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Title: Improving Postoperative Pain Management In General And Obstetric Surgery Patients At Regional Hospital Of Prizren, Kosovo

Poster Number PW0001

Authors
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Aim of Investigation
Test the feasibility of using a Plan-Do-Study- Act cycle to improve management of post-surgical pain at the Prizren Regional Hospital in Kosovo. The project was carried out in the context of pilot within IASP's post-operative pain management improvement project led by the International Pain Registry (IPR) and Developing Countries (DC) Working Groups (WGs). Hospitals in Kosovo face severe shortages of medications. Analgesics are limited in terms of quantity and range.

Results
The work was carried out from December 2014 – November 2015. Data was collected from 322 general and 213 obstetric surgery patients. The most common general surgery procedures were cholecystectomy (open and laparoscopic); hernia repair and appendectomy; for obstetrics it was Caesarian Section. Baseline data indicated that patients experienced severe pain. General surgery: Worst pain was (average ± SD) 7.0 ± 1.8; patients spent an average of 30% of POD1 in severe pain. 22% of patients would have liked additional pain medication. For obstetric surgery: Worst pain was 7.2 ± 1.6;
patients spent an average of 40% of POD1 in severe pain; 46% of patients would have liked additional pain medication. After consulting IPR and DC-WG members, a local team of physicians (anesthesiologist and surgeons) and nurses selected a range of changes in practices; they were implemented over a period of 6 months. Interventions included: teaching staff to assess pain; preparing forms to record the measurements in recovery room; setting up a recovery room in obstetrics; educating patients including evaluation of pain by numerical or verbal rating scale; infiltrating the surgical wounds of all patients; intending to administer analgesics routinely, guiding nurses to administer analgesics and uterotonic separately; increasing the proportion of obstetric patients receiving spinal analgesia. Analyses of the PROs in the second phase of data collection (1 month) indicated clinically significant changes in both wards; the difference for general surgery was a medium effect size and for obstetrics it was a large effect size. Examples of PROs, for general surgery: worst pain was 5.6 ± 1.3; patients spent an average of 23% of POD1 in severe pain; 0 patients would have liked additional pain medication. For obstetrics: worst pain was 5.9 ± 1.2; patients spent an average of 24% of POD1 in severe pain; 1.4% of patients would have liked additional pain medication.

**Conclusion**

Over a period of 11 months, staff from two wards at the Prizren Regional Hospital, collected pain-related PROs and processes, they used the findings to implement extensive changes in pain management. The changes brought about clinically relevant improvement in PROs in both wards. Long term plans consist of preparing and implementing pain management guidelines and protocols on a national level, devising pathways for routine assessment of pain on a national level, and to increase the number and variety of analgesics in Kosovo.
Title: Effect Of Diluted Nitrous Oxide On The Pain Of Heroin Addicts During Withdrawal

Poster Number PW0002

Authors
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Aim of Investigation
To investing the analgesic effect of diluted nitrous oxide on the pain of heroin addicts during withdrawal.

Results
There was no significant differences of VRS score, HR and SaO2 between the two groups before treatment (Z=0.198, t=0.315, t=1.299, P>0.05). There was remarkable significance on the VRS scores of 2 minutes after treatment between two group (Z=6.554, P<0.01). There was no significant difference between two group 2 minutes after treatment in HR and SaO2 (t=1.079, t=0.284, P>0.05).

Conclusion
The diluted nitrous oxide can reduce the pain score of heroin addicts during withdrawal. It shows an obvious analgesic effect. It may be applied in the symptoms control for the opioids addictives during withdrawal.
Title: Interaction Between Methylphenidate, Methadone And Different Antidepressant Drugs In Mice, And Possible Clinical Implications

Poster Number PW0003

Authors
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Aim of Investigation
Preclinical studies in rats showed that MPH has an analgesic effect when given alone or in combination with morphine. In the present experiments we studied the interaction of acute doses of MPH with sub threshold doses of methadone and different antidepressant medications. Next, we studied the interaction of increasing doses of MPH with chronic methadone using implanted mini pumps.

Results
The addition of a sub threshold dose of venlafaxine, desipramine and clomipramine to MPH produced significant augmentation of MPH antinociceptive effect with each medication (p<0.05). No interactions were found when sub threshold doses of escitalopram and methadone were added to acute doses of MPH. On the other hand, addition of increasing doses of MPH to chronic methadone given for 2 weeks using osmotic mini pumps induced augmentation of the antinociceptive effect of chronic methadone exclusively at high dose of MPH.

Conclusion
These findings may implicate the need of an excessive attention to the administration of MPH given to MMT patients. The findings of the no interaction between MPH and escitalopram may hint to the possibly safe co-administration of methylphenidate and SSRIs to depressed ADHD patients. Further studies are needed before these possible clinical implications can be validated.
Title: Stable Gastric Pentadecapeptide Bpc 157 Counteracts Muscular Pain After Intramuscular Succinylcholine Application In Rats

Poster Number PW0004

Authors
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Aim of Investigation
The effect of pentadecapeptide BPC 157 on pain was the aim of our study. We know that BPC 157 through interaction with NO-system, is acting like protector for muscles and nerves. So, we tested the hypothesis that the succinylcholine, like local and systemic threatening effect (muscle pain) should depend on NO-related mechanisms in a particular way, and that both N(G)-Nitro-L-arginine methyl ester (L-NAME), NOS-blocker, and L-arginine, NOS-substrate, would both exhibit an aggravating effect in rat.

Results
Results were identical in the test animals receiving 10 mcg and 10 ng BPC 157. Pentadecapeptide BPC 157 completely eliminated pain in all combinations and hyperalgesia. No violent screaming upon light touch appeared in IM succinylcholine-rats. These were all identical by L-NAME and by L-arginine and counteracted by BPC 157 co-administration. CK values were several times higher in rats receiving a combination of 0.9 % NaCl + L- arg +Sux and 0.9 % NaCl + Sux. In other combinations of animals that are combinations received BPC 157 had a smaller increase in CK compared to the NO system.

Conclusion
Succinylcholine both local and systemic threatening effect is dependent on NO-related mechanisms in a particular way, since both L-NAME, NOS-blocker, and L-arginine, NOS-substrate exaggerated pain caused by succinylcholine and L-NAME-aggravation and L-arginine-aggravation, and these effects are consequently counteracted by stable gastric pentadecapeptide BPC 157. SO, we concluded that BPC 157 suppress muscle pain, also in particular relation with NO-system. We hope the research would be continued through clinical studies.
Title: An Audit Of Implementation Of Pain As The 5th Vital Sign By Ward Nurses In A University Medical Center

Poster Number PW0005

Authors
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Aim of Investigation
'Pain' as the 5th vital sign was launched in April 2012 in University Malaya Medical Centre, Kuala Lumpur, Malaysia. All patient observation records were altered to include 'pain assessment' in addition to the other four vital signs. A series of workshops were conducted for all ward staff nurses and senior nursing staff over a period of six months before the launch to emphasize the importance of pain assessment for improved patient care. Two months after the launch a random audit of 100 medical records showed that only a small percentage were recording severity of pain on patient charts. This follow up audit was conducted to see if there has been any improvement.

Results
One hundred and sixty seven (167) complete data collection forms were available for analysis. Of these only 31 patients (18.5%) were managed by the APS. Pain scores were recorded in all but 4 patients. However, 53/167 (31.7%) patients were not asked if they had any pain, but pain scores charted anyway. Of these, 13 were children, 14 were in the ward awaiting surgery and another 10 patients were in for investigations. In 114 patients pain scores were recorded after they were assessed by the nurses, mainly using a verbal rating scale. In 33/114 (28.9%) patients, the severity of pain was under-estimated and the pain scores were much lower than that elicited by the APS nurse. Of the audited recorded, the majority of nurses were not using the designated Numerical Rating Scale (NRS) ruler of the hospital or the FLACC scale. They were also not taking any action for pain scores > 4. in patients who were managed by the APS, the assessment of pain was more consistently carried out and patients had lower pain scores.

Conclusion
The routine assessment of pain in patients in the hospital continues to be inadequately documented and not optimum despite a large number of workshops, weekly ward rounds, inclusion of pain
management lectures in nursing schools and efforts to make pain 'visible.' The reasons for this state may be multifactorial. It could be nurse's attitudes or poor knowledge on their part. It could also be that the junior-most trainee nurses are given the responsibility for all ward observation including assessment of pain which needs a more mature understanding. Clearly a new strategy is needed to change the attitude of nurses – like getting senior nurses involved in these activities. Audits such as this can be brought to the attention of senior management in charge of quality to strategize on the next move.
Title: An Investigation Of Hospital Anxiety And Depression Status With Pain Perception In Neurosurgical Patients: The Clinical Practice Perspective

Poster Number PW0006

Authors
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Aim of Investigation
The experience of pain is known virtually to all mankind apart from those unfortunate individuals who have congenital insensitivity to pain. Discovering the function of emotional status remains one of the greatest challenges for healthcare personnel. The experience combines sensory qualities, indicating the exact location of damage, an unpleasant emotional state, and related 'pain behavior' such as avoidance. Despite recent advances in the understanding of the complex nature of pain and the introduction of new technologies, such as patient controlled and epidural analgesia, there is evidence to suggest that pain management in the health service remains poor, with many patients suffering unacceptable levels of pain, leading to potential delays in recovery and psychological trauma. Pain is not simply the end product of a linear sensory transmission system; it is a dynamic process that involves continuous interactions among complex ascending and descending systems. It is evident from the preceding review that there has been a considerable focus of research upon the role of psychological factors in the experience of acute pain. These factors have included emotional responses and the role of personality, cultural, patients' belief and social support about their pain. The subjective intensity of pain relates to different perceptions, meanings, attitudes, beliefs and emotional responses in different groups with different cultures and ideologies. Individual response to pain is influenced by a typical cultural pattern of beliefs about pain and how one should react to it. For example, in Eastern philosophy it is believed that those who suffer from pain and other difficult life events will derive spiritual value. From Hippocratic medicine through the modern theory of Melzack and Wall, the concept and physiopathology of pain has been developed over the course of time, assuming in some instances a religious or philosophical view and in others a more scientific meaning. People have developed very different words to express pain. The Arabic language has hundreds of words to express pain, while European languages are more limited. In the West culture, the emphasis is on understanding the nature of pain is stable through bodily performance and explained the issue of spirituality in the same way. While that spiritual energy...
performance higher than of the physical impact and not to the similar body properties. In other words, for some religious devotees, the experience of pain is to be borne as a recognition of devotion and acceptance. Recognition of the spiritual dimension and its function as a vital component of human well-being has led to an increased interest in its effects upon perception of health and illness, yet very little progress has been made in identifying possible intervention methods for enhancing spirituality.

Results
This study was cause and a comparative examination Anxiety shows significant positive correlations with dimensions of MPQ in sensory, affective, miscellaneous, word chosen (p<0.05) and total rating (p<0.01), but depression only shows significant positive correlations with dimensions of affective, sensory and pain total rating (p<0.05) (Table 1). Table 2 shows the groups' mean scores on HADS anxiety. It is evident that patients show a decrease in mean anxiety from the first to second time T-tests provides the following measures: a) Main effect of time on anxiety - to assess whether anxiety changes over time regarding to the operation. The main effect of time was significant, indicating that, overall, anxiety reduced significantly for patients after operation (T=9.22, df=45, p<0.01). It revealed a significant effect of time of test, confirming that after operation showed a reduction in depression scores over time (T=8.52, df=45, p<0.01). Depression Table 2 shows mean scores on depression for the patients at the two assessment periods. T-test revealed a significant effect of time of test after operation, confirming that the result showed a reduction in depression scores over time (T=7.52, df=45, p<0.01). As in the case of anxiety scores above, the scores on depression were also considered as a function of the proportion of patients falling within the low to severe categories, and these are shown in Table 2. Pain Scores Table 2 shows the Patients' mean scores on the McGill Pain Questionnaire as a function of the first and second testing period. As in the case of the scores on the emotional variables above, t-test was applied to the data. The following results were found for the various dimensions of the McGill Pain Questionnaire. i) Total Pain Scores - There was the main effect of time (T=9.88, df=45, p<0.001) and the interaction of the time before and after operation. ii) Sensory Pain Scores - As in the case of total scores, only the main effect of time interaction were significant (T=10.25, df=1.45, p<0.001). iii) Evaluative Pain Scores – It show a marked decline in the emotional nature of their pain experience over time, as confirmed by test results (T=4.44, df=1.45, p<0.004). iv) Affective Pain Scores - The study group show a further significant reduction in their affective experience of pain over time as confirmed by the significant interaction (T=8.41, df=1.45, p<0.003). v) Miscellaneous and Word Count Dimensions – Analysis of these more general assessments of the impact of pain confirm that the result show a marked and significant reduction.

Conclusion
The researchers have concluded that the main problems for such patients are both emotional distress and physical symptoms. The outcomes of this study show that patients have more emotional function, it could be relevant to their culture in nature. The evidence reviewed points to substantial commonalities, but also some differences and interactions between physical and psychological pains. It is also evident that operation itself has an influence during the treatment because the patients showed a reduction in their scores on anxiety, depression, emotional distress and pain from the first to second questionnaire. In summary, the patients in this sample have more emotional status than the population norm. They
also report considerably greater degrees of emotional distress when compared to population norms. Their most common source of emotional function is prior to surgical intervention. Suggestions for future research need more discussed, including methodological and conceptual considerations. At the time when patients completed the post-operative questionnaires, in this study, they have experienced a resurgence of hope; this means that operation has reduced the emotional status. Perhaps if the questionnaires are repeated three months after the surgery, it can be used to evaluate the emerged helplessness and hopelessness. Researchers have concluded that the main problem for such patients is emotional distress rather than physical symptoms. Therefore one implication of this might be that psychological intervention may be more effective than the conventional 'medical' treatment administered in the Hospital and clinic environment. Beyond these ways of current approach in study of pain with various theories, there are also important roles that theories play unconsciously in everyone's mind, which is not accounted with these current views. This is the psychological formatting in unity package of theory. In this suggestion that the aspects of how theories are implicated in the analyst's understanding of investigations is one version and an extension of the way in which people ordinarily express their personal assertiveness, conscious and unconscious relationship, formulated and unformulated psychological insight and theories about people in understanding other people according to self-exploration. This marks an important avenue for further research and discussion or develops some more details in explanation of 'Master Key Theory' in geometric perspective. It may angle the period of 2015 + and 'The future Decades of Pain Control and Research' as they are exposed to the new debate and bring the ignorance of the physiological specializations at the edge of the world's knowledge which could progress productive science facts. The limitation of this study was difficult in recruiting the control group, because there were no interventions designed throughout the study.
Title: What Do Patients Think Of Post-Op Pain Management?

Poster Number PW0007

Authors
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Aim of Investigation
To assess patient satisfaction with post operative pain control. Assess level of patient education on post operative pain control. Find ways to improve quality of postoperative pain management.

Results
82 male, 103 female East 66/70 returned (16NPT, 50 POW) West 119/130 returned (20 Singleton, 99 Morriston) Overall response 92.5%

Conclusion
Samples size was small. However, findings indicated that education (patients & staff) is needed in relation to the general population of postoperative patients. Some results obscured due to lack of data (25-72hrs), pain scores may have been better. Comments corroborates literature review, eg pts ask for analgesia was given (90-94%) or there was a delay. ?Pain not seen as a priority.
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**Title:** The Effects Of Some Mitochondrial Modulators On Thermonociception

**Poster Number** PW0008

**Authors**
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**Aim of Investigation**
Mitochondrial diseases are a clinically heterogeneous group of disorders that arise secondary to a dysfunction in the mitochondrial respiratory chain. Patients with mitochondrial disease frequently suffer from different types of pain, such as headache, neuropathic pain, muscle pain and abdominal pain. In this study, we assessed the effect of some mitochondrial (mt) modulators on acute thermonociception. We tested mt-ALDH2 modulators (nitro-glycerine-NTG and disulfiram-DSF) mt-ATP modulators (cobalt choride-CoCl2, riboflavin- RBF and methylene blue-MB) and free radicals modulators (curcumin-CCR, ascorbic acid-ASC and pramipexole -PRX).

**Results**
The effect induced by a single dose of mitochondrial modulators varied not only with the drug, but also with time. Thus, the pain assessed by TFT was inhibited in the first hour by MB, DSF, NTG, PPX, and AAS, but after 4h all tested drugs had an analgesic effect except vitamin C. The PBC was more than 50% for CCR and DSF. For CoCl2, RBF, ASA and PPX, the PBC was between 30 and 40%. The PBC was less than 10% for the rest of the drugs. Nociception as assessed by HPT was increased by CoCl2 and ASC and reduced by all the other drugs. The PBC was >50 % for MB, CCR and RBF and > 40% for the other substances. In the control groups, the PBC was less than 20% for both TFT and HPT.

**Conclusion**
Our results show that a single dose of the drugs able to interfere with the mitochondria respiratory chain induces chances in thermonociception. Moreover, the effect is different and seems to depend on the spinal (TFT) or supraspinal (HPT) integration of thermonociception. In our study, the ATP and free radicals modulators produced the most important changes in pain perception as assessed by the HPT, while the TFT was mainly influenced by the ALDH2 and the free radicals modulators. Acknowledgments:
Research supported by Executive Agency for Higher Education & Research Funding (UEFISCSU) Romania, project PNIII PCE201130875.
Title: The Comparative Evaluation Of The Intensity And Quality Of Acute Postoperative Pain After Open And Robotic-Assisted Radical Prostatectomy Surgery

Poster Number PW0009

Authors
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Aim of Investigation
Greater understanding of men's postoperative pain experience following prostatectomy is needed to guide treatment and inform patients of their likely surgical outcomes. We explored the comparative intensity and quality of men's acute postoperative pain following open radical retropubic (RRP) and robot-assisted radical (RARP) prostatectomy.

Results
Most men reported mild-to-discomforting present pain intensity (PPI ≤2/5; n=307, 92.2%) and received a mean proportion of 26% of their available analgesics. For 14 men however, PPI was 'distressing', 'horrible' or 'excruciating' (PPI>2/5; 4.2%). These men received a mean proportion of 27% of their available analgesics (p=.868). There was no effect of surgical approach on PPI (p=.273) or the severity of sensory (Md=9/42, IQR=9; p=.634), affective (Md=1/14, IQR=1; p=.229) or miscellaneous (Md=1/17, IQR=4, p.355) aspects of pain quality. However, severity of evaluative pain (eg. annoyance, trouble) was higher (p<.05, r=-.11) following RRP (Md=1/5, IQR=0) than RARP (Md=1/5, IQR=2). Chi-square tests of independence indicated no effect of surgical approach on the prevalence of sensory and affective pain dimensions experienced. The most prevalent sensory dimensions of pain irrespective of surgery type were: dullness (84.4%); misc. sensory pain (71.5%); constrictive pressure (57.4%); traction pressure (46.2%); temporal (rhythmic - 43.5%); incisive pressure (41.7%) and punctuate pressure (37.8%). The sensory dimensions of brightness (30%), spatiality (movement - 30%) and thermality (heat - 13.2%) were less prevalent. The affective dimension of tension (47.4%) was common. Men were unlikely to report fear (11.4%), misc. affective pain (5.1%), or to perceive pain as autonomic (11.1%) or punishing (8.4%). Prevalence of evaluative pain was higher among RRP than RARP patients (p<.001, phi=-.23). Although severity and prevalence of sensory pain were the same irrespective of surgery, men in each surgical group had a different experience of its dimensions. Constrictive pressure was significantly more likely to be experienced as 'pressing' (zres=2.1) by RRP and 'cramping' (zres=2.1) by RARP patients (p<.005,
Cramer's $V = 0.235$); dullness as 'hurting' (adj. $z_{res} = 2.5$) by RRP and 'aching' (adj. $z_{res} = 2.1$) by RARP patients ($p < 0.05$, Cramer's $V = 0.184$). Surgical approach also had a significant effect on the experience of evaluative pain. RRP patients were significantly more likely to evaluate their pain as 'annoying' ($z_{res} = 2$; $p < 0.001$, Cramer's $V = 0.275$). RRP patients also experienced greater bother than RARP patients ($p < 0.05$, $r = -0.11$).

**Conclusion**

Surgical approach moderately impacted the sensory and evaluative experiences of acute pain following prostatectomy and had a small effect on the prevalence and severity of evaluative pain. RRP patients reported different sensations of constricting pressure, dullness, bother and annoyance compared to RARP patients. Furthermore, men who underwent RRP found pain more annoying or troubling. Approximately 5% of men reported intense pain that was distressing, horrible or excruciating. These men failed to receive adequate pain management. There were no other differences in pain experience between surgical groups. These findings inform communication about men's likely postoperative outcomes following prostatectomy and may help prepare men for their acute postoperative recovery.
Title: Patient Processes For Attributing A Numerical Rating To Postoperative Pain Intensity After Total Knee Joint Replacement Surgery: A Qualitative Study

Poster Number PW0010

Authors
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Aim of Investigation
An 11-point numerical rating scale (NRS) is commonly used after surgery as a unidimensional measure of pain intensity, however little is known about patients' approach to and application of the scale. This qualitative study examines the processes patients use to select and communicate a number representative of their postoperative pain intensity.

Results
Two key processes emerged: 1. Calibration involved using the scale's structure and personal experience as a frame of reference to locate pain intensity and define anchor points. 2. Contextual Modification identified dimensions other than intensity, that patients incorporate into the calibration process to manage the dynamic nature of their pain as well as to navigate the routines and uncertainties of the clinical environment necessary to achieve analgesia.

Conclusion
Our findings suggest that numerical pain ratings reported by patients represent a complex interplay of personal and contextual factors, rather than just their current pain intensity and the validity of using them as the basis for pain management decisions is questionable. Rather the NRS should be considered a starting point for comprehensive clinical assessment and underscores the need for a more systematic, standardised application of the NRS clinically.
Title: Area Under The Psychophysical Curve As The Measure Of Pain Habituation

Poster Number PW0011

Authors
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Aim of Investigation
In the literature, pain habituation (PH) was usually measured by the change in pain threshold before and after repetitive painful stimulation. However, this measure merely depicts the alteration of subjective ratings at the pain threshold, leaving the extent of psychophysical shift beyond this point unrepresented. To circumvent this issue, we propose a novel method by exploiting the psychophysical curve (PPC) to estimate the degree of PH. We examine if a linear regression using a power function can improve the evaluation of PH in humans.

Results
Instead of simply reflecting an alteration in pain threshold, dAUC demonstrated the capability to capture the whole changes in psychophysical function to different magnitudes of painful stimulation.

Conclusion
The estimation using the power function is straightforward and contains the full information developed during the process of pain habituation. Future studies will be conducted to investigate if this approach is better than calculating the change in pain threshold to represent the degree of PH.
Title: Comparing Assessment Of Pain Severity Using Visual Analog Scale (VAS) And Numerical Rating Scale (NRS) In Patients With Chronic Pelvic Pain (CPP)

Poster Number PW0012

Authors
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Aim of Investigation
To assess the agreement between Visual Analogue Scale (VAS) and Numerical Rating Scale (NRS) in patients with Chronic Pelvic Pain.

Results
We obtained 344 ratings of pain, from 43 patients using the NRS and VAS rating scales. 67% of patients surveyed were female, mean age was 47y. Although mean NRS scores were around 0.35 units higher than VAS scores, and Bradley-Blackwood test result was rather poor, the Pearson's correlation and Lin's concordance correlation revealed substantial agreement between NRS and VAS versions for Q4 (r= 0.965), (ρc = 0.952, 95% CI 0.926–0.978) and Qs (r = 0.946), (ρc = 0.93, 95% CI 0.889 – 0.97) respectively. Scales Q1, Q2 and Q3 showed less good agreement. The Bland-Altman plots were generally satisfactory.

Conclusion
Both NRS and VAS rating scales can be used to report pain severity in patients with chronic pelvic pain. NRS and VAS have good agreement to measure current pain severity and overall BPI composite severity in patients with chronic pain. NRS scores are reported higher than VAS score, for all scales. Chronic pelvic pain researchers and clinicians should be aware that the VAS and NRS pain reporting scales should only be used interchangeably when assessing the current and composite severity scores.
Title: Pain Associated With Diabetic Neuropathy In Patients With Type 2 Diabetes From Primary Care: Signs And Symptoms Of Anxiety And Depression

Poster Number PW0013

Authors
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Aim of Investigation
The aim of this study was to evaluate signs and symptoms of anxiety and depression in patients with pain related to diabetic neuropathy enrolled in the Diabetes Program of the Brazilian Public Health System Primary Care.

Results
The sample consisted of 140 patients with type 2 diabetes, mostly females aged 18-60 years, and 93% presenting pain related to diabetic neuropathy. The use of the Hospital Anxiety and Depression Scale showed 36% of patients presenting signs and symptoms of anxiety and 29% of depression, and part of the sample 18% presented both conditions simultaneously.

Conclusion
Taking into account the results obtained it can be suggested the importance of holding the emotional evaluation of patients enrolled at the Diabetes Program of the Brazilian Public Health System Primary Care. This procedure could help to identify the real needs of this population based on the Public Health Surveillance precepts including comprehensive care.
Title: The Pain Modulation Index: A Novel Self-Reporting Questionnaire To Determine Levels Of Endogenous Pain Modulation In People With Chronic Pain

Poster Number PW0014

Authors
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Aim of Investigation
The aim of this study was to develop and preliminarily validate a novel self-reporting questionnaire that identifies key symptoms associated with changes with endogenous pain modulation in people with chronic pain.

Results
PMI scores were significantly higher in CP patients compared to healthy controls (p<0.000001). Findings were similar with both pain and global symptom subscales (p<0.000001 / p<0.000001). We also found significantly higher PMI scores in CP patients with constant pain versus those intermittent pain (p=0.007). The chronic pain group had a significant reduction in CPM (92% + 21.6 SD vs 109% + 13.1 SD, P=0.003) and baseline pressure pain threshold (44.9 ± 14.7 SD n/cm² vs 59.0 + 14.9 n/cm², P<0.0002) compared with controls. Those with constant pain also showed significantly reduced CPM (p=0.01), but not baseline pressure pain threshold (p=0.79) compared to CP patients with intermittent pain. PMI total scores were moderately and significantly correlated with changes during CPM (r=−0.43, p=0.004). There was a moderate negative correlation between CPM levels and PMI global symptom scores (r=−0.44, p=0.003) but only a weak correlation with pain symptom scores (r=−0.34, p=0.03). Additionally, there were moderate negative correlations between pressure pain thresholds at baseline and the PMI total (r=−0.48, P<0.002), pain symptom subscale (r=−0.48, P<0.002) and global symptom subscale (r=−0.45, P<0.001). The strongest correlations between the PMI and other psychological function measures lay with pain anxiety (r=0.76, p<0.000001), and pain self-efficacy (r=0.76, P<0.0000001). Preliminary Cronbach’s alpha scores were 0.96 (PMI-total), 0.92 (pain symptom subscale) and 0.93 (global symptom subscale).

Conclusion
A self-report questionnaire that is able to reliably detect alterations in pain modulation would be a
valuable clinical tool. It would be a large step forward in making the assessment and treatment of chronic pain more rigorous and effective. Based on our initial findings, the PMI appears to correlate with both baseline pressure pain thresholds and CPM suggesting that it is indicative of pain modulation. The differences in strength of correlations between the two subscales of the questionnaire suggests that the pain symptom subscale may have a stronger link to central sensitisation due to bottom-up nociceptive inputs, whereas the global symptom sub-scale may have a stronger link with top-down pain modulation. However, further studies in a larger sample of people with chronic pain are needed to explore the value of individual items in the questionnaire and to refine the ability of the questionnaire to reliably detect changes in pain modulation.
Date: 09/28/2016 03:15:00 PM

**Title**: Systematic Administration Of B Vitamins Inhibits Behavioral And Neurochemical Signs Of Diabetic Neuropathic Pain In Rats

**Poster Number** PW0015

**Authors**
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**Aim of Investigation**
Diabetic neuropathic pain (DNP) continues to possess major clinical challenge. The specific cellular and molecular mechanisms underlying DNP remain elusive and its treatment are limited. B vitamins have been used in aiding in treating some syndromes associated with diabetic neuropathy. We investigated treatment effects of B vitamins on DNP and the associated neurochemical alteration in rats.

