sheds new light on the functional plasticity of a specific subset of nociceptive DRG neurons, namely IB4-\(\text{A}\delta\) neurons to mechanical stimulation and reveals a novel mechanism that could underlie the mechanical hypersensitivity associated with CRP.
Title: Assessment Of Human Nerve Fiber Properties With Perception Threshold Tracking

Poster Number PTH432

Authors
T. Hoberg, L. Vestergaard, K. Hennings, L. Arendt-Nielsen, C. Mørch

SMI®, Department of Health Science and Technology, Aalborg University, Denmark., Aalborg, Denmark, Center for Neuroplasticity and Pain (CNAP), SMI®, Department of Health Science and Technology, Aalborg, Aalborg, Denmark

Aim of Investigation
Aim: Small nerve fibers can be selectively affected in peripheral neuropathies. Existing clinical neurophysiological technologies cannot assess the properties of small fibers. The aim of the study was to assess the membrane properties of small and large nerve fibers using the novel perception threshold tracking (PTT) technique and use topical application of lidocaine/prilocaine to modulate the response.

Results
Results: Application of lidocaine/prilocaine cream did not lead to significant changes of large-fiber-associated thresholds, however several changes were found for small-fiber-associated thresholds. With quantitative sensory testing significant changes were detected for cold detection threshold (p = 0.002), warm detection threshold (p = 0.002), and pinprick stimulation (p = 0.002). With PTT significant differences in thresholds were found for small fiber stimulation in the following conditions: rectangular electrical pulse of 1ms (p = 0.002), rectangular electrical pulse of 50μs (p = 0.002), the strength duration time constant (p = 0.019) and rheobase (p = 0.002). For conditioning pulses there were significant differences detected for depolarizing threshold electrotonus 20ms (p = 0.034), depolarizing threshold electrotonus 80ms (p = 0.05), and hyperpolarizing threshold electrotonus 80ms (p = 0.006).

Conclusion
Conclusions: The novel PTT technique may be useful for assessment and diagnosis of small fiber neuropathy as it may provide information about small fiber membrane properties. This study confirms that the technique is able to assess the membrane properties of both small and large nerve fibers in an experimental model of small fiber neuropathy based on automatic detection of perception thresholds.
Title: Identification And Characterization Of Pain-Specific Trpv1 Interactors

Poster Number PTH433

Authors
J. Sondermann, R. Abdelaziz, L. Avenali, M. Schmidt

Max Planck Institute of Experimental Medicine, Goettingen, Germany

Aim of Investigation
The transient receptor potential vanilloid 1 (TRPV1) channel is a polymodal sensor of a variety of irritants and noxious hot temperatures. The involvement of TRPV1 in different pain modalities has been well documented and together with its enriched expression in dorsal root ganglia (DRG) renders TRPV1 a promising target for novel analgesics. However, several TRPV1 antagonists that reached clinical trials are challenged by severe side effects because of their interference with the physiological function of TRPV1. An interesting alternative to TRPV1 blockage might be the targeting of such TRPV1 interaction partners that are specific for e.g. inflammatory or neuropathic pain. This strategy would provide a means to suppress pathological pain states while leaving nociceptive pain intact. However, little is known about the protein scaffold of TRPV1 during different pain states. Our aim is therefore, to identify and characterize TRPV1 interactors that are specifically formed under inflammatory pain.

Results
The analysis of the MS data revealed a significant regulation of the TRPV1 interactome upon induction of inflammatory pain. Using the Database for Annotation, Visualization and Integrated Discovery (DAVID) we performed GO analysis to get insights into altered cellular processes and protein networks among identified members of the interactome. Amongst others, the GO terms 'protein localization' and 'protein transport' were found to be enriched hinting towards alterations of TRPV1 trafficking during pathological states. Immuunochemical studies suggested co-expression of several candidates in DRG. The close proximity of TRPV1 and identified candidates was further substantiated by PLA validating our MS data. The functional relevance of one interaction for TRPV1-mediated nociceptive signaling was assessed by RNAi-mediated candidate knockdown followed by calcium imaging in DRG cultures. Interestingly, these functional studies revealed differences in TRPV1-mediated neuronal responses to capsaicin in DRG isolated from CFA-injected mice. Follow-up experiments will focus on in vivo modulation of selected candidates in order to evaluate their role for TRPV1-dependent pain behavior and inflammatory pain.
Conclusion
Our data show that members of the TRPV1 interactome are dynamically regulated during pain. Therefore, our data strongly suggest that protein-protein interactions specific for pathological pain exist. The knowledge about interactions occurring only during pathological states and whether they are pain-promoting or analgesic offers the opportunity to achieve analgesia by either stimulating or destabilizing those interactions without interfering with nociceptive pain and other physiological processes, respectively. Such findings can have important implications for the development of novel analgesics with higher efficacy and less side effects. In addition to revealing novel TRPV1-specific mechanism of painful conditions, the further investigation of the TRPV1 interactome paves the way for the characterization of unknown players for pathological pain as well as somatosensation in general.
Title: The Role Of Axonal Transport Disruption In The Development Of Axonal Mechanical Sensitivity Along Intact Nociceptive Axons

Poster Number PTH434

Authors
G. Goodwin, A. Dilley
University of Sussex, Brighton, west sussex, Brighton and Sussex Medical School, Falmer, United Kingdom

Aim of Investigation
The mechanical properties of regenerating axonal sprouts at a neuroma have been well described. However, work from our laboratory (1), and that of others (2), has shown that inflammation (neuritis) can cause intact nociceptive axons to become mechanically sensitive. Such axonal mechanical sensitivity (AMS) may drive movement-evoked radiating pain, and may be in part responsible for symptoms in those patients with neuropathic pain who do not have signs of an overt nerve injury. The mechanisms underlying AMS are not well understood. Our previous studies have revealed a reduction in axonal transport at the neuritis site (3), and we have shown that transported components are necessary for the development of AMS along inflamed axons (4). To better understand the role of axonal transport disruption in the development of AMS, we have used the anti-mitotic agent vinblastine to disrupt axonal transport. The local application of vinblastine to the rat sciatic nerve disrupts axonal transport in the absence of inflammation and causes intact C-fibre axons to develop AMS (4). In this study, we have investigated the time course of vinblastine-induced AMS and have examined the force-discharge relationship. Furthermore, we have begun to elucidate the channels that are responsible for such mechanical sensitivity.

Results
C-fibre axons became mechanically sensitive at the treatment site, which developed rapidly from day one (15.8%) and peaked on day four (n=5; 27.6%, p<0.05 compared to the sham group (n=3; 0%), Fisher Exact test). By day 14, the mechanical sensitivity had recovered. The mean thresholds for AMS was 103 (range 40-204mN; n=3). There was a positive relationship between force applied and firing rate (r² = 0.65). The average firing rate at 50% of maximum force was 4-8.5 Hz. 50uM ruthenium red caused a 38.5% increase in the threshold of mechanical sensitivity (n=1). The mean number of spikes elicited by 173 mN force decreased from 22.6 to 12.6 (-44.2%).
Conclusion

Axonal transport disruption causes the rapid, yet reversible, development of mechanical sensitivity along intact axons. This reversibility of AMS is consistent with the short time course of axonal transport disruption (3). The range of thresholds for AMS indicates that these axons are highly responsive to mechanical stimulation. A change in the force-discharge relationship by ruthenium red suggests that ion channels blocked by this agent may be in part responsible for the AMS. These channels include the transient receptor potential (TRP) family of channels. We have hypothesised that TRP channels transported to the periphery are accumulating at the treatment site, leading to a hot spot of mechanical sensitivity. Finally, the vinblastine lesion may provide a more sensitive method for determining the channels responsible for noxious mechanical transduction.

Title: Establishing Myelinating Cocultures With Human Ipscs To Study Demyelination And Nociception In Peripheral Neuropathies

Poster Number PTH435

Authors
A. Clark, M. Kaller, S. Rinaldi, D. Bennett

University of Oxford, Oxford, United Kingdom

Aim of Investigation
Human induced pluripotent stem cells (iPSCs) have opened up new methods to better understand disease and have created opportunities for therapeutic approaches. Rapid progress has been made in establishing protocols for the differentiation of iPSCs into specific cellular lineages, including neural crest derivatives such as sensory neurons and Schwann cells. Our aim is to coculture these neural crest derivatives to understand important interactions and signaling pathways between these human cells that mediate processes including myelination, protein trafficking and neuronal excitability.

Results
We have investigated signalling between the neuron and glial by interacting with the neuregulin pathway, using small molecules to block its receptor or enzymatic cleavage we can modulate the levels of myelination. Furthermore we have transfected the neurons with AAVs containing a neuregulin construct and we observe a dose dependent increase in the levels of myelination. In order to assess the clinical relevance of our model, we incubated the myelinating cocultures with antibodies directed against the disialoysl epitopes present on GD1b and GT1b gangliosides. These antibodies are detected in predominantly sensory variants of the inflammatory neuropathies, including Guillain Barre syndrome, and can be associated with demyelination, sensory loss, and pain. Previously generated mouse monoclonal antibodies with this specificity bind to unmyelinated axons and nodes of Ranvier in the myelinated cocultures. Long term incubation with the antibodies significantly reduced the extent of myelination compared to untreated controls at 4 weeks. We are currently advancing this model further by differentiating Schwann cells from human iPSCs. We have applied these Schwann cells to iPSC-derived sensory neurons to create an entirely human myelinating co-culture. RNA-sequencing has confirmed their similarity to human cadaver derived primary Schwann cells. When cocultured with human iPSC derived neurons, they successfully align with the axon and form MBP positive internodes. We are in the process of differentiating Schwann cells from iPSCs derived from patients with acquired...
and inherited neuropathies. These patients often have some degree of demyelination and a record of chronic pain.

**Conclusion**

We aim to create human myelinating cocultures from iPSCs in order to study axon-glia interactions in a system disrupted by mutations that influence myelination and nociception. Our goal is to use these in vitro models to study disease pathophysiology and progression.
Title: A Novel Method To Study Tumor-Nerve Interaction For Oral Cancer Pain

Poster Number PTH436

Authors
S. RUPAREL, M. Bendele, L. Chodroff, A. Wallace, V. Valenzuela

University of Texas Health Science Center At San Antonio, san antonio, TX, University of Texas Health Science Center At San Antonio, San Antonio, TX

Aim of Investigation
Pain is often the presenting and the top ranked symptom in oral cancer patients, leading to significant reduction in quality of life. Pain in these patients is of multifactorial etiology and unlike other cancers is produced at the primary site of the tumor even when the tumor is still quite small in size. This suggests that tumor cells control the activity of surrounding nociceptors leading to the activation of pain pathways. It is therefore crucial to understand the interaction of oral tumor cells with surrounding nociceptors to delineate mechanisms by which oral cancer produces pain. The current study developed and validated a novel orthotopic in vivo tongue cancer model that mimics patient symptoms. Moreover, using this model, we have established a novel electrophysiology method that allows us to study tumor-nerve interactions at the site of primary tumor growth.

Results
Our data show that HSC2 injected mice produced observable tumors by day 9 post inoculation whereas NOK injected mice showed no visible growth. The tumor was well vascularized as well as innervated with sensory and sympathetic fibers. In addition, tumor growth produced a significant reduction in feeding behavior that was reversed by analgesics like indomethacin (5 mg/kg) and tramadol (20 mg/kg) as well as produced a central nociceptive state as measured by CPP. HSC2 tumor bearing mice also showed reduced threshold to von Frey testing in the vibrissal pad suggesting facial pain, indicating central sensitization of the V2 trigeminal nerve. We were also able to successfully dissect the tumor-tongue and the lingual nerve and record increased nerve discharges upon mechanical stimulations and compare with normal tongues.

Conclusion
Our in vivo orthotopic tumor model is the first oral cancer pain model that reflects patient symptoms. We have now used this model to develop a tumor-tongue electrophysiology method that allows
studying interactions of tumor and peripheral nerve fibers in several different ways. Currently we are characterizing the different types of fibers with different stimulus modalities to determine the effect of oral tumor on sensory firing. Supported in part by William and Ella Owen's Foundation and American Cancer Society.
Title: Ultra Short Diode Laser Stimulation For Investigation Of Heat Transduction Mechanisms In Native Rat Drg Neurons And Cells Heterologously Expressing The Capsaicin-Receptor Trpv1

Poster Number PTH437

Authors
D. Rosenberger, E. Jubileum, U. Binzen, W. Greffrath, R. Treede
Heidelberg University, Mannheim, Germany

Aim of Investigation
To characterise the molecular mechanisms for the transduction of ultra short near-infrared laser heat stimulation.

Results
When challenged with laser stimuli of 0.7 mJ (135 mW, 5 ms) 61 % of DRG neurons (n = 115) displayed a significant increase in \([\text{Ca}^{2+}]_{i}\). All laser-sensitive DRGs were also sensitive to capsaicin (10 μM), indicating expression of rTRPV1, but none of the capsaicin-insensitive neurons (n = 10) was laser heat sensitive. Of rTRPV1 transfected and capsaicin-sensitive HEK cells (n = 990) 87 % were also sensitive to laser stimuli, whereas of the capsaicin-insensitive ones (i.e. insufficient transfection; n = 318) only 9.1 % and of mock transfected cells (n = 722) 3.5 % showed a significant laser response. However rTRPV1-HEK cells displayed a significant larger increase in \([\text{Ca}^{2+}]_{i}\) than DRG neurons at this stimulus intensity (265.3 ± 4.4 % vs 144.3 ± 3.7 %; p < 0.01). The threshold in native DRG neurons at a stimulus intensity of 35 mW was 78 ms (2.7 mJ; n = 25) and disproportionately decreased when increasing laser power (to 4.6 ms at 135 mW; 0.6 mJ; n = 115). rTRPV1-HEK cells had similar thresholds ranging from 9.1 ms at 80 mW (0.7 mJ; n = 142) to 1.7 ms at 190 mW (0.3 mJ; n = 150). An overlap of the laser spot with about one third of a neuron was required for induction of \([\text{Ca}^{2+}]_{i}\)-transients throughout the whole cell (n = 16), spreading faster than temporal resolution (≈ 331 μm/s; n = 20). Amplitudes increased with higher overlap, suggesting contribution of \([\text{Ca}^{2+}]_{i}\)-influx through laser targeted heat-activated \([\text{Ca}^{2+}]_{i}\)-channels. Heat and capsaicin-sensitivity were highly dependent in both cell types (p < 0.001, χ-test, respectively). Hence, the application of the competitive TRPV1 antagonist capsazepine (10 μM) resulted in a significant reduction of the \([\text{Ca}^{2+}]_{i}\)-transients to about 40 % of the response in vehicle-treated neurons (1.1 and 17.9 mJ; n = 20; p < 0.01, respectively) and to 78 % in rTRPV1 positive HEK cells (0.7 mJ; n = 1926; p < 0.001).
Conclusion

These results demonstrate that Ca\(^{2+}\)-dependent heat transduction mechanisms in native nociceptive neurons and rTRPV1 expressing HEK cells can be activated by ultra short (< 2 ms, 190 mW) diode laser stimulation. In both cell types laser heat responses mainly depend on the expression of the capsaicin-receptor TRPV1. When rapidly heating a small volume, less laser energy is needed for cell activation at higher power and shorter duration of stimuli, due to reduction of lateral diffusion. Spatially confined stimulation of cells leads to an activation of targeted heat-gated Ca\(^{2+}\)-channels, indicating underlying spatial summation mechanisms. Our laser systems provide a platform for investigating heat transduction mechanisms with high spatial and temporal resolution at a high cell throughput. Furthermore, translational research is simplified since comparable lasers stimuli can easily be transferred directly to human pain experiments.
Title: Role Of 5-Ht Receptors In Peripheral Nociceptive Processing In Mice

Poster Number PTH438

Authors
E. Nascimento Junior, T. Romero, M. Dutra, I. Duarte, B. Fiebich, M. Coelho

Federal University of Piauí, Parnaíba, Piauí, Federal University of Minas Gerais, Department of Pharmacology, Belo Horizonte, Minas Gerais, Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, University of Freiburg Medical School, Freiburg, Germany

Aim of Investigation
5-Hydroxytryptamine (5-HT, serotonin) is a cell-derived vasoactive amine, mainly released by platelets (in humans), mast cells (in rodents) and endothelial cells. It is a regulator of smooth muscle in the cardiovascular system and the gastrointestinal tract, an enhancer of platelet aggregation, and a neurotransmitter in the central nervous system. 5-HT receptor subtypes have been described in different tissues and demonstrated to be involved in painful and inflammatory conditions. Although 5-HT is implicated in the regulation of a number of physiological processes and their malfunctions, including those related to inflammation, the exact sites and mechanisms of its action still remain under investigation. The aim of this study is to investigate the role played by 5-HT and its receptors in the peripheral nociceptive response in mice.

Results
Intraplantar (i.pl.) injections of 5-HT (10, 20, 40 or 80 μg/paw; 20 μl) induced mechanical allodynia in mice. Pretreatment (-10 min; 20 μl; i.pl.) with isamoltane (5 μg; 5-HT1B antagonist) and ketanserine (1 μg; 5-HT2A antagonist) did not affect the mechanical allodynia. On the other hand, the mechanical allodynia was reverted by BRL 15572 (10 μg; 5-HT1D antagonist) and SB 269970 (25 μg; 5-HT7 antagonist) and exacerbated by ondansetron (20 μg; 5-HT3 antagonist).

Conclusion
The results indicate that 5-HT, by its interaction with 5-HT1D and 5-HT7 receptors, play an important role in the peripheral nociceptive processing. Interestingly, 5-HT3 receptors may mediate antinociceptive effect under the experimental conditions used in this study.
Aim of Investigation
Brain-derived neurotrophic factor (BDNF) is expressed in a subset of small-diameter primary afferent (DRG) neurons, and is upregulated following peripheral nerve injury. It is unclear, however, how this upregulation contributes to chronic pain states, or even whether BDNF signaling influences acute pain processing. Attempts to study primary afferent-derived BDNF using gene deletion approaches are confounded by the fact that BDNF is essential for normal DRG development. To address this limitation, we used a tamoxifen-inducible Cre approach to delete BDNF selectively from primary afferent neurons in adult animals, and analyzed the consequences of this deletion in a battery of tests of pain and itch processing.

Results
After one week of tamoxifen treatment, BDNF conditional knockout (cKO) mice showed greater than 90% reduction in primary afferent BDNF mRNA (assayed by qPCR), but no change in spinal cord or brain levels. Baseline mechanical thresholds in these animals were normal, as were responses to all pruritogens tested. However, the latency to respond in tests of acute heat pain sensitivity increased by at least 50%, suggesting that BDNF selectively contributes to the transmission of pain messages carried by TRPV1-expressing primary afferents. Unexpectedly, these same animals also displayed a three-fold increase in the duration of their response to injection of capsaicin into the hindpaw. Ongoing studies are assessing BDNF's contribution to behavior in tissue and nerve injury with formalin, carrageenan, spared-nerve injury and paclitaxel.

Conclusion
As noxious heat exerts its effects in large part via TRPV1, these divergent responses to noxious heat and capsaicin are clearly paradoxical. However, although TRPV1-expressing afferents are critical for the
detection of capsaicin-induced nocifensive behavior, deletion of TRPV1 does not completely eliminate responses to noxious thermal stimulation. This suggests that there are other, yet unidentified heat-sensitive channels that mediate nocifensive behavior, and that these channels and TRPV1 might be differentially regulated by BDNF. The first step toward addressing this question is to establish the extent to which BDNF is associated with TRPV1-expressing afferents. Unfortunately, BDNF antibodies are notoriously unreliable, making it difficult to characterize BDNF expression with immunohistochemistry. To this end, we have generated a Cre-dependent BDNF-reporter line that is presently under study.
Date: 09/29/2016 09:30:00 AM

Title: Involvement Of P2X4 Receptor Of Dorsal Root Ganglion On Streptozotocin-Induced Diabetic Peripheral Neuropathic Hyperalgesia In Rats

Poster Number PTH440

Authors
C. Parada, G. dos Santos, M. Athie, I. Bonet, F. Farias, C. TAMBELI, C. Muller, J. Teixeira

State University of Campinas - UNICAMP Institute of Biology, Campinas, Sao Paulo, State University of Campinas, Campinas - SP, Brazil, State University of Campinas, Campinas/SP, Brazil, INSTITUTE OF BIOLOGY - UNIVERSITY OF CAMPINAS, CAMPINAS, SÃO PAULO, PharmaCenter Bonn, Pharmaceutical Chemistry I, University of Bonn, Bonn, Germany

Aim of Investigation
Diabetic Peripheral Neuropathy (DPN) manifests in 50-60% of types I and II diabetic patients and is the major cause of limb amputation. There are evidences that the activation of P2X4 receptors expressed in spinal cord glial cells is essential for neuropathic pain processes. However, no studies to date have investigated the involvement of glial cells’P2X4 receptor from dorsal root ganglion (DRG) on DPN. Therefore, the aim of this study was to investigate the role of P2X4 receptors in glial cells of DRG on established mechanical hyperalgesia in streptozotocin-induced DPN in rats. Diabetic Peripheral Neuropathy (DPN) manifests in 50-60% of types I and II diabetic patients and is the major cause of limb amputation. There are evidences that the activation of P2X4 receptors expressed in spinal cord glial cells is essential for neuropathic pain processes. However, no studies to date have investigated the involvement of glial cells’P2X4 receptor from dorsal root ganglion (DRG) on DPN. Therefore, the aim of this study was to investigate the role of P2X4 receptors in glial cells of DRG on established mechanical hyperalgesia in streptozotocin-induced DPN in rats. Diabetic Peripheral Neuropathy (DPN) manifests in 50-60% of types I and II diabetic patients and is the major cause of limb amputation. There are evidences that the activation of P2X4 receptors expressed in spinal cord glial cells is essential for neuropathic pain processes. However, no studies to date have investigated the involvement of glial cells’P2X4 receptor from dorsal root ganglion (DRG) on DPN. Therefore, the aim of this study was to investigate the role of P2X4 receptors in glial cells of DRG on established mechanical hyperalgesia in streptozotocin-induced DPN in rats.
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**Results**
The i.p. STZ administration (5 consecutive days) increased rats' blood glucose levels on days 7, 14, 21 and 28 after first STZ administration. In these hyperglicemic animals, a significant decrease in mechanical threshold started from the 14th day and continued to decline until the end of the protocol on 28th day, when compared with control group (p<0.05, two-way ANOVA, Bonferroni test). The P2X4 receptor antagonist administration (PSB-15417, at doses of 0.3, 1 and 3 mM - i.t. and 1 mM - i.gl.) significantly blocked the STZ-induced decrease of mechanical threshold at 1 and 3 hours after i.t. and i.gl. PSB-15417 administration (p<0.05, two-way ANOVA, Bonferroni test), when compared with its vehicle. The antisense-ODN against P2X4 receptor intrathecal administration (4 consecutive days) significantly blocked the STZ-induced decrease of mechanical threshold at 24 and 48 hours after the last antisense-ODN administration (p<0.05, two-way ANOVA, Bonferroni test) when compared with its mismatch. There is an increase of P2X4 receptor expression in DRG (L5) of STZ-induced DPN group (p<0.05, unpaired t-test) when compared with control group.