**Results**
STZ-induced DNP in rats exhibited significant thermal hyperalgesia and mechanical allodynia associated with increased excitability of DRG neurons manifested as a decrease in action potential current threshold, increase repetitive discharge and spontaneous activity, and increased expression of P2X2/3 receptors in DRG neurons and p-ERK1/2 and p-CREB in DRG and SC. In vivo single injection of VBC (B1/B6/B12 at 33/33/0.5mg/kg,i.p.) transiently, significantly reduced the thermal hyperalgesia. Repetitive administration of the VBC (B1/B6/B12 at 33/33/0.5 mg/kg/d, 7-10 days) significantly inhibited thermal hyperalgesia and suppressed the increased DRG neuron excitability and increased expression of P2X2/3, p-ERK1/2 and p-CREB.

**Conclusion**
These findings provide evidence that B vitamins can effectively suppress DNP and the associated neurochemical alterations, and support the clinical use of VBC in treating DNP.
Title: An Educational Intervention To Assess Knowledge Of Chronic Non-Cancer Pain Among Family Physicians In Pakistan

Poster Number PW0016

Authors
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Aim of Investigation
To assess the knowledge of chronic non cancer pain (CNCP) among the family physicians and to evaluate the impact of an educational workshop for improving understanding of CNCP among family Physicians in province of Punjab, Pakistan.

Results
In our study, a total of 147 (67 female and 80 males) family physicians participated, 5 workshops delivered over a period of 24 weeks. More than half (54%) of all participants and 80% of female participants were between 20 and 30 years of age and all participants were under 50 years of age. Preliminary results showed overall a positive trend in improvement of family physicians' knowledge towards CNCP assessment and management as a result of participating in the workshop. Of those 142 participants who submitted pre and post-tests 129 completed all questions in both pre and post tests and 138 completed more than 14 questions. In only 4 questions, more than 50 % of participants recognize the correct answer in both pre and post-test. One question was misunderstood as 28% changed their correct answer to an incorrect answer in the post-test and only 5% got it right in both. For one other question more than 75% of participants answered incorrectly in both pre- and post- tests. However, with 8 questions participants showed a significant increase in answering correctly (P<0.05); 5 of those questions were from the section of knowledge of CNCP and 3 items were from the management of CNCP

Conclusion
To our knowledge, this is a first study that evaluate knowledge of CNCP among Family Physicians in Pakistan and to measure the consequence of trying to improve that knowledge. Evidence of improved
knowledge was measured but also evidence of increased confusion and unchanged deficits in knowledge. This study illustrates the need and the opportunity for improving understanding of CNCP knowledge and its management amongst general practitioners in Pakistan.
Title: Lowered Threshold For Self-Motion Perception To Galvanic Vestibular Stimulation In Patients Suffering From Weather-Related Pain

Poster Number PW0017

Authors
J. SATO, S. Aono, H. Sakurai, A. Saito, M. Toda, T. Ushida

Aim of Investigation
Several clinical studies have demonstrated a consistent relationship between changes in barometric pressure and pain intensity in patients with chronic pain. We have demonstrated that the barometric pressure sensor located in the inner ear (vestibule) contributes to the mechanism of weather-related pain. However, it has not been known whether the vestibule of patients with weather-related pain is more sensitive than that of healthy subjects. The present study, therefore, aimed to investigate the threshold for self-motion perception to galvanic vestibular stimulation (GVS) in patients with weather-related pain.

Results
The average perception threshold of subjects with weather-related pain (0.09 ± 0.02 [mA], mean ± SE) was significantly lower than that of weather-independent pain group (0.20 ± 0.03) and healthy control group (0.32 ± 0.04). The amplitude ratio of disappearance threshold to the perception threshold of subjects with weather-related pain was significantly lower than that of healthy control group.

Conclusion
These results showed that patients with weather-related pain are sensitive to vestibular inputs. From these results, it is suggested that one of the characteristics of the weather-related pain is to have different susceptibility to vestibular inputs.
Title: Towards A Taxonomy Of Musculoskeletal Pain Disorders That Is Mechanism-Based And Clinically Applicable

Poster Number PW0018

Authors
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Aim of Investigation
To develop a taxonomy for musculoskeletal (MSK) pain conditions that merges insights from pain pathophysiology and rheumatological clinical classification for both clinical and scientific uses.

Results
Two sets of taxonomic reforms will be presented. The first conforms to the format required by ICD which remains anatomically- or disease-based. This comprises four main categories: chronic musculoskeletal pain from persistent inflammation; chronic musculoskeletal pain associated with structural changes; chronic musculoskeletal pain due to disease of the nervous system; and chronic primary musculoskeletal pain (to include spinal pain and widespread pain). The second prefers classification by pain mechanisms and identifies conditions characterized by nociceptive pain and primary hyperalgesia and those characterized by nociplastic pain and secondary hyperalgesia.

Conclusion
The authors contend that the somatic dimension of musculoskeletal pain conditions is better conceptualized by incorporating underlying pain pathophysiology into conventional labels rather than by describing MSK pain as different disease entities or as 'pain syndromes'. These proposed new taxonomic sets are not mutually exclusive and can probably be integrated for clinical purposes, not only in pain clinics but also in rheumatology and primary care settings. Although they refer only to the somatic or biomedical dimension of the complex experience of musculoskeletal pain, they can be readily integrated with the psychological and social axes of an evolving taxonomy.
Title: Validation And Application Of A Core Set Of Patient-Relevant Outcome Domains To Assess The Effectiveness Of Multimodal Pain Therapy (Vapain: Study Protocol And Update)

Poster Number PW0019

Authors

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Aim of Investigation
Pain management approaches underwent a significant change of paradigm over the last decades. Over the last years, multimodal pain therapy (MPT) has been established internationally as a special type of therapy accounting for bio-psycho-social considerations in diagnostic and therapy. MPT seems to be effective, but comparability of studies is strongly limited due to diversity study designs and used outcome measurements. The presented study aims to develop a core outcome set consisting of a minimum of outcome measures deemed necessary for medical and therapeutic decision making, which must be measure in all clinical trials and non-randomized intervention studies.

Results
Results of systematic review on domains in effectiveness studies in MPT will be presented. Basing on these results the conducted online survey to estimate relevant and possible outcome domains in MPT revealed drifting apart interests of the different stake holders. During a subsequent presence meeting a preliminary consensus on 8 outcome domains could be achieved and in another online survey accomplished by definitions of the relevant domains. A first systematic review on psychometric properties for one domain (pain intensity) showed enormous lack of evidence for important pain intensity scales. In focus groups addressing patients view on measurement instruments for pain intensity scales the problematic issues of this scales were supported by the patient representatives.

Conclusion
To identify outcome domains of a comprehensive therapy approach such as MPT requires a face to face discussion to ensure that all important opinions are heard. The impossibility of a consensus during an online survey therefore has overcome and a consensus has been achieved. The perspective of patient...
representatives was important at several critical turning points and had a strong influence on the
development of the COS. The subsequent step in developing COS to identify relevant measurement
instruments of high psychometric property (here pain intensity measurement instruments) was
hampered by lacking evidence and obvious problems in content validity of the investigated scales. New
considerations arose out of the discussion of patient representatives where the high individuality of
pain experience and accordingly the problems to design scales were emphasized and imply that
measuring pain intensity as outcome might not be appropriate for interpretability and feasibility of
outcome assessment.
Title: Interventional Pain Management Services In Subsaharan Africa: A Multi-Disciplinary Treatment Approach

Poster Number PW0020

Authors
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Aim of Investigation
This review discusses the urgent need for interventional pain management services in sub Saharan Africa.

Results
Worldwide, about half of patients with chronic pain report low back pain, among other conditions; one fifth report widespread pain while one third report shoulder pain(1). People seek healthcare for pain not only for diagnostic evaluation and symptom relief, but also because pain interferes with daily activities, causes worry, emotional distress and undermines confidence in one's health. When pain persists for weeks or months, its broader effects on well being can be profound. Psychological health and performance of social responsibilities in work and family life can be significantly impaired. Delays in treatment or lack of appropriate facilities for treating chronic pain conditions are particularly damaging. The multi-disciplinary treatment approach can be expanded with better outcomes if appropriate interventional pain therapies can be employed in the management plan. The limitation of this enhanced conservative treatment could be lack of the technical skills and appropriate equipment in most health centres in sub Saharan Africa.

Conclusion
Approximately 10 to 20 percent of patients in primary care (2) experience chronic pain and it is the most personally compelling reason for seeking medical attention. There is urgent need for interventional pain management services in sub Saharan Africa.
Title: Assessment Of The Convergent Validity Of The Tampa Scale For Kinesiophobia For Temporomandibular Disorders- Japanese Edition: A Preliminary Study

Poster Number PW0021

Authors
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Aim of Investigation
We developed the Tampa Scale for Kinesiophobia (TSK) for Temporomandibular Disorders (TMD) Japanese edition (TSK-TMD-J) and confirmed its high internal consistency, test-retest reliability, and responsiveness. This preliminary study aimed to investigate the convergent validity of the TSK-TMD-J.

Results
Mean intensity of subjective pain was 25.4±25.0 mm in VAS. Mean range of mouth opening was 41.7±9.0 mm. The total score in TSK-TMD-J was 27.8±4.7. Activity avoidance and somatic focus scores in TSK-TMD-J were 15.9±2.9 and 11.9±2.3, respectively. The total score in TSK-TMD-J was correlated with the helplessness score in the PCS and the general health perception (GH) score in SF-36 (r=0.48, p<0.01 and r=-0.51, p<0.01, respectively). The activity avoidance score in TSK-TMD-J was also correlated with the helplessness score in PCS and the GH score in SF-36 (r=0.37, p<0.05 and r=-0.44, p<0.05, respectively). The somatic focus score in TSK-TMD-J was correlated with the rumination and helplessness scores in PCS and the GH score in SF-36 (r=0.48, p<0.01; r=0.53, p<0.01; r=-0.50, p<0.01, respectively).

Conclusion
The total and subscale scores in TSK-TMD-J might be reflect a reduction in subjective health perception. Many questions in subscales except GH assess physical activity based on mobility. Therefore, TSK-TMD-J only showed significant correlation with GH. Moreover, patients who were afraid of moving their jaw may fear pain or vice versa because the total and subscale scores of TSK-TMD-J showed significant correlations with the helplessness scores in PCS. Further studies with larger sample sizes will be required through our sample size calculations based on the results of this preliminary study.
Date: 09/28/2016 09:30:00 AM

Title: Inflammatory Serum Protein Profiling Of Patients With Lumbar Radicular Pain One Year After Disc Herniation: Analysis Of Biomarkers For Better Understanding Of Pain Pathophysiology

Poster Number PW0022

Authors

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Aim of Investigation
In this explorative study we investigated the serum inflammatory protein profile in patients suffering from severe lumbar radicular pain following disc herniation one year after the start of the pain symptoms. The control group was patients with the same disease, whom had become free from pain.

Results
We found clear overall difference in the serum cytokine profile between the chronic pain patients (n=23; VAS 8-10) versus the patients that had recovered from the radicular pain (n=22; VAS 0-1) from the same cohort, followed over 12 months from the start of their symptoms of disc herniation. Given a false discovery rate (FDR) of 0.10 or 0.05, we identified 41 and 13 proteins respectively, which were significantly up-regulated in the patients with severe pain one year after disc herniation.

Conclusion
The present data demonstrated that sciatica patients with a chronic pain outcome have increased levels of inflammatory proteins in serum one year after disc herniation. This is to our knowledge the first broad protein serum profiling study of patients with chronic lumbar radicular pain. An inflammatory PEA-based 'fingerprint' in these persistent pain patients was demonstrated. We conclude that serum proteins are measurable molecular markers of patients that develop persistent pain after disc herniation. The pathophysiological relevance of these proteins remains to be investigated. Multiplex
analysis of inflammatory biomarker patterns may provide some information on pain pathophysiology, and perhaps give insights regarding prognosis and choice of treatment.
Title: Management Of Chronic Perineal Or Lower Abdominal Pain

Authors
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Aim of Investigation
Chronic perineal or lower abdominal pain is encountered quite often in a pain treatment clinic, but its treatment is difficult in many cases. They come to the pain clinician most of the time after unsuccessful treatment by specialists of other disciplines.

Results
Average current age of the patients is 77.0 (Median 76.0, SD ±4.5). The age at which the pain started is 66.1 (Median 69.0, SD ±5.8), and the average age of the first visit to our clinic is 73.8 (Median 74.5, SD ±5.3). Average duration of pain before coming to our clinic is 6.1 years (Median 7.2, SD ±7.8) and we treated them at an average duration of 4.2 years (Median 5.0, SD ±5.4). Their pain ranged from perineal, perineal-anal, anal and lower abdominal. Treatment strategy included medication (pregabalin, amitryptiline, narcotic, etc), near infra-red radiation, spinal cord stimulation and regular consultation. Complete pain relief is difficult in most of the cases and the effective method is dependent on the patient’s condition. One male patient with anal pain developing after coloscopic examination responded to spinal cord stimulation. One female patient with low abdominal pain of unknown etiology is resistant to any treatment including spinal cord stimulation but the pain is barely controlled with oral morphine.

Conclusion
Perineal and lower abdominal pain is difficult to control partly due to complex sensory and sympathetic innervation of the region. However, many patients with this problem come to the pain treatment clinic. It is important to listen to their complaint carefully understanding their suffering and try to use proper strategy to cope with the pain.
Title: Diagnostic Accuracy Of Neck Tornado Test As A New Screening Test In Cervical Radiculopathy

Poster Number PW0024

Authors
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Aim of Investigation
Cervical radiculopathy (CR) is defined as pain in a radicular pattern in one or both upper extremities related to compression and/or irritation of one or more cervical nerve roots with the existence of a cervical disc herniation or other lesions that decrease the dimension of the foramen on MRI or CT as a criterion standard. The Spurling’s test, one of the most commonly applied provocative test in cervical radiculopathy (CR), is a highly specific, and only low to moderately sensitive examination. To introduce a new provocative test to examine the neck and cervical spine in CR, Neck Tornado Test (NTT), and to compare the diagnostic accuracy with an acknowledged physical examination, the Spurling’s test.

Results
In the Spurling’s test and NTT: sensitivity was 55.22 (43.32-67.13) % and 85.07 (76.54-93.61) % (p<0.0001); specificity was 98.53 (95.67-101.39) % and 86.76 (78.71-94.82) % (p=0.0026); the PPV was 97.37 (92.28-102.46) % and 86.36 (78.08-94.64) % (p=0.0075); the NPV was 69.07 (59.87-78.27) % and 85.51 (77.2-93.81) % (p=0.0423); accuracy was 77.04 (69.94-84.13) % and 85.93 (80.06-91.79) % (p=0.0252).

Conclusion
The Neck Tornado Test is a sensitive test with superior diagnostic accuracy for CR diagnosed by MRI. Therefore, Neck Tornado test can be useful clinically as a screening test, and help to confirm CR by MRI.
Aim of Investigation
Chronic pain (CP) patients have an increased risk of developing cognitive impairment, a recognized factor in the prognosis of behavioral disorders and therapeutic success, but still lack adequate screening in clinical routine. Therefore, we evaluated the Japanese version of the Montreal Cognitive Assessment (MoCA-J) for its suitability in assessing cognitive performance in CP patients in comparison to the commonly used mini-mental state examination (MMSE).

Results
[Experiment 1] CP patients performed poorly in cognitive domains, especially in lexical fluency (mental flexibility) and working memory. The MMSE or TMT-B discriminated more weakly than the VFT. The VFT identified patients with cognitive impairment with a sensitivity of 76.9% and specificity of 100% for a cut-off value of <13 words per minute. The MoCA-J correlated well with problems in locomotion (rs=0.938, p<0.001). There were no significant differences in the results of pain-related tests, motor functions, and QOL, before- and 3 months after-intervention. [Experiment 2] Pain-related tests, NRS, PDAS, and PCS, correlated with VBM analysis comparing local volumes. Significant regions included bilateral-paracentral lobules (right and left, rs= -0.44 and -0.47, respectively), which are part of the primary somatosensory area; bilateral-anterior cingulate cortex (rs=0.53 and 0.55), left-medial-superior frontal gyrus (rs=0.52), left-anterior hippocampus (rs=0.52), left-rolandic operculum (rs=0.44), which is part of the secondary somatosensory area and language, and left inferior occipital gyrus (rs= -0.46) (all p<0.05).
Conclusion
The MoCA-J represents a suitable cognitive screening tool for CP patients. The VFT can be performed quickly, and is one of the sub-sections of both MoCA and FAB. The VFT demonstrated good sensitivity and specificity levels, covering executive function, which appears to play an important role in the cognitive performance of CP patients. In CP patients with lower back pain, we also found changes in the local volume of cognitive regions of the brain, including the limbic system and fronto-striatal projections, which have an important association with the VFT and executive functions. Since management for CP with SMC alone was not an effective remedy, it has been suggested that additional rehabilitative therapies are also necessary. In the future, MoCA-J could be used as a cut-off for effectual therapeutic response, including physical therapy (exercise) and cognitive behavioral therapy.
Date: 09/28/2016 09:30:00 AM

Title: Influence Of Pain Catastrophizing On Intensity Of Pain In Patients With Different Chronic Pain Diseases

Poster Number PW0026

Authors
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Aim of Investigation
Intensity of pain is easily modified by emotions or way of thinking. Pain catastrophizing is known to be correlated with intensity of pain in several chronic pain disease. However, it is unclear that these relationships are identical in any type of chronic pain diseases. In this study, we clarified the relationships in patients with five representative chronic pain diseases.

Results
There were significant relationships between maximal NRS and PCS in patients with post herpetic neuralgia (r=0.45) and fibromyalgia (r=0.62). On the other hand, the significant relationships were not seen in patients with complex regional pain syndrome, spinal canal stenosis, lumbar spinal canal stenosis or atypical facial neuralgia.

Conclusion
From these results, in patients with post herpetic neuralgia and fibromyalgia, severe pain tend to lead them negative thinking (pain catastrophizing), and conversely, negative thinking might make them feel severe pain. It is also suggested that the relationship between pain catastrophizing and intensity of pain is different among chronic pain diseases.
Title: Long-Term Treatment With Methylphenidate For Pain And Mental Fatigue After Traumatic Brain Injury

Poster Number PW0027

Authors
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Aim of Investigation
Traumatic brain injury (TBI) may cause long-lasting post-concussive symptoms, such as mental fatigue and concentration difficulties and this may become the main hindrance for returning to work and studies. There is currently no effective treatment for long-lasting mental fatigue. In this hypothesis generating study the long-term effects of methylphenidate on mental fatigue, cognitive function, pain and safety were assessed.

Results
After six months follow-up, effects on Mental Fatigue Scale (MFS), depression, anxiety and cognitive function (processing speed, attention, working memory) were significantly improved compared to baseline data (<i>p</i>&lt;0.001 respectively). Pain was not improved as measured with VAS but the patients tolerated their pain much better. Heart rate was significantly increased (<i>p</i>=0.01), while blood pressure was not changed.

Conclusion
Individuals suffering from prolonged symptoms after TBI reported reduced mental fatigue and improved cognitive functions with long-term methylphenidate treatment. They tolerated pain better. It is suggested that methylphenidate can be a treatment option for long-term mental fatigue and cognitive impairment after a TBI, but further randomized control research is warranted.
Title: The Proposed Classification Of Chronic Musculoskeletal Pain For Icd-11

Poster Number PW0028

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Aim of Investigation
Chronic pain syndromes, including chronic musculoskeletal pain (MSK), are not represented in the current International Classification of Diseases (ICD) in a systematic manner. This very large category is characterized by different definitions and classifications according to countries and medical specialties. This has deprived patients, clinicians and administrators of an appropriate reference base for problems characterized primarily by pain and its attendant loss of function and amenity. The current ICD10 MSK classification refers to underlying rheumatologic diseases and anatomical disorders of the MSK system but does not integrate all chronic MSK pain dimensions. The International Association for the Study of Pain (IASP) has long campaigned for improvements in this classification system.

Results
In the proposed classification chronic pain has been pragmatically defined as pain that persists or recurs for more than 3 months. Chronic musculoskeletal pain embraces that which arises as part of an identifiable disease process directly affecting bone(s), joint(s), muscle(s) or related soft tissue(s). This includes chronic musculoskeletal pain due to persistent inflammation or associated with structural changes affecting bones, joints, tendons or muscles. Musculoskeletal pain of neuropathic origin will be cross-referenced to 'neuropathic' pain and conditions such as non-specific back pain or chronic widespread pain will be cross-referenced to 'chronic primary pain'.

Conclusion
In the context of the overall classification proposal, several improvements can be expected. For the first time chronic musculoskeletal pain syndromes will be represented in the ICD in a comprehensive and systematic manner, including all dimensions, thereby improving their recognition. It is hoped that in time this will translate into improved assessment for patients and access to multimodal management towards relief of pain and improvement in function.
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Title: Bowel Function Index: Evaluating Opioid-Induced Constipation In Patients With Moderate-To-Severe Pain From Culturally And Geographically Diverse Countries

Poster Number PW0029

Authors
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Aim of Investigation
Constipation is a common class effect of opioid analgesics. Many patients report that opioid-induced constipation has a negative impact on their quality of life and impairs activities of daily living. The Bowel Function Index (BFI) was developed to provide a patient-reported assessment of constipation symptoms in individuals with chronic pain. Studies validating the BFI have shown it to be a reliable instrument to measure symptoms of opioid-induced constipation. In an exploratory, post hoc analysis we evaluated the presence and nature of constipation using BFI in patients with opioid-induced constipation who participated in clinical trials from diverse locations worldwide across a range of pain settings.

Results
In total, 2644 patients from 24 countries (Asia, North America, Europe and Australia) who participated across 11 trials were included in this analysis. The trials comprised randomized, controlled, double-blind, phase III (n=7); randomized, controlled, cross-over, phase III (n=1); randomized, controlled, double-blind, phase II (n=1); open-label, uncontrolled, phase III (n=1); and observational, cross-sectional (n=1) studies. Mean (SD) total BFI scores at baseline in each of the 11 studies ranged from 56.9 (21.5) to 67.4 (20.5). Cohen's effect size (f=0.472) indicated a strong effect regarding similarity of baseline BFI scores across the trials and the transformed correlation coefficient of r=0.427 represented good correlation of BFI scores between the studies. Baseline BFI scores showed little variation across geographical regions. Mean (SD) BFI scores of the three studies conducted in North America (n=953 in total) ranged from 63.2 (25.0) to 64.1 (30.0), and mean BFI (SD) in an Asian trial of 202 patients (conducted in China, Japan, South Korea, Singapore and Thailand) was 61.5 (23.0). Data pooled from five studies conducted in Europe revealed mean (SD) baseline BFI scores of 61.1 (23.6) in Western Europe (n=808) and 63.7 (20.1) in Eastern Europe (n=204).
Conclusion
This study demonstrates that the validated BFI is a useful tool to evaluate opioid-induced constipation globally. In patients with moderate-to-severe pain participating in clinical trials, BFI revealed that opioid-induced constipation is remarkably similar across patients from a range of ethnic groups and countries. Medical writing support was provided by Siân Marshall of SIANTIFIX Ltd, Cambridgeshire, UK, funded by Mundipharma Research GmbH & Co.KG. Copyright for the Bowel Function Index is owned by Mundipharma Laboratories GmbH, Switzerland, 2002; the BFI is also the subject of European Patent Application Publication No. EP 1,860,988 and corresponding patents and applications in other countries.
Title: Observational, Multicentre Study Evaluating The Bowel Function Index For Constipation In Asian Countries

Poster Number PW0030

Authors
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Aim of Investigation
Opioid-induced bowel dysfunction is a common yet under-managed class effect of opioid analgesia. The validated Bowel Function Index (BFI) provides a reliable measure of patient-reported constipation symptoms in individuals with chronic pain. In this study, BFI was evaluated in patients from China, Japan, South Korea, Singapore and Taiwan.

Results
Demographic characteristics were balanced across constipated (n=134) and non-constipated (n=68) groups: mean age was 60 years, 56% were male, 96% were Asian and mean body mass index was 22.5 kg/m2. Cancer was the primary cause of pain for most constipated (72%) and non-constipated (60%) patients. As anticipated, constipated patients had harder stools, fewer bowel movements and greater laxative intake vs non-constipated patients. Mean (SD) total BFI scores were also greater in constipated (61.5 [23.0]) vs non-constipated (11.4 [15.6]) patients, as were BFI item scores: 'ease of defaecation': 67.2 (24.5) vs 15.5 (23.3); 'feelings of incomplete evacuation': 48.8 (33.2) vs 10.4 (19.8); 'patient judgement of constipation': 68.4 (26.1) vs 8.3 (16.7). BFI scores were not influenced by age or gender. Mean (SD) BFI scores were high for constipated patients from each country (China 65.5 [20.8]; Japan 57.8 [23.6]; South Korea 66.6 [15.8]; Singapore 65.7 [16.5]; Taiwan 53.2 [30.4]), while BFI scores in non-constipated patients were within the reference range (0–28.8) for non-constipated patients with chronic pain, ranging from Japan: 3.6 (4.8) to Singapore: 19.7 (19.5). These findings are consistent with prior studies in Europe (Ueberall et al. J Int Med Res 2011;39:41–50). For constipated patients, internal consistency for BFI was high: Cronbach's alpha = 0.77 and remained above the threshold for good internal reliability (0.70) with each BFI item deleted (alpha = 0.87–0.92). Spearman's rank correlation of
each BFI item and total score indicated high inter-item correlation (r=0.45–0.71, p<0.0001). In contrast, in non-constipated patients, Cronbach’s alpha for BFI = 0.67 and increased >10% with each item deleted, indicating lower reliability, and inter-item Spearman’s rank correlations were not significant (these findings were anticipated in non-constipated patients since BFI is a tool to assess 3 constipation parameters). Correlations between BFI item scores and bowel habits (stool frequency, stool consistency and laxative intake) were r=-0.40 to 0.08 and -0.29 to 0.26 for constipated and non-constipated patients, respectively.

**Conclusion**

This study demonstrated that BFI is a valid, reliable and sensitive tool for assessing opioid-induced constipation in patients receiving analgesia in Asia, with outcomes similar to prior studies in Western patients with chronic pain. This study was funded by Mundipharma Research GmbH & Co.KG. Medical writing support was provided by Siân Marshall of SIANTIFIX Ltd, Cambridgeshire, UK, funded by Mundipharma Research GmbH & Co.KG. Copyright for the Bowel Function Index is owned by Mundipharma Laboratories GmbH, Switzerland, 2002; the BFI is also the subject of European Patent Application Publication No. EP 1,860,988 and corresponding patents and applications in other countries.
Title: Comparison Of Three Pain Assessment Scales In Different Patient Groups, Patients’ Preferences, And Need For Treatment

Poster Number PW0031

Authors
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Aim of Investigation
The purpose of this study was threefold: a) to compare three pain severity scales: vertical and horizontal numeric rating scales (NRS), and a verbal descriptive scale (VDS) in four patient groups; b) to evaluate which of the three scales patients prefer to use; and c) to assess where on the three scales patients feel they need treatment for their pain. Differences were assessed between the four patient groups and according to sex.

Results
Data were analyzed from 70 rheumatic and 70 cancer patients, 67 patients in geriatric rehabilitation, and 68 postoperative patients (N=275). The mean age was 64.7 years (sd=18.0, range 18-95) and 51% were women. The three pain scales were strongly correlated, both in the total sample and in the four patient groups, p<0.001, and differentiated between pain severity in the respective groups and according to sex, p<0.05. The verbal descriptive scale was the preferred instrument to use (≥50%) in all four patient groups. The mean score for the total sample, on when patients felt they did not need treatment, was 2.0 (mild) on the VDS, and 2.8 and 2.6 on the NRSs. Patients felt they needed treatment, although not urgent, when their pain was 2.8 (moderate) on the VDS, and 4.3 on average on the NRSs. Urgent need for pain treatment was felt when mean pain severity was 4.3 (severe) on the VDS and 7.9 on the NRSs. Women rated pain severity for urgent pain treatment higher than men on all three scales, p<0.05. Similarly, mean pain severity was higher when elderly patients needed urgent treatment,
compared to patients with rheumatism and cancer on the VDS, and rheumatic patients on the NRSs, p<0.05.

**Conclusion**
The three pain scales were found to be strongly correlated in the four different patient groups and can be used interchangeably to assess pain severity. The preferred scale of choice was the verbal descriptive scale. Patient assessment of when they needed treatment on the scales corresponded to mild, moderate and severe pain cut-points reported in the literature.
Title: Training Subjects To Report Their Pain More Accurately Improves Study Power: Results Of A Randomized Placebo-Controlled Study Of Pregabalin Versus Placebo In Painful Diabetic Neuropathy

Poster Number PW0032

Authors
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Aim of Investigation
Clinical trials of analgesics have been plagued by the insensitivity of pain outcome measures due in large part to large variability in subject's pain reports. Previous studies have shown that subjects differ greatly in the accuracy with which they report their pain, and that these differences in pain reporting skill predict ability to discriminate effective drugs from placebo in clinical trials. To date no studies have examined the effectiveness of methods to train subjects to report pain more accurately on the sensitivity of trials to discriminate analgesics from placebos. To this end, we have developed an Evoked Pain Training (EPT) method, aimed to train subjects to be better discriminators (connoisseurs) of their pain experiences. The aim of the current study was to assess the effects of the EPT on patients' ability to discriminate drug from placebo in a double-blind crossover trial of pregabalin in a population of patients with painful diabetic neuropathy (PDN).

Results
Ninety-nine subjects were screened and 67 subjects (37 females) with a mean age (±SD) of 56.4±10.8 were included in the safety population. Per-protocol population included 53 subjects who completed the entire study. Subjects' pain reporting skills, calculated as R-squared values, improved during training, from 0.543 at the screening visit, to 0.550, 0.601, 0.650 and 0.706 during EPT visits 1 to 4, respectively. No significant differences were found in changes in average pain between pregabalin (mean± SD, 1.02±1.96) and placebo (0.80±1.81) (p=0.533, SES=0.090) in the overall (trained and untrained) population. Subjects who underwent EPT (n=29) demonstrated positive SES (0.339), with a trend (p=0.084) toward statistical significant superiority of pregabalin (0.93±2.16) vs. placebo (0.21±1.166), while untrained subjects (n=24) demonstrated negative SES (-0.149) (i.e. placebo outperformed pregabalin), with no statistically significant differences (p=0.502) between pregabalin (1.14±1.62) and placebo (1.57±2.27). Training effects on secondary pain endpoints were consistent with the primary endpoint.
Conclusion
The results of the first study phase demonstrated that subjects’ ability to accurately and reliably report their pain is a trainable skill that improves upon training. The second study phase resulted in a failed trial, in which pregabalin, a drug with a known efficacy, failed to demonstrate statistical superiority over placebo in the entire cohort. However, subjects who were trained to report their pain accurately did demonstrate positive SES with a trend toward superiority of pregabalin over placebo, while untrained subjects demonstrated negative SES (placebo did better than pregabalin). Training subjects to more accurately report their pain before entering into analgesic clinical trials by the EPT dramatically enhances the study power to discriminate between drug and placebo. This can translate into more efficient clinical drug development programs, which are based on smaller studies, with fewer clinical sites (that will further reduce variability and will enhance study power) and may shorten overall drug development time.
A Classification Of Chronic Pain Syndromes For ICD-11

Poster Number PW0033

Aim of Investigation
Chronic pain is a major source of suffering affecting an estimated 20% of people worldwide and accounts for 15-20% of physician visits. However, currently chronic pain syndromes are not represented in the International Classification of Diseases (ICD) in a systematic manner. The International Association for the Study of Pain (IASP) has long campaigned for improvements in the classification system.

Results
Chronic pain has been recognized as pain that persists past the normal time of healing and has lost its warning function. In the proposed classification this has been pragmatically defined as pain that persists or recurs for more than 3 months. Seven further subdivisions (chronic primary pain, chronic cancer pain, chronic postsurgical and posttraumatic pain, chronic neuropathic pain, chronic headache and orofacial pain, chronic visceral pain and chronic musculoskeletal pain) will be spelled out. In all these categories, pain is either the sole, or a leading, complaint of the patient and requires special treatment and care. For chronic pain as well as all the further pain syndromes, a number of optional specifiers can be used to indicate pain severity (consisting of pain intensity, pain-related distress and disability), the time course, and the presence of evidence for psychosocial factors.

Conclusion
A major challenge in the development of the classification was finding a rational organizing principle that is applicable for all selected diagnoses, but that also fits into the general ICD-11 framework. Since even in the ICD several classification principles coexist, the task force had to adopt a compromise. The seven diagnostic groups represent such a compromise. Although far from perfect, several improvements can be expected from this classification: Chronic pain as a condition that requires special consideration and treatments will be much better expressed than ever before in ICD and chronic pain conditions that
were neglected in former ICD-versions now will be represented, e.g. chronic cancer pain, chronic neuropathic pain.
Aim of Investigation
Patients with chronic pain are faced with limited therapeutic options. Moreover, the clinical diagnosis of pain is largely subjective. In order to identify novel therapeutics and objective diagnostic criteria, we seek to better understand the mechanisms of signal processing in the brain associated with pain. Our lab showed that a model of neuropathic pain enhances low-frequency power in somatosensory cortex (LeBlanc et al. 2014), and that cortical power is attenuated using a novel T-type calcium channel with analgesic properties (LeBlanc et al. 2016), suggesting that cortical power correlates with neuropathic pain.

Results
Our data show increased power in primary somatosensory cortex (S1) and prefrontal cortex (PFC) in awake, freely-behaving rats with acute, inflammatory or neuropathic pain. In the neuropathic pain model, coherence between PFC and S1 is significantly increased at a late, but not early, time point during the development of nociceptive behavior. Treatment with ibuprofen (non-steroidal anti-inflammatory), pregabalin (calcium channel blocker) or mexiletine (sodium channel blocker) attenuates power and S1-PFC coherence.

Conclusion
Our data suggest that cortical power correlates with pain, analgesia and the transition from acute to chronic pain.
Title: Trial Of Mindfulness-Based Pain Management In A Small Private Clinic

Poster Number PW0035

Authors
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Aim of Investigation
Mindfulness is said to be the third-generation cognitive behavioral therapy. Not only can it change responses to sensory events, but it has a strong theoretical basis. Around the world, mindfulness has been used in various fields such as psychotherapy, education, welfare and medical care. In the Japanese medical field, facilities are limited, and mindfulness has been adopted particularly in the private clinics. Although the technique tends to be limited to psychologists or psychiatrists, mindfulness-based pain management can be effective even when performed by a pain clinician who is not an expert in psychology or psychiatry, but in interventional therapy.

Results
Improvement in PCS scores was seen in both cases. In addition, improvements in NRS, PDAS and HADS-Anx scores, and worsening of HADS-Dep were seen in Case 1; however, improvement in HADS-Dep, worsening of NRS, and worsening of PSEQ and HADS-Anx scores were seen in Case 2. This decrement in NRS and psychological scores was seen in a single episode of care, but gradually improved. Case 1 NRS 10/10→3/10 PDAS 46/60→39/60 HADS-Anx 16/Dep 13→Anx 9/Dep 15 PCS 50/52→36/52 Case 2 NRS 8/10→10/10 PSEQ 20/60→17/60 HADS-Anx 5/Dep 15→Anx 8/Dep 10 PCS 36/52→27/52

Conclusion
Mindfulness therapy has a cognitive aspect and a behavioral aspect. On the cognitive side, one learns the relationship between 'thought' and 'emotion.' On the behavioral side, one practices meditation. Mindfulness meditation is characterized by focused attention and open monitoring practices. Focused attention may reduce pain by disrupting the communication of sensory experience as pain; the non-evaluative stance of open monitoring reduces an experiencer’s tendency to get caught up in pain. From various reports, mindfulness-based cognitive behavioral therapy produces changes in the activity of the brain, and in one’s environment, cognitions, and behaviors, and has been found to cause a change in
emotions. Pain is also reduced by these mechanisms. These case studies suggest that a brief mindfulness intervention performed by a non-specialist can improve both physical and psychological conditions of patients with chronic pain. The results also raise the possibility that even pain clinicians in small clinics can provide comprehensive medical treatment to patients without the multidisciplinary approach of general hospitals. One potential drawback is that it is difficult to allocate sufficient time for mindfulness classes in the everyday practice of private clinics in Japan. We therefore carried out a shortened version of the mindfulness class. We believe that some benefit could also be obtained by incorporating teaching materials for self-learning, combined with frequent visits to the clinic over a short period of time.
Title: The Proposed Classification Of Chronic Postsurgical And Chronic Posttraumatic Pain For ICD-11

Poster Number PW0036

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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 postsurgical and chronic posttraumatic pain. This contrasts with the fact that chronic pain frequently develops after surgical interventions or as a consequence of accidental injuries. The incidence of chronic pain after multitrauma lies in the range of 46 to 85%. The International Association for the Study of Pain (IASP) has long campaigned for improvements in the classification system.

Results
In the proposed classification chronic pain has been pragmatically defined as pain that persists or recurs for more than 3 months. Chronic postsurgical pain is pain that begins after a surgical procedure at the site of the surgery and lasts at least three months. Chronic posttraumatic pain is defined in a parallel manner as chronic pain that develops after a tissue injury (including burns) at the site of the trauma and persists at least three months after this initial event.

Conclusion
In the context of the overall classification proposal, several improvements can be expected. For the first time chronic postsurgical pain and chronic posttraumatic pain will be represented in the ICD. Due to the different causality (surgical intervention vs. accidental injury) and also from a medico-legal perspective, a separation between postsurgical pain and pain after all other trauma was regarded as useful despite the fact that similar processes may underlie the ensuing pain syndrome. The new diagnoses will allow to code postsurgical and posttraumatic pain syndromes in a comprehensive and straightforward manner, thereby improving the recognition of chronic postsurgical and posttraumatic pain. It is hoped that this increased recognition in time will translate into improved pain relief and access to multimodal treatments.
Title: Further Evaluation Of The Japanese Version Of The Pain Self-Efficacy Questionnaire

Poster Number PW0037

Authors

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Aim of Investigation
The current study aims to evaluate the psychometric properties of the original ten- and four-item short-form versions of the Pain Self-Efficacy Questionnaire (PSEQ) with Japanese chronic pain patients.

Results
Confirmatory factor analyses revealed that both versions of the PSEQ showed an acceptable fit to the data (Original: χ² (33) = 91.00, p < .01, χ² / df = 2.76, SRMR = .04, RMSEA (90% CI) = .11 (.08-.13), GFI = .90, CFI = .95, PNFI = .68, and AIC = 135.00; Short form: χ² (2) = 5.16, p < .08, χ² / df = 2.58, SRMR = .02, RMSEA (90% CI) = .10 (.00-.21), GFI = .99, CFI = .99, PNFI = .33, and AIC = 21.16). Adequate internal consistencies were also observed (10 item version: α = .94; 4 item version: α = .90). Both versions of the PSEQ had moderate correlations with pain intensity (NRS, original r = -.38; short-form r = -.38), pain interference (PDAS, original r = -.59; short-form r = -.56), pain catastrophizing (PCS, original r = -.68; short-form r = -.66), depression (HADS depression scale, original r = -.68; short-form r = -.66), anxiety (HADS anxiety scale, original r = -.56; short-form r = -.54) and health-related quality of life (EQ5D, original r = .65; short-form r = .64).

Conclusion
Both the original and the short-form versions of the PSEQ demonstrated sound psychometric properties in a sample of Japanese patients with chronic pain. The findings suggested an extended utilization of the short-form PSEQ for assessing self-efficacy in Japanese chronic pain patients.
Date: 09/28/2016 09:30:00 AM

**Title**: One-Sheet,10-Item Questionnaire For Spinal Pain: An Expert Nurse Intently Listens To Patients’ Complaints For Ten Minutes Before Physician Consultation

**Poster Number** PW0038

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**Aim of Investigation**
The spine is the most frequent anatomical site of pain that originates from cervical, thoracic, lumbar and sacrum lesion. Spinal pain is not a clinical entity but a symptom, with different stages of impairment, disability, chronicity and handicap. Spinal pain is complex, and consists of several spinal disorders. Symptoms vary from localized spinal pain or motion pain to numbness, radiating pain, or motor/sensory disturbances at upper/lower extremities. There are problems in acquiring useful information by questionnaire. That is, 1) time-consuming, 2) difficulty to get accurate pain history, 3) many modifying factors such as occupational/socioeconomic/psychological effects, 4) there are neck/back specific pain scales, but none for whole spine, 5) much effort is paid to numerical pain rating scales for outcome evaluation. For example, several validated methods or standardized measures by an international group of back pain researchers are available to assess the symptom outcome after treatment. However, the time required to administer these instruments is a major obstacle to their widespread use because numerical rating scales are typically used to measure intensity. Moreover, little research has focused on questionnaires used for diagnosis at the first consultation. Since 2008, I have developed a new questionnaire for outpatients of spinal pain as a clinical listening tool to gather information concerning patient's whole life. This questionnaire is patient- complaint-based diagnosing tool, and consists of the following ten items: 1) Pain severity/frequency/distribution & daily dysfunction (open-ended questions and self-pain drawing), 2) Past history and medication, 3) History of operation, 4) Occupation & income, 5) Smoking & drinking habits, 6) Sleep quality, 7) Healthy lifestyle habits, 8) Living situation, 9) Fears and hopes about pain, 10) Patient expectations. The aim of Investigation is to introduce this questionnaire of spinal pain, which is summarized on a single sheet by an orthopedic nurse. It could be used in routine outpatient clinics to get precise diagnosis and begin treatment smoothly. I have also researched the time needed to complete this questionnaires.
Results
The mean question time was 10 minutes (5 minutes or less; 19%, 6-10 minutes; 49%, 11-15 minutes; 24%, 16-20 minutes; 7%)

Conclusion
This questionnaire is available for primary care physicians to diagnose or manage spinal pain at clinical examinations. Using this, physicians can quickly focus on specific problems and ask additional questions without needing the time to 'listen to' a long list of possible symptoms. Our spinal surgeon decide the pathoanatomical site of pain from whole spine. For accurate diagnosis, I use the following classification of spinal disorders based on both therapeutic anatomical targets and pathology, A; Alignment, B; Bone, C; Cord, D; Disc, E; Epidural space, F; Frava and other ligament, and G; Ganglion and nerve root. After I decide the anatomical site by using this questionnaire and clinical examination, patients are sent to radiological testing to evaluate pathology. This flowchart of diagnosis, first by questionnaire, followed by decision of the anatomical site of pain, and finally pathology of pain, is very useful and efficient. In conclusion, listening to patients is time-consuming, but the patients need this. I propose that 'listening' nurses should be one therapy method, where the patient can talk about their complaints without hesitation or restraint. In addition, it is very useful for physicians to easily choose the treatment option.
Title: A Prospective Study To Determine Agreement Between Two Methods Of Percentage Pain Reduction And Compare Self-Reported Pain Assessment Instruments In Chronic Low-Back Pain Patients Treated With Epidural Steroid Injections

Poster Number PW0039

Authors
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Aim of Investigation
The purpose of this study was to estimate the degree of agreement between calculated percent pain reduction (CPR) and perceived percentage pain reduction (PPR) in chronic lower back pain patients undergoing epidural steroid injection (ESI). This study also assessed the degree of correlation for three single item pain intensity scales (Numeric Rating Scale [NRS], Verbal Descriptor Scale [VDS], and Visual Analog Scale [VAS]), two multidimensional pain assessment instruments (Brief Pain Inventory [BPI], Short Form McGill Pain Questionnaire 2 [SF-MPQ-2]), and a multiple-item functional tool (Oswestry disability Index [ODI]).

Results
At 30-minutes post-procedure, the PPR and NRS-based CPR differed by -0.3 (95% CI: -3.6 to 3.0; P-value: 0.970), and the PPR and VAS-based CPR differed by 3.1 (95% CI: -0.2 to 6.3; P-value: 0.125). At 7-days post-procedure, the PPR and NRS-based CPR differed by -5.4 (95% CI: -11.6 to 0.8; P-value: 0.157), and the PPR and VAS-based CPR differed by -3.1 (95% CI: -9.3 to 3.0; P-value: 0.506). Correlation coefficients of pain ratings between the single item pain intensity scales (NRS, VAS, VDS) ranged from 0.51 to 0.78 at the pre-procedure stage, 0.80 to 0.92 at 30-mins post-procedure, and 0.81 to 0.95 7-day post-procedure. Correlation coefficients of pain ratings between the multiple-item and multidimensional scales (ODI, BPI interference vs severity, and SF-MPQ-2) ranged from 0.37 to 0.55 at the pre-procedure stage, and 0.64 to 0.81 7-day post-procedure.
Conclusion
Our results demonstrate agreement between PPR and CPR (both NRS-based and VAS-based) at 30 minutes post-ESI. The NRS-based CPR and PPR at 30 minutes post-ESI had the highest level of agreement (95% Confidence interval: -3.6 to 3.0; P-value: 0.970). However, at 7-day post-ESI, the PPR and NRS-based CPR had reduced agreement (-5.4 difference; CI: -11.6 to 0.8), per the 5% parameter of agreement. These findings suggest that PPR and CPR (based on NRS and VAS) can be used interchangeably in chronic lower back pain patients to assess changes in pain symptoms 30 minutes after ESI. The VAS-based CPR may reflect changes in pain symptoms more accurately than the NRS-based CPR 7 days after ESI. The single item pain intensity scales (NRS, VAS, VDS) demonstrated moderate to very high correlation with each other at all three time points in the study (CC: 0.51 to 0.95). Correlation between the VAS and VDS was moderate (CC: 0.51). The generally high correlation noted amongst NRS, VAS, and VDS support their use interchangeably in assessment of lower back pain after ESI. The multidimensional and multiple-item instruments (ODI, BPI severity and interference, and SF-MPQ-2) demonstrated less inter-scale correlation then did the single item pain intensity scales. These scales showed moderate to high correlation at seven days post-ESI (CC: 0.64 to 0.81). Pre-injection correlation between the ODI, BPI, and SF-MPQ-2 was weak to moderate (CC: 0.37 to 0.55), with the lowest correlation between the ODI and BPI severity (CC: 0.37). The inconsistent correlation between the ODI, BPI, and SF-MPQ-2 suggests that these tools are not always interchangeable and may be a function of the differences between the specific items tested on these tools.
Title: The Proposed Classification Of Chronic Visceral Pain For Icd-11

Poster Number PW0040

Authors
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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 represented unsystematically is chronic visceral pain. Current classification of chronic visceral pain does not provide a clear indication of aetiology and/or mechanism, which has been improved in the new classification. The International Association for the Study of Pain (IASP) has long campaigned for improvements in the classification system.

Results
Chronic visceral pain is persistent or recurrent pain that originates from the internal organs of the head/neck region and the thoracic, abdominal and pelvic cavities. The pain is usually perceived as referred visceral pain in the somatic tissues of the body wall in the areas receiving the same sensory innervation as the internal organ. In these areas secondary hyperalgesia is common. Chronic visceral pain will be further subdivided according to the major underlying mechanisms, such as persistent inflammation, vascular mechanisms, obstruction/distension, traction/compression, etc. Pain due to cancer will be cross-referenced to the chapter chronic cancer pain and chronic primary visceral pain to chronic primary pain.

Conclusion
In the context of the overall classification proposal, several improvements can be expected. For the first time chronic visceral pain syndromes will be represented in the ICD in a comprehensive and systematic manner, thereby improving the recognition of chronic visceral pain. This classification combines information about pain location with that related to aetiology and mechanisms. It is hoped that this increased recognition in time will translate into improved pain relief and access to multimodal treatments.
Title: Procedural Pain And Palliative Care: Preliminary Results Of The French Survey Spdol

Poster Number PW0041

Authors
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Aim of Investigation
To assess the current state of procedures, the associated pain, the analgesia used, in patients hospitalized in a Palliative Care Hospital (PCH)

Results
59 patients with a median age of 72 years (IQR: 62 - 81), with a 21/38 Male/Female ratio, patients with cancer (88.1 %) were included. The analgesic treatments concerned 50 (84.7 %) of them. The analgesics administered were opioids (87.5 %), grade II (2.1 %), grade I (10.4 %) and neuropathic pain treatment (23.7 %). The anxiolytic treatments concerned 32 patients (54.2 %), among which 16 at a sedative dose. Among the 603 procedures, 40.4 % were performed by a pair-work, 28.7 % by a nurse and 25.2 % by an assistant nurse. The most frequent procedures were: 444 nursing care (73.6 %), 54 punctures and skin-breaking procedures (9 %), 29 physiotherapy (4.8 %). 40 patients (67.8 %) were able to self-assess their pain, 316 procedures (52.4 %) were assessed with the NRS and 543 procedures (90 %) with the ALGOPLUS® scale. Specific analgesia was administered for 18.6 % of procedures, mainly opioids (subcutaneous: 37.5 %, bolus: 33 %, oral form: 9.8 %). Among the 96 procedures prepared with a specific analgesic, 47 (49 %) remained painful when they were carried out.

Conclusion
This survey shows that procedural pain is still present in PCH and that analgesia remains insufficient, including with the association of sedation. Enhancement of analgesic practice is required
Title: Pain Prevalence During Admission To A Tertiary Hospital In Argentina

Poster Number PW0042

Authors
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Aim of Investigation
The pain prevalence during admission to hospitals worldwide is highly variable, with estimates ranging from 16.7 to 76.9%. However, knowledge about pain prevalence in Latin America is limited. The aim of this study was to determine the pain prevalence during admission to our hospital.

Results
A total of 736 adult patients were recruited, including 416 women (56.52%). Their ages ranged from 18 to 94 years. The pain prevalence 48 hours after admission was 56% (95% CI 52.7 to 60.1). The pain prevalence in the clinical, surgical and obstetric groups was 36.58% (95% CI 31.36 to 42.05), 70.21% (95% CI 64.50 to 75.49) and 76.98% (95% CI 68.64 to 84.01), respectively. The median pain intensities in the three groups (clinical, surgical, and obstetric) were 7 (RIC 2), 7 (RIC 3) and 7 (RIC 3).

Conclusion
There was a high pain prevalence during admission to our hospital, especially in the obstetric and surgical units. Therefore, it is necessary to generate formal research protocols at the institutional level.
Aim of Investigation
In a prospective cohort study we aimed to describe the determinants of long term pain related functional limitations following a recent onset neck or low back pain in a general population.

Results
Analyses show that higher age (>50 years) was associated with increased pain related functional limitations (β=0.02, p=0.005). No significant associations were found for gender, educational levels, marital status or heavy physical work. All pain related variables measured at baseline; pain intensity at present (β=0.02, p<0.001), time since first pain episode (β=0.28, p=0.003), frequency of previous episodes per year (β=0.63, p<0.001), similar pain reports in both neck and low back (compared to only neck pain) (β=1.13, p<0.001) were associated with more pain related functional limitations. In addition, poor self-reported general health (β=-0.90, p<0.001), higher body mass index (β=-0.45, p=0.001), symptoms of depression (β=-0.11, p=0.003) and symptoms of fatigue (β=-0.43, p<0.001) at baseline were associated with pain related functional limitations. Self-reported somatic disease (medical conditions or musculoskeletal conditions), smoking or psychological factors (symptoms of anxiety, loneliness or insomnia) were not found to associate with pain related functional limitations the following year.

Conclusion
In persons reporting new incidents of neck or low back pain we found that pain related factors at baseline as well as age, body mass index, poor self-reported general health and symptoms of depression and fatigue contributed as predictors in the development of long term pain related functional
limitations. The identification of such symptoms is thus relevant in the planning of interventions for patients with recent onset of symptoms.
Title: Acute Pain And Related Outcomes In Surgical Patients: Retrospective Analysis Of A Large Us Electronic Health Record Database

Poster Number PW0044

Authors
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Aim of Investigation
Several efficacious and well-established analgesic options are available to physicians treating acute pain in surgical patients, and there is growing evidence for the advantages of patient-centered approaches to postsurgical pain management. Still, recent reports indicate that acute pain control is inadequate in the majority of patients, such that they experience significant pain following surgery. If not managed appropriately, excessive postsurgical pain can contribute to adverse short- and long-term postsurgical outcomes. The objective of the present study was to examine the prevalence, progression, and potential impacts of postsurgical pain in a large sample of US surgical patients.

Results
The study population included 110,145 patients. The most common procedure types were abdominal/pelvic surgery (n=46,623), cardiovascular surgery (n=23,033), and orthopedic/spine surgery (n=19,870). Prior to surgery, n=53,963 (49.0%) of patients overall had severe baseline pain (maximum pain score 7-10), while n=20,559 (18.7%) had moderate pain (maximum pain score 4-6), and n=35,623 (32.3%) had no or mild pain (maximum pain score 0-3). A similar trend was observed for the majority of surgery types examined. Patients with severe baseline pain typically experienced a decrease in pain following surgery (mean maximum baseline pain score (± SD): 8.9 ± 1.1; mean maximum pain score on postsurgical day 1: 6.2 ± 3.3). Conversely, patients with moderate baseline pain experienced minimal changes in pain level, on average (mean maximum baseline pain score: 5.0 ± 0.8; mean maximum pain score on postsurgical day 1: 4.4 ± 3.2), and patients with no or mild pain typically experienced an increase following surgery (mean maximum baseline pain score: 0.7 ± 1.2; mean maximum pain score on postsurgical day 1: 3.0 ± 3.3). There was an association between maximum baseline pain and length of hospital stay (LOS) such that patients with severe pain typically had the longest length of stay (8.2 days), followed by patients with moderate pain (7.2 days), and no or mild pain (6.8 days). Last pre-discharge
pain score in patients with a LOS <15 days was, on average, 5.3 ± 3.4 for patients with severe baseline pain, 3.5 ± 3.1 for patients with moderate baseline pain, and 2.3 ± 3.0 for patients with no or mild baseline pain, suggesting that, generally, patients are discharged only after pain is controlled.

Conclusion
This analysis identified important potential associations between pain outcomes and LOS and pain severity in the pre-surgical period. These findings provide initial insights into potentially relevant risk factors in the broad surgical population and are supportive of the importance of patient-centered pain management approaches in surgical patients.
Title: Factors That Impede The Efficient Management Of Acute Pain In Abidjan Emergency Mobile Service

Poster Number PW0045

Authors
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Aim of Investigation
Acute pain is the most commonly experienced type of pain throughout the world many guidelines have been published on his management. However treating acute pain is a challenge in our practice. The aim of investigation is to identify factors that impact negatively on the efficient management of acute pain, by physicians in abidjan prehospital emergency service

Results
1873 procedures were performed by the prehospital emergency medical service. Painful diseases accounted for 299 (16%). Number of physicians involved is 22. According to seniority in the medical practice there were 75% who were less than 5 years experience, 4 were between 5 and 10 years, and 2 had more than 10 years medical experience. According to the qualification, 3 doctors were in specialization of anesthesia and intensive care, 2 were in training of Emergency Medicine, 17 were general practitioners According to clinical conditions there were 8 cases coronary pain, abdominal pain 59 cases, trauma accidents by highway 112, femur fractures by fall height 9, 10 isolated headache, secondary transmission among patients sedated and analgesia 111. There was no assessment of pain (or EVA, or EN), the type of analgesic used was 90% acetaminophen, in 6 cases was used NSAID diclofenac. The was no femoral block. The choice of analgesic strategy was based on the availability of painkillers at the time of patient care. There were no cases of use of morphine.

Conclusion
Several decades after the published recommendations for management of acute pain we are still facing with the unavailability of morphine, the misconceptions recommendations, lack of real training on the management of acute pain, cultural habits and lack of interest of health authorities on a true medical staff training policy in our geographic area. Acute pain seemed remain to be for a long time a fatality in our developing countries
Title: Who Is At Risk Of Initiating Long-Term Opioid Treatment?