**Conclusion**
The results suggest the essential role of P2X4 receptor of the DRG in STZ-induced DPN. Therefore, this purinergic receptor present in peripheral nerve system (DRG) may be an interesting therapeutic target for the control of neuropathic pain in patients with diabetes.
Title: Interaction Of Trpv1 And Ano1 In Drg Neurons

Poster Number PTH441

Authors
Y. Takayama<sup>,2</sup><sup>,3</sup>, M. Tominaga<sup>,2</sup><sup>,3</sup>

Okazaki Institute for Integrative Bioscience, Okazaki, Japan, National Institute for Physiological Sciences, Okazaki, Japan, The Graduate University for Advanced Studies, Okazaki, Japan

Aim of Investigation
Capsaicin receptor TRPV1 is activated by various noxious stimuli, and the stimuli are converted into electrical signals in primary sensory neurons. It is believed that cation influx through TRPV1 causes depolarization, leading to the activation of voltage-gated sodium channels, followed by action potential generation. Anoctamin 1 (ANO1), a calcium-activated chloride channel, also expresses in TRPV1-positive DRG neurons. Therefore, we hypothesized that calcium entering into the cells through TRPV1 activation induces ANO1 activation followed by depolarization in DRG neurons because the intracellular chloride concentrations are maintained at a high level due to low expression of potassium-chloride co-transporter type 2. Here, we suggest the interaction between TRPV1 and ANO1 in DRG neurons and the pain enhancement mechanism.

Results
Capsaicin-activated currents were significantly larger in HEK293T cells expressing both TRPV1 and ANO1 than in cells expressing TRPV1 or ANO1 alone. Furthermore, direct interaction between TRPV1 and ANO1 was suggested by immunoprecipitation in both HEK293T cells and in DRG, which could effectively drive the TRPV1-ANO1 functional interaction through the increase in intracellular calcium. Similarly, in mouse DRG neurons, capsaicin-activated inward currents were significantly inhibited by a specific ANO1 antagonist, T16Ainh-A01 (A01) in the presence of a high concentration of EGTA, but not BAPTA. And the concomitant administration of A01 inhibited capsaicin-evoked action potential generation in DRG neurons probably through the interaction because A01 did not affect the action potential generations by current injection and the currents of voltage-gated sodium, potassium and calcium channels. Capsaicin-evoked pain-related behaviors were inhibited by A01.

Conclusion
TRPV1 and ANO1 work as receptors activated by noxious stimuli in sensory nerve endings. It is believed
that activation of the two channels causes cation influx and anion efflux, respectively, both of which lead
to depolarization. We show that ANO1 is activated by calcium ions entering neurons through TRPV1
activation based on their physical binding on the cell membrane. Indeed, both capsaicin-activated
inward currents in sensory neurons and capsaicin-induced pain-related behaviors in mice were
significantly inhibited by ANO1 blockade. Thus, the interaction between TRPV1 and ANO1 functions is a
pain-enhancing mechanism.
Title: Transcription Factor Sp4 Is Expressed In Nociceptors And Required For Persistent Hyperalgesic States

Poster Number PTH442

Authors

University of California, San Francisco, San Francisco, CA, University of California, San Francisco, San Francisco, CA, Erasmus MC, Rotterdam, CA, Wakayama Medical University, Wakayama, Japan, Wakayama Medical University, Wakayama, Japan

Aim of Investigation
The development of persistent pain and hyperalgesia, whether initiated experimentally by an immune-mediated response (Complete Freund's Adjuvant – CFA), excess in neurotropic factor (Nerve Growth Factor – NGF) or exposure to platinum-based chemotherapeutic agents (Oxaliplatin - OX), rely in part on changes in gene expression within the nociceptive neurons residing in the peripheral sensory ganglion. Building on our understanding of the transcriptional machinery responsible for TRPV1 expression in nociceptors (Xue et al. J. Neurochem 2007), and its relationship to the Sp1-like transcription factor family (Chu et al. Mol Pain 2011), we have now studied transcription factor Sp4 in mouse dorsal root ganglion – DRG neurons, the consequence of its genetic reduction on pain behaviors induced by CFA, NGF and OX and its pharmacologic blockade.

Results
Immunofluorescence of wt. DRG tissue sections revealed that 90% of DRG neurons with Sp4 + nuclei were < 400 m2. Approximately 81% of Sp4+ staining DRG neurons also stained positive for other nociceptive markers: TRPV1 (42%), IB4 (35%) or both (~4%). Pain Behaviors: No significant differences were found between baseline thermal or cold paw withdrawal latencies nor mechanical thresholds of wt. versus Sp4 +/- mice. CFA – induced a persistent decrease in the thermal withdrawal latency for 10 days. In contrast CFA - treated Sp4 +/- mice, showed only a transient decrease in withdrawal latency (2-6hr), returning to control levels for the duration of the study. In a parallel set of experiments, Sp4+/- mice developed only transient mechanical allodynia that returned to baseline by day 10. Oxaliplatin OX (3mg/kg) in wt. mice induced a decrease in mechanical threshold and cold plate latency beginning at 24 hours and lasting up to three weeks. In contrast, OX- injected Sp4+/- mice failed to develop persistent
mechanical or cold allodynia. Treatment of OX – injected mice with the Sp1-like transcription factor inhibitor, mithramycin (MTM) (100 mcg/kg) (Zavala et al. Neurosci Lett. 2014), reversed both the mechanical and cold plate allodynia. Cultured DRG neurons derived from OX – treated wt. mice had the greatest percentage of cold – responding neurons. In contrast, DRG neurons derived from mice initially treated by OX then by MTM, showed a reversal of this phenomenon, with a reduction of cold-responding neurons.

**Conclusion**

Transcription factor Sp4 is expressed in a subset of specialized DRG neurons likely associated with nociception. Heterozygous Sp4 +/- mice developed only transient pain behaviors following treatments with CFA, NGF and OX. Studies with an Sp1-like factor inhibitor reversed OX – induced pain behaviors and mimicked the Sp4+/ condition. Sp4 represents a factor that may play an important role in the control of nociceptive gene expression under conditions of cellular injury and inflammation.
Title: Do Changes In The Endocannabinoid System Account For Higher Efficacy Of Peripherally-Restricted Cannabinoids In Alleviating Chronic Pain Symptoms Versus Their Antinociceptive Effects?

Poster Number PTH443

Authors
Y. Mulpuri, D. Dang, B. Schmidt, H. Seltzman, I. Spigelman

UCLA School of Dentistry, Los Angeles, CA, NYU College of Dentistry, New York, NY, Center for Drug Discovery, Research Triangle Institute International, Research Triangle Park, NC

Aim of Investigation
We developed a series of synthetic peripherally-restricted cannabinoids (PRCBs) and demonstrated the absence of central nervous system (CNS) side effects and minor antinociceptive effects (changes in latency of tail-flick responses to radiant heat) of PRCBs compared to the brain-permeant cannabinoid, HU-210 (Mulpuri et al, Soc. Neurosci. Abstr. Vol. 37:173.21, 2012). However, PRCBs are highly effective at alleviating mechanical allodynia symptoms in rodent models of cancer, sciatic nerve entrapment (SNE)-induced neuropathy, and chemotherapy (cisplatin)-induced peripheral neuropathy (CIPN). Here we tested the hypothesis that the higher efficacy of PRCBs in alleviating chronic pain symptoms versus their antinociceptive effects is due to cancer or neuropathy-induced alterations in the endocannabinoid system.

Results
Paw cancer (inoculated with human oral carcinoma cells) mechanical allodynia was ~75% suppressed by 0.6 mg/kg systemic PrNMI (4-{2-[(-1E)-1[4-propynaphthalen-1-yl]methylidene]-1H-inden-3-yl]ethyl)morpholine). In SNE rats, 0.6 mg/kg intraperitoneal PrNMI increased ipsilateral mechanical thresholds by 29 ±2 g, but only by 8 ±4 g in sham rats. In CIPN rats, 0.25 mg/kg intraplantar PrNMI increased mechanical withdrawal thresholds by 25 ±4 g. CB1R immunofluorescence was previously shown to increase in L5 DRG of paw cancer mice (Guerrero et al., Neurosci. Lett. 12:77-81, 2008). By contrast, neither the receptors nor the endocannabinoid system enzymes were significantly upregulated in DRG of SNE or CIPN rats. DAGL and MAGL were significantly downregulated in CIPN versus control rat DRG.
Conclusion
Our data suggest that in the SNE neuropathy and CIPN, increased efficacy of PRCBs is not due to increases in cannabinoid receptor expression.
Title: 50B11 Cells As A Peripheral Sensory Nociceptive Neuron Model For Neurotrophin Signalling.

Poster Number: PTH444

Authors
Flinders University, Adelaide, South Australia, University of Applied Sciences Kaiserslautern, Zweibrücken, Germany, Flinders University of South Australia, Adelaide, SA

Aim of Investigation
Stimulation and sensitization of nociceptive neurons with cell bodies in dorsal root ganglia (DRG) play an important role in the development of chronic and neuropathic pain. Investigations of nociceptive DRG neurons are limited by the absence of a suitable cellular high-throughput model. The aim of this study was to establish whether an immortalized rat embryonic DRG cell line (50B11) can be used as a model for the investigation of sphingolipid and neurotrophin specific nociceptive signalling in DRG neurons.

Results
Stimulation of 50B11 cells with forskolin for 24h (10 µM, n = 5) induced a significant increase in differentiation indicated by the increase in neuritogenesis. The increase in neurite length of differentiated cells remained constant whereas the percentage of differentiated cells decreased over 96h. Co-treatment with NGF (100ng/ml) had no additional effect on the proportion of differentiated cells or neurite length, but significantly increased the response of 50B11 cells to capsaicin (n=5). The majority of differentiated cells showed co-labelling for the markers of nociceptive neurons, isolectin B4 and calcitonin-gene related peptide, and expressed TRPV1, P2X3, TrkA and p75NTR receptor proteins. Differentiation with either forskolin and/or NGF was sufficient to reduce the calcium increase in response to ATP and increase calcium in response to capsaicin. Differentiation induced by forskolin/NGF also increased the relative mRNA expression levels for brain derived neurotrophic factor (Bdnf) decreased mRNA levels for the sphingosine kinase 2 (Sphk2) isoform but not for sphingosine kinase 1 (Sphk1)(n = 6). However, forskolin but not forskolin/NGF significantly increased mRNA levels for the neurotrophin receptor p75 with a similar trend in the low expressed neurotrophin TrkA receptor.

Conclusion
Taken together our data indicate that the 50B11 cell line shows characteristics of nociceptive neurons with growth factor-dependent changes of the nociceptive phenotype. This suggests that the cell line is a...
valuable tool for a high-throughput model system for the study of nociceptive signaling events downstream of TrkA and TrpV1 activation in peripheral nociceptors and suggest that independent regulation of sphingolipid synthesizing enzymes plays an important role in these nociceptive pathways.
Title: Hypotonicity-Induced Cell Swelling Activates Trpa1

Poster Number PTH445

Authors

Mandom Corporation, Suita, Osaka, Japan, Graduate School of Pharmaceutical Sciences, Osaka University, Suita, Osaka, Japan, Okazaki Institute for Integrative Bioscience, National Institute for Physiological Sciences, Nationa, Okazaki, Aichi, Okazaki Institute for Integrative Bioscience, Okazaki, Japan, Okazaki Institute for Integrative Bioscience, National Institutes of Natural Sciences, Aichi, Japan, Mandom Corporation, Osaka, Japan

Aim of Investigation
Hypotonic solutions can cause local pain sensation especially in the nasal and ocular mucosa. However, the molecular mechanisms of the pain sensation are still unknown. TRP channels are well recognized for their contributions to sensory transduction, responding to a wide variety of stimuli, including temperature, nociceptive stimuli, touch, osmolarity changes and pheromones. Among TRP channels, TRPV4 was reported to be an osmo- and mechano-sensor that could be activated by several chemicals as well as warmth. However, the role of TRPV4 in nociception is still under debate. TRPA1 has been proposed for the involvement in detection of a variety of chemical stimuli, including allyl isothiocyanate (AITC), a main component of mustard oil. Hypotonic conditions occurring after tissue damage and diseases often lead to allostynia. Although TRPA1 was reported to play a role in mechanical hyperalgesia, the role of this channel in sensing hypotonic conditions is still unknown. Therefore, we hypothesized that TRPA1 might be involved in nociception under hypotonic conditions in humans.