Poster Number PW0046

Authors
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Aim of Investigation
Chronic non-cancer pain (CNCP) is treated increasingly with long-term opioid therapy which is reported to be associated with severe side effects and concurrent use of benzodiazepine (BZD). Epidemiological data regarding long-term opioid and BZD use among CNCP patients is sparse. This study aimed to identify risk factors associated to long-term opioid and BZD use in the Danish population.

Results
Female gender, short education, heavy smoking, sedentary lifestyle and obesity were identified as risk factors for long-term opioid use. Furthermore, poor health-related quality of life was strongly associated with long-term opioid use. Higher risk of using BZD was associated with female gender, short education, heavy smoking, sedentarity and CNCP patients treated with or without opioids.

Conclusion
Sociodemographic factors and health-related life style seemed to be important risk factors for long-term opioid and BZD use. These results deserve attention due to uncertainties on the analgesic effect of opioids for CNCP and the potential deleterious consequences of both medications.
Title: Increased Disability In Pain Patients With Restless Legs Syndrome

Poster Number PW0047

Authors
P. Andersen, E. McGehee, R. Vrads, H. Vaegter

Aim of Investigation
Aim of Investigation: The primary aim of this study was to investigate the prevalence of Restless Legs Syndrome (RLS) in patients with chronic widespread pain (CWP: spinal pain + pain in all four extremities), chronic low back pain (LBP: pain in the lower back without pain referral below the knees) and pain in multiple spinal areas (MSPA: pain in more than one spinal area) referred to a multidisciplinary pain clinic. Secondary aim was to investigate its possible impact on clinical pain, disability and quality of life.

Results
Results: In all, 118 patients were included (mean age: 47.3±13.4 years; 79 women). 35 patients (29.7%) fulfilled the criteria for RLS by answering 'yes' all 4 questions. There were no significant difference in the proportion of patients with RLS between CWP (12/34, 35%), LBP (11/24, 46%), and MSPA (12/25, 48%; Chi Square, P > 0.7). Age and disability was significantly increased in pain patients with RLS compared with pain patients without RLS (P < 0.05).

Conclusion
Conclusions: Restless Legs Syndrome has a high prevalence in patients with chronic pain across different pain conditions. As patients with RLS demonstrate higher levels of disability, early diagnosis and management of RLS may improve treatment outcome.
Aim of Investigation
This Danish nationwide survey aimed to analyse the associations between chronic pain, opioid use and sexuality in the general adult population.

Results
Sample characteristics were as follows: 50.0% men, mean age 46.7 years, 49.0% married, and 26.0% had basic school as highest completed education. The prevalence of chronic pain was 26.7%. Dissatisfaction with sexual life was reported by 21.3% of the individuals with chronic pain (26.6% of those on long-term opioid use, 22.4% on short-term opioid use, and 20.8% of those not on opioids) and 16.6% of individuals without chronic pain. The odds ratio of being dissatisfied or very dissatisfied with one's own sex life was 2.21 (95% CI: 1.51-3.25) times higher among long-term opioid users with chronic pain than among individuals without chronic pain. The odds ratio was also higher for non-opioid users with chronic pain (1.42, 95% CI: 1.25-1.60). Absent or low libido was reported by 23.9% of the individuals with chronic pain (39.3% of those on long-term opioid use, 30.7% on short-term opioid use, and 21.6% of those not on opioids) and 13.3% of individuals without chronic pain. The odds ratio of absent or low libido was 2.66 (95% CI: 1.91-3.68) times higher among long-term opioid users with chronic pain than among individuals without chronic pain.

Conclusion
Chronic pain was associated with dissatisfaction with sexual life and absent or low libido in this national representative survey. In addition, long-term opioid use was associated with increased odds ratio for these issues. Further investigation on this area is necessary.
Title: Medical Cannabis (Mc) For Chronic Pain Management: Characteristics Of New License Applicants

Poster Number PW0049

Authors
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Aim of Investigation
The overall aim of the present study is to set up a registry on the use of medical cannabis (MC) for the relief of chronic pain in a large patient population in Israel. It is structured to collect data prospectively on the effectiveness and safety of MC and to identify predictors for success\ failure of MC treatment. The study has recently begun. This is a preliminary report on the characteristics of the first group of patients with chronic pain for whom a MC license use application has been submitted.

Results
Thus far, 86 patients (45M/ 41F) wereRequested. Their mean (±SD) age is 49(±16) years old. Thirty four percent are employed either full or part time, 23% are retired and 32% are supported by social security. Pain diagnoses are neuropathic pain in 75%, musculoskeletal pain in 70%, and dysfunctional pain in 17%, headache and visceral pain in 14% (each), and cancer pain in 3% of the study population. As can be seen, most of the patients are diagnosed with concomitant pain etiologies. Mean pain duration is 10.3±10.5 years (ranging from 1-50 years). Approximately 80% of the cohort uses 2-5 analgesics agents currently. Currently, patients comprise the following analgesics: anti-consultants (45%), strong opioids (34%), over the counter medications (32%), weak opioids (32%), anti-depressants (30%) and non-steroidal anti-inflammatory drugs (21%). Mean pain intensity scores are 8.0±1.4 (i.e., severe pain); moderate level of disability (PDI, 6.5±1.8); high levels of catastrophizing (PCS, 36.7±10.9); sleep quality by PSQI revealed that 47% reported very poor sleep quality; moderate level of anxiety (GAD, 9.7±6.0) and poor QOL (EQ5, 4.9±1.8).

Conclusion
The preliminary findings of this ongoing study suggest that patients with chronic pain for whom MC use has been recommended, suffer from severe pain of diverse etiologies, express high scores in a large
range of associated symptoms and report low quality of life. Further long-term data collection will shed light on the safety and effectiveness of MC in reducing pain and associated symptoms.
Title: The Burden Of Pain In Musculoskeletal Disorders In Chile

Authors
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Aim of Investigation
To estimate the burden of selected musculoskeletal disorders in Chile and the relative impact of chronic pain in the total burden.

Results
The national prevalence of CMP was 17.9%, with higher rates observed in OA-K and CLBP. Almost a quarter (23.4%) of the total national disability corresponds to the pain domain, and 4.5% was actually associated to CMP, corresponding to 281,606 years lived with disability (YLDs). CLBP caused 341,676 YLDs, out of which 82,318 YLDs belonged to the pain disability domain, which represented 1.7% of the whole national disability. CSP produced 64,797 YLDs (14,635 YLDs due to pain), whereas OA-H and OA-K caused 74,615 and 171,036 YLDs, out of which 18,535 and 39,764 YLDs were attributed to pain respectively. At a national level, pain caused by OA-H accounted for 2.8% of the total disability. FMY and MYS were responsible of 85,288 and 57,791 YLDs, out of which 17,068 and 13,553 YLDs were due to pain respectively. CLBC and OA-K are in the top position of diseases explaining the highest national burden. Relevant differences by sex and age were also observed.

Conclusion
The pain domain of disability accounts for almost 25% of the whole disability at a population level. The burden due to musculoskeletal disorders occupies the top positions of the ranking of diseases with highest disability. Future research should focus on possible interventions to reduce this burden and improve the quality of life of patients suffering chronic pain.
Title: Association Between Pain Characteristics And Frailty In Community-Dwelling Older Adults

Poster Number PW0051

Authors
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Aim of Investigation
The aim of this study is to investigate the association between pain characteristics and frailty in community-dwelling older adults.

Results
Prevalence of frailty and prefrailty was 4.9% (n = 26) and 36.2% (n = 192), respectively. The number of chronic musculoskeletal pain locations was more with the progression of frail status [median (interquartile range), robust: 0 (0–1); prefrailty: 1 (0–2); frailty: 2 (1–3); <i>p</i> for trend < 0.001]. The pain severity was higher with the progression of frail status [median (interquartile range), robust: 0.75 (0–2); prefrailty: 1.13 (0–2.5); frailty: 1.88 (0–4.25); <i>p</i> for trend < 0.001]. Multinomial logistic regressions controlling confounding factors showed that the pain severity was significantly associated with frailty (ROR: 1.49, 95% CI: 1.09–2.05) and that the number of chronic musculoskeletal pain locations was significantly associated with frailty (ROR: 1.53, 95% CI: 1.13–2.07) and prefrailty (ROR: 1.19, 95% CI: 1.02–1.39).

Conclusion
Pain characteristics, regardless of number or severity, were associated with frailty even after adjusting for confounding factors. Interventions for pain management may help to prevent or to improve frailty in community-dwelling older adults.
Title: Symptom Burden And Quality Of Life In Hemodialysis Patients With Chronic Pain

Poster Number PW0052

Authors
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Aim of Investigation
Chronic pain is a multidimensional phenomenon with physical, psychological, and social components, and is an important problem for 50% of hemodialysis (HD) patients with end-stage renal disease. Our study aimed to collect information on chronic pain and physical - emotional symptoms among HD patients in Japan, and to compare physical - emotional symptoms and quality of life (QOL) in patients with and without chronic pain.

Results
One hundred and six patients, 61 males and 45 females, aged 31-89 years were interviewed. 70 (66%) reported chronic pain and 43 (40.6%), moderate to severe pain. HD patients with moderate to severe chronic pain had more in the overall score of symptom burden (10.6 ± 4.4 versus 8.3 ± 5.3, P = 0.01) and higher in the total DSI symptom-severity score than patients with mild chronic pain or acute pain, or no pain (26.4 ± 16.6 versus 17.6 ± 13.8, P = 0.002). Patients with chronic pain showed significantly lower QOL scores in eight subscales of the SF-36.

Conclusion
Our research indicates the importance of addressing chronic pain in improving the burden of symptoms and low QOL of HD patients.
Title: Psychosocial Factors For Headache In Slovenia

Poster Number PW0053

Authors
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Aim of Investigation
Headache is a common disabling condition related to high health system burden. It can be deleterious for psychological and social well-being. In Slovenia psychosocial factor for headache are not well established. To identify population groups at very high risk for headache and thus enable more focused prevention actions in Slovenia

Results
We noticed high odds for risky stress behaviour (OR yes vs. no =1.99; P<0.001), sleep behaviour (OR < 6 vs. 8 hours/day = 1.23; P<0.001) and coffee drinking behaviour (OR > 1cups vs. no coups/day = 1.58; P<0.001) in headache subjects. In addition, we found the highest odds in women (OR women vs. men=1.99, P<0.001), aged 25-29 years (OR 25-29 vs. 70-74 = 6.10, P<0.001), participants with the lowest (OR primary vs. postgraduate =1.34, P=0.082).

Conclusion
In Slovenia, intellectual/leading position women, aged 25-29 years, were identified as the largest population sub-group at high risk for frequent headache disorders with stress behaviour.
Title: The Impact Of Chronic Pain On Depression And Daily Life Activities In Hemodialysis Patients With End-Stage Renal Disease

Poster Number PW0054

Authors
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Aim of Investigation
In Japan, the elderly dialysis population is steadily growing and has a high burden of chronic health conditions, such as poor physical and psychological functioning, which, along with low physical mobility, decrements quality of life. Furthermore, chronic pain is a common problem in the elderly, and is often associated with significant physical disability and psychosocial problems. Our study aimed to investigate the relation between chronic pain, depressive state, and physical activity in Japanese HD patients.

Results
Eighty-four patients with end-stage renal disease, 49 males and 35 females, aged 32-86 years with chronic HD were interviewed. 45 (52.3%) reported chronic pain and 31 (36.0%), moderate to severe pain. There was a higher prevalence of locomotive syndrome in patients with moderate or severe chronic pain compared to patients with mild chronic pain or acute pain, or no pain (74.2% vs. 22.6%, odds ratio [OR] = 9.24, p = 0.000) and patients with chronic pain showed significantly higher scores on the Locomo-25 (31.0±19.6 vs. 13.6±16.9, p = 0.000). Although chronic pain showed significantly higher scores on the GDS-15 (6.3±3.2 vs. 4.7±3.6, p = 0.014), there was no association between chronic pain and the presence of depression.

Conclusion
Our findings demonstrate that chronic pain was found to be closely related to decreasing physical activity in Japanese HD patients.
Title: Pain Self-Efficacy Mediates The Relationship Between Pain Catastrophizing And Depression

Poster Number PW0055

Authors
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Aim of Investigation
It is recognised that psychological variables contribute to outcomes in those with chronic pain (CP). Depression has been found to account for 20% of the variance of pain intensity and pain interference (Hawthornthwaite, Sieber & Kerns, 1991). Research has found that an estimated 40-50% (Gatchel & Okifuki, 2006) of those with CP have depression. Examining the mechanisms which underlie depression in CP is especially important as the specific mechanisms by which cognitive behavioural therapy (CBT) treats depression and pain in CP are still unclear (Burns, Day & Thorn, 2012). The CBT method in treating CP focuses on reducing pain catastrophizing (PC) and enhancing coping by increasing coping variables such as pain self-efficacy (PSE). Despite this approach, the individual contributions of PC and PSE to depression in CP have not fully been examined. PC has been found to account for as much as 40% of depression (Nicholas, Coulston, Asghari & Mahli, 2009) and PSE is also a significant predictor of depression (Turner, Eresk & Kemp, 2005). Turner, Jenson and Romano (2000) found that PC significantly predicted depression in CP but did not independently contribute to physical disability when pain beliefs and coping were included in the model. On outcomes of pain, stiffness and fatigue, PSE remains the only a significant independent predictor when PSE and PC are both entered as predictors (Somers, Kurakula, Criscione-Schrieber, Keefe & Clouse, 2012). Therefore it is hypothesised that although PC is a predictor of depression, the relationship between PC and depression is mediated by PSE.

Results
As predicted, PSE fully mediated the relationship between PC and depression. PC was a direct predictor of depression (R²=.09, F(1, 60)=6.50, p=.013, β=.11) and PSE (R²=.32, F(1, 60)=25.58, p<.001, β=.47). PSE, itself, directly predicted depression (R²=-.19, F(2, 59)=5.92, p=.0045, β=-.18). In the mediation model, i.e. when PC and PSE were entered into the model together, the direct relationship between PC and depression was no longer significant (R²=.03, F(2, 59)=5.92, p=.605, 95% CI [-.07, .13]). In this
mediation model, the relationship between PC and depression was fully mediated via PSE ($\chi^2=.19$, 95% CI [.05, .35]) and indicated a medium effect size.

**Conclusion**
These results indicate that PC is only related to depression via the effect of PSE suggesting PSE may underlie PC in depression. Catastrophic thinking and PSE may both contribute to feelings of helplessness, reduction in pleasure from activities and reduced motivation for goals leading to global depressed mood. This finding is important as it may be that improvements in PC and depression seen post-treatment are influenced by improvements in PSE. Focusing on reducing PC in those with CP and depression may not be sufficient to improve outcomes. An approach which combines reductions in PC and improvements in PSE should be prioritised.
Title: The Relationship Between Sexual Abuse And Chronic Pain

Poster Number PW0056

Authors
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Aim of Investigation
The purpose of this study is twofold: 1. first, to examine the incidence of history of childhood sexual abuse in individuals with heterogeneous chronic pain assessed in the Interdisciplinary Chronic Pain Management Program of the Michael G. DeGroote Pain Clinic; and 2. second, to investigate the relationship between childhood sexual abuse and chronic pain by comparing scores on pain-related variables of individuals with a history of sexual abuse to those without.

Results
The incidence of sexual abuse in individuals initially assessed at the Michael G. DeGroote Pain was 16.0% (10.7% for males and 20.1% for females). Those with a history of sexual abuse tended to have higher scores on the Activities Engagement (AE) subscale of the Chronic Pain Acceptance Questionnaire (CPAQ) (p = 0.042) and on the Contemplation subscale of the Pain Stages of Change Questionnaire (PSOCQ) (p = 0.037). There also tended to be gender differences in terms of the Pre-contemplation subscale of the PSOCQ (p = 0.054) in favor of males.

Conclusion
The results suggest that a) the incidence of sexual abuse in individuals with heterogeneous chronic pain assessed at an interdisciplinary chronic pain management program is similar to that of the general population, and b) a relationship between sexual abuse and adaptation to chronic pain as measured by the PSOCQ and CPAQ. The latter findings have not been previously reported.
Aim of Investigation
Dardsatya aims to provide and promote supportive care to improve the quality of life of patients suffering from cancer and non-cancer disease and also focus on accessibility of supportive care to individuals who need it. Basic training and education about whole patient assessment, goals of care, pain and symptom management, psychosocial and spiritual support to nurses, doctors, families and patients are the main focus of Pall Train project.

Results
Till February 2016, education and training was given to improve awareness and sensitize people about basic palliative care services across 11 hospitals, 2 schools, 4 medical colleges, 9 community health centers including 545 health care workers training about basic palliative care and end of life care. Till January 2016, 119 patients were visited for home care, 47 patients were provided with nursing care and assistance at home. Psycho-social and spiritual counseling was done to improve the quality of life. End of life care was given to 63 patients at home and 13 patients in the hospital.

Conclusion
There is a need for more quality supportive care initiatives in India. Development of a palliative care delivery system is essential for the society and nation. Doctors and nurses need proper education and training to acquire the necessary knowledge, attitude and skills to deliver good palliative care to patients. Dardsatya is aiming to provide local solutions to local problems and sensitize healthcare workers and general people about palliative care. Visit www.dardsatya.com to know more about 'Pall Train' project.
Title: Pain Content Within A United States Credentialing Examination For Physicians

Poster Number PW0058

Authors

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Aim of Investigation
Successful completion of the United States Medical Licensing Exam (USMLE) is a requirement for medical licensure in the United States and Canada. The USMLE consists of three steps that test candidates on basic science and clinical knowledge, as well as clinical skills for the proper, unsupervised, general practice of medicine. We undertook a review of the USMLE to assess test questions for inclusion of pain core competencies, pain topics and public health issues related to pain.

Results
The data comprised 12 spread sheets, with a pool of 3728 questions available for review. A total of 1506 questions were reviewed. 432 questions were assessed as including pain. 232 questions (15.4%) were classified as fully (n=94) or partially (n = 138) related to pain and were included in analysis. Pain was represented in all four domains. Domain 2, pain assessment, was most heavily emphasized, with 205 (88.36%) fully and partially related questions, while Domain 1, what is pain, received substantially less emphasis with 42 (18.1%) questions. Domain 3, pain management and treatment, was noted in 55 (23.7%) questions, and clinical context (Domain 4) was noted in 36 (15.5%). A similar trend was observed in an examination of the pain competencies. The competency most frequently covered was 2.1 (use of valid tools for assessing pain) which was documented in 185 questions (79.7%). The next three competencies with the highest number of fully and partially related to pain questions include:
competency 3.4. Development of a Pain Treatment Plan with 44 questions (19.0%); competency 1.1 - Nature of Pain with 27 questions (11.6%); and competency 4.1. Needs of Special Populations with 19 questions (8.2%). Other competencies were tested in at least one question.

**Conclusion**
To our knowledge, this is the first review of pain content within a national credentialing examination any health profession. Pain was represented throughout the three-step exam. However, the vast majority of these questions related to assessment of pain, with much less emphasis found on other domains (what is pain, how is pain treated, and how does context affect pain). This review of the USMLE suggests that pain assessment is amply represented as a topic in the exam, but a greater focus on the nature of pain, pain treatment and context may be warranted to ensure comprehensive knowledge of pain management. These data may be helpful for educators who seek to develop balanced competency-based educational outcomes for pain to guide curriculum redesign. The emphasis on assessment rather than other aspects of pain and its treatment may be relevant to understanding the role of education in some pain-related public health problems seen in the US, such as a high prevalence of chronic pain and high rates of opioid prescribing.
Title: Promoting Quality Pain Care Through Education And Mentoring Of Primary Care Clinicians

Poster Number PW0059

Authors
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Aim of Investigation
The aim of this investigation was to assess the impact of the UC Davis Project ECHO Pain Management TeleMentoring Program, a peer-to-peer video conference mentoring program designed to support primary care clinicians and interprofessional teams in their mission to provide high quality pain care. The program convened and led an interactive learning community where clinicians at the forefront of health care have the opportunity to learn more about core pain management topics from multi-disciplinary specialists in pain management.

Results
Forty participants (53% response rate) in Project ECHO session 1 and/or session 2 responded to a web-based survey focused on qualitative assessments of quality and impact. Seventy percent reported a change in prescribing patterns as a result of participating in ECHO; while two-thirds (66%) reported working on tapering patients on opioid medications. Over three-quarters of respondents (77%) reported that they feel better able to identify patients abusing medications as a result of participating in the project. A theme in respondents' comments indicated the project changed the way participants view treating pain patients and provided a better understanding of addiction.

Conclusion
Pain is the most common reason individuals seek health care. However, comprehensive pain management education is not a sufficient part of prelicensure education leaving primary care clinicians unprepared to address the complex, multidimensional nature of pain in practice. With inadequately managed pain and abuse of prescription opioids both growing public health concerns, novel approaches to education are necessary to support the existing primary care workforce who are at the frontline of
delivering pain care. This program demonstrates that an interactive, distance-based mentoring approach can have a positive impact on the quality of pain care delivered by primary care clinicians. An evaluation of claims data to assess quantitative changes in clinician behavior is currently underway. This project was supported through a grant from the California Health Care Foundation.
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**Title:** Impact Of Pain Education In Developing Countries: Results Of A Follow-Up Survey Of Participants From Iasp Pain Management Camps In Southeast Asia

**Poster Number** PW0060

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**Aim of Investigation**
IASP Pain Management Camps have been organised in conjunction with the biennial conference of the Association of South East Asian Pain Societies (ASEAPS) since 2011. We aimed to determine the impact of this pain education on the participants of the pain camps, which included doctors, nurses and other healthcare workers from ASEAN countries, Bangladesh, Bhutan, Mongolia, Nepal and Sri Lanka..

**Results**
42 participants from 14 countries responded, giving an overall response rate of 73.7%. 50% were anaesthetists, 10% neurologists and the remaining from other specialties. 79% were working in the public sector. 93% of participants indicated that the knowledge learned at the pain camp was used 'moderately' or 'a lot' in their current work and 83% found that the pain camp had been a 'very useful' or 'extremely useful' experience and made a difference for them as healthcare providers within the area of pain. On a scale of zero to 10, the level of participants' involvement increased from an average of 5.95 to 8.81 in the area of 'clinical pain management' and from 4.77 to 8.12 in the area of 'pain education and training'. 67% had been involved in organizing a local pain education activity since returning from the pain camp. 6 participants had attended an IASP or ASEAPS conference before the pain camp, and this increased to 25 after the camp. The majority of pain camp participants have kept in touch with others from the same pain camp, mainly through social media.

**Conclusion**
The Southeast Asian IASP Pain camps had a positive impact on participants' knowledge of pain as well as
on the pain services in their countries, their involvement in pain education and local pain societies and attendance at IASP/ASEAPS conferences. The survey suggests that there is a beneficial effect on pain education and pain management of these IASP funded pain camps. Based on this we recommend IASP continue to support this type of educational activity.
Title: Exploring People’s Feelings And Thoughts About Pain In Response To A Multimedia Experience Of Facial Expressions Of Pain

Poster Number PW0061

Authors
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Aim of Investigation
Helping people understand the affective (feelings) and cognitive (thoughts) aspects of pain has become an important education strategy in the management of chronic pain. People learn differently. Facial expressions communicate pain and individuals respond to painful faces in different ways. Abstract conceptualization may be a way to increase understanding about pain, though this premise does not appear to have been examined. This study investigated responses to a multimedia experience of facial expressions of pain in relationship to participants' feelings and thoughts about pain.

Results
27 individuals (n=15 female) participated in the study; 19 individual interviews and one focus group (n=8). Average age was 38 years (range 21-82). 10 reported having chronic pain (average Brief Pain Inventory score=4.45, average Pain Self-Efficacy Questionnaire (PSEQ)=25.5), 9 a relationship with a person who has chronic pain (average modified PSEQ=32) and 8 as pain free (average modified PSEQ=33.5). Key themes were identified with strong consistency between interviews and the focus group. Participants predominantly expressed feelings of surprise and empathy when viewing the video images. For example, many people were surprised that one person with multiple facial piercings had lower tolerance to ice immersion. There was a tendency for participants to relate to individuals in the videos who reacted in the same way that participants perceived they would react themselves. For example some participants related to videos of people who were more expressive, and others more stoic videos, consistent with what they anticipated their own response would be. Participants' explanations for the different way people responded to pain were highly variable ranging from the simple to the complex. The majority of participants reported their perceptions towards pain had changed after viewing and reflecting on the multimedia presentation. This included a realisation that people could be in pain but may not outwardly express it. For several participants, the multimedia
presentation evoked more empathy or understanding towards people in pain, and the expression that pain is a subjective experience.

**Conclusion**

The multimedia experience provided an interesting mechanism to trigger participants' self-reflection about their pain and the pain of others. Themes identified support the supposition that viewing facial expressions of pain can impact people's understanding of pain. For some people, abstract conceptualization of pain using multimedia may be a useful tool to assist in better understanding their pain, or the pain of others.
Title: Correlations Among Goal Attainment, Psychological Factors, And Pain In Patients Recovering From Total Knee Arthroplasty

Poster Number PW0062

Authors
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Aim of Investigation
Psychological factors have been reported to affect chronic pain after total knee arthroplasty (TKA). Successful goal attainment is integral to the psychological factors that can influence and prevent the development of postoperative chronic pain. This study aimed to determine the correlations among goal attainment, psychological factors, and postoperative pain.

Results
We found a significant correlation between COPM-performance and PCS-rumination \((r = -0.38, p < 0.01)\), COPM-performance and PCS-helplessness \((r = -0.65, p < 0.01)\), and COPM-performance and PCS-magnification \((r = -0.40, p < 0.01)\). There was also a significant correlation between COPM-performance and HADS-anxiety \((r = -0.49, p < 0.01)\) as well as HADS-depression \((r = -0.52, p < 0.01)\). There was also a significant correlation between COPM-satisfaction and NRS \((r = -0.24, p < 0.05)\), COPM-satisfaction and PCS-rumination \((r = -0.41, p < 0.01)\), COPM-satisfaction and PCS-helplessness \((r = -0.64, p < 0.01)\), and COPM-satisfaction and PCS-magnification \((r = -0.42, p < 0.01)\). Additionally, there was a significant correlation between COPM-satisfaction and HADS-anxiety \((r = -0.43, p < 0.01)\) as well as HADS-depression \((r = -0.50, p < 0.01)\). The multiple regression analysis showed that PCS-helplessness \((\beta = -0.59, p < 0.01)\) and HADS-depression \((\beta = -0.24, p < 0.05)\) were significantly associated with COPM-performance \((R = 0.47, p < 0.01)\). Furthermore, PCS-helplessness \((\beta = -0.57, p < 0.01)\) and HADS-depression \((\beta = -0.21, p < 0.05)\) were significantly associated with COPM-satisfaction \((R = 0.45, p < 0.01)\).

Conclusion
The results suggest that goal attainment as measured by the COPM (performance and satisfaction) can influence pain (PCS-helplessness) and depression (HADS-depression). Therefore, we think there is a
need for clinical intervention, with the goal of reducing the helplessness and depression felt by this patient population. Lastly, the data highlights the importance in assessing the COPM of patients undergoing TKA.
Title: Breaking Down Silos: Developing Interprofessional Case-Based Learning Modules About Pain Management

Poster Number PW0063

Authors

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Aim of Investigation
To collaboratively develop and test a set of interprofessional case-based training modules for students of prelicensure health professional schools about key issues in clinical pain management. Target learners include medical, nurse practitioner, physician assistant, social work, and pharmacy students. All materials developed from this project (including facilitator guides; detailed module content; and fully-developed case studies) will be made available worldwide and free of charge.

Results
Participant feedback on surveys conducted after both pilots was strongly positive. Using a 5-point scale ranging from 0 (strongly disagree) to 5 (strongly agree) the overall weighted mean score on a set of questions about the value of the educational modules was 4.4 / 5.0 from the June, 2015 pilot, and 4.6 / 5.0 from the January 2016 pilot. Qualitative data confirm and expand on these data, with participants strongly endorsing the value and need for interprofessional education programs, as well as the value and importance of the specific content covered in the piloted modules.