Results
We clarified the ability of human TRPA1 (hTRPA1) to respond to physical stimulus, and we evaluated the response of hTRPA1 to cell swelling under hypotonic conditions. We observed the modulation of hTRPA1 activity induced by AITC under hypotonic conditions using a Ca-imaging method. Moreover, cell swelling in hypotonic conditions evoked single-channel activation of hTRPA1 in a cell-attach mode when the patch pipette was attached after cell swelling under hypotonic conditions but not before swelling. Furthermore, the single-channel currents activated by cell swelling were inhibited by known hTRPA1 blockers. Since pre-application of thapsigargin did not affect the single-channel activation of hTRPA1
induced by cell swelling, changes in intracellular calcium concentrations were not related to the activation of hTRPA1 by physical stimuli.

**Conclusion**
Our findings suggest that cell swelling causes TRPA1 activation in cells under hypotonic conditions and that the TRPA1 activation could result in pain sensation in nasal and ocular mucosa.
Title: Examination Of The Role Of Endogenous Opioids In The Insensitivity-To-Pain Phenotype Of An Adult-Onset Nav1.7 Knockout Mouse

Poster Number PTH446

Authors
L. Deng, S. Shields, R. Reese, J. Kaminker, D. Hackos

Department of Neuroscience, Genentech, South San Francisco, CA, Department of Bioinformatics, Genentech, South San Francisco, CA

Aim of Investigation
Loss-of-function mutations in Nav1.7 lead to complete insensitivity to pain (CIP) in humans and a CIP-like phenotype in Nav1.7 KO mice. It has recently been suggested that up-regulation of endogenous opioids in DRG neurons following removal of Nav1.7 directly contributes to this insensitivity to pain phenotype. This is a distinct mechanism compared to the previous view that Nav1.7, the prominent TTX-sensitive Nav channel expressed in small-diameter DRG neurons, is required for the excitability of peripheral nociceptors. To examine this potential role of endogenous opioids in detail, we took advantage of an adult-onset Nav1.7 KO mouse that allows complete removal of Nav1.7 from the DRGs and sympathetic nervous system within 6-8 weeks following i.p. dosing with tamoxifen. These mice show a near complete deficit in heat nociception and acute mechanical nociception, providing multiple sensory modalities in which to assess the role of endogenous opioids.

Results
We observed a small 2-3 fold increase in the expression level of the preproenkephalin mRNA (Penk) within 2-3 weeks following tamoxifen injection which was more prominent in female vs. male mice. Despite the small fold-increase, RNAseq analysis demonstrated that Penk appears to be the most up-regulated gene observed following Nav1.7 deletion. However, in the tail flick assay for heat nociception, 2 mg/kg i.p. naloxone failed to reverse the analgesia due to loss of Nav1.7. This same dose of naloxone was able to reverse morphine-induced analgesia in the same assay. Additional naloxone experiments were conducted using the Hargreaves and Randall-Selitto assays.

Conclusion
Here we show that adult-onset removal of Nav1.7 does appear to cause a small 2-3 fold increase in Penk
mRNA expression in the DRG. However, it is unclear whether this increase in Penk expression contributes significantly to the CIP-like phenotype in Nav1.7 KO mice.
Title: Pharmacological Inhibition Of Nav1.7 With An Isoform-Selective Blocker In Wildtype Mice Largely Recapitulates The Phenotype Of Mice With Adult-Onset Genetic Deletion Of Scn9A

Poster Number PTH447

Authors
S. Shields, R. Reese, L. Deng, G. Bankar, S. Howard, D. Hackos

Genentech, South San Francisco, CA, Xenon Pharmaceuticals, Burnaby, British Columbia

Aim of Investigation
Our ultimate goal is to develop novel pain drugs that work by selectively targeting Nav1.7. To support this effort, our preclinical investigation takes a two-pronged approach: 1. We have generated a conditional knockout mouse model in which scn9a, the gene that encodes the voltage-gated sodium channel Nav1.7, can be deleted in adulthood. This model should demonstrate the maximal possible effect of selective blockade of Nav1.7 in adults. 2. We have developed a small molecule inhibitor tool compound that potently blocks mouse Nav1.7 (GX-3585; IC50: 9.6 nM) and is >10-fold selective over other voltage-gated sodium channel family members (Nav1.5, Nav1.6, Nav1.8). With these tools, we aimed to investigate the potential for Nav1.7 inhibition to provide meaningful anti-nociception and/or anti-allodynia in animal models of acute and chronic pain.

Results
Mice with adult-onset deletion of scn9a display a profound insensitivity to most modalities of acute pain. However, while cold alldynia in the SNI model was reversed or prevented by Nav1.7 removal, static mechanical alldynia was unexpectedly preserved. In wildtype C57Bl/6 mice dosed orally with GX-3585, we observed significant analgesic effects in tests of acute nociceptive thresholds of multiple modalities, in line with the expected action of an effective Nav1.7 inhibitor. Furthermore, significant anti-allodynic effects were observed in chronic pain models as well, largely recapitulating the behaviors observed in our Nav1.7 conditional knockout mice.

Conclusion
Here we show preclinical proof-of-concept evidence that selective pharmacological inhibition of Nav1.7 could be an effective strategy to provide pain relief.
Title: Mu-Delta Hetero-Dimerization And Peripheral Opioid Tolerance In Neuropathic Rats

Aim of Investigation
Background: Recent reports suggest that chronic morphine exposure upregulates mu-delta (µ-δ) heterodimers in specific rat brain regions involved in pain signaling (e.g., rostro-ventral medulla, nucleus accumbens).1 Moreover, increase in brain heterodimer levels may be linked to morphine tolerance, suggesting that the heteromer may play a role in central opioid tolerance.2 However, the role of peripheral µ-δ heterodimers in primary sensory neurons has not been examined, particularly after nerve injury and peripheral opioid tolerance. Aims: 1. To determine the effects of nerve injury and peripheral opioid tolerance on µ-δ heterodimer formation. 2. To determine if blocking heterodimerization in dorsal root ganglion (DRG) of neuropathic rats or using mu-delta heterodimer biased agonist alters neuropathic pain behavior and opioid tolerance.

Results
Results: DALDA attenuated SNL-induced mechanical allodynia (10 mg/kg) and thermal hyperalgesia (0.2 mg/kg) in rats. Repeated (3 days b.i.d) treatment with DALDA (10 mg/kg s.c) in SNL rats resulted in the development of tolerance to its inhibition of mechanical allodynia, but not thermal hyperalgesia. SNL led to a decrease in MOR expression and µ-δ heterodimers in injured primary sensory neurons (L5 DRG), but an increase in heterodimer levels in uninjured L4 DRG. In SNL rats, repeated DALDA and morphine treatment led to further increase in µ-δ heterodimers in both L4 and L5 DRG neurons. Blocking µ-δ heterodimer formation, using continuous infusion of the tat-peptide (500ng/day for 7 days), did not prevent development of tolerance to DALDA-induced inhibition of mechanical allodynia. In contrast, systemic administration of CMY5-1010 inhibited mechanical allodynia and thermal hyperalgesia in SNL rats at high (2 mg/kg s.c) but not at low dose (0.2 mg/kg s.c). Under chronic morphine tolerance condition, CMY5-1010 significantly inhibits both mechanical and thermal pain behavior at lower dose (0.2 mg/kg s.c).
Conclusion
Conclusion: These findings suggest an increase in μ-δ heterodimerization in primary sensory neurons after nerve injury and the development of peripheral opioid tolerance. However, blocking μ-δ heterodimer formation was not effective in preventing peripheral opioid tolerance. Rather, a μ-δ heterodimer agonist attenuated nerve injury-induced pain, especially after opioid tolerance.
Title: Mir-15B Role In The Oxaliplatin-Induced Neuropathic Pain

Poster Number PTH449

Authors
A. Sakai, N. Ito-Kuroki, N. Miyake, K. Miyake, T. Okada, A. Sakamoto, H. Suzuki
Nippon Medical School, Tokyo, Japan

Aim of Investigation
Although oxaliplatin is a key drug for colorectal cancer therapy, peripheral neuropathic pain seriously limits its availability as a dose-limiting adverse effect. Furthermore, the oxaliplatin-induced neuropathic pain can persist even after the chemotherapy has been stopped. However, the molecular mechanisms underlying the persistent neuropathic pain remains poorly understood and therefore no effective prophylaxis is available in clinical practice. MicroRNA is a noncoding small RNA involved in a variety of pathophysiology including cancer and neuropathic pain. Here, we examined the miRNA involvement in the oxaliplatin-induced neuropathic pain.

Results
Mechanical allodynia, but not thermal hyperalgesia, was induced at 7 days after first oxaliplatin injection and sustained at 28 days. miR-15b expression level was increased following the development of pain in the L5 DRG. Injection of AAV vector encoding the miR-15b gene effectively upregulated the miR-15b expression in the L5 DRG neurons. miR-15b overexpression caused significant mechanical allodynia in intact rats. Luciferase assay revealed that candidate target genes predicted by TargetScan were downregulated by miR-15b.

Conclusion
miR-15b-mediated translational repression may have a causal role in persistent neuropathic pain induced by oxaliplatin.
Title: Spinal Nociceptive Transmission From The Lower Urinary Tract

Poster Number PTH450

Authors
N. Akimoto, A. Hakozaki, M. Kawatani<sup>,1</sup>, K. Imoto<sup>,3</sup>, M. Kawatani<sup>,1</sup>, H. Furue<sup>,3</sup>

Department of Information Physiology, National Institute for Physiological Sciences, Okazaki, Japan,
Department of Neurophysiology, Akita University Graduate School of Medicine, Akita, Japan,
School of Life Science, The Graduate University for Advanced Studies, Okazaki, Japan

Aim of Investigation
Sacral spinal dorsal horn receives synaptic inputs not only from somatic but also from visceral afferent fibers, and has important roles in integrating the sensory information and controlling pelvic organ's functions including the lower urinary tract functions. Sensory information including nociceptive sensation from the pelvic organs is known to be conveyed to the sacral dorsal horn mediated by small myelinated Adelta and unmyelinated C afferent fibers. However, little is known about how the sacral dorsal horn receives pelvic sensory information in vivo.

Results
A subpopulation of dorsal root ganglion neurons were visualized with a retrogressive tracer, Fast-Dil injected into the bladder wall, and were different from the groups of the neurons retrogradely labelled with Fluoro-Gold injected into the urethra. Sacral dorsal horn neurons in vivo elicited action potentials in response to bladder filling and voiding. The sacral dorsal horn neurons were classified into two types based on their responsiveness: Type A neurons show a burst of action potentials that correlated to the rise in intravesical pressure during voiding, and type B neurons elicited firings at the peak pressure. Both groups of sacral dorsal horn neurons received inputs from slow conducting afferent fibers and type B neurons elicited action potentials by electrical urethra stimulation. Furthermore, in cystitis model rats, the action potential frequency of type B's responses at the peak pressure did not changed in comparison with that in normal rats. However, type B neurons responded to intravesical capsaicin which increased the micturition frequency.

Conclusion
Sensory information including nociceptive sensation from the bladder and urethra was separately
conveyed to the different types of sacral dorsal horn neurons, and the precise pattern of spike timing in each group of the neurons may be needed to implement appropriate micturition.
Title: Effects Of Ethanol On Gabaergic Synaptic Transmission In The Rat Spinal Dorsal Horn.

Poster Number PTH451

Authors
A. Yamada<sup>,2</sup>, M. Ohsawa, K. Kume, K. Imoto<sup>,3</sup>, H. Furue<sup>,3</sup>

National Institute for Physiological Sciences, Okazaki, Japan, Department of Neuropharmacology, Graduate School of Pharmaceutical Sciences, Nagoya City University, Nagoya, Japan, School of Life Science, The Graduate University for Advanced Studies, Okazaki, Japan

Aim of Investigation
Ethanol is known to be a potent modulator of synaptic transmission, and affect neural network function in the CNS. However, it is not fully understood how ethanol modulates nociceptive transmission. In the present study, we investigated the effects of acute ethanol on synaptic transmission in the spinal dorsal horn.

Results
SG neurons exhibited spontaneous excitatory postsynaptic currents (EPSCs) under voltage-clamp conditions at a holding potential of -70 mV. Bath-application of ethanol did not change the frequency and amplitude of spontaneous EPSCs. On the contrary, ethanol increased the frequency and amplitude of spontaneous inhibitory postsynaptic currents (IPSCs) at a holding potential of 0 mV. Venus-positive neurons in the spinal dorsal horn elicited action potentials in response to current injections through the recording pipette under current-clamp conditions. The firing properties of the neurons were similar to those of inhibitory neurons reported in previous studies. Venus positive neurons did not exhibit spontaneous firings at their resting membrane potentials. Ethanol evoked action potentials in the Venus-positive neurons.

Conclusion
Acute ethanol excites GABAergic neurons and augments GABAergic synaptic responses in the superficial dorsal horn. This spinal GABAergic augmentation by ethanol may have an antinociceptive action.
Aim of Investigation
NMDA receptor plays a key role in central sensitization, which is a mechanism of neuropathic pain after injury to the nervous system. N-methyl-D-aspartate receptor 2B (GRIN2B), a NMDAR subunit, has glutamate binding site and phosphorylation sites, and it interacts with postsynaptic density protein-95 (PSD-95). Therefore, we investigated to find out the role of GRIN2B related signaling pathway in neuropathic pain after peripheral nerve injury.

Results
In this study, 1) protein expression of GRIN2B increased within 4 days after SNL. This period was development phase of mechanical hypersensitivity in the ipsilateral side of the hind paw, and intrathecally administrated Ro 25-6981 reverted it more effectively than in the late phase. 2) GRIN Ser1303 phosphorylated until 21 days after SNL. The interaction between Ser1303 and CaMKII increased in the early phase, and AIP increased the mechanical hypersensitivity more than in the late phase. In contrast, the interaction between Ser1303 and PKC appeared in the late phase, and CHE reverted that in this phase more effectively than in the early phase. 3) The interaction between Ser1303 and PSD-95 was getting increased until 21 days after SNL. AIP and Ro 25-6981 reduced that in the early phase, but CHE did not.

Conclusion
Thus, our results suggested that the interaction between GRIN2B Ser1303 and PSD-95 may be a possible connector to turn the development phase of neuropathic pain into the maintenance phase after peripheral nerve injury.
Title: Phosphosrylation Of Serine 10 In Histone H3: A Novel Epigenetic Marker In The Spinal Cord Following A Burn Injury

Poster Number PTH453

Authors
J. Torres Perez, I. Nagy

Imperial College, London, United Kingdom, Imperial College London, London, United Kingdom

Aim of Investigation
Burn injury is the main source of accidental tissue damage. Controlling pain in burn injury patients, which is one of the most excruciating pain sensations that can be experienced, is still a major clinical challenge and an unmet medical need. Sensitisation, which depends on transcriptional changes, in spinal dorsal horn neurons plays a crucial role in the development of persistent pain in tissue injury, including burn injury. Phosphorylation of serine 10 in histone 3 (pS10H3) is a post-translational modification with a critical role in the regulation of transcriptional changes in neurons. The aim of the investigation is to study whether a scalding-type burn injury model up-regulates the expression of pS10H3 in spinal dorsal horn neurons.

Results
Western blotting detected a ~15 kDa mass band corresponding to pS10H3 and the statistical analysis revealed a significant up-regulation of pS10H3 after burn injury in the ipsilateral spinal cord (normalised densitometry ratio of pS10H3 and β-actin in burn: 3.22±0.42, n=4, in control: 1.27±0.22, n=4; p=0.006, Student's t-test). Immunolabelling revealed the expression of pS10H3 immunopositive nuclei of neurons in laminae I and II. The number of immunolabeled nuclei was around 10 cells per sections at 5 minutes post-injury. This expression level gradually returned to baseline levels at later time points. Sham injury did not induce up-regulation in pS10H3 expression in the spinal cord. At 5 minutes post-injury, 57±8.12% (n=4) of the pS10H3 immunopositive neurons were also positive for pERK1/2, whereas 84.74±1.85% (n=4) of the pERK1/2 immunopositive neurons showed pS10H3 staining. At 30 minutes post-injury, 72.2±7.73% (n=4) of the pS10H3 immunopositive nuclei expressed cFos, whereas 66.98±14.54% (n=4) of the cFos immunopositive nuclei were also immunolabelled for pS10H3.
Conclusion
We postulate that pS10H3 is novel epigenetic marker for nociceptive processing in superficial spinal dorsal horn neurons following a burn injury in the peripheral tissues.
Title: Less Efficacious Conditioned Pain Modulation As Measured With Upper Limb Nociceptive Flexion Reflex In Chronic Unilateral Knee Osteoarthritis: A Pilot Study

Poster Number PTH454

Authors
E. Lim, Y. Zhao, B. Viriyasaksathian, L. Lim, H. Hosain, K. Tan

Department of Physiotherapy, Singapore General Hospital, Singapore, Health and Social Sciences Cluster, Academic Programmes, Singapore Institute of Technology, Singapore, Department of Clinical Research, Singapore General Hospital, Singapore, Division of Research, Singapore General Hospital, Singapore, Department of Anaesthesiology, Singapore General Hospital, Singapore, Singapore

Aim of Investigation
Chronic knee osteoarthritis (OA) is a major cause of disability, and it poses a substantial economic burden in Singapore. A less deficient conditioned pain modulation (CPM), which is also known as counter-irritation and a commonly used paradigm to evaluate endogenous pain inhibitory function in humans, has been demonstrated in chronic knee OA. However, the use of quantitative sensory testing (e.g. pressure pain threshold), which relies more on cognitive processes, has often been used as the test stimulus in CPM studies. To our knowledge, there has not been any studies which have used a neurophysiological measure to evaluate CPM in chronic musculoskeletal pain conditions. Therefore, we aimed to use the upper limb nociceptive flexion reflex (NFR) threshold to compare CPM between healthy participants and patients with chronic knee OA.

Results
Fourteen healthy participants and 9 patients with chronic unilateral knee OA were recruited. Compared to healthy participants, patients with chronic unilateral knee OA exhibited a 34.5% (95% confidence interval [CI] 6.32 to 62.7, P =0.019) reduction in CPM. The 2-way ANOVA showed that there was a time main effect [F(2,20) = 5.534, P = 0.012], and time by condition interaction effect [F(2,20) = 3.707, P = 0.043]. No other effects were identified. The mean pre-heat NFR and during-heat NFR thresholds (standard error, SE) were 14.9 (2.09) mA and 19.7 (2.36) mA respectively in the healthy control group. In contrast, the mean pre-heat and during-heat NFR thresholds (SE) were 16.2(2.61) mA and 16.7 (2.93) mA respectively in the chronic knee OA group.
Conclusion
The results suggest a less efficacious CPM amongst patients with chronic unilateral OA knee, as evident with the use of upper limb NFR threshold. This infers an impaired endogenous pain inhibition in response to the noxious thermal stimulus, which supports the presence of a dysfunctional internal pain modulatory system among subjects with chronic unilateral knee OA. However, due to the small sample size, further studies are warranted to confirm this preliminary finding.
Title: Incision-Induced Hyperalgesia In Adult Rats: Sexually Dimorphic Response To Prior Neonatal Incision And Perioperative Minocycline

Poster Number PTH455

Authors
S. Walker, O. Moriarty, Y. Tu, M. Salter, S. Beggs

UCL Institute of Child Health, London WC1N 1EH., United Kingdom, The Hospital for Sick Children, Toronto, Toronto, ON, Hospital for Sick Children/University of Toronto, Toronto, Ontario

Aim of Investigation
Adult incision-related hyperalgesia is enhanced following prior neonatal incision. Microglial priming in the spinal dorsal horn contributes to this enhanced response, as increased hyperalgesia in adulthood is accompanied by an increased degree and duration of microglial reactivity [2]. Furthermore, administration of microglial inhibitors at the time of adult injury reduced both the enhanced behavioural response and microglial reactivity in male rats [2; 3]. Microglia are critical contributors to pain signalling; however, neuroimmune responses may be sexually dimorphic, and inhibition of microglial activation has been shown to alleviate peripheral nerve injury-induced pain hypersensitivity in male but not female mice [4]. We aimed to further characterise the impact of prior neonatal incision in rats, and to investigate the effect of microglial inhibition with minocycline at the time of neonatal injury. We also sought to determine whether these effects were sex-dependent.

Results
Neonatal minocycline treatment prevented enhanced hyperalgesia following adult incision in male but not in female rats with a neonatal priming injury. This sex-specific effect following adult incision was quantifiable in both behavioural and EMG responses. Primed male rats treated neonatally with minocycline did not differ from rats without prior incision in mechanical or EMG responses. Minocycline also partially attenuated the neonatal incision-induced increase in Iba1 in the medial lumbar ipsilateral spinal dorsal horn at P6 in male but not in female rats. Neonatal incision increased neuronal cell death in the ipsilateral dorsal horn in both sexes. Minocycline had no effect on incision-induced cell death, but also did not paradoxically increase apoptosis in the developing spinal cord [1].

Conclusion
These results suggest that sex differences in microglia-neuron signalling are generalizable across rodent
Title: Spinal Network Activity In Response To Noxious And Innocuous Electrical Stimulation

Poster Number PTH456

Authors
C. Greenspon, I. Devonshire, R. Mason, V. Chapman, G. Hathway

University of Nottingham, Nottingham, Please select..., University of Nottingham, Nottingham, United Kingdom, University of Nottingham, Nottingham, -- SELECT --, School of Life Sciences University of Nottingham, Nottingham, United Kingdom

Aim of Investigation
The responses of single neurones in the spinal cord to different stimuli has been well characterised through the use of single-unit electrophysiology. Communication between these neurones, or between different populations of neurones in the spinal cord has been less well studied. These network properties within the dorsal horn of the spinal cord may convey important information with regard to the integration and encoding of information that are relayed to the brain and evoke nociceptive behaviours. The aim of this study was to characterise how spinal networks respond to a range of electrical stimuli assessing both multi-unit activity and field potentials.

Results
Analysis of the LFP revealed a pattern that allowed channel accurate alignment between rats. LFPs at the centre of the observed deflection increased in amplitude as stimulation intensity was increased up to 5 mA, at which point no further increase in amplitude was evident. CSD analysis revealed several superficial and deep sinks. Sink response significantly decreased as stimulation intensity increased ($r = -0.886; p = 0.045$). The magnitude of the sink response varied according to the depth, with larger magnitudes recorded in the superficial dorsal horn ($r = 0.582; p = 0.032$).

Conclusion
Our data suggest that spinal cord neuronal networks can be elucidated and characterised with multi-array techniques. The differential responses of the superficial and deep dorsal horn networks to varying levels of electrical stimulation suggests that this technique may be a useful tool for pursuing the deconstruction of the spinal networks using other types of stimulation and pharmacological interventions alongside this method of recording.
Title: Activation Of Lanthionine Synthetase C-Like 2 Protein (Lancl2) Attenuates Spinal Neuroinflammation And Neuropathic Pain In Rats

Poster Number PTH457

Authors
H. Weng, D. Maixner

University of Georgia College of Pharmacy, Athens, GA

Aim of Investigation
Spinal neuroinflammation plays a critical role in the genesis of neuropathic pain. LANCL2 is implicated in the regulation of inflammation in the periphery but its role in the nervous system is unknown. In this study, we determined the role of LANCL2 in the genesis of neuropathic pain.