Conclusion
Collaboratively-designed interprofessional learning modules can help break down the academic 'silos', in which students in health care professions can become isolated. The programs developed in this project successfully brought together groups of learners who do not typically interact and provided a forum and learning framework in which the students learned from each other as much as from course facilitators. The structures, curricula, case studies, and didactic content developed by this project were designed to be easily replicated for teaching interprofessional groups of students. Pain appears to be a useful focus
for differing professions to learn about and with each other. More broadly, the processes used to develop these materials may encourage others to develop similar modules in pain management and, perhaps, other branches of health care as well. Acknowledgments/Disclosures: This investigation and program was funded by the Josiah Macy Foundation with support from the Milbank Foundation and Mayday Fund.
Title: Investigation Of Factors That Influence The Steps Per Day In The Early Stages After Total Knee Arthroplasty

Poster Number PW0064

Authors
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Aim of Investigation
Total knee arthroplasty (TKA) aims to mitigate knee pain and improve quality of life by increasing the patient's level of activity. Therefore, it is important to improve the ability to walk during the early postoperative stage. The aim of this study was to measure the steps (per day) as an evaluation of walking ability during the early postoperative stage and investigate the factors that influence the steps, which will be beneficial for rehabilitation in the early postoperative stage.

Results
A significant correlation was found between steps and age (r = −0.20), knee pain (r = −0.32), muscle strength of knee extension (r = 0.33), PCS (r = −0.21), and PSE (r = 0.33). The results of the multiple regression analysis identified age (β = −0.15; p = 0.16), knee pain (β = −0.24; p = 0.02), muscle strength of knee extension ( β = 0.18; p = 0.09), and PSE ( β= 0.16; p = 0.13), indicating that knee pain is a significant element influencing steps (R = 0.22; p < 0.01).

Conclusion
Knee pain was identified from the multiple regression analysis as a factor strongly correlating with steps. This finding clarifies the necessity for rehabilitation during the early TKA postoperative stage to endeavor to reduce knee pain through adequate pain management including medication and icing. In addition, a correlation was found between muscle strength of knee extension, PCS, and PSE and steps. Therefore, it is important to reduce a patient's catastrophic thinking about pain not only by focusing on muscle strength during postoperative rehabilitation but also by presenting the means to reduce postoperative knee pain over a period of time. It is also necessary to conduct patient education that will improve self efficacy by increasing the postoperative activity level with pacing, which will not aggravate any knee pain.
Title: Student Selected Components (SSCs): Short Courses In Pain For The Undergraduate Student

Poster Number PW0065

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Aim of Investigation
'Tomorrow's Doctors' is a UK document that sets out the General Medical Council's (GMC) requirements for teaching undergraduate medical students (Tomorrow's Doctors, 2009). It places 'the doctor as a scholar and a scientist' at the top of its list of outcomes for graduates. Since understanding the physiology of pain is imperative to effective diagnosis, treatment and management of patients, it is important that basic pain education is firmly placed in the undergraduate curriculum. This is mainly achieved through core lectures and clinical rotations. However, for many students, an interest in pain extends beyond the basic curriculum. At the Brighton and Sussex Medical School (BSMS), we developed Student Selected Components (SSCs) that allow students to experience practical elements of basic pain education and research in a small group learning environment. SSCs are optional modules, which run over 7-8 weeks during the term. Here, we have described how this was achieved.

Results
Both SSCs have successfully run for over four years. They are highly rated by the students, with average scores of 3.9/4 for interest, usefulness and overall quality of delivery. Moreover, both SSC leaders are named in person as best aspect of the module. Typical comments have included: 'fantastic experience', 'really interesting', 'fun as it was hands-on', 'it allowed us to integrate our knowledge with a real patient', 'best SSC I have done' and 'well put together and thought out'. Comments praise in particular the valuable skills and knowledge that is applicable in the subsequent clinical years. Both SSCs are repeatedly oversubscribed, with high numbers of students selecting these as first choice.

Conclusion
An understanding of the physiology of pain is essential for good clinical practice, especially since pain is reportedly the most common symptom presented to a clinician. At BSMS, we have achieved this through interactive lectures as well as the development of two SSCs that provide a diverse learning experience for second year students with an interest in the field to expand their knowledge.
Importantly, the format of these SSCs is in line with GMC's Tomorrows Doctors. Finally, we have also developed a local Pain Network with the aim of engaging clinicians, therapists and basic scientists in pain education. It is hoped that such an initiative will stimulate experts into developing and delivering further novel and creative teaching sessions that fulfill a students want of this common but equally complex symptom.
Title: Communication About Pain: A Comparative Analysis Between The Twitter Profiles Of The Sociedad Española Del Dolor (Spanish Pain Society) And The American Pain Society

Poster Number PW0066

Authors
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Aim of Investigation
In a world increasingly digitized, the way in which we are taking care of our health is changing rapidly, and this includes the use of social media. The aim of this study was to analyze how two organizations of pain specialists create messages and communicate about pain, by looking into the content that they share on their Twitter profiles: the Sociedad Española del Dolor (SED; Spanish Pain Society; (@Sedolor)) and the American Pain Society (APS; (@AmericanPainSoc)). Specifically, the objectives of this work were to study: (1) the type of contents that they share, (2) the target of those messages, (3) the most recurrent topics, (4) the content that engages the most to users, and (5) the type of language that is being used.

Results
As expected, all the content is pain-related. Most tweets contain links to other medical or scientific sources, and visual content is poor (e.g., the APS profile just contains 18 pictures). Mostly, the content is addressed to professional audiences. Topics are diverse, and in both profiles news-related tweets are the ones that are shared the most. Engagement is low as shown by the low number of likes, retweets and replies from users. Neither the APS nor the SED interact with users, and their profiles do not share information on a daily basis (sometimes, several days go by without tweeting). In terms of language, both the APS and the SED combine technical tweets with some others that use a more plain comprehensive language addressed to general audiences.
Conclusion
The use of social media is growing in the organizations that have been analyzed; however there is still a lot to do, on the basis of what is being recommended by communication experts. For example, these organizations should elaborate more the contents that are being shared, including multiple forms of communication, like info graphs or videos (contents that are more likely to generate greater engagement with users, according to experts in communication). Furthermore, the nature of these tools is bidirectional, and in the profiles that were analyzed, messages only went in one direction. In short, these organizations would benefit from developing a clear social media strategy, in order to improve communication in this changing environment.
Title: Mis-Trafficking Of Neuropeptides Underpin Congenital Insensitivity To Pain In Cltcl1 Mutation Carriers

Poster Number PW0067

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Aim of Investigation
Congenital insensitivity to pain sensing is a very rare phenotype; however the identification of causative genes has yielded novel targets for pain treatment and often unexpected insights into pain pathways. We aimed to identify novel components of the pain sensing system, potentially relevant as therapeutic targets, by studying patients unable to feel pain yet lacking mutations in previously known pain genes.

Results
We report a novel recessive disorder characterised by congenital insensitivity to pain, inability to feel touch, and moderate mental retardation. Having identified a potential mutation in CLTCL1 (CHC22), p.E330K, we confirmed pathogenicity by demonstrating a disrupted ability of CHC22 to mediate endocytosis. CLTCL1 is significantly upregulated in the developing human brain and displays an expression pattern indicative of a role in early human neurodevelopment. In both of our cell models there was a significant down-regulation of CHC22 upon the onset of neural differentiation, which we have proved to be an essential step in pain neuron development. Furthermore, knockdown of CHC22 induced neurite outgrowth in neural precursor cells, which was rescued by stable overexpression of siRNA resistant CHC22 but not by mutant CHC22. Using state-of-the-art quantitative proteomics we have identified the protein complement of clathrin coated vesicles in neuronal cells and report that CHC22 functions in the sorting of a subset of trophic neuropeptides to the regulated secretory pathway. In the absence of CHC22, SCG2 positive endosomes containing both NPY and BDNF are trafficked to neurite tips where they are secreted and exert an autocrine differentiation signal to the developing neuron.

Conclusion
Our results reveal an essential and non-redundant role for CHC22 in neural crest development and in
the genesis of pain and touch sensing neurons. Unexpectedly, we demonstrate the secretion of a number of neuropeptides to be dependent on CHC22 function, many of which have also been reported to affect postnatal pain sensing. Hence further identification and characterisation of the cargoes trafficked by CHC22 represent plausible targets for analgesic development.
Title: Genetic Variation In Adrb2 And Pain

Poster Number PW0068

Authors
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Aim of Investigation
Adrenergic β2 receptors (ADRB2) and other key proteins of the adrenergic system modulate pain and several other physiological and psychological phenotypes, such as cardiovascular and lung function and stress-responses. Genetic variation can change the level of expression or functional properties of proteins. Genetic variation in ADRB2-gene can lead to alterations in the amount, availability, or function of ADRB2-receptors. Here, we aim to characterize the effects of variation in ADRB2-gene on pain and opioid requirements in human patients.

Results
Rs17108817, rs11957757, and several other ADRB2 SNPs were associated with experimental and postoperative pain phenotypes. The strongest associations were seen in cold pain intensity (rs17108817 & rs11957757, 2-way ANOVA, genotype effect, p<0.0001). Both SNPs were also associated with tolerance to cold pain (cold withdrawal time, genotype effect, p<0.05).

Conclusion
Conclusions. Our results suggest that ADRB2 and genetic variation in ADRB2-gene are involved in the modulation of human pain responses.
Title: The Association Between Parental Knowledge Of Genetics And Parental Attitudes In Genotypic Pediatric Pain Research

Poster Number PW0069

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Aim of Investigation
This study examined the association between parental knowledge of genetics and parental attitudes towards enrolling children in genotypic pain research.

Results
Of the 32 interviews, 46.8% (n=15) of parents stated they had little or no knowledge of genetics. The educational level of parents with little or no knowledge of genetics ranged from some secondary education 60% (n=9), bachelor's degree 26.6% (n=4), master's degree 6.7% (n=1), to doctoral degree 6.7% (n=1). No parent with little or no knowledge of genetics stated they would enroll their child in minimal risk genotypic pediatric pain research unless there was a direct benefit to their child. Twenty-five percent (n=8) of parents stated they had some knowledge of genetics. The educational level of parents with some knowledge of genetics ranged from some secondary education 50% (n=4), bachelor's degree 12.5% (n=1), master's degree 25% (n=2), to doctoral degree 12.5% (n=1). Of the parents who self-reported some knowledge of genetics, two parents from different interviews (educational level secondary education) stated they would enroll their child in minimal risk genotypic pediatric pain research. The educational level of parents who felt they understood genetics, 21.8% (n=7), ranged from some secondary education 14.2% (n=1), bachelor’s degree 28.6% (n=2), master’s degree 28.6% (n=2), to doctoral degree 28.6% (n=2). Only one parent who self-reported an understanding of genetics (educational level PhD) stated they would enroll their child in minimal risk genotypic pediatric pain research. This parent had a genetics background and was employed in the field. Educational level was unavailable for 2 mothers. Parental sources of genetic knowledge influenced parent's attitude and willingness to hear about a genetic study but did not affect parent's decision to participate in genotypic research. Of the 46.8% (n=15) of parents who reported they had no source of genetic information, no parent was interested in hearing about a genetic study. When parents with some of knowledge of genetics or parents who felt they understood genetics were interviewed, only three parents stated they
would enroll their child minimal risk genotypic pediatric pain research. Twenty-five percent (n=8) received their information through personal experience (genetic testing during their pregnancy), 12.5% (n=4) received genetic information from a friend or family member, 12.5% (n=4) received genetic information from television, the Syfy channel, and 3.1% (n=1) had formal education in genetics.

**Conclusion**

There is a complex nonlinear relationship between parental knowledge of genetics and parent's attitude toward genomic research. Although it seems intuitive that a public less knowledgeable about genetics will have negative attitudes toward genetic research, the converse of that statement is not evidence-based. Previous data has demonstrated that knowledge of genetics may in fact result in a more discriminating public and a reluctance to participate in genomic research. Our findings support earlier research in adults suggesting that parental educational level is not a significant factor in the decision to enroll children in minimal risk genotypic pain research. More research exploring parental knowledge and attitudes towards genotypic pediatric pain research is needed to draw definitive conclusions. Funding: Sigma Theta Tau International Honor Society of Nursing #5971.
Aim of Investigation
Catechol-O-methyltransferase (COMT) is a key enzyme in the control of bioactive amines, such as epinephrine, norepinephrine, and dopamine. Thus, COMT contributes to an array of complex phenotypes, including pain perception and closely related ones, such as mood, cognition, and stress response. The COMT gene carries multiple single nucleotide polymorphisms (SNPs) that can modify the activity of the enzyme independently or combined into haplotypes, through multilocus genetic effects. Such pleiotropic diversity of the enzyme and high variability of the gene likely explain why COMT is one of the most studied genes in human pain genetics, and why it has been challenging to replicate findings from association studies. In this report, we will present recent advances that shed some light into the complex contribution of COMT to pain phenotypes.

Results
In study 1, we identified and replicated findings that the minor A allele of SNP rs165774 is protective against risk of TMD and experimental pain sensitivity. Finding this marker led to the discovery of alternative isoform (a)-COMT, which was shown in silico to feature a distinct and yet functional C-terminus. In vitro results confirmed that (a)-COMT is catalytically active and displays unique substrate specificity, exhibiting activity with dopamine but not epinephrine. We proposed contribution of the protective allele to decreased pain sensitivity through increased dopaminergic rather than decreased
adrenergic tone, characteristic of reference isoforms. In study 2, the COMT high pain sensitivity (HPS) haplotype showed robust interaction with stress in both cohorts, and number of HPS haplotype was positively associated with pain sensitivity in non-stressed, but not in stressed individuals. In the post-MVC cohort, there was additional modification by sex: the HPS-stress interaction was apparent in males, but not in females.

**Conclusion**
Findings of the two studies provide further understanding of the relationship between COMT and pain. We present an additional functional COMT marker that contributes to individual variability in pain phenotypes, along with a previously uncharacterized isoform of COMT that seems to play an essential role in pain signaling. We also demonstrate that stress and sex are fundamental components that should be evaluated in future studies aiming to investigate this complex relationship.
Aim of Investigation
Temporomandibular disorders (TMD) represent a major source of chronic orofacial pain, but their etiology is not well understood. The Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA) cohort study identified a number of intermediate phenotypes associated with increased risk of TMD. Two major psychological risk factors for TMD include heightened somatic awareness and stress. We have previously examined genetic polymorphisms in a genome-wide association study (GWAS) of TMD. Here, we have subjected two psychological risk factors for TMD to genetic association analysis in order to identify additional polymorphisms underlying genetic risk for TMD.

Results
One SNP was significantly associated with somatic symptoms: rs76842050, located in an intron of the semaphorin 4B gene on chromosome 15 (SEMA4B, beta=-7.68, p=2.23x10^-8). Another SNP was significantly associated with psychological stress: rs62205074 (beta=-2.0, p=2.7x10^-8), located on chromosome 20 within an intron of the FAM217B gene and near the protein phosphatase gene PPP1R3D.

Conclusion
The genetic architecture of TMD may include novel genes and pathways identifiable by association with psychosocial risk factors. In particular, semaphorin genes play a role in axon growth and regeneration.
and have been linked to neuropathic pain, suggesting a role for this system in increasing somatic symptoms.
Title: Pain Factors Associated With Arginine Vasopressin Receptor 1A Snp (Rs10877969) In Patients With Sickle Cell Disease

Poster Number PW0072

Authors

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Aim of Investigation
Pain, a multidimensional problem, is the classic symptom of individuals who have sickle cell disease (SCD) and is the most prevalent reason for treatment in the emergency department and for hospitalization. In a previous study, a pain-related single nucleotide polymorphism (SNP) was identified in the vasopressin receptor gene (AVPR1A) in patients with SCD and has been associated with sex and perception of stress in other pain studies. The aim of this study was to explore relationships between rs10877969 genotypes and self-reported pain and stress in adult outpatients with SCD.

Results
The frequency of rs10877969 homozygous CC genotype was 30 (28%), heterozygous (CT) was 44 (41%), and homozygous TT genotype was 33 (31%). The mean pain intensity scores were 3.8±3.1 for pain now, 3.1±2.7 for least pain, and 5.4±3.5 for worst pain. Thirty five (33%) patients reported stress aggravated their pain and 72 (67%) did not. Age, sex, and pain intensity scores were not associated with genotype at a statistically significant level. Genotype and citing stress as a pain aggravator were significantly related (p=0.002); 10% of patients with CC genotype cited stress, compared with 48% of patients with CT and 33% of patients with TT.

Conclusion
Among individuals with SCD, the AVPR1A SNP rs10877969 genotype was significantly associated with citing stress as a pain aggravating factor, but was not significantly associated with patient sex, age, or pain intensity. Results support the need for future pain studies to determine whether individuals with SCD who have a T allele at rs10877969 are more sensitive to stress as a pain aggravating factor.
**Title:** In Vivo Characterization Of Mice Expressing Painless Ngf Mutant And Its Implication In The Pathogenesis Of Hereditary Sensory Autonomic Neuropathy Type V (Hsan V)

**Aim of Investigation**
Hereditary sensory and autonomic neuropathy type V (HSAN V) is a rare genetic disorder characterized by the loss of pain perception. Because of the insensitivity to pain, HSAN V patients often develop serious orthopedic problems, posing an enormous medical challenge. The genetic analyses in Swedish cases identified a mutation in nerve growth factor (NGF) gene in which arginine 100 was replaced by tryptophan (R100W). In vitro studies revealed that R100W NGF mutation results in an altered affinity to p75-neurotrophin receptor as well as an impaired maturation/secretion. However, the understanding of the pathogenesis of HSAN V has been hampered by the lethality of transgenic mice carrying NGF R100W mutation. Alternatively, we have utilized knock-in mice expressing mutant human NGF in which arginine 100 was substituted by glutamic acid (hR100E), which possesses similar receptor binding/signaling properties to R100W mutant without significant compromise in maturation/secretion. In this study, we characterized the in vivo effects of NGF R100E mutation on pain-related phenotypes to elucidate the mechanisms underlying the insensitivity to pain in HSAN V.

**Results**
There was no significant difference in mechanical and heat sensitivity at the baseline between hWT and hR100E mice. The development of mechanical hypersensitivity following CFA injection was modestly reduced in hR100E mice, while CFA-induced heat hypersensitivity in hR100E mice did not differ from that of hWT mice. The duration of nocifensive responses following the formalin injection was also similar between hR100E and hWT mice. The immunohistochemical data showed that hR100E mice had similar densities of TrkA positive neurons in the DRGs and CGRP positive nerve fibers in the sciatic...
nerves compared to those in hWT mice. The microCT scanning revealed no significant difference in the BMD between hWT and hR100E mice.

Conclusion
While hR100E mice showed a modest reduction in the mechanical hypersensitivity following the joint inflammation, hR100E mice failed to recapitulate the phenotypes of HSAN V patients. This disparity may indicate that altered NGF signaling caused by R100 mutation only plays a minor role in the pathogenesis of HSAN V. Rather, the reduced maturation/secretion of NGF caused by R100W mutation may be essential for the abnormal nociceptive innervation and the development of the insensitivity to pain.
Title: Delivering Transgenic Tools To Primary Afferent Neurons Using Aav9

Poster Number PW0074

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Aim of Investigation
The general circuitry responsible for pain perception is well understood; however, we still have limited knowledge of the detailed circuitries involved. In particular, the neuronal networks of the dorsal horn - the first point in the pain pathway where peripheral inputs, descending and local inputs are integrated and modulated – are still not fully defined. One approach of studying the neuronal populations involved is to utilise a wide array of genetic tools, such as genetically encoded calcium indicators (GECI) or Cre recombinases. These tools can provide visual readout of neuronal activity or be used to knock out or express genes of interest, respectively. A major challenge to the use of such tools is their delivery to a specific neuronal population or subtype. Viral vectors, such as adeno-associated viruses (AAV), are one of the options available for controlling expression of transgenes in neurons. AAVs are non-pathogenic viral vectors that can carry up to 4.7 kb of genetic code and have multiple serotypes of which some possess strong neuronal tropism and as a result are useful for studying neuronal populations, e.g. serotype 9 (AAV9) possesses the capacity for anterograde and retrograde transport in neurons. We have investigated the use of AAV9 in delivering various genetic tools to neuronal populations that are part of the dorsal horn circuitry, particularly aiming at targeting the primary afferent neurons.

Results
Intrathecal delivery of 5ul of 2.5x10 gc/ml AAV9-eGFP resulted in eGFP labelling in the majority (67%, ±7%) of lumbar and cervical DRG neurons, while thoracic DRGs had significantly lower proportion of eGFP-positive cells. In the spinal cord, afferent fibres entering the superficial laminae of the dorsal horn, as well as those projecting in the dorsal columns, are clearly labelled with eGFP. When using AAV9-GCaMP6s, cultured DRG neurons that are positive for GCaMP6s show robust increase in fluorescence following depolarisation of DRG neurons in vitro. A significant increase in GCaMP6s signal in the L4 DRG neurons was evident in vivo following mechanical stimulation of the foot. Finally, intrathecal administration of AAV9-Cre into GCaMP6s-STOP-floxed mice resulted in expression of...
functional GCaMP6s in the L4 DRG neurons, evident by a robust increase in fluorescence <i>in vivo</i> in response to electrical stimulation of the hindlimb.

**Conclusion**
Intrathecal injection of AAV9 can be successfully used to deliver transgenes to the DRG neurons, and the transgenes are shown to retain their functionality in the cells, as shown by GCaMP6s and Cre experiment shown using GCaMP6s and Cre retain their functionality in the cells. This approach has wide applications, including delivering GECI for in vivo or in vitro imaging, as well as Cre-dependent knock-down of genes or expression of transgenic tools. In the future, GCaMP6s delivered using this method will be an important tool to investigate primary afferent activity in healthy animals and chronic pain models in vivo, as well as to study the effect of knock down of particular genes in the DRG neurons.
**Aim of Investigation**
Migraine is a common and debilitating neurological disorder characterised by unilateral throbbing, severe headaches, often accompanied by nausea, photophobia and phonophobia. Existing research has revealed changes in resting neural activity in migraineurs even between migraine attacks and it has been hypothesised that on-going altered functioning of the trigeminal system may underlie these changes including the pathogenesis of the migraine itself. Furthermore, it has been suggested that migraineurs have reduced endogenous analgesic mechanisms which may result in altered pain processing even between migraine attacks. In this study we aimed to determine if the sensitivity of the trigeminal system was altered in migraineurs between attacks (interictal) by measuring brain activity during the application of noxious heat stimuli to the orofacial region. We hypothesised that migraineurs would show altered activity patterns in the trigeminal system compared with controls including in regions known to be involved in mediating endogenous analgesia such as the prefrontal cortices.

**Results**
Despite no difference in applied temperature (migraineurs: 47.9°C, controls: 47.6°C), migraineurs showed significantly reduced pain rating when compared to controls (4.3±0.7 and 6.1±0.5 out of 10, respectively; p=0.001). Despite reduced pain intensity ratings, migraineurs displayed increased signal intensity changes in a number of brain regions. These included a region encompassing the anterior cingulate cortex (ACC) and bilateral medial prefrontal cortices (mPFC). In contrast, migraineurs displayed reduced signal intensity changes in the contralateral secondary somatosensory cortex (S2).

**Conclusion**
This data revealed that during a noxious heat stimulus, when compared to controls, migraineurs show greater activity in regions associated with pain modulation such as the cingulate and dorsolateral prefrontal cortices. These data suggest that even between attacks, migraineurs have altered central
processing of noxious information; with greater activity in areas associated with affective-emotional processing rather than sensory-discriminative, as seen in controls. This raises the possibility that reduced responsiveness of brain regions involved in endogenous pain control may result in the prolongation of pain during migraine attacks.
Title: Reduced T2 Relaxation Times Indicating Glial Activation In Chronic Neuropathic Pain

Poster Number PW0076

Authors

Aim of Investigation
We recently showed that orofacial neuropathic pain is associated with an increase in infra-slow (<0.1Hz) brain activity oscillations in the spinal trigeminal nucleus at a similar frequency to calcium waves that are released from astrocytes1. This finding is consistent with the observation in post-mortem tissue of long-term astrocyte activation in the dorsal horn of individuals with neuropathic pain2, supporting the theory that astrocyte activation is involved in the generation of infra-slow oscillatory activity and the constant perception of pain. To further test this hypothesis, the aim of the present study was to investigate astrocyte activation in living humans with neuropathic pain using structural magnetic resonance imaging (MRI). The MRI measure, T2 relaxation rate, is indicative of astrocyte activation2, so we propose that in individuals with orofacial neuropathic pain (NP), T2 relaxation rate will be reduced in the ipsilateral (to pain) spinal trigeminal nucleus, and other parts of the ascending pain pathway.

Results
T2 relaxation rates were significantly reduced in NP subjects in the ipsilateral (to ongoing pain) spinal trigeminal nucleus (mean±SEM: controls: 130.1±1.6, NP: 119.2±2.2, p=0.00009) and the contralateral primary somatosensory cortex (controls: 141.1±4.2, NP: 116.6±5.0, p=0.0002). In addition, significant reduction in NP subjects occurred in the contralateral medial prefrontal cortex (controls: 136.0±2.2, NP: 122.6±2.5, p=0.00007), contralateral cingulate cortex (controls: 124.5±2.4, NP: 111.9±2.1, p=0.00009) and contralateral primary motor cortex (controls: 127.9±3.1, NP: 113.2±2.9, p=0.0004). In no region was T2 relaxation rate increased in NP subjects compared with controls. The ipsilateral spinal trigeminal cluster overlapped with the region we have previous shown to display increased infra-slow oscillations and furthermore we found a significant correlation between T2 relaxation time and infra-slow
oscillations in the patient group ($r = 0.54$, $p = 0.03$). That is, the greater the reduction in T2 relaxation time, the greater the increase in resting infra-slow oscillation power.

**Conclusion**
These findings reveal decreased T2 relaxation time within the spinal trigeminal nucleus and primary somatosensory cortex of individuals with orofacial neuropathic pain. The results also reveal that decreases in T2 relaxation are related to increases in infra-slow oscillations, particularly in the region of the primary afferent synapse. Combined with previous findings, these results suggest that neuropathic pain following nerve injury results in long-term astrocyte activation, which causes an increase in infra-slow oscillation within the ascending pain pathway. Astrocyte activation results in significantly altered synaptic function including increased synaptic sensitivity, so the increased glial activation in NP may alter activity in ascending pain pathways and contribute to the constant perception of pain.
Aim of Investigation

There is substantial evidence from animal models to suggest that the development and maintenance of chronic pain relies, in part, on alterations within the descending pain modulation network. Although behavioral studies have suggested that patients with chronic musculoskeletal pain are less able to efficiently engage this circuitry, it is only recently that neuroimaging research has identified structural alterations in the brainstem that might support such deficits. Further insights into the functioning of descending modulation circuitry in chronic musculoskeletal pain may be achieved by studying patterns of on-going activity using resting state functional magnetic resonance imaging (fMRI). In particular, we have recently shown that infra-slow oscillations (0.03-0.06Hz) in the neural signal are increased in pain processing pathways in individuals with chronic neuropathic pain. The objective of the present study was to identify whether temporomandibular disorder (TMD), a chronic musculoskeletal pain condition, is associated with an altered pattern of resting oscillations in areas within the brainstem that modulate nociceptive transmission. Furthermore, the current study aimed to assess whether TMD is associated with altered resting state interactions between components of the brainstem descending modulation system.

Results

Compared to controls, the TMD group displayed significantly greater fractional power of infra-slow oscillations in multiple brainstem regions of the descending modulation network, including the midbrain periaqueductal grey and the region of the nucleus raphe magnus. Additionally, functional connectivity analysis revealed that in TMD subjects, the nucleus raphe magnus displayed significant greater connectivity with other brainstem areas involved in pain modulation including the periaqueductal gray matter bilaterally and the region encompassing the parabrachial nucleus. There was no significant linear
relationship between mean pain intensity, scan pain or pain duration on fractional power or nucleus raphe magnus functional connectivity strength.