Results
LANCL2 was expressed in the spinal dorsal horn neurons but not in microglia or astrocytes. Protein expression of LANCL2 in the spinal dorsal horn was reduced in rats 10 days after nerve injury, which was accompanied with increased expressions of Iba1, GFAP, phosphorylated ERK, and TNF alpha. Genetic knockdown of spinal LANCL2 by siRNA produced mechanical allodynia and thermal hyperalgesia, and induced the changes of Iba1, GFAP, ERK, and TNF alpha similar to those in rats with pSNL. Activation of LANCL2 with abscisic acid (20 mg/kg/day, i.p.; starting before surgery and then daily for 9 day) increased LANCL2 protein expression in the spinal cord, and attenuated the development of neuropathic pain. These were simultaneously associated with the reduction of protein expressions of Iba1, GFAP, ERK, and TNF alpha in the spinal dorsal horn of rats with pSNL.

Conclusion
Our study for the first time indicates that LANCL2 plays a critical role in the regulation of neuroinflammation in the CNS, and suggests that targeting the LANCL2 signaling pathway could be a novel strategy for the management of neuropathic pain.
A Novel Template-Matching Technique For Quantification Of In Vivo Single-Unit Dorsal Horn Projection Neurons For Exploring The Effects Of 10-Khz Spinal Cord Stimulation

Poster Number PTH458

Authors
D. Lee, M. Smith, K. Bradley, S. McMahon

Nevro Corporation, Redwood city, CA, King’s College London, London, United Kingdom, King’s College London Faculty of Life Sciences & Medicine, London, United Kingdom

Aim of Investigation
We have developed an in vivo experimental protocol to study the effect in the rat spinal cord of high frequency 10kHz spinal cord stimulation on electrophysiological (EP) activity of superficial dorsal horn projection neurons. To confirm that these studied units were projection neurons, we used antidromic stimulation from the cervical spinal cord [1]. Often with in vivo preparations, the extracellular potentials measured from microelectrodes include not only single-unit action potentials (AP) from the target neuron, but also APs from neighboring neurons, which makes measuring the target neuron's activity a difficult challenge. Laborious 'by-eye' evaluations are then necessary to visually discern the target neuron's APs from surrounding neuronal network activity. Here we report a novel, semi-automated template-matching technique that we have developed specifically for our protocol, but which may be useful in other EP evaluations when the target neuron can be robustly and reproducibly evoked.

Results
All three templates (T1, T2, T3) showed biphasic morphology with positive peaks followed by negative peaks. Within each experimental preparation, templates had consistent latencies and amplitude, but the morphologies were slightly different between templates. In general, the first template (T1) had higher similarity with action potentials from hind limb afferent nerve stimulation. Applying different ST's to select target unit firing provided various outcomes: low ST's sometimes identified background noise (or neighbor neuron firings); high ST's occasionally missed unit firings from the target neuron. Reasonable ST's were ~32% error in power for template-matching, with some adjustment necessary for different preparations.

Conclusion
Using repetitive antidromic stimulation at the C2 spinal vertebrae level of the spinal cord, activated
Title: Assessment Of Thermo-Nociceptive Pathways In Healthy Volunteers And Sci Patients

Poster Number PTH459

Authors

Spinal Cord Injury Center, University of Zurich. University Hospital Balgrist, Zurich, Switzerland, Chair of Neurophysiology, University of Heidelberg, Medical Faculty Mannheim, Mannheim, Germany, ICORD, University of British Columbia, Vancouver, Canada, Chair of Neurophysiology, University of Heidelberg, Medical Faculty Mannheim, Mannheim, GERMANY

Aim of Investigation
Neuropathic pain is viewed as the consequence of a lesion or disease affecting the somatosensory system (Jensen et al. 2011). Even though the assessment of spinothalamic pathways for noxious heat using the established and validated methods like laser evoked potentials (LEPs) and contact heat evoked potentials (CHEPs) (Treede et al. 2003, Chen et al. 2001) is important in the diagnostic confirmation of neuropathic pain conditions (Treede et al. 2008), there is no objective electrophysiological method for the evaluation of the non-noxious pathway for cooling. Clinically, however, cold hyperalgesia and allodynia are frequently reported plus symptoms in patients suffering from neuropathic pain (Finnerup et al. 2003). Moreover, there is evidence suggesting the existence of a specific pathway for non-noxious cooling both in the periphery with cold-specific receptors in the superficial skin layers (Hensel et al. 1974), as well as in the spinal cord with neurons responding specifically to cold stimuli (Craig et al. 1994).

Results
We characterized cold evoked potentials (CEPs) applied to different dermatomes of the body in healthy volunteers with respect to possible modulation of cold perception and evoked potentials under experimental conditions. Finally, we began to investigate the relationship between altered cold perception and cortical responses in patients with defined lesions of the spinal cord. Contact cooling by nominally 5 °C from an adaptation temperature of 35 °C produced a slight, non-painful cool perception with less habituation compared to noxious heat pulses. Contact cooling of the glabrous and non-glabrous skin in different dermatomes reliably elicited cortical potentials. Mean amplitudes of these N2/P2 vertex potentials were 16 ± 2.1 µV for CEPs and 17.5 ± 2.6 µV for CHEPs. The responses displayed intensity coding as they increased with higher stimulus intensities. VAS ratings to CHEPs stimulation of
the C6 dermatome were 23 ± 6 (mean ± SEM; n = 12). Ratings of cooling stimuli were not perceived as painful and were rated at 7 ± 3 on a scale of 0-100 (0 being no perception, and 100 the most intense cooling imaginable). CEPs latencies were shorter than CHEPs latencies (N2 323 ms vs. 397 ms, t-test; p<0.01). Local desensitization with 8% capsaicin abolished cortical responses and perception of heat stimuli, whereas CEPs and cool perception remained unaffected. Sensitization with 40% menthol for 30 minutes enhanced cool perception and shortened CEPs latencies. In patients with spinal cord lesions affecting the anterolateral quadrant, CHEPs and CEPs were both severely impaired. In a patient with cold hypersensitivity CEPs amplitudes were moderately reduced, however, CHEPs amplitudes did not display any significant alterations.

Conclusion
CEPs are a novel method to study non-noxious thermo-sensory pathways for cooling. In the peripheral nervous system CEPs are conducted through distinct, capsaicin-insensitive A delta fibres, which might be of diagnostic value in the neurophysiological evaluation of small fibre neuropathies. In the spinal cord, the ascending pathways conducting non-noxious cooling appear to be located in the anterolateral spinal cord, and are lost together with CHEPs after lesion to this area. In patients with defined spinal lesions CEPs may provide further insight into differential impairments of thermo-nociceptive pathways and somatosensory dissociation. To what extent CEPs represent a useful and complimentary method to CHEPs / LEPs in the assessment of spinothalamic pathways warrants further investigation.
Title: Morphology And Function Of Gastrin-Releasing Peptide Expressing Excitatory Interneurons In The Spinal Dorsal Horn

Post Number PTH460

Authors
A. Bell, A. Dickie, N. Iwagaki, E. Polgar, M. Gutierrez-Mecinas, A. Todd

University of Glasgow, Glasgow, United Kingdom

Aim of Investigation
Numerous interneurons are present in the superficial dorsal horn of the spinal cord and these cells regulate the transmission of information perceived as touch, pain, or itch. Despite the importance of these cells, our understanding of their roles in the neuronal circuitry is limited by the difficulty in identifying functional populations. Gastrin-releasing peptide (GRP) is expressed in a neurochemically distinct population of excitatory interneurons in the dorsal horn. It has been suggested that GRP release from these cells plays an important role in the spinal transmission of non-histaminergic itch. This study aimed to determine the neuronal morphology of these GRP-expressing interneurons. Additionally, to test the hypothesis that GRP release is critical for the transmission of itch we evaluated the response of GRP-expressing cells to both noxious and pruritic stimulation.

Results
The dendritic trees of GRP-EGFP cells appear to be morphologically heterogeneous, and do not demonstrate islet or vertical morphology. The majority have dendrites that are elongated in the rostro-caudal axis and remain within the same lamina as the soma. Cluster analysis using dendritic morphometrics was unable to differentiate GRP-expressing neurons from other morphologically heterogeneous groups of interneurons previously reconstructed in our laboratory. Axonal arbors frequently exit the slice at the cut surface suggesting that they may be more extensive than observed. Axons extend both rostrocaudally and mediolaterally beyond the dendritic tree, and in some cases this is very extensive. They remain predominantly in the lamina of the cell and rarely enter lamina I. GRP-expressing cells seldom express fos or phosphorylate ERK following intradermal chloroquine. The proportion of all neurons in the activated zone that showed either pERK or Fos was 21% and 18%, respectively. Of the GRP immunoreactive cells only 3% and 7% were pERK- or Fos-immunoreactive respectively. ERK phosphorylation also seldom occurred in GRP-immunoreactive cells following pinch or heat stimulation. During our studies we noticed that GRP cells were rarely present in areas of the dorsal...
horn which somatotopically represent glabrous skin. Primary afferents from hairy skin can be identified using vesicular glutamate transporter 3 (VGLUT3) immunofluorescence and there are significantly fewer GRP-EGFP cells in zones of the dorsal horn not innervated by VGLUT3 expressing primary afferents. However GRP-EGFP cells do not appear to receive synaptic contacts from these afferent fibres.

**Conclusion**
The dendritic trees of GRP-expressing excitatory interneurons appear to be morphologically heterogeneous. Despite their characteristic axonal arborisation and distinct somatotopic distribution their functional role remains unclear. Based on the lack of activation of GRP+ neurons following itch stimulation, they do not appear to have a major role in itch transmission.
Conditional Pain Modulation: Effect Of Interventions In Different Chronic Pain States

Poster Number PTH461

Authors
S. Ramaswamy, V. Mehta, B. Kidd, R. Langford, L. Casey, K. Poply, A. Bahra, T. Wodehouse

Barts Health, London, United Kingdom, Pain and Anaesthesia Research Centre, St Bartholomew's Hospital, London, United Kingdom, Pain and Anaesthetic Research center, London, West Smithfield, St Bartholomew's Hospital, London, United Kingdom, Pain and Anaesthesia Research Centre, London, West Smithfield, Pain and Anaesthesia Research Centre, Barts Health NHS Trust, London, United Kingdom, Pain and Anaesthesia Research Centre, London, United Kingdom, Pain and Anaesthetics Research center, London, West Smithfield

Aim of Investigation
Conditional pain modulation (CPM) is a psychophysical paradigm used to describe the diffuse noxious inhibitory control (DNIC) and is an objective measure of the endogenous descending pain modulation. This is thought to be one of the main driving mechanisms for the central sensitization in chronic pain. CPM has been found to be abnormal in a variety of chronic pain states. It has also been associated with an increased incidence of acute and chronic postoperative pain. Patients with low CPM also had a better response to interventions such as duloxetine in patients with painful diabetic neuropathy. This suggests that CPM may also possibly have a predictive value and hence may be useful tool for phenotyping patients with chronic pain. The Pain and Anaesthesia Research Centre (PARC) based at St Bartholomew's hospital, London, has an established Quantitative Sensitive Testing (QST) laboratory. The aim of this study is to monitor the consistency of the changes in the CPM following an appropriate clinical intervention in different chronic pain states.

Results
The results for the different pain models are summarized as below: 1) 14 patients with FM had –ve baseline CPM. CPM was normalized in all these patients following pregabalin. 2) 11 patients with CIH had –ve baseline CPM. ONS normalized CPM in all patients. 3) 16 patients with CBURL had –ve baseline CPM. Steroid injection normalized CPM in 14 of these patients. Three months later 10 patients from this group went on get PRF treatment. Of these 5 patients maintained their CPM. PRF normalized/maintained CPM in all patients. 4) 19 patients with knee OA had –ve baseline CPM. TKR
normalized CPM in 17 of these patients. Very few patients in different pain models (2 in FM group, 3 in CIH group, 3 in original CBURL group and 1 in OA group) had normal baseline CPM. This was maintained in all but the 2 patients in FM group. 19/20 patients in the control group had a normal CPM.