**Conclusion**
These data reveal that chronic nociceptive pain is associated with altered on-going activity and greater temporal coupling within the descending pain modulation network. Although the mechanisms responsible for this difference are unknown, eliminating these activity changes may provide pain relief in individuals suffering from chronic musculoskeletal pain conditions such as TMD.
Aim of Investigation
Pain is an enigma being an unique and complex experience that always includes three dimensions: sensory, affective and cognitive. Among these factors of pain cognition, perceptual decision making of pain is at heart of a broad spectrum of theories, and evidence suggests impaired pain discrimination process in chronic pain conditions. In previous neuroimaging studies, activation related to the decision process of pain seem to be inconsistent across different studies. Without including non-pain and non-memory conditions, it is impossible to demonstrate the mapping specific to the pain decision. The current study aims to investigate pain-specific neural substrates during the decision process.

Results
The difficulty ratings between pain discrimination (PD) and nonpain discrimination (ND) were comparable, which allowed us to directly compare brain activity between PD and ND without the confounding of difficulty. Correct rates for all four trial types [PD, pain categorization (PC), ND, nonpain categorization (NC)] were significantly higher than the chance level (50%), suggesting that subjects correctly performed decisions in our study. Regarding fMRI results, a hippocampal-parietal network (hippocampus and posterior parietal cortex) was activated specifically during PD ['(PD-PC)-(ND-NC)'].

Conclusion
The main novel finding disclosed in current study is the distinct neural correlates underlying pain discrimination. These findings complement the neural basis for the cognitive modulation on pain.
Title: Multivariate Pattern Analysis In Individuals With Musculoskeletal Pain Utilizing Structural Or Functional Mri: A Systematic Review

Poster Number PW0079

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Aim of Investigation
The aim of this study was to systematically review the evidence relating to findings generated by multivariable pattern analysis (MVPA) following structural or functional magnetic resonance imaging (fMRI) to determine if this analysis is able to: a) Discriminate between individuals with musculoskeletal (MSK) pain and healthy control participants b) Predict pain perception in healthy individuals stimulated with a noxious stimulus compared to those stimulated with a non-noxious stimulus.

Results
Fourteen articles were identified and included for review. Analyses were limited by significant study heterogeneity, including small sample size, variable MRI methodologies and limited patient subgroups. All studies were cross-sectional in nature. Five studies investigated patients with painful conditions versus comparative controls, reporting the ability of machine-learning (ML) algorithms to differentiate patient groups. The remainder of the studies utilized healthy control participants (using them as their own controls), during experimental pain paradigms aimed to investigate the ability of ML to differentiate individuals stimulated with noxious stimuli from those stimulated with non-noxious stimuli. In the studies involving patient groups, three investigated chronic low back pain, two investigated fibromyalgia (FM), with one study each investigating complex regional pain syndrome, knee osteoarthritis and rheumatoid arthritis respectively. There is conflicting evidence regarding whether structural MRI with ML algorithms can distinguish between patient groups and healthy controls. Two studies demonstrated >75% sensitivity and specificity in distinguishing cLBP from HC, with one study demonstrating similar values for OA and CRPS classification. However, another study demonstrated that although classification accuracy, based upon brain volumes ranged from 53 to 76% (for FM), self-report measures of mood and pain intensity demonstrated significantly higher accuracy rates. There is limited
evidence that various ML algorithms when combined with fMRI may be able to differentiate between cLBP and HC. In the healthy cohort studies, multiple studies demonstrated that various classifiers in different scanners and different healthy populations are successfully able to discriminate painful heat from non-painful warmth with accuracy between 70-94%. A small number of included studies demonstrated that ML classifiers are successfully able to discriminate between physical pain and emotional pain with high sensitivity (>85%) and specificity (73-100%).

**Conclusion**
In conclusion, there is emerging and preliminary evidence that MVPA analyses of structural or functional MRI is able to discriminate between patients and healthy controls, and also discriminate between noxious and non-noxious stimulation. However, further research is required in different patient populations, with standardized methodological criteria to assist with further translation of these results to determine their full clinical utility.
Title: Nurses Engage In Emotional Labor: Underlying Their Professional Empathic Neural Mechanism

Poster Number PW0080

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Aim of Investigation
Empathy is the essential ability to understand other's pain and imagine own pain. However, the empathetic ability differ in individuals, even between professions: physicians down-regulate their pain empathy response (Jean D et al., 2010). The aim of this study is to test the hypothesis 'Nurses are compassionate' which is rumored as an urban legend, using voxel-based morphometry (VBM) and resting-states functional magnetic resonance imaging (rsfMRI) techniques.

Results
We found low IRI score tendency in N group. N group showed significant decreased gray matter volume in the right striatum (cluster FDR p = 0.012) in comparison with C group. In rsfMRI analysis seeding the right striatum cluster, we found Significant increased connectivity in right dolso-lateral prefrontal cortex (DLPFC) in C group (cluster FDR p = 0.048), especially strong covariation (cluster FDR p < 0.001) in Personal distress (sub-scale in IRI) in comparison to N group.

Conclusion
In Nurses, the brain region involved in positive emotion showed decreased gray matter volume and decreased functional connectivity with DLPFC, representing emotion regulation, have found. The current representation suggests that nurses down-regulate their empathetic response as professions through realistic perspective, similar to physicians.
Title: Correlation Between Voxel-Based Morphometric Values Of The Brain And Pain Assessment Scale Scores In Patients With Chronic Pain

Poster Number PW0081

Authors

Aim of Investigation
Voxel-based morphometry (VBM) is a method to examine morphological changes in the brain, and has been a focus of brain morphology research in recent years. In this study, morphological changes in the brain were examined using VBM, and pain assessment was conducted using the PDAS (Pain Disability Assessment Scale), PCS (Pain Catastrophizing Scale), and HADS (Hospital Anxiety and Depression Scale), in 92 patients with chronic pain. Our purpose was to examine common morphological changes in the brain in chronic pain patients with CRPS (complex regional pain syndrome), fibromyalgia, cervico-omobrachial syndrome, and chronic low back pain using VBM and to determine the relationship between such brain changes in amygdala and scores from each scale.

Results
In patients with chronic pain, VBM analysis showed significant decreased gray matter volumes in the amygdala, the dorsal entorhinal cortex (BA 28), and the anterior entorhinal cortex (BA 34) on both sides. VBM analysis showed significant decreased gray matter volumes in the fusiform gyrus and the cerebelum on right side, and the superior temporal pole on left side. There was a negative correlation between gray matter volume of the the left amygdala and PCS scores.

Conclusion
The amygdala is a nucleus playing a central role in the processing of negative emotions, such as fear and anxiety, and a region with possibly marked influences on patients with chronic pain. In the present
study, the decrease in the volume was more marked on the right side, suggesting an association of pain with such changes in the amygdala. Further analysis is needed to clarify this point.
Title: Neural Correlates Of Localized Thermal Comfort And Discomfort In Young And Elderly Participants

Poster Number PW0082

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Aim of Investigation
Research in human ergonomics suggests an association between feelings of thermal comfort and optimal warmth of the physical environment (Parsons, 2014). The sensation of physical warmth includes feelings of emotional warmth and pleasantness (Rolls et al 2008) and activates areas of the brain associated with pleasure (Kühn&Gallinat 2012). Processing of subjective pleasantness associated with more localized stimuli, however, has largely been neglected, and very little is known regarding changes in the experience of comfort with age. Here we directly investigate the relationship between brain activity, local thermal stimulation, and feelings of comfort and discomfort in young and elderly healthy controls.

Results
Hedonic reports of comfort and discomfort associated with each temperature were collected continuously while in the scanner and are averaged across participants in 30 second epochs. For both groups, greatest discomfort was associated with the highest (43°C) temperature. Lower temperatures were generally more comfortable. Elderly participants, however, reported less comfort for lower temperatures and less discomfort for the highest temperature. Nevertheless, there was large variability in hedonic reports for both young and elderly participants. For many participants, feelings of comfort and discomfort changed and overlapped during a single sequence. These dynamic changes in hedonics were captured during fMRI and demonstrated temperature driven comfort in primary somatosensory cortex in elderly participants and temperature driven discomfort in primary somatosensory cortex in young participants.

Conclusion
Elderly participants were generally more comfortable with higher temperatures and more
uncomfortable with lower temperatures in comparison to young participants. Most participants, however, demonstrated highly fluctuating experiences of comfort and discomfort during the same temperature delivery. fMRI data analysis of temperature driven hedonic reports captured that variability and indicated a 'hedonic flip' in primary somatosensory cortex when processing increasing temperatures. In elderly participants increased S1 activity was tuned to changes that evoked comfort while in young participants increased S1 activity was tuned to changes that evoked discomfort.
Title: The Role Of Respondent Appetitive And Aversive Learning In Subacute Back Pain

Poster Number PW0083

Authors
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Aim of Investigation
The relevance of classical conditioning in the generation and persistence of pain syndromes has already been shown (Nees et al., 2010; Flor, 2000; Linton et al., 1984). Previous research led to the assumption that emotional learning may play a major role in the development of chronic back pain. Chronification may develop along emotional learning via appetitive and aversive respondent conditioning. Aim of this study is to test how these learning processes relate to subacute pain perception and whether the assumed shift from nociceptive brain areas to regions known to be involved in the processing of emotions (Hashmi et al., 2013) is related to respondent learning mechanisms to identify target characteristics for the transition from acute to chronic pain. Special focus will be laid on extinction which is supposed to be impaired in individuals with a high risk for the development of chronic back pain. We propose that subjects with subacute back pain (SBP) show enhanced aversive conditioning and reduced appetitive conditioning with a delayed extinction of aversive conditioned responses, which is associated with a higher involvement of emotional brain circuits (amygdala, insular and prefrontal cortex).

Results
The data indicate the pleasant touch is a valid bodily-related US, with significant learning-related brain activation in the insula and the amygdala during the acquisition phase for the CS+ versus the CS-. Moreover, we show data on the relation of learning and subacute back pain that indicate stronger aversive compared to appetitive conditioning, on a neural and peripheral physiological level, with effects observed both in the acquisition and extinction phase.

Conclusion
Until now the usability of a pleasant body-related touch as an appetitive US was hardly studied in the MR environment, but may serve as valid stimulus in the context of body processes and related disorders such as (chronic) pain. We were able to show significant learning-related brain activation during
appetitive learning in the amygdala and insula. Moreover, subacute back pain may differentially change aversive versus appetitive learning processes, which could serve as risk factor for the development of chronic back pain. Supported by the Deutsche Forschungsgemeinschaft (SFB1158/B03 to FN/HF)
Title: Resting State Functional Connectivity Of Periaqueductal Gray And Primary Somatosensory Cortex Is Associated With Individual Differences In Conditioned Pain Modulation

Poster Number PW0084

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Aim of Investigation
Conditioned Pain Modulation (CPM) is a behavioural paradigm used to test the efficacy of the pain modulatory system. In this paradigm, a tonic pain stimulus induces a generalized modulatory response, and reduces pain perception of a test stimulus. Subjects are instructed to only rate and attend to the test stimulus. There are notable inter-individual differences in CPM, and these have been shown to predict the likelihood of the development of post-operative chronic pain and responses to pain medication (Yarnitsky et al., 2012). Despite this clinical relevance, the underlying mechanism of these inter-individual differences remain poorly understood. CPM has been associated with descending modulatory systems and a key descending modulatory region within the brain is the periaqueductal gray (PAG) (Gebhart, 2004). We therefore investigated whether resting state functional connectivity of PAG to the rest of the brain was associated with individual differences in CPM.

Results
Average participant threshold was 45.64 (s.d=1.75), with a mean 6/10 stimulation of 46.90 (s.d=1.19). The mean CPM value was 1.64 (s.d=1.38), indicating reduced ratings in the CPM condition. Values ranged from -.67 to 5.67. When adding CPM values as a regressor of interest in our analysis of resting-state PAG connectivity, we found that the connectivity between PAG and left S1 was significantly associated with CPM.

Conclusion
Resting state connectivity of modulatory and sensory processing areas is associated with individual differences in the pain modulation profile.
Title: Higher Pain Rating Results In Lower Variability Of Somatosensory Cortex Activation By Painful Mechanical Stimuli

Poster Number: PW0085

Authors

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Aim of Investigation
The aim of this study was to find pain-related brain activity which corresponds to self-report pain ratings based on degree of response and repeatability.

Results
Although the average PSCs for trice stimuli conducted in one session increased in accordance with pain ratings in the somatosensory cortex (S1) and anterior cingulate cortex (ACC), there was a different response between S1 and ACC when subjects rated intense pain; a stable response in S1 against a variable response in ACC.

Conclusion
These results imply that there are different cognitive responses between sensory discrimination and affective component to constant painful stimulus each time.
Title: Voxel-Based Morphometric Values Of The Brain In Patients With CRPS, Fibromyalgia, And Cervico-Omo-Brachial Syndrome

Poster Number PW0086

Authors
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Aim of Investigation
Voxel-based morphometry (VBM) is a diagnostic imaging technique to analyze brain morphology. Our purpose was to examine characteristic morphological changes in the brain in chronic pain with CRPS (complex regional pain syndrome), fibromyalgia, and cervico-omo-brachial syndrome using VBM.

Results
In patients with CRPS (N=9), VBM analysis showed significant decreased gray matter volumes in the amygdala, the dorsal entorhinal cortex (BA: Brodmann area 28) and the anterior entorhinal cortex (BA 34) on right side. In patients with fibromyalgia (N=5), VBM analysis showed significant decreased gray matter volumes in the amygdala, the dorsal entorhinal cortex (BA 28) and the anterior entorhinal cortex (BA 34) on both sides. In patients with cervico-omo-brachial syndrome (N=10), VBM analysis showed significant decreased gray matter volumes in the amygdala, the dorsal entorhinal cortex (BA 28) and the anterior entorhinal cortex (BA 34) on both sides, the anterior hippocampus, and the caudate nucleus on right side. The right amygdala, BA 28 and BA 34 showed a decrease in gray matter volume more so than in the left side in CRPS patients.

Conclusion
In the present study, there were lateral differences in the volume of the amygdala, BA28 and BA34 in CRPS patients. The decrease in the volume was more marked on the right side, suggesting lateral differences in the function of the amygdala, BA28 and BA34 in CRPS patients. Further analysis is needed to clarify this point.
Title: Cortical Correlates Of Ciguatoxin-Induced Cold Allodynia: A Functional MRI Study In Human Subjects

Poster Number PW0087

Authors
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Aim of Investigation
Cold pain states like cold allodynia are specific and frequent pain symptoms for which patients seek medical care and for which there is still lack of effective or curative therapy. Cold allodynia occurs as a major symptom of neuropathic pain states or nerve injury. This includes also increased neuronal excitability at the primary afferent level caused by fish poisoning with ciguatoxins (CTXs) that act as sodium channel activator toxins in humans. The disease is of particular scientific interest, because cold allodynia occurs in up to 94% of patients without presence of heat or mechanical allodynia.

Results
CTX induced a significant increase of cold pain threshold from 6.05 ± 2.29°C (Mean ± SEM) before injection to 23.07 ± 0.77°C after injection while it did not affect the heat pain threshold. The most prominent BOLD changes were found during ramp-shaped temperature changes. Changes in BOLD signal during cold allodynia were located in the frontal lobe (BA 9 and BA 10), in the anterior insula, anterior cingulate cortex, and in subcortical areas. The contrast analysis showed that the majority of these changes were stronger during cooling of the CTX site than of the control site and reduced during periods of constant cooling. Brain areas which responded to ramp-shaped cooling during cold allodynia were always located bilateral and appeared in the medial insula, in the medial cingulate cortex (MCC), the secondary somatosensory cortex S2, in frontal areas and in the cerebellum. Almost all of these areas had no change in BOLD-signal during the warming stimuli.

Conclusion
Our findings demonstrate that a CTX-induced substantial peripheral sensitization to phasic cooling stimuli in Ad-fibers [Vetter et al., EMBO J 2012, 31:3795-808] is retrieved in all activated areas in the...
brain, including insula, cingulate cortex, frontal lobe and the secondary somatosensory cortex and may be the defining feature of this pain percept. The silencing of most affected brain areas during warming of the affected skin may explain the beneficial effect of warming often described by ciguatera patients. Acknowledgements: Funding for this project was obtained through the German research council (Zi1172/3-1) and the EFIC Gruenenthal Grant 2012.
Title: Altered Resting State Functional Connectivity Is Associated With Fatigue And Pain In Patients With Chronic Fatigue Syndrome

Poster Number PW0088

Authors

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Aim of Investigation
Myalgic encephalitis/chronic fatigue syndrome (CFS) is a debilitating disorder characterized by disabling fatigue and cognitive dysfunction. Recent work from our laboratory and others' utilizing arterial spin labeling functional magnetic resonance imaging (ASL fMRI) indicates CFS patients have lower resting state regional cerebral blood flow (CBF) in several areas associated with various aspects of higher cognitive function including anterior cingulate cortex (ACC) and parahippocampal gyrus. This regional hypoperfusion may underlie CFS pathogenesis. The current report compared functional connectivity of hypoperfused regions between CFS patients and healthy controls (HC).

Results
CFS patients demonstrated greater functional connectivity relative to HC in bilateral superior frontal gyrus, ACC, and left inferior temporal gyrus to regions including precuneus, right postcentral gyrus, posterior cingulate gyrus, and thalamus. In contrast, HC patients had greater functional connectivity than CFS in ACC, left parahippocampal gyrus, bilateral pallidum, and right inferior occipital gyrus to regions including right insula, right precentral gyrus, and hippocampus. Subsequent correlation analysis indicated lower parahippocampal gyrus connectivity to left post central gyrus was significantly associated with greater fatigue ratings ($r=-.71, p=.001$). Similarly, greater ACC connectivity to posterior cingulate, left thalamus, and left hippocampus was associated with fatigue ($r=.56, p=.02$) and clinical pain ratings($r=.42, p=.03$).

Conclusion
The current report demonstrates these regions show altered functional connectivity in CFS patients
compared to their healthy counterparts, providing evidence that brain network abnormalities may be associated with CFS symptomatology.
Title: Accuracy Of Machine Classification Algorithms Using Structural MRI And Self-Report Features In Patients With Chronic Pain

Poster Number PW0089

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Aim of Investigation
Chronic fatigue syndrome (CFS) is a disorder associated with pain, severe fatigue, and neurocognitive impairments. CFS is characterized by central nervous system (CNS) abnormality as indicated by multiple neuroimaging modalities. Several studies have used machine learning (ML) techniques to determine the effectiveness of magnetic resonance imaging (MRI) features in classifying individuals with chronic pain conditions from healthy controls (HC). However, when compared, MRI features have not outperformed those obtained via self-report (SR). These techniques have not yet been applied to CFS, nor have SR and MRI features been combined in these tasks. The current investigation aimed to compare the performance of sMRI and SR features in the classification of HC and patients with CFS.

Results
The sMRI model achieved 75.76% accuracy and included only the right cuneus. Higher but comparable performance was achieved with the SR (accuracy = 90.91%) and sMRI + SR (accuracy = 93.94%) models. In both, all SR features except anger were retained. In the sMRI + SR model, estimates from the parietal, occipital and temporal lobes, insula, precuneus, cuneus, caudal anterior cingulate cortex, parahippocampal area, hippocampus, pallidum, caudate, and postcentral gyrus were retained. Models displayed poor performance in high and low base rates for NPV and PPV, respectively. SR and sMRI + SR models achieved PPV and NPV greater than 80% for base rates ranging from 30%-80%.

Conclusion
This is the first ML-based analysis of neuroimaging features in patients with chronic pain and CFS. Our results demonstrate similar performance to previous ML studies of chronic pain conditions and, likewise, depict greater performance for models using SR features than sMRI alone. Findings suggest that combining SR measures with sMRI may increase performance. The role of abnormalities in the occipital...
and temporal cortices, and basal ganglia in CFS were supported. Future studies using similar approaches to distinguish from among patients with similar conditions are recommended.
Title: Inter-Individual Differences On Pain Sensitivity And Functional Brain Connectivity Are Modulated By Bdnf Val66Met Polymorphism In Fibromyalgia

Poster Number PW0090

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Aim of Investigation
Several studies have already suggested that single nucleotide polymorphisms could play a relevant role in the development and maintenance of pain and affective symptoms in fibromyalgia by modulating pain sensitivity. The Val66Met polymorphism of BDNF gene could be one candidate due to its relevant role in the central sensitization that contributes to chronic pain conditions. Previous studies have further demonstrated that chronic pain patients with the Met allele of the Val66Met polymorphism displayed higher amplitudes of the pain-evoked brain potentials than pain-free individuals. The present study was aimed to analyze differences due to the functional Val66Met polymorphism of the BDNF gene on functional brain connectivity (resting-state fMRI) and pain sensitivity in fibromyalgia patients.

Results
Forty-one fibromyalgia patients carried at least one Met allele (met carriers) and 51 were Val homozygotes. The BDNF Val66Met genotype distribution was in Hardy-Weinberg equilibrium. Met carriers displayed lower cold pain tolerance, as well as higher pain sensitivity to mechanical stimuli than Val homozygotes. Analyses of functional connectivity at rest revealed that greater connectivity between anterior cingulate cortex and insula, insula and postcentral gyrus, amygdala and thalamus, amygdala and middle frontal gyrus, and secondary somatosensory cortex and frontal lobe in Met carriers than in Val homozygotes. In addition, cold pain tolerance was negatively correlated with connectivity of postcentral gyrus and middle frontal gyrus, whereas high anxiety was correlated with increased connectivity of insula and thalamus.

Conclusion
The present study revealed that FM patients carrying a Met allele of the Val66Met polymorphism of the
BDNF gene were more sensitive to painful mechanical and thermal stimulation than Val homozygotes. Moreover, Met carriers displayed increased connectivity of anterior cingulate cortex, insula, amygdala, thalamus, somatosensory cortices and frontal lobe than Val homozygotes. Data suggest that BDNF Val66Met polymorphism could modulate pain sensitivity and resting-state brain connectivity in FM patients. These findings provide further support for the notion that fibromyalgia is not a discrete entity and that different physiological mechanisms could be involved in the maintenance of pain and affective symptoms.
Title: Central Opioidergic Dysregulation In Fibromyalgia: A PET And FMRI Study

Poster Number PW0091

Authors
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Aim of Investigation
We previously reported that µ-opioid receptor (MOR) availability is reduced in several pain-processing brain regions in fibromyalgia (FM) patients and that they have increased levels of endogenous opioids in cerebrospinal fluid, compared to healthy controls. In the present study, we compared resting MOR binding potential (BP) with pain-evoked brain activity and clinical pain levels in FM patients, to determine how regional differences in the endogenous opioid system are related to evoked and clinical pain in FM. If regional variations in MOR availability are found to be significantly correlated with regional pain-evoked activity and levels of clinical pain, this would provide strong evidence that the endogenous opioid system is participating in the pathogenesis of FM.

Results
The whole-brain correlational approach yielded 7 FWE-corrected clusters in which BOLD and MOR BP were positively associated. These regions were primarily ones that are known to be involved with antinociception and descending inhibition, including the dorsolateral prefrontal cortex (r = .81, p < .001 FWE) and multiple rostral anterior cingulate cortex clusters (all r > .67; all p < .02 FWE). In these regions where reduced MOR BP was associated with decreased pain-evoked BOLD, both BP and BOLD were consistently negatively correlated, in some cases significantly, with clinical affective but not sensory pain levels.

Conclusion
These findings are the first to link endogenous opioid availability to pain-evoked brain activity in a clinical pain population. Our data suggest that dysregulation of the endogenous opioid system in FM (e.g. MOR downregulation due to chronic overstimulation) could lead to less pain-evoked excitation in antinociceptive brain regions, resulting in hyperalgesia, allodynia, and higher levels of clinical pain – a
process akin to endogenous-opioid-induced hyperalgesia. These findings also strengthen our contention that exogenous opioids are unlikely to be efficacious in FM due to an already dysfunctional opioidergic system, and support a plausible mechanism through which long-term opioid use could worsen pain by exacerbating an existing neurobiological vulnerability in this population.
Aim of Investigation
Short-term memorisation of nociceptive events seems to involve cortical regions involved in the sensory and cognitive dimensions of pain. However, the timing of these activations and how these regions interact are not known. The aim of the study is to highlight cortical regions involved in a painful short-term memory task and their interactions, and to compare them with short-term memorisation of non-painful somatic and auditory stimuli.

Results
When stimuli had to be memorized, early components of evoked potentials showed increased amplitude relative to the control task in regions involved in affective and cognitive aspects of somatosensory system (anterior insula, prefrontal cortex, anterior cingulate cortex). Moreover a late negative response, from 300 ms to 800 ms after stimulation, was observed in response to painful and non-painful somatosensory stimuli during the memorisation period in these same regions, which also showed alpha and beta desynchronisation during the retention phase of all memory tasks.

Conclusion
Increasing of evoked potentials' amplitudes for all types of stimuli when subjects had to memorize suggests an increased attentional shift toward the stimulation, leading to both enhanced arousal and anticipation. The late negativity occurring during memorisation of both painful and non-painful stimuli may be tentatively related to the maintenance of somatosensory intensity in working memory. Alpha and beta desynchronisations during the retention phase, with a larger effect for painful stimuli, might be related to cognitive processing sustaining active maintenance of pain-related information in short-term memory.
Title: Association Of Bdnf Val66Met Polymorphism With Hippocampal Volume Plasticity In Primary Dysmenorrhea

Poster Number PW0093

Authors
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Aim of Investigation
Hippocampus plasticity is highly associated with pain and stress experience. Persistent pain may induce stress-like alterations in hippocampal neurogenesis. Brain-derived neurotrophic factor (BDNF) plays a key role in hippocampal neurogenesis. A single-nucleotide polymorphism producing a valine (Val) to methionine (Met) substitution at codon 66 (Val66Met) in the human BDNF gene is thought to disrupt activity-dependent secretion of BDNF and associated with abnormal cortical morphology. Primary dysmenorrhea (PDM) patients suffer from cyclic cramping pain in the lower abdomen or pelvis that starts with the menstruation and lasts for 24-72 hours. Our recent studies highlighted that the Taiwanese PDMs exhibit a significantly higher BDNF Met/Met prevalence, implicating that females with BDNF Met/Met homozygous may have an increased risk of PDM. In the present study, we hypothesize that the BDNF Met allele PDMs might exhibit smaller hippocampus volume than Val homozygous PDMs and that the changes in hippocampal volume may be dependent on duration of pain history.

Results
For the ROI-based analysis, we found the PDMs had significant smaller hippocampal volumes than HCs. The BDNF Met allele PDMs (Met/Val and Met/Met) had smaller hippocampal volumes than Val homozygote. The Val homozygous PDMs had larger hippocampal volume than Val homozygous HCs. For the voxel-wise one-way ANOVA analysis, we found a significant BDNF Val66Met genotypes effect in PDM (FWE corrected, p < 0.05) on the right posterior hippocampus. No correlation was found between
hippocampal volume and psychological scores. Finally, we found that the longer cyclic pain experiences, the smaller right hippocampal volume was in the Val homozygous PDMs.

**Conclusion**

The present study showed a significant BDNF Val66Met genotype effect in PDM on bilateral hippocampal volumes, especially at the right posterior part. The BDNF Val66Met polymorphism is the important factor about BDNF secretion. Based on the neurotrophic model, cycling pain is thought to be a stress source which leads to decrease the expression of BDNF and induces atrophy of the hippocampus. Our findings of the altered hippocampal volume in PDM suggest the association of the BDNF Met allele with a heightened risk for hippocampal neurogenesis when cyclic pain occurs. Moreover, the BDNF Val homozygotes may exert a neuroprotective effect on the microglial hyperactivation induced hippocampal damage in the early stage of cyclic pain. Therefore, early treatment of cyclic pain affords an opportunity to retard the atrophy of hippocampal neurons. It can be important to take the current finding into consideration in the future genetic neuroimaging studies and clinical practice of PDM.
A National Survey Of Pain Clinics Within The United Kingdom And Ireland Focusing On The Constitution Of The Multidisciplinary Team And The Incorporation Of The Extended Role

Title: A National Survey Of Pain Clinics Within The United Kingdom And Ireland Focusing On The Constitution Of The Multidisciplinary Team And The Incorporation Of The Extended Role

Poster Number PW0094

Authors
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Aim of Investigation
A National survey was conducted to review the current service provision in all known adult chronic pain clinics in the UK and Ireland. The survey focused on variations in the provision of multidisciplinary staffing and also the extended role of different healthcare professionals. Multidisciplinary team (MDT) working is essential to the management of complex chronic pain patients and previous audits have highlighted potential inconsistencies of approach as well as variable compliance with national guidelines. Financial pressures have led to alternate ways of staff utilisation with variable degrees of success.

Results
Of the 188 clinics contacted, 143 completed the survey, giving us a response rate of 76%. 85% of clinics surveyed had a MDT clinic. 21% had monthly MDT meetings, 43% met weekly, 3% met daily, 29% did not have MDT meetings and 4% met sporadically. The majority of clinics (81%) had a consultant led service. The Survey examined the presence of non-consultant led clinics. 71% of clinics had specialist pain nurse led clinics, 49% physiotherapist led clinics and 45% had psychologist led clinics. The respondents were asked for their impression regarding the safety and cost effectiveness of the nurse led clinics being utilized for the expressed purpose of seeing new referrals to the clinic. 47.5% of respondents stated that nurse led clinics were safe, while 45% stated they were unsafe and 7.5% were undecided. 58% of respondents stated that nurse led clinics were cost effective, 34% stated that they were not cost effective and 8% were undecided. In contrast, with regards to nurse led follow up clinics, 93% of respondents stated that this was safe and 91.5% stated it was cost effective. The perceived financial viability of each pain clinic within the health service was surveyed. 30% of clinics were reported to
operate on a cost-neutral basis, while 37% of the clinics were running at a surplus and 11% at a loss. 22% of the clinics were uncertain.

**Conclusion**
The high response rate of the survey increases its validity. The survey reveals that the majority of Pain Clinics have adopted the MDT approach as is recommended by the National Health Service England report. However, there is significant variability of both the composition of the MDT and also the working patterns of the individual healthcare practitioners. The survey reports the successful use of the extended roles for specialist nurses in follow up clinics. In contrast, the survey highlights that a large proportion of clinicians surveyed have reservations about both the effectiveness and the safety of utilizing specialist nurses in the extended role to see new referrals of complex pain patients to pain clinics.
Title: Costs And Consequences Of Chronic Pain Due To Musculoskeletal Disorders From A Health System Perspective In Chile

Poster Number PW0095

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Aim of Investigation
Chronic pain is a prevalent and distressing condition for patients with an associated high burden to the healthcare system and society. There is evidence of inadequate management which can be partly explained by the lack of clinical guidelines, their actual scarce implementation in the clinical practice and the health system unawareness regarding the magnitude of the problem. The aim of this research was to estimate the expected costs and consequences of chronic pain caused by musculoskeletal diseases from the health system perspective in Chile.

Results
On average, the annual expected cost due to musculoskeletal chronic pain was estimated in USD $1,266.7 million, equivalent to 13% of the total 2016 public healthcare national budget. The 95% Bayesian credibility interval (BCI) shows an interval between USD $717.8 million and USD $2,090.2 million, revealing significant uncertainty. OA of the knee and LBP account for most of the total cost, 35.9% and 26.6% respectively. Depression attributed to chronic pain is another important consequence accounting for USD $40.4 (BCI 95% $21.0 – $68.1) million in patients with LBP followed by CSP with USD$ 27.1 (BCI 95% 14.6 – 45.2). Productivity losses also account for and important cost even though early retirement caused by these musculoskeletal diseases and presentism were not measured. In addition, each year chronic pain generates on average a loss of 166,001 YLDs related to the main musculoskeletal diseases.

Conclusion
Chronic pain is a common health problem in Chile that generates important costs and health losses to
the health system. A better management of chronic pain can improve patients quality of life and reduce costs to the health system.
Aim of Investigation
In recent years there has been widespread concern in the United States about an emerging 'epidemic' of abuse and addiction to prescription opioids, with consequent emergency department visits and overdose deaths. More recently, cities are reporting an 'epidemic' of heroin abuse / addiction. Both phenomena have been attributed to liberal opioid prescribing, a trend that began in the late 1980s. Unanswered questions include: To what extent are adverse events (including addiction) the results of opioid prescriptions; i.e., are providers providing medications to people who are harmed by them? To what extent are the upsurge in heroin use and its associated consequences sequelae of having been prescribed opioids therapeutically, and also to what extent are they a consequence of the widespread availability of prescription opioids in society. Opioid addiction, when comorbid with chronic pain, occurs more commonly in those with preexisting substance use disorder. It is also widely believed that many of those with heroin addiction 'came in through the pain door;' i.e., they became addicted as a result of having received licit opioids for pain, and migrated to heroin when access to prescription opioids was impeded. However, there is little information available concerning the natural history of heroin addiction. It is established that there is a high prevalence of substance use disorders in patients with chronic pain, and conversely, a high prevalence of chronic pain in those with opioid use disorders. Studies suggest that when chronic pain patients have comorbid substance use disorders, the substance use disorder typically preceded the pain. This data argues against the notion that pain treatment caused the addiction. The situation is complicated by evidence that physicians are not so much creating 'iatrogenic addiction' as supplying those already addicted with a legitimized source of drugs. Evidence suggests that physicians are prescribing COAT preferentially to those who are at greatest risk of harm and for whom there is least evidence of likely benefit, given that virtually all studies of long term opioid therapy exclude subjects with pre-existing substance use disorders. There is cause for concern about unintended consequences of the liberalization of opioid prescribing. Fatal poisonings involving opioids more than tripled between 1999 – 2006, from ~ 4000 to 13,800.
**Results**

Results: 16/75 subjects were female. The average age of onset of substance use was 14 years old. Most started with marijuana (23/75) followed by alcohol (22/75) and alcohol plus marijuana (22/75). The mean age at first opioid use was 21.2 and for heroin was 24. Among those who started their substance use with opioids and later used heroin, the average interval between initiating opioids and using heroin was 5 years. Average age of 1st harm was 18.7 years at which time most subjects were using multiple substances. The substance of first harm was not quantified as that information was often not available. 27/75 patients had engaged in harmful substance use prior to initiation of opioids, and 18/75 experienced harmful substance use and opioid initiation at the same age. 20/75 patients had started opioid use prior to having negative consequences of other substance use. 9/75 did not use other opioids at all. Age at 1st harm is missing for 1 subject. Of the 75 cases, 43/75 started heroine at least 2 years after they started opioids, however, 9/75 used no other opioids prior to heroin or after. 11/75 started heroin within 1 year of other opioid onset. 2/75 started heroin before other opioids. 10/75 started heroin and other opioids at the same age.

**Conclusion**

Conclusions Most patients with heroin addiction in this population arrived via a 3-step process: They initiated substance use in early adolescence with marijuana or alcohol and quickly showed signs of a substance use disorder. Subsequently, their use expanded to include recreational use of prescription opioids, some of which was obtained legitimately, and some obtained illicitly. After a variable period of time, they began use of heroin, typically with nasal insufflation. In this population, periods of using licit, prescribed opioid analgesics were typically intermediate between non-opioid and heroin substance use disorders. Prescription drugs, even when obtained through licit means, were typically used recreationally. Discussion The findings of the present study suggest that heroin addiction is one stage of an evolving process that begins with alcohol and marijuana abuse/addiction and in which abuse of prescription opioids is an intermediate step. The role of health care providers in this process seems to be two-fold – prescribers supply opioids (and benzodiazepines) to patients with pre-existing substance addiction / abuse, and contribute to the pool of opioids that are available for diversion and illicit consumption. These data along with prior studies suggest that it is unusual for medical prescribing to initiate the addiction process; however, it may well promote a transition from other substances (e.g. alcohol and cannabis) to opioids. Of course, prescribing can also lead to addiction relapse in those who are recovering from a prior addiction. Although the dramatic increase in heroin addiction has paralleled a similar increase in opioid prescribing, it is not established that prescribing opioids to patients leads them to develop heroin addiction. Rather, the increased availability of prescription opioids in the population has promoted their recreational use, which is a step in the transition from alcohol / marijuana to heroin. It is unknown whether this has increased the overall prevalence of substance use disorders in the country, whether it has led those with preexisting substance use disorders to migrate to heroin, or whether those with alcohol / marijuana use disorders would have migrated to heroin without the intermediate step. A common belief regarding the spike in heroin abuse is that, because of opioid prescriptions for pain, some patients became addicted and turn to heroin when access to prescription analgesics is impeded. This appears to be incorrect, as recreational use of prescription opioids was a more likely prelude to heroin use than was prescription use. Together, the available information
indicates that screening for abuse of alcohol and marijuana prior to prescribing opioids is essential to safe management, since patients with this history are at risk for transition to more deadly forms of substance use.
Title: Have Smart Phones Made Pain Physicians Smarter?

Aim of Investigation
To look at use of technology and scope of various smart phone based applications in daily life of a pain physician.

Results
The various useful smart phone applications include Whatsapp, Practo, Lybrate, 1mg, Medscape, Uptodate, Doxper etc. Social mobile applications like Whatsapp can be used for networking amongst pain physician and serves as a source of sharing knowledge and latest news. They can be used as a mode to connect with patients, provide them information about an ailment, post procedural instructions and videos for physical therapy. Practice management applications like Practo and Lybrate help to digitize our practice, enhance efficiency, maintain professional calendar and improve patient experience. It increases online profile visibility of a physician too. Lybrate can also be used to follow an outstation patient via text, audio or video consultation which can be made chargeable if desired. Updated medical information is readily available applications like Medscape and Uptodate medical resources. Similarly for availability and cost of pharmacological agents, applications like 1 mg can be a handy tool for all young physician. Doxper is another interesting mobile based application which is working on electronic medical record keeping. Here doctor would write with a special pen on dotted sheet of paper which is handed as usual to patient and file is stored in digital format via bluetooth in the doctor’s phone or laptop. Many more similar useful applications are available for physicians but they come at the cost of privacy and associated legal issues.

Conclusion
It is a personal perspective of using various application based products available in market. There are various advantages and disadvantages associated with use of advanced technology in the lives of a professional pain physician. The major advantages being internet based cognitive therapy, ensuring adherence to therapy, better patient management and experience, cost effective method for
communication and decrease in emergency visits to clinic. Few disadvantages include loss of privacy for the physician and legal issues involved especially in the case of emergencies.
Date: 09/28/2016 09:30:00 AM

Title: Bioethical Approach In Pain Management Of Elderly In Everyday Practice

Poster Number PW0098

Authors
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Aim of Investigation
The Institute of Gerontology and Palliative Care Belgrade (IGPC) provides medical care to frail aged, suffering severe diseases, many of whom are terminally ill and on a high level of functional dependency. High ethical principles, such as respect of personal autonomy, dignity and integrity, are incorporated in everyday medical practice and nursing care of elderly treated in their homes. It is spotlighted how ethical principles are involved in pain management of elderly treated by IGPC. Personal right on decision about medical treatment should be jeopardized by impairments due to advanced age, psychiatric comorbidity, but also due to outer factors (e.g. lack of information or inappropriate knowledge and attention of professionals). THE AIM of the research was to assess whether the pain management of elderly in IGPC is consistent with bioethical principles.

Results
Study was conducted on N=98 (63f/35m) patients, 78.9±7.7 years old, with one or more pain syndromes (N=127). The third of the study population was functionally disabled (31.6%) and received continuous, formal and informal, caregiver support (24 hours). 30.6% (N=30) suffered mental disease. Many, 85.6% (N=83 conscious patients), preserved capacity to understand the process of pain treatment, including autonomy in making decisions. 13.4% (N=13) were confused and one (N=1) was in coma. Economical integrity (retired with regular incomes, N=98) was preserved, as well as, psychosocial protection from spouse (46.9%) and family members (10.7%). Formal caregiver support was provided for 37.5% patient who lived alone. More than half suffered strong or the most intense pain (55.1%, 70/127), 22% (28/127) moderate, 11.8% (15/127) slight and 11% (14/127) unknown. However, mainstay of pain pharmacotherapy was NSAIDs, 58.8% (625.0/1063.4 DDD/1000/d). Moderate and strong opioids (e.g. morphine 38.3, hydromorphone 28.6, fentanyl TD 40.8, tramadol 102.0 DDD/1000/d) comprised 23% of
pain pharmacotherapy. Patients ceased proposed pain pharmacotherapy because of lack of analgesia (43.6%), side effects (28.2%), unknown (6.4%) and other (21.8%). There were no significant difference due to gender (p=0.29), age (p=0.84) or presence of mental disease (p=0.64) p>0.05.

Conclusion
Health care professionals need to understand that, despite of advanced age, huge medical problems and barriers (e.g. functional, cognitive, economical and social), this frail population preserve autonomy in making decisions about medical treatment that should not be underestimated. Much more responsibility, medical knowledge, respect and empathy is needed in the pain management of elderly. Effective pain control have to provide suitable pain relief, taking care to preserve the dignity, integrity and vulnerability of elderly.
Date: 09/28/2016 03:15:00 PM

Title: Appropriateness Of Self-Report And Observational Pain Scales With Dementia Severity

Poster Number PW0099

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Aim of Investigation
Pain is common in residential aged care facilities (RACFs) but prevalence is difficult to estimate. Dementia is a major barrier as the ability to self-report pain becomes increasingly limited as dementia becomes more severe. Behavioural and observational pain assessment scales have been devised to measure pain in those with advanced dementia, but are they also appropriate in less demented cohorts? Current pain management guidelines suggest self-report plus observation scales may be most appropriate for pain identification in aged care settings when the resident has dementia, but evidence directly testing this is limited and the guidelines provide little additional evidence base.

Results
The prevalence of pain diminished with increasing dementia severity in cases that could self-report pain (None 66%, MCI 61%, Mod 43%, Severe 39%). This pattern was not replicated when using the Abbey (None 67%, MCI 38%, Mod 42%, Severe 57%), PAINAD (None 62%, MCI 43%, Mod 43%, Severe 57%) and NOPPAIN (None 47%, MCI 33%, Mod 30%, Severe 34%) scales at established cut-offs. Performance of the three observational tests on classification function for each category of dementia severity was also calculated. Sensitivity was higher than specificity for the Abbey and PAINAD scales in the no impairment (Abbey: 81.0% sensitivity, 60.5% specificity; PAINAD: 69.0% sensitivity, 53.5% specificity; NOPPAIN: 59.5% sensitivity, 79.1% specificity) and severe dementia categories (Abbey: 80.0% sensitivity, 67.5% specificity; PAINAD: 80.0% sensitivity, 67.5% specificity; NOPPAIN: 48% sensitivity, 75% specificity). Conversely, specificity was higher than sensitivity for the Abbey and PAINAD in the mild impairment (Abbey: 60.8% sensitivity, 92.2% specificity; PAINAD: 63.3% sensitivity, 82.4% specificity; NOPPAIN: 51.9% sensitivity, 92.2% specificity) and moderate dementia (Abbey: 61.8% sensitivity, 71.1% specificity; PAINAD: 61.8% sensitivity, 64.4% specificity; NOPPAIN: 44.1% sensitivity, 77.8% specificity) categories.
Conclusion
Pain prevalence profile with dementia severity changes whether using self-report or observational pain scales to measure pain. As dementia worsened the prevalence of self-reported pain decreased. This pattern was not replicated using observational pain assessment scales. Instead, pain prevalence was highest in those with no or minimal cognitive impairment, reduced in those with mild and moderate impairment, and increased again with severe cognitive impairment. This pattern was more marked with the Abbey and PAINAD observational scales and would suggest that there are limitations on using observational scales dependent on the severity of cognitive impairment.
Date: 09/28/2016 09:30:00 AM

**Title:** The Assessment And Management Of Pain In Older People By Nurses In Acute Care: A Focused Ethnography

**Poster Number** PW0100

**Authors**

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**Aim of Investigation**

This study used focused ethnography to explore the clinical practices of nurses during pain assessment and management of hospitalised older people. Older people constitute over a third of all admissions to acute care (Australian Institute of Health and Welfare (AIHW) 2014) and comprise up to 50% of the inpatient population (AIHW 2014), they also have the longest hospital stay (AIHW , 2014) which predisposes them to adverse and iatrogenic events (Ackroyd-Stolarz, Guernsey, MacKinnon, & Kovacs, 2009; Vaglienti & Grinberg, 2004). Pain is one of the main reasons why older people (65 years and over) present to hospital (Carr et al., 2014; Daoust, Paquet, Lavigne, Sanogo, & Chauny, 2014; Dawood, Dobson, & Banerjee, 2011). Of concern is that older people often have pre-existing multiple pain sites and types associated with chronic and complex diseases (Abdulla et al., 2013; Herr, 2010; Perry, 2009). During hospitalisation older people also succumb to pain inflicted during medical and surgical interventions (Czarnecki et al., 2011; Rawe et al., 2009). The research shows that being in pain leads to negative outcomes for older hospitalised people; there may be complications associated with unrelieved pain such as falls (Titler, Shever, Kanak, Picone, & Qin, 2011), disrupted sleep (Bowman, 1997; Gardner, Collins, Osborne, Henderson, & Eastwood, 2009), increased distress (Westman, Boersma, Leppert, & Linton, 2011), atelectasis (Thornlow, Oddone, & Anderson, 2014), and side effects associated with analgesic medications (Edwards, Pandit, & Popat, 2006; Thornlow, Anderson, & Oddone, 2009). Pain decreases cognition (Ji et al., 2010) and increases the risk of cascading iatrogenic events with multiple complications (Thornlow et al., 2009) prolonging hospitalisation and increasing the risk of further adverse events (Kerr et al., 2010). Discharge may be delayed (Elliott et al., 2014) and unrelieved temporary pain may become chronic (Brennan, Carr, & Cousins, 2007). Pain also predisposes older patients to delirium (Robinson & Vollmer, 2010), which if untreated can lead to death (Silverstein, Timberger, Reich, & Uysal, 2007). Hospitalisation with unrelieved pain also leads to increased risk of negative outcomes for older people who are cognitively impaired (Australian Institute of Health and
Welfare, 2014; Herr, Coyne, McCaffery, Manworren, & Merkel, 2011; Malloy & Hadjistavropoulos, 2004). However, despite this, little is known about the factors that impact on how nurses assess and manage pain in older people in acute care.

**Results**

Analysis of data showed that when caring for older patients with pain, nurses showed leadership by acting as problem solvers around pain issues and concerns, that they mentored new nurses in relation to pain care, they questioned them about the rationales for their approaches and they provided education to staff, albeit within the limitations of their own knowledge. There were tales of success from the nurses, how they assessed and rated pain, pain that they acknowledged as real and genuine, and of how quality improvement audits shaped what they did. Older patients talked of not being heard by nurses when in pain, of enduring pain, of having to retell their pain histories often, of being moved around from ward to ward, and of being a good patient or an unpopular patient. The older people in this study spoke about how difficult it was for them to provide one numerical pain score in the light of their multiple pain sites and types. Observations revealed pain assessment was mediated by a set of census based social rules, rituals and routines for pain care. There was a lack of continuity of pain care provision from shift to shift, ward to ward, and hospital to hospital. This resulted in the development of a range of barriers to pain care provision. Barriers to the provision of culturally congruent pain care for the older person in this study related to a lack of uptake by the nurses in this study of evidence based best practice (EBP) guidelines into their clinical pain care provision practices, despite the availability and proliferation of evidence available for them to use. Furthermore the nurses themselves had devised a set of social rules for the provision of pain care that was based on a combination of a lack of knowledge about pain and older person care in the presence of inconsistent clinical leadership which lacked clarity of roles. The implication was that the nurses in this study did not utilise the application and use of EBP within their experiences of being a mentor, leader or educator for the junior transitional nurses. Moreover on observation the clinical practices of the nurses in this study were often lacking in the application of EBP and the implication for the older person was that their experiences of pain care provision were less than optimal. Assumptions about pain and older person care held by the nurses has directed their actions and behaviours within their own set of social rules. Of particular salience was the finding that the older person was often excluded from pain management decision making, and beliefs held that they would not disclose their pain. The system barriers to effective pain management, specifically the focus on auditing was a strong factor that impacted and guided negatively the way that nurses provided pain care.

**Conclusion**

Before undertaking this study, little was known about how nurses in acute care undertake the assessment and management of pain for the older person in acute care. The aspects of nursing culture that will impact on nursing practices when assessing and managing pain in the older person within acute care were noted to be the lack of uptake and implementation of EBP guidelines into clinical practices. The presence of culturally mediated barriers and facilitators to aspects of their clinical practices were identified as being contributors to not implementing EBP guidelines such as the use of social rules devised by the nurses in this study. This focused ethnographic study has identified the culturally
mediated array of social rules in place that are devised by nurses when an absence occurs of ready access to EBP guidelines, policies and procedures. Whilst these social rules are a best fit for the nurses within a clinical environment, they are typified by an organisational drift away from patient-centred care philosophies, and their presence acts as a major barrier for the provision, implementation and translation into clinical practice of EBP for pain care provision for the older person. The perceptions and experiences of those older persons receiving pain care provision when their pain story was lost and their pain care provision lacked continuity were explored. In summary, this study has identified that the existence of numerous culturally mediated sets of social rules devised by nurses for pain care provision of the older person in the acute care system is a major barrier for delivery of culturally congruent pain care for this group of patients. The implication for those older persons who are the most vulnerable cannot be understated. This study has identified how a perfect storm can occur when there is lack of knowledge about implementation, translation, and adaptation of EBP to provide support for nurses within their clinical practices, and how this will impact on their ability to provide continuity of pain care provision for the older hospitalised person. Furthermore, in the presence of an all pervading climate of overt ageism, a lack of education, no undertaking of research, and leadership which lacked clarity of roles as well as a climate of organisational drift in combination, this study has shown how this can exert an all-pervading barrier for the provision of pain care for the older person. The implication for the older person in acute care is waiting and enduring in pain. The study has shown that for those older persons who are the most vulnerable their experiences were of suffering in pain. To conclude, the main facilitating aspect present for the provision of culturally congruent pain care for the older person is that nursing is a profession and therefore able to conduct research into its own clinical practices in order to understand them and to potentially undertake change.
Aim of Investigation
Age-related diseases and physiological changes create barriers for older people to participate and benefit from multidisciplinary pain management. The primary aim of this study was to assess the feasibility of offering multidisciplinary pain management specifically tailored for the needs of older people who would not usually be suitable for management in a mainstream multidisciplinary pain clinic. Additionally, indices of frailty, co-morbidity and cognitive status were examined for associations with changes in pain report before and after multidisciplinary pain management.

Results
Patients' ages ranged from 63.5 – 93.7 years (mean 80.1, SD = 7.1) with females representing 76%. The mean number of co-morbidities was 7.2 (SD 1.9), with the average number of daily medications being 10.2 (SD = 4.1). Clinical frailty was present in 66.3%. Cognitive impairment was present in 39.4%. All patients were able to complete a 3 hour assessment on a single visit, rather than having this broken up over multiple visits. Follow up psychometric scores were available on 80.5% of 124 eligible patients, on average 130.4 days after initial attendance. At presentation the average pain scores over the preceding 24 hours were 6.0 (SD = 1.9) and at review 4.6 (SD = 2.1) (p<0.001). A >30% reduction in pain was reported by 41.2% of patients, and >50% reduction by 21.6%. Corresponding results for 'interference in general activity from pain' were 7.1 (SD = 2.5) and 4.9 (SD = 2.8)(p <.0.001). A >30% reduction in interference was reported by 55.1% of patients, and >50% reduction by 40.4%. Changes in pain report did not differ between groups with or without cognitive impairment, or those who were clinically frail or not frail. Compared with the non-frail, patients who were frail reported less improvement in interference in general activity (p<0.008). A trend for greater improvement with increased numbers of co-morbidities did not reach statistical significance (r=0.2, p=0.057).
Conclusion
Older patients who may not be suitable for a mainstream Multidisciplinary Pain Clinic may gain significant benefit from a multidisciplinary approach specifically designed to deal with pain in the setting of frailty, co-morbidities and cognitive impairment.
Date: 09/28/2016 09:30:00 AM

**Title:** Advance Care Planning (Acp) Using Peace And Pace Models To Help Reduce Inappropriate Hospital Admissions For Older Adults: A Pilot Study To Evaluate Healthcare Professionals’ Views Of Service Delivery

**Poster Number** PW0102

**Authors**
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**Aim of Investigation**
To identify the barriers, facilitators and similarities associated with the delivery and implementation of two different models of Advance Care Planning (ACP) provided by two groups of healthcare professionals. The first GP led model used a document called PACe (Proactive Anticipatory Care Plan) and the second is a nurse led model with community geriatrician oversight used a model called PEACE (Proactive Elderly Persons' Advisory CarE). The former document is a variation of the PEACE document. The PEACE plan is a document to help guide healthcare professionals in delivering the best care to frail, older people with life-limiting illnesses (such as those with Parkinson's, advanced dementia and cancer) who are anticipated to be in the last year of their life and reside in a care home. It records discussions between the older person and/or their representatives and the geriatric team about what that best care might look like in the future when the older person’s health starts to decline further. Discussions may cover topics such as pain management, feeding, infections and whether coming back to hospital might be a beneficial or detrimental event for the older person. For example, discussions might include the use of morphine to help alleviate symptom burden at the end of life and such discussions may include family members but would be guided by the patient themselves.

**Results**
The PEACE Tool: there was considerable trepidation expressed by the nursing staff in relation to leading the pilot albeit with community geriatrician oversight. Five themes emerged from the data: PEACE as a tool to inform future care and treatment preferences; the importance of existing relationships; reflective practice; medical support as a fundamental PEACE facilitator and difficulties associated with PEACE in its current format. The PACe Tool: experiences of using the tool were wide ranging and participants spoke of having adapted the tool to suit their own needs. Five main themes emerged from
the data: the importance of existing relationships; creates and focuses conversation; a 'go to' document; reflective practice and difficulties associated with the PACe tool.

Conclusion
The findings suggest that the PEACE and PACe documents have the potential to improve care at the end of life by documenting the future care and treatment preferences of older adults with a life limiting illness by obtaining information from a range of sources- older adults themselves or in the case those who are cognitively impaired, the views of relatives, carers and health care staff using a 'best interests' approach. Both the PEACE and PACe tools are, in themselves, evidence enough to highlight the progress made to develop resources for ACP. Based on the findings from this study, these tools have demonstrated progress, but there is still a clear need to improve ACP delivery systems. Health care providers continue to indicate that patient volume, increasing patient complexity, the need to share information with multiple providers and an increasing paperwork burden has adversely affected quality ACP delivery. An increasing and ubiquitous use of health information technology, such as electronic health records and electronic health record-tethered patient portals, affords opportunities to streamline communication methods between various providers and their patients to help provide seamless end of life care.
Title: Pain Burden Among Patients Receiving Community-Based Palliative Care: A Retrospective Cohort Analysis

Poster Number PW0103

Authors

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Aim of Investigation
Palliative care provides support to seriously ill patients and their families and aims to manage symptom burden associated with chronic illness. It has been recognized that symptom distress triggered by chronic pain can be substantial. The aim of our study was to determine prevalence and predictors of pain and pain-related distress in community-dwelling chronically ill patients served by a U.S.-based, urban, specialist-level community-based palliative care program.