**Conclusion**

Central sensitization is thought to be one of the main driving mechanism in different chronic pain models. This perhaps allures to a unified underlying mechanism. In this study we have demonstrated that CPM is abnormal in majority of patients in different chronic pain models. Following an appropriate intervention, CPM reverses to normal in most (all but 2 patients with –ve baseline CPM) of these patients. Interestingly, 2 (FM) patients with +ve baseline CPM became –ve following intervention. In contrast CPM was found to be +ve in 95% of the control group. In future, to establish the role of CPM as a phenotypic marker for chronic pain interventions, we need to analyze the effect of the interventions on a larger pool of patients with positive and negative baseline CPM. We have currently established such a database in our centre, following ethics approval, which we hope will help us to answer this question in future.
Title: Zinc Transporter-3 Mediated Sex Differences In Acute Inflammatory Pain

Poster Number PTH462

Authors
C. Fan, B. McAllister, R. Dyck, T. Trang

University of Calgary / Hotchkiss Brain Institute, Calgary, Alberta, University of Calgary, Calgary, Alberta

Aim of Investigation
Zinc is abundant in the central nervous system (CNS), and its activity is implicated in neuropathic and inflammatory pain. Intracellular zinc is sequestered into synaptic vesicles by the vesicular zinc transporter ZnT-3, the localization of which is tightly regulated by the adaptor complex AP-3. Vesicular zinc release into the synaptic cleft regulates pain transmission via inhibition of post-synaptic N-methyl-D-aspartate receptors. In this study, we found that ZnT-3 is also expressed in microglia, which are resident immune cells in the CNS. Under physiological conditions, microglia are in a surveillance state, with a small cell body and long processes that actively survey the environment. In the presence of damage and/or infection, microglia adopt a more activated state with a larger cell body, shorter processes, and they increase the expression of cell surface markers, such as ionized calcium-binding adapter molecule 1 (Iba1). Aberrant microglia activation has been implicated in the development of neuropathic and inflammatory pain. Additionally, studies have shown that microglia activation can be triggered by extracellular zinc in vitro. Emerging evidence suggests that males and females have distinctly different pain mechanisms and that microglia, in particular, play a differential role in the modulation of pain in males and females. Furthermore, sex hormones have been shown to modulate synaptic zinc levels by regulating the expression of the δ subunit of AP-3. The sex hormone estrogen has been shown to decrease synaptic zinc release by disrupting AP-3 expression. Thus, we investigated whether there are sex differences in the acute inflammatory pain response of female ZnT-3 knockout and wild-type mice compared to males. In the present study, we asked whether ZnT-3 is critically involved in the sequelae of inflammatory pain and whether sex differences exist in this mechanism.

Results
We found that there was no significant difference between ZnT3 knockout and wild-type male mice in the phase I formalin response. However, phase II of the formalin response was significantly enhanced in male ZnT-3 knockout as compared with wild-type mice. In contrast, we found no difference in phase I or II formalin responses in female ZnT3 knockout and wild-type mice. We also determined that the deletion...
of ZnT-3 in male mice was associated with lower expression of the microglial marker, Iba1, in naïve male mice.

**Conclusion**
Collectively, our findings indicate that ZnT-3 is expressed in microglia and that the deletion of ZnT-3 is associated with lower basal levels of microglial activation. Our results also indicate that zinc transport mediated by ZnT-3 plays a critical role in the central sensitization associated with phase II of the formalin response in male mice; however, this mechanism does not appear to important in female mice.
Title: Noradrenergic Inhibition Of Spinal Hyperexcitation Elicited By Cutaneous Cold Stimuli In Rats With Oxaliplatin-Induced Allodynia: Electrophysiological And Behavioral Assessments

Poster Number PTH463

Authors
S. Choi<sup>,2</sup>, S. Kim, S. Oh, H. Furue<sup>,4</sup>

Department of Physiology, College of Korean Medicine, Kyung Hee University, Seoul, Korea, Department of Information Physiology, National Institute for Physiological Sciences, Okazaki, Japan, Department of Neurobiology and Physiology School of Dentistry, Department of Brain and Cognitive Sc, Seoul, Korea, School of Life Science, The Graduate University for Advanced Studies, Okazaki, Japan

Aim of Investigation
The goal of this study was to investigate the spinal action of noradrenaline on cold-evoked hyperexcitation observed in wide dynamic range neurons (WDR) of rats with allodynia induced by an oxaliplatin.

Results
* Total sum of the behavioral assessment scores were markedly higher in the oxaliplatin-administered group than those in the vehicle-treated group. * The frequency of the cold-elicited firing in oxaliplatin-administered rats was significantly higher than that in the vehicle treated rats. * Noradrenaline inhibited cold-elicited action potentials in oxaliplatin-administered rats. * The spinal application of noradrenaline produced the most potent inhibition rate (87.2%). Clonidine (75.9%) and phenylephrine (68.8%) also showed a strong, but slightly lower, suppressive effect, whereas isoprenaline exhibited low effect (26.5%). * Being consistent with these electrophysiological data, behavioral results with intrathecal injection of noradrenaline and its agonists showed that α2 and alpha 1 agonists, but not beta agonist, induced significant analgesic effects.

Conclusion
Our study demonstrates a significant increase in frequency and duration of the spinal WDR neuronal firings in response to peripheral cold stimulation in oxaliplatin-administered rats. Moreover, we suggest that the inhibitory effect of spinal noradrenaline on oxaliplatin-induced cold allodynia is mediated by activation of alpha 2 and alpha 1 adrenoceptors, but not by beta adrenoceptor.
Title: Spinal Dorsal Horn Cholinergic System And Nociceptive Information Processing

Poster Number PTH464

Authors
D. Dhanasobhon, M. Medrano, S. Kavraal, I. Yalcin, R. Schlichter, M. Cordero-Erausquin

Institut des Neurosciences Cellulaires et Intégratives (INCI), Strasbourg, France, Université de Strasbourg, Strasbourg, France

Aim of Investigation
At the spinal level, an endogenous cholinergic tone modulating nociceptive behaviors has been documented in rodents and humans. Clonidine and morphine analgesia are involved in the release of spinal acetylcholine and the downstream activation of spinal cholinergic receptors. The spinal cholinergic tone is thought to be abolished in neuropathic conditions. One potential source of this acetylcholine is the spinal Dorsal Horn (DH) cholinergic interneurons; which have been previously reported in mice and monkeys. The project aims to elucidate the role of the dorsal spinal cholinergic system in the modulation of sensory information in naïve and neuropathic animals.

Results
Our behavior data showed the presence of a cholinergic tone modulating mechanical thresholds and demonstrated that it is still present, although reduced, after neuropathy. In both states, nicotinic and muscarinic cholinergic receptors are involved. Similarly, in vivo recordings illustrated ACh tone modulating brush and pinch responses in DH neurons of naïve mice. In cuff animals, alterations in these responses were observed, thus highlighting the changes observed from the behavior. Our in vitro recordings suggest that the cholinergic interneurons receive inhibitory inputs from deeper laminae and that these inputs are elevated following to neuropathy, potentially explaining the reduction in the tone observed in behavior. In addition, they are indirectly connected by the subset of nociceptive primary afferents expressing TRPV1, demonstrating their involvement in nociceptive processing.

Conclusion
Altogether, we have demonstrated that the spinal endogenous cholinergic tone has a role in defining mechanical nociceptive threshold in both naïve and neuropathic conditions. The cholinergic interneurons are well integrated in the DH network and connected indirectly to a subset of incoming
nociceptive fibers. Better understanding the spinal cholinergic system can pave way to alternative pain therapy.
Title: Co-Administration Of Melatonin Prevents Morphine Tolerance Via The Regulation Of Glutamate Transmission In Spinal Cord In Rats.

Poster Number PTH465

Authors
J. Kao<sup>,2</sup>, C. Wong

Department of Medical Research, Cathay General Hospital, Taipei, Taiwan, Department of Pharmacology, National Defense Medical Center, Taipei, Taiwan, Department of Anesthesiology, Cathay General Hospital, Taipei, Taiwan

Aim of Investigation
Morphine is the most widely used analgesic for treating moderate to severe pain in clinical practice. However, morphine tolerance is frequently encountered when long-term use that limits its effectiveness. Co-administration of a second drug which could attenuates morphine tolerance and improves the antinociceptive effect of morphine is the pain control paradigm in clinical. As known, pineal hormone melatonin is a remarkable molecule for sleep regulation. Recently, melatonin was demonstrated to exert antinociceptive effect in experimental animal models. In this study, we explored the combined effects of melatonin and morphine on morphine tolerance development.

Results
Our data show that co-administration of melatonin prevents morphine-induced tolerance. The morphine-induced upregulation of NR1 and the morphine-induced downregulation of GLT-1 were revered by co-administration of melatonin.

Conclusion
Co-administration of melatonin prevents morphine-induced tolerance in rats via the regulation of glutamate transmission in spinal cord in rats.
Title: Contribution Of Presynaptic Hcn Channels To Excitatory And Inhibitory Inputs In Rat Spinal Substantia Gelatinosa Neurons

Poster Number PTH466

Authors
T. Liu, S. Peng, L. Li, D. Zhang, C. Xie, X. Hu

the First Affiliated Hospital of Nanchang University, Nanchang, China

Aim of Investigation
Hyperpolarization-activated cyclic nucleotide-gated (HCN) channels are widely distributed in nervous system and are known to be involved in neuropathic pain disorders. The HCN channel family comprises four homologous isoforms (HCN1-HCN4). Our previous studies found that HCN channel-induced current are observed in nearly 50% of spinal lamina II (substantia gelatinosa, SG) neurons which play a pivotal role in regulating nociceptive transmission to the spinal dorsal horn from the periphery. In order to know in detail a role of HCN channels in regulating nociceptive transmission, we investigated the subcellular localization and the contribution of presynaptic HCN channels to excitatory and inhibitory inputs in SG neurons.

Results
All isoforms of HCN channels were found in superficial spinal dorsal horn. Among them, HCN1-HCN3 were seldom co-expressed with VGAT (markers of inhibitory presynaptic terminal) and VGLUT2 (markers of excitatory presynaptic terminal). On the contrary, HCN4 was highly co-expressed with VGAT and less co-expressed with VGLUT2. 10 microM of ZD7288 (antagonist of HCN channel) superfused for 10 min did not affect both sEPSCs and sIPSCs of SG neurons. However, at a higher concentration of 50 microM, ZD7288 significantly decreased both the frequency but not the amplitude of sEPSCs and sIPSCs. These inhibitory effects were also found in the superfusion of another HCN channel blocker cesium chloride.

Conclusion
We conclude that HCN isoforms are differently expressed in presynaptic terminals of SG neurons. HCN4 but not HCN1-HCN3 is enriched in inhibitory presynaptic terminal and less expressed in excitatory presynaptic terminal. Our data further indicate that both of the excitatory and inhibitory inputs in rat spinal SG neurons are suppressed by presynaptic HCN channels resulting in the modulation of nociceptive transmission.
Date: 09/29/2016 03:15:00 PM

Title: Role Of Spinal G Protein-Coupled Kinase 2 In Electroacupuncture Anti-Allodynic

Poster Number PTH467

Authors
Y. Zhou, L. Hu, Y. Wang, Q. MaoYing

Fudan University, Shanghai, China, Fudan University, Shanghai, -- SELECT --

Aim of Investigation
This study was designed to investigate the possible role of spinal GRK2 in EA anti-allodynic in a model with complete Freund's adjuvant (CFA) induced inflammatory pain.

Results
Single EA treatment at day 1 after CFA injection remarkably alleviated CFA induced mechanical allodynia two hours after EA. Repeated EA displayed significant anti-allodynic effect from 2nd EA treatment and a persistent effect was observed during the following treatments. Furthermore, data from western blot analysis demonstrated that the attenuated expression of spinal GRK2 induced by CFA injection was reversed by EA treatment. However, down-regulation of spinal GRK2 by intrathecal exposure of GRK2 antisense 30 mins after EA treatment completely eliminated both the transient and persistent anti-allodynic effect by EA treatment.

Conclusion
The attenuation of spinal GRK2 completely reversed both the transient and long-term anti-allodynia effect by EA treatment on inflammatory pain. The results supported that the spinal GRK2 played an important role in EA anti-allodynia on inflammatory pain.
Title: Synaptic Pruning Within The Dorsal Horn Observed After Traumatic Nerve Injury Using A Novel Stereological & Automated Quantification System Of Synaptic Puncta

Poster Number PTH468

Authors
S. West, D. Bennett


Aim of Investigation
Following peripheral nerve injury a plethora of central changes occur within the dorsal horn of the spinal cord, including enhanced excitatory and reduced inhibitory tone, increased proliferation of glial cells, as well as putative changes to the physiological and anatomical connectivity of central and primary afferent neurons. Recent data suggest that substantial re-wiring of specific circuits within the dorsal horn are causally linked to the hypersensitivity seen after peripheral nerve injury (for review see West et al. Neuroscience, 2015; 300:254-75). Here, an overall assessment of dorsal horn connectivity was undertaken to attempt to understand the global changes to synaptic connections throughout the dorsal horn, through the quantification of synaptic puncta within this region. This level of analysis provides an overview of the myriad neuronal circuits present within the dorsal horn, and may help to uncover important shifts in dorsal horn circuitry following lesions to peripheral nerves. This work can be divided into two key aims: 1. To develop a methodology to quantify synaptic puncta throughout the dorsal horn, using immunofluorescence and confocal microscopy, which produces robust, unbiased data on synaptic number, size and shape within user-defined regions. To avoid potential biases arising from quantifying 3-dimensional objects from a 2-dimensional image representation, the aim was to develop an method to assess 3D image stacks of synaptic puncta. 2. To apply this methodology to the dorsal horn of the spinal cord and assess the global synapse distribution patterns in this region in the naive dorsal horn, as well as the effects of peripheral nerve injury to these distributions.

Results
Histochemical labelling of synaptic puncta was first performed with pepsin treatment only, which showed significant improvement of the labelling of PSD95 and Synaptophysin puncta, with a punctate distribution throughout the neuropil. However, pepsin alone resulted in poor penetration of labelling and background labelling of neurites. Pre-treatment with heat and proteinase K was hypothesised to improve the penetration of pepsin & improve synapse labelling. These pre-treatments significantly
increased labelling intensity and depth, and eliminated background neurite labelling seen with pepsin-only tissue, and thus was utilised for synaptic assessment. Image deconvolution was optimised by acquiring images of fluorescent beads of known size. Image deconvolution showed a significant improvement in the FWHM in the lateral and axial planes of thresholded bead images. This method also showed significant improvements in signal to noise and resolution of images of synaptic puncta, and produced accurate 3D thresholded representations of synaptic objects for automated quantification. To assess synaptic puncta in user-defined regions in an unbiased manner, automated stereological algorithms were developed to quantify object number in a defined region of interest independent of object size, shape or orientation, with rules adapted from the di-sector probe. The unbiased nature of these algorithms were established in synthetic datasets of objects with known densities and varying sizes, shapes and orientations. Pilot analysis across mouse dorsal horn enabled the assessment of ~30,000 PSD95 and ~40,000 SynaptoPhysin puncta per animal using this system. Synapse assessment in naïve rats throughout laminae I-III revealed a significant alteration of PSD95 across laminae (p<0.01, one-way ANOVA), with large increases in PSD95-positive synapse number within lamina IIi (p<0.05 Dunnett’s Lamina IIi v. Lamina I, IIo & III), consistent with previous electron microscopy data (McNeill et al. 1988). Following unilateral rhizotomy in the rat a significant reduction in PSD95+ puncta is seen throughout all superficial laminae (two-way ANOVA, p<0.01), with a significant reduction in all groups (lamina I, IIo, III; bonferroni post hoc p<0.001 for all). Furthermore, 21 days post SNL in the rat there was a significant reduction in PSD95+ puncta seen in lamina III (p<0.01, two-way ANOVA, Bonferroni post hoc), while synapse number remain consistent in other laminae. Synapse assessment in naïve mice through laminae I-III revealed a significant increase in PSD95+ puncta from lamina I to lamina IIi, which dropped in lamina III; but an increase in SynaptoPhysin+ puncta from lamina I to lamina IIi which remained elevated in lamina III (p<0.01, one-way ANOVA). 21 days post SNI in the mouse revealed a significant reduction in PSD95+, but not SynaptoPhysin+ puncta, in lamina IIi (p<0.05, two-way ANOVA, Bonferroni post hoc), with puncta in other laminae unchanged.

**Conclusion**

The work presented here has made substantial progress in developing an automated and unbiased assessment system for synaptic puncta, and observing important changes in synaptic global distribution patterns in the dorsal horn following peripheral nerve injury paradigms. The histological development demonstrated here produces synaptic labelling of significant intensity and labelling depth to allow automated assessment of 3D synaptic puncta. This high fidelity signal is essential for the subsequent analysis of synapses, and is where many previous attempts at similar analyses have failed (Schmitz et al. 2014). Image deconvolution proved a vital step for automated analysis of synaptic puncta. Without deconvolution, objects were often merged following the thresholding step, making assessment of synapse number difficult to perform in an automated manner. However, following deconvolution, the extra resolution and signal to noise obtained produced very accurate thresholding of objects, and enabled the application of automated object analysis algorithms. The development of improved automated object analysis algorithms to implement an unbiased quantification of 3D objects in irregular ROIs across image stacks presented a unique challenge. The method extends the logical of the di-sector probe commonly employed in stereological studies to irregular ROIs - regions which more closely resemble the areas found in the CNS. Analysing the whole ROI as opposed to several spaced di-sector
probes had a number of significant advantages: The images were analysed in a very efficient manner, with no areas in ROIs avoiding quantification; a bias due to distribution patterns of objects was avoided which would otherwise potentially skew data collected at several evenly spaced intervals; and implementing the analysis across the whole ROI circumvented problems with long and narrow ROIs. Distribution patterns of synapses through the dorsal horn revealed some interesting patterns. The most conspicuous was the difference in lamina III between PSD95 and SynaptoPhysin in the mouse. This may reflect the increase in a separate population of synapses, likely inhibitory glycinergic synapses which are present in this lamina (Foster 2015). Rhizotomy surgery in the rat demonstrated the methods ability to accurately assess synaptic numbers. Rhizotomy is known to eradicate synapses in the dorsal horn (Chung 1989), which was affirmed with this method. Finally, the reduction in PSD95 puncta observed after peripheral nerve injury was a robust measurement demonstrated in two nerve injury paradigms across two species. We hypothesise this loss is due to loss of input from the IB4+ C fibres. In the mouse, this was not accompanied by loss of SynaptoPhysin, suggesting either SynaptoPhysin is absent from this synaptic population; or the breakdown of the synapse begins with PSD95, and SynaptoPhysin loss may occur at later time points. We acknowledge the Wellcome Trust for funding this work.
Title: Stimulus Predictability Modulates The Withdrawal Strategy To Nociceptive Stimulation In Humans

Poster Number PTH469

Authors
F. Jure, F. Arguissain, J. Biurrun Manresa, T. Graven-Nielsen, O. Andersen

Center of Neuroplasticity and Pain (CNAP), SMI®, HST, Aalborg University, Aalborg, Denmark

Aim of Investigation
The nociceptive withdrawal reflex (NWR) is elicited when a nociceptive stimulus is detected, and resulting in a withdrawal of the limb to prevent potential tissue damage. In this process, neural mechanisms, biomechanical strategies and muscular activity are integrated. Previous studies of modulation of lower limb NWR indicate that the NWR response is modulated by stimulation site, intensity, frequency, and by supraspinal activity like ongoing cognitive processes. The aim of the present study was to investigate the supraspinal modulation of the biomechanical withdrawal strategy of human lower limb reflexes due to the predictability of repetitive nociceptive stimulus.

Results
The mean RTh in TA was 6.2 mA (range 3.3 – 9.5 mA), whereas the mean PTh was 13.2 mA (range 8.5 – 24.5 mA). Results show a significant main effect of condition for NWR amplitude on the BF muscle (F1,10 = 6.16; p = 0.032), whereas no significant effects were found on the TA muscle. With regards to probability of occurrence, the ANOVA also showed significant main effect of condition for BF muscle (F1,10 = 7.35; p = 0.022), whereas no significant effects were found on the TA muscle.

Conclusion
The predictability of the nociceptive stimulus modulates the biomechanical withdrawal strategy of the lower limb in humans. Thus, this study shows that the NWR from the BF muscle is larger and the probability is higher when the stimulus is unpredictable. On the other hand, the activity and the probability of eliciting NWR in the TA muscle remain unchanged in relation to the predictability. These results indicate that descending control plays a major role for the withdrawal reflex strategy and stimulation site is not the only predictor.
Title: Cortical Mechanisms Of Sensory Amplification In Visceral Pain Conditions

Poster Number PTH470

Authors
F. Tu, R. Silton, K. Dillane, K. Polnaszek, S. Harte, K. Hellman

NorthShore University HealthSystem, Evanston, IL, Loyola University in Chicago, Chicago, IL, UNIVERSITY OF MICHIGAN UM/Chronic Pain & Fatigue Research Ctr, ANN ARBOR, MI

Aim of Investigation
Individuals with visceral pain conditions commonly report increased somatic symptoms that interfere with daily life functioning, suggesting widespread sensory amplification. We have previously shown that dysmenorrhea and somatic symptoms are associated with worsened bladder pain. Since cortical amplification has been reported in some chronic pain conditions, we hypothesized that sensory input may be amplified in primary sensory cortices of women with visceral pain, potentially explaining the relationship between multiorgan pain and generalized report of sensory unpleasantness. To characterize patterns of abnormal cortical activity associated with somatosensory amplification, we modified an unpleasant visual task for use with simultaneous electroencephalography (EEG).

Results
Dysmenorrhea sufferers were more likely to report significant bladder distension pain (12/36) than healthy controls (1/11, p < 0.05). Those with dysmenorrhea and bladder hypersensitivity (p < 0.01) and those with PBS (p < 0.05) reported significantly higher levels of experimental visual unpleasantness compared to healthy controls. The magnitude of self-reported menstrual pain after NSAID treatment (r = 0.27, p < 0.05) and experimental bladder pain (r = 0.46, p < 0.001), was correlated with heightened self-reported visual unpleasantness. Visual unpleasantness was also positively correlated with increased visual-evoked activity in occipital cortex (r = 0.35, p < 0.01). Although women with bladder hypersensitivity did not have more visual evoked activity in occipital cortex (p = 0.76), they had significantly more frontal beta/gamma (20-40 hz) oscillatory activity during the visual task across all trials (p < 0.01).

Conclusion
We replicated our prior finding that many women with moderate-to-severe dysmenorrhea exhibit enhanced bladder distension pain. A key difference between those with and without experimental
bladder pain is sensory amplification of unpleasant visual stimuli. The observed relation between self-report of visual unpleasantness and evoked occipital cortex activity suggests enhanced cortical activity is one contributor to somatosensory amplification. As bladder pain conditions were not related to increased occipital activity, neither increased synaptic excitability nor modulation of visual cortex explains our task-specific observed sensory amplification. Instead, results suggest that frontal cortical networks associated with higher order processing may amplify sensory unpleasantness.