Results
The sample of 894 patients of a mean age of 72.3 years (SD=14 years, range 18-100) included 56.2% women; 67.5% patients were English-speaking and 22.2% were Spanish-speaking. Most prevalent diagnoses were congestive heart failure (36.3%) and cancer (30.4%). At the time of enrollment into the palliative care program, KPS ranged from 20-70 (median 60). Upon referral, almost half of the patients (46.9%, N=420) had pain. The pain was perceived as distressful by 96.2% (N=404) of the patients; 38.9% (N=157) of patients rated the pain-related distress as moderate or severe. The significant predictors of pain prevalence upon referral were age (p<.0026) and sex (p<0.05), indicating that older patients and women are significantly more likely to have pain. Sex also predicted pain-related distress at the enrollment. Both prevalence of pain and pain-related distress changed over time. After two at-home visits by palliative care team, pain prevalence in the sample decreased by 7.6%, from 46.9% to 39.3%. Further, there was a significant change (p<0.0001) in pain-related distress after two visits; 32.6% of patients reported a decrease in distress, 51.1% reported no change and 16.2% reported an increase in pain related distress.
Conclusion
The findings confirmed that prevalence of pain and pain-related symptom burden are high among community-dwelling chronically ill patients at the time of enrollment into palliative care; women and older patients are at higher risk. Overall, after receiving palliative care services, both the prevalence of pain and pain-related distress decreased. The findings support the importance of pain management in community-dwelling populations with advanced illness and suggest that palliative care programs can yield favorable patient related outcomes in a pain population. These findings can inform future development of palliative care programs.
Title: Validity And Reliability Of The Thai Version Of Pain Self-Efficacy Questionnaire

Poster Number PW0104

Authors
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Aim of Investigation
The Pain Self-Efficacy Questionnaire (PSEQ) was originally developed to assess self-efficacy beliefs in chronic pain patients. It is based on Bandura's concept of self-efficacy. Belief in self-efficacy influences the coping strategies, physical and psychological function, and therapeutic outcome in chronic pain patients. The PSEQ has already been translated into various languages. We conducted this prospective study to determine the psychometric properties of the Thai version of Pain Self-Efficacy Questionnaire (Th-PSEQ) in Thai chronic nonmalignant pain patients.

Results
The psychometric properties of the Th-PSEQ were calculated. The Th-PSEQ had high internal consistency (Cronbach's alpha 0.924) and moderate retest reliability (intraclass correlation coefficient 0.524). It was significant correlation with pain score, the DASS21, the RMDQ and the EQ-5D-5L.

Conclusion
The psychometric properties of the Thai version of PSEQ was confirmed. It was consistency with previous findings in other languages of the same scale. For Thai chronic nonmalignant pain patients, pain self-efficacy beliefs were associated with levels of pain severity, physical disability, depression, anxiety, stress and general health status. The Thai version of PSEQ was a reliable Thai clinical questionnaire for assessment of pain self-efficacy.
Title: Comparing Cold Pressor Test And Ischemic Pain Test In Relation To Pain Substances In Healthy Subjects

Poster Number PW0105

Authors
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Aim of Investigation
This study was aimed at finding a relationship between pain modulators in the blood and physiological pain in apparently healthy Nigerians. It also aimed at establishing a pilot study for finding reference values for plasma levels of substance P, serotonin and tryptophan for the first time among Nigerians.

Results
Results from cold pressor test revealed pain intensity to be 5.79 ± 0.25 cm, pain threshold 28.77 ± 2.32 sec and pain tolerance 143.62 ± 24.39 sec, while those from ischemic pain test were: pain intensity - 6.32 ± 0.28 cm; pain threshold - 67.05 ± 4.44 sec and pain tolerance - 121.50 ± 10.93 sec. Blood plasma level of substance P was 116.52 ± 20.53 pg/mL, serotonin 454.18 ± 30.16 ng/mL and tryptophan 12.77 ± 0.67 µg/mL. There was negative correlation between CPT pain threshold and plasma substance P, CPT pain tolerance and plasma substance P and CPT pain threshold and plasma serotonin. There was however a positive correlation between CPT pain intensity and plasma serotonin. There was significant positive correlation between IPT pain threshold and serotonin and weak positive correlation with substance P. IPT pain tolerance also has significant positive correlation with serotonin and weak positive correlation with substance P.

Conclusion
In conclusion, the regression formulas may aid in using cold pressor test to predict blood substance levels of the measured pain modulators in a low resource setting like Nigeria where ELISA test is very expensive. This can also serve as a pilot study for a nationwide survey of the measured parameters.
Title: Global Health: Population Data In A Community Pain Clinic In Tehran, Iran

Poster Number PW0106

Authors
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Aim of Investigation
To describe the pain and demographic characteristics of patients attending a community pain clinic in an urban area of Middle Eastern Region (MER).

Results
The population consisted of 128 females (mean age 47.7 years) and 73 males (mean age 43.9 years). Preliminary analysis shows that younger men presented with single site MSK problems and low pain interference on the BPI, while older females over 55 tended to present with multisite-widespread pain and high BPI pain interference scores. Further analysis will outline the nature of pain problems, as well as possible differences between genders and age groups.

Conclusion
The current study provides the first detailed information about demographics and pain characteristics of patients attending a community pain management clinic in an urban MER area. The results of this study should inform future research in other MER settings and help outline differences and similarities with other urban pain management clinics in North America.
Aim of Investigation
To examine the association between playing online games and pain intensity in 12 body locations.

Results
Averagely, participants reported pain intensity from 1.66 to 3.57 after playing online games, specifically, pain in head (1.85), eye (3.57), neck (3.29), shoulder (3.40), upper arm (2.41), forearm (2.40), wrist (3.02), finger (2.59), upper back (2.64), low back (2.45), hip (2.81), and knee (1.66). Female players reported higher pain intensity than male ones in eye, neck, shoulder, upper arm, wrist, upper back, and hip. Moreover, age was positively related to pain in upper arm, forearm, wrist, finger, and knee. Education, annual income, the history and intensity of playing online games were not associated with pain intensity in all locations.

Conclusion
Playing online games may be related to the intensity of pain in various body locations after playing games. Gender and age may predict the intensity of pain in some body locations.
Title: Safety And Effectiveness Of Ultrasound-Guided Peripheral Nerve Blocks: Audit At A Tertiary Care Hospital

Poster Number PW0108

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Aim of Investigation
Peripheral nerve blocks (PNBs) provide effective (1) analgesia to the areas of the body innervated by individual plexuses or single nerves. These nerves can be blocked by local anesthetics using various techniques. The key requirement for a successful regional block is an optimal distribution of local anesthetic solution in the proximity of nerve structures. Properly administered PNBs have negligible effects on the cardiovascular and respiratory systems. Different techniques have been used in clinical practice to guide local anesthesia (LA) injections, ranging from nerve localization by anatomical landmarks to nerve stimulation and ultrasound guidance (2). After the introduction of ultrasound, ultrasound guided regional anesthesia (UGRA) became an area of interest and gained popularity among anesthesiologists as 'an era of regional anaesthesia under direct visual control' (2). UGRA has the benefits of directly visualizing the target nerve, surrounding tissues, and LA spread (3) with more rapid block onset times (4), higher success rates (5) and a prolongation of both surgical anesthesia and postoperative analgesia (6, 7). Though it has been documented that the complications associated with UGRA use are extremely rare, (2) studies have shown a range of complications, varying from early complications like erythema, hematoma, or edema overlying the block placement site, minor neurologic injuries (numbness, tingling, pain, altered sensation), local anesthetic systemic toxicity, nausea, vomiting, block failure, pneumothorax, and hemidiaphragmatic paresis (HDP) (1) to late complications like persistent neurological deficit, infection and myalgias. Currently, data about the frequency of complications after ultrasound guided peripheral nerve block is scanty. With advancements in ultrasound guided technique, more evidence is needed to evaluate benefits and complications compared to conventional guidance techniques. So far, no data is available in developing countries like Pakistan. The use of ultrasound is becoming popular in our country but due to limited resources and training, this facility is still underutilized. Department of Anaesthesiology, Aga Khan University Hospital has started to use the ultrasound for PNB since January 2013. As this is important that any new
technology should be evaluated, this audit was designed to assess the safety and effectiveness of PNB using US.

Results
In the last two years, 299 patients received US guided regional block as a part of their anesthesia care. The average age of the patients was 44.57 ±16.64 years. Hypertension (29.1 %) was the commonest co-morbid followed by diabetes mellitus (16.41 %), kidney disease (7%), asthma (4.7 %), heart disease (5.7 %) and anemia (4 %). 99.85% of the blocks were performed by the consultant anesthesiologist. In 92% of the patients the nerve blocks were inserted for the purpose of analgesia. Whereas the methods used for nerve localization were mainly ultrasound guided alone (92%), by nerve localization (0.3%), as well as both nerve stimulation and ultrasound were used in about 6.7%. Catheter was left in situ in 3.7% of the patients. The drug used as local anesthetic was mainly bupivacaine alone, 205 patients were asleep at the time of peripheral nerve block insertion. In 7.4% patients the nerve blocks were inserted after second attempt, the rest of the patients were successfully blocked in first attempt. Vascular puncture was the only complication which occurred at the time of peripheral nerve block insertion. Out of 299 patients, 139 patients (46.5%) received tranverse abdominus plane block (TAP block). Other blocks were supraclavicular nerve block ( 16.7% ), interscalene nerve block (12.7 %), femoral nerve block (9.7%), axillary (3.3%), popliteal (3%) and miscellaneous ( 5.4% ). Pain was assessed by static and dynamic scores using visual analogue scoring system. Majority of the patients ( upto 69. 7 %) remained pain free for 12 hours postoperatively. However mild pain was observed when patients were at rest in approximately 17 % cases and moderate pain was 8.4 to 16 %. A small percentage ( 2.3 % ) of the patients had severe pain in the recovery room and their pain persisted till 12 hours though got lessened in intensity after 2 hours ( 0.7%). When asked to make movements, approx 30 % patients had no pain, whereas mild pain was observed in approx 41.1% of patients, moderate pain was 29.4% to 36.1%, severe pain was 6.7 % which also lowered down to be present in 4.3% of the patients at 12 hours. Analgesics prescribed included opioids n=78 (26.1%), paracetamol n=125 (41.8%) and NSAID n= 17 (5.7%). Regarding motor/sensory block, there were 6.7 % patients who complained of weakness and partial sensory block in RR and 1 % patients reported weakness and numbness till 12 hours postoperatively. These patients were then followed for the next 24-48 hours till the symptoms resolved. No patient had motor or sensory block after 24 hours. Patients were also assessed for sedation status. In 83.8% of the patients, limbs have been protected from pressure and were supported by soft padding and they were helped in walking, whereas in approx 16% of the patients, this couldn't be done as the patients got discharged within 6 hours postoperatively.

Conclusion
This audit showed that complications associated with ultrasound guided nerve blocks are very few. Despite of the use of ultrasound guidance along with nerve stimulator, the effectiveness of these blocks seems to be near 70 %. With advancements in US technique, further studies are required to evaluate benefits and complications in comparison with conventional techniques.
Title: Somatosensory Processing And Pain Experience In Extremely Preterm-Born Young Adults: Sex And Modality-Specific Effects

Poster Number PW0109

Authors
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Aim of Investigation
Persistent alterations in somatosensory processing and pain experience have been reported in children following neonatal intensive care. Greater change in those requiring neonatal surgery or higher numbers of procedural interventions suggest correlations with the degree of tissue injury or pain exposure. We previously reported generalized reductions in baseline thermal sensitivity in 11 year old children born extremely preterm,[2] and have now re-evaluated sensory function and pain report in the same cohort.

Results
Sensitivity to all thermal modalities was reduced in EP males, and to a greater degree in those with prior neonatal surgery (EP+surgery); whereas values in EP females did not differ significantly from TC. Pressure pain thresholds (both digit and knee) were also significantly higher in EP+surgery males only. Testing on the chest wall confirmed a generalized decreased sensitivity in EP males; whereas more marked localised changes adjacent to thoracic scars were present in males and females. Sensitization to repeated punctate stimuli (increased WUR) was more common adjacent to thoracic scars in EP females. EP females had reduced CPT tolerance (immersion time <30secs) and higher associated pain scores. In those tolerating CPT, pressure thresholds significantly increased both during (15secs) and were maintained after (50-90secs) the conditioning stimulus. Sensory outcomes did not differ significantly between TC males and females. The incidence of current pain was higher in females (headache and musculoskeletal) than males (predominantly musculoskeletal pain), but was not altered by EP status. In females with current pain, pain intensity was similar, but interference due to pain was greater in the EP vs TC group.

Conclusion
Alterations in sensory processing following preterm birth and neonatal intensive care persist until early
Title: Opioids For Cancer Pain In Children And Adolescents: Part I Of A Cochrane Suite Of Reviews

Poster Number PW0110

Authors
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Aim of Investigation
The Suite WHO guidelines on pharmacological treatments for persistent children's pain, acknowledge that pain is a public health concern of major significance around the world. In the past, pain was often dismissed and left untreated, assuming that children quickly forgot about painful experiences. Views have improved over time and relief of pain is now seen as important. Zero - 18 year olds account for 27% (1.9 billion) of the world's population. We know little about their pain management needs, seen through only 12 paediatric reviews (by the pain group) in the Cochrane Library. We identified a need to summarise the evidence in child and adolescent pain using pharmacotherapies. Through a focus group of leaders, we have identified seven priority areas in chronic and cancer pain (examining opioids, NSAIDs, antidepressants, anti-epileptics, and paracetamol). The first Title investigating opioids for the use of cancer pain has been completed, the results follow. Background As one of the leading causes of mortality and morbidity in the world today, childhood cancer is a major health concern (second leading cause of death in the USA and Europe, and rising in African and Asian regions). Leukaemia is the leading cancer (30% Europe – 34.1% USA); lymphomas among the most common in the African regions; and viral related cancers the most common among Asian regions. All childhood cancer rates are rising worldwide with approximately 10,380 of zero - 15 year olds expected to be diagnosed with cancer by the end of 2016. However, over 80% of paediatric cancer patients have shown survival rates of 5 years or more. Developed countries see cancer pain related to diagnostic and therapeutic procedures, whereas developing countries tend to see cancer pain caused by the progressed tumour itself. Opioids are used worldwide in medicine for treating pain, but less so within paediatric pain management. Objectives To assess the analgesic efficacy and adverse events of opioids used to treat cancer pain in children and adolescents between the ages of zero - 18 years, in any setting.
Results
The search identified 663 papers, of which two authors independently screened 511 Titles and abstracts. We included no studies in this review as no studies met the eligibility criteria.

Conclusion
Discussion From a practical point of view, we can see what is available in child friendly doses - liquid morphine in mg/mL is the most common. However, most remaining sustained-release opioids may be at too high a dose for most of the paediatric population, such as sustained release tablets and fentanyl patches. Conclusion There is no high quality evidence for the use of opioids to treat cancer pain in children and adolescents. This is a disappointing outcome as children have specific needs and we are extrapolating from adult data alone. In practice, although there is no evidence in a clinical scenario, we do know that opioids are being used. Taking a broader scope of the suite of reviews, some pharmacotherapies (which we intentionally separated) are likely to provide more data than others. Thus, the results were as expected considering that randomised controlled trials in children are known to be limited. The results will assist to inform policy making decisions for funding future clinical trials into opioid treatment of child and adolescent pain, therefore, any results (large or small) are important to capture a snapshot of the current opioid evidence. Acknowledgement & Disclosure (not included in character count) Institutional support is provided by the Oxford Pain Relief Trust. The National Institute for Health Research (NIHR) is the largest single funder of the Cochrane Pain, Palliative & Supportive Care Review Group. This review was carried out under the Programme Grant ID: 13/89/29 – Addressing the unmet need of chronic pain: providing the evidence for treatments of pain. The authors have no potential conflicts of interest to declare.
Title: Interest Of Nitrous Oxide As An Analgesic In Dental Care

Poster Number PW0111

Authors

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Aim of Investigation
More and more studies have been conducted in order to assess the benefit / risk of the 50 % nitrous oxide/oxygen (EMONO). But published data evaluating the addiction risk associated to its use is scarce. Indications are extremely broad and involve many medical specialties. Even in the particular context of dental care, their term of use varies greatly between countries, as their indications. The purpose of this study was to investigate effects of EMONO sedation used in paediatric dentistry. The analgesic effect and anxiolysis was particularly assessed, as part of the expected effects of nitrous oxide.

Results
A total of 76 patients were included in this study. They were aged 3-13 years (mean 6.6 years). The sex ratio was in favor of girls (48/76, 63%). For 29% (22/76) of these patients, this was the first dental care and for 53% (40/76) their first treatment experience under EMONO. Regarding the effects felt by the child, 29 (40%) described analgesia and 44 (62%) described anxiolysis under EMONO use. Anxiolytic effect and analgesia were associated only in 33% of children (24/71). After a multivariate statistical analysis, none of these variables appeared significantly associated with an extended EMENO duration.

Conclusion
Regarding the effects felt in all patients, it is coherent to find anxiolysis as the most effective one corresponding to the indication of EMONO. However, we found that only 62% of patients presented an anxiolytic effect, which seems rather low for expected major effect in this EMONO indication. Just after anxiolysis, relative analgesia is also one of the major known effects of nitrous oxide. In our group of patients analgesia is only the 4th one and concerns only 29 of the 72 patients (40%). The analgesic potential of nitrous oxide in the oral sphere can be also discussed based on these treatment sessions. Nevertheless, these results from the child's responses should be considered with caution, especially because analgesia remains a difficult criteria to assess by children. It is important to consider that in
France, patients admitted for dental treatment under nitrous oxide are in a difficult clinical situation, since dental care in a classical way have generally failed. The effectiveness of the nitrous oxide previously discussed through the analgesia and anxiolytic perceptions is therefore to be analyzed in this context. Indeed, these treatment sessions under EMONO, initially provided in order to reconcile the patient with classical dental care, are very often the only alternative to general anesthesia. Since treatments have been achieved even with a difficult patient cooperation, it is considered that the care was a success. In our study, on 76 patients, only one patient could not be processed as expected. EMONO represents a considerable advantage as long as it remains within the limits of its indication.
Aim of Investigation
Circumcision is one of the most common surgeries in male infants. It is seldom medically indicated but it is often practiced for religious or cultural reasons. However, data on acute pain after circumcision in children is rare. Aim of this study was to assess information of pain intensity after pediatric circumcision in clinical routine.

Results
156 patients were assessed. Their mean pain on the first post-operative day after circumcision was 4.06±3.2. 57 (36.7%) boys had pain levels of 6 or higher. 53 out of 154 (34.4%) boys felt very tired after the operation (2 missing answers). 21 out of 155 (13.5%) would have wished for more pain medication (1 missing). During surgery, 124 (96.1%) patients received general and regional anesthesia and 5 (3.9%) patients received only regional anesthesia (27 missings). Regional anesthesia is split into 22 (17.5%) neuraxial and 104 (82.5%) peripheral techniques (30 missings).

Conclusion
Some 20 years ago and in some countries even today, circumcision is executed without proper anesthesia. In the 6 hospitals in this study, patients received at least general anesthesia, often combined with regional techniques. Even so, circumcision is a painful surgery. The amount of patients with severe pain is still too high. From a medical point of view, the necessity of circumcision without medical indication should be critically discussed. Furthermore, there is room for improvement of pain management after this frequent surgery. Some religious groups demand that the children are circumcised relatively early after birth. Our study was restricted to children of 4 years or older. There is no evidence that younger children experience less pain after circumcision.
Title: Health Care Professionals’ Perceptions Of Pain Practices In Neonatal Units In Kenya

Poster Number PW0113

Authors
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Aim of Investigation
To describe health care professionals' perceptions of procedural pain practices and barriers to pain treatment in neonatal units in Kenya.

Results
Three main categories emerged; (a) pain treatment practices, (b) contextual challenges to pain practices and (c) feasible pain treatment interventions. Health care professionals acknowledged that neonates undergoing painful procedures were rarely treated for the pain. Participants attributed this undertreatment to understaffing and competing care priorities, inaccurate perceptions about the safety of analgesics and poor clinicians' attitudes towards pain in nonverbal neonates. Mother-driven pain treatment interventions such as breastfeeding, kangaroo care and facilitated tucking were considered appropriate in these resource-limited settings on account of their availability and safety.

Conclusion
Health care professionals acknowledged the gross undertreatment of procedural pain; and identified potentially viable pain treatment interventions that could improve pain practices in Kenya. Strategies to (a) create awareness among health care professionals about pain, (b) implement effective treatments for pain such as breastfeeding and kangaroo care and (c) actively engage parents during procedures are warranted to address the undertreatment of procedural pain in Kenya and other resource-limited settings.
Aim of Investigation
Intraplantar injection of complete Freund's adjuvant (CFA) in adult rats induces a local inflammatory response and accompanying decreases in thermal and mechanical nociceptive thresholds. µ-opioid receptor (MOR) signalling plays an important role in the physiological response to this pain; following resolution of inflammatory pain, blockade of these receptors via the administration of naltrexone temporarily unmasks hyperalgesia initially caused by the inflammmogen. This constitutive MOR activity (MOR<sub>CA</sub>) can be observed for several months following recovery. We have previously shown that opioid receptor signalling pathways undergo extensive postnatal maturation. This study aimed to examine whether MOR<sub>CA</sub> plays the same role in pain resolution following inflammatory injury early in life, and which regions of the CNS are involved in this signalling.

Results
Intraplantar injection of CFA at P1 did not cause a significant decrease in PWT vs saline, despite the presence of significant inflammation for up to 7 days (2-way ANOVA; n = 15; P > 0.05). Subsequent s.c. injection of NTX had no effect on PWT following intraplantar CFA injection (2-way ANOVA; n = 7-8; P > 0.05). In contrast, injection of CFA at P10 or 21 caused a significant decrease in paw withdrawal threshold that resolved in 7 days. Subsequent s.c. injection of NTX caused a decrease in mechanical threshold in rats that received CFA at P10 or 21, but had no effect in rats that did not receive CFA (2-way ANOVA with Bonferroni post-hoc test; n = 3; P < 0.05). Examination of NTX-mediated reductions in PWT normalised to baseline indicated significant age-dependent variations in MOR<sub>CA</sub> (mean ± SEM: P1 - 6.5% ± 11.2; P10 - 48.9% ± 10.7; P21 - 70.1% ± 5.1; 1-way ANOVA with Bonferroni post-hoc test, P<0.03 P1 vs P10; P<0.01 P1 vs P21). Examination of the role of endogenous opioid peptide-expressing nuclei in this phenomenon revealed significant age-dependent effects of microinjection of NTX into the RVM and PAG following resolution of CFA-induced inflammation.
**Conclusion**

Intraplantar injection of CFA at P1 does not induce a decrease in PWT despite the presence of significant inflammation, in contrast to P10, P21 and adult rats. MOR<sub>CA</sub> is involved in the resolution of acute inflammatory pain induced in 10 and 21 day old rats – administration of NTX unmask hyperalgesia long after the initial tissue injury. This does not occur following injury at P1. Opioid receptor signalling within descending pathways in the brainstem and midbrain play a role in this process, in addition to intrinsic signalling within the dorsal horn of the spinal cord. These findings suggest that inflammatory nociception and associated constitutive MOR activity following tissue injury alter/mature significantly during the postnatal period.
Title: School Functioning In Adolescents With Chronic Pain

Poster Number PW0115

Authors
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Aim of Investigation
This study sought to examine the differences in school functioning between adolescents with and without chronic pain. We also explored the associations between school functioning and pain intensity and other pain-related variables (depression, anxiety and pain catastrophizing) and examined the role that these variables might play in school functioning in the group of adolescents with chronic pain.

Results
Differences between adolescents with and without chronic pain were found in that the former had lower levels of school functioning and higher absenteeism. Results also confirmed the significant associations between school functioning and pain catastrophizing, pain intensity, depressive and anxiety-related symptoms. However, absenteeism was only significantly related to the maximum pain intensity. Depressive symptoms and pain intensity levels emerged as the sole predictors of school functioning in adolescents with chronic pain.

Conclusion
The results provide additional evidence of the role of modifiable psychosocial factors in school functioning. This information provides useful insights for helping adolescents with chronic pain to learn more effective pain coping strategies in the school setting. Furthermore, this information could help to develop preventive treatment programs aimed at reducing absenteeism and improving school functioning among adolescents with chronic pain.
Title: Barriers That Impede The Provision Of Pain Care To Neonates By Nurses In Jordan

Poster Number PW0116

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Aim of Investigation
The purpose of this study was to describe perceived barriers impeding pain assessment and management among neonatal nurses in Jordan.

Results
Factors influencing effective neonatal pain care practices should be investigated to close the evidence-practice gap and improve the pain assessment and management of neonates. Neonatal pain misconceptions, ineffective interprofessional communication, inadequate training on neonatal pain management, and concerns about pain medications' side-effects were barriers impeding effective pain care practices. One of the main issues hindering nurses' effective practice of neonatal pain care was the underuse of structured pain measurements, especially around painful procedures (72%). Furthermore, nurses indicated minimal knowledge about pain medication for neonates (66%), and fearing their side effects on neonates (50%). Also the nurses received inadequate training on neonatal pain care during both their initial orientation (24%) and while in service (19%). Nurses perceived low interprofessional appreciation of any inputs into pain care decisions (72%). Finally, only 39% of nurses supported involving parents in their infants’ pain.

Conclusion
Future efforts for improving evidence-based neonatal pain care should focus on the nurses and the organizational factors that influence neonatal pain care practices. Efforts for improving neonatal pain best care should focus on improving the nurses' knowledge about neonatal pain, increasing competencies and involvement in pain management options, and improving channels of professional communication about neonatal pain.
Title: Pain-Free Children's Hospital Zagreb, Croatia

Authors
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Aim of Investigation
To show the improvement of the quality of care and patients' satisfaction by organisation of Pain Clinic since 2001 and Acute Pain Service (APS) since 2011 in Children's Hospital Zagreb.

Results
APS was formed 5 years ago using 'Nurse based, anesthesiologists supervised' model. Protocols for postoperative analgesia have been made, pain intensity is regularly measured by age-appropriate scales (VAS, FLACC, Numerical 1-10) and adequate interventions are performed. Questionaire for patient/parental satisfaction with postoperative analgesia is used. More than 5500 operations are performed yearly in Children's Hospital Zagreb, types of operations are abdominal, thoracic, urogenital, orthopaedic, plastic, neurosurgical, ENT. Postoperative pain is of different intensity, duration and analgesia needs. Patients age ranges from premature newborns to 18 years old adolescents, weight range is from less than 1 kg to more than 100 kg. Postoperative analgesia should be adequately planned, using pharmacological methods or regional analgesia with peripheral and central nerve blocks. Regional blocks are US controlled, single dose or continous therapy by implanted catheters. Pain Clinic was established fifteen years ago for the treatment of children with chronic pain. There are patients with migrenous or tension headaches, neuralgias, neuropathic pain (CRPS I or II), oncology patients with malignant pain and children with chronic non-malignant pain of orthopedic, immunorheumatologic or posttraumatic origin. In Pain Clinic detailed pain history is taken, where pain characteristics, duration, intensity are evaluated. Pain questionaire, clinical examination, diagnostic methods as MR imaging, CT, EEG, TCCD, US, Rtg are used. From 2002 to 2016 2622 patients, boys 1263 (48.2%) and girls 1659 (51.8%) were treated. Median age was 13,1 (+- 4,3) years. Treatment was pharmacological (titration of opioids, NSAID, adjuvant therapy with antiepileptics and antidepressives) in 30% of patients, non-pharmacological (TENS, laser, acupuncture) in 65%, and regional analgesia in 5% of patients. Non-pharmacological methods were laser therapy in 52.5%, acupuncture in 25.1%, TENS in 19.5% of patients. Invasive methods like trigger points infiltration and peripheral nerve blocks were
used in 5% of patients. With US control the number of invasive interventions is growing. Types of pain treated were musculoskeletal pain in 39.6% of children, headache in 27.7% and malignant pain in 31.5% of children. Musculoskeletal pain was of rheumatic origin in 37.6% of patients, posttraumatic in 30.6% and orthopedic in 31.8% of patients. Headaches were migraneous in 39%, and tension in 61% patients. Types of malignant pain were somatic 69.9%, visceral 13.1%, neuropathic 5.2%, mixed 9.8%. Therapy success was significant, mean VAS at the beginning of treatments was 6.9, at the end 3.7 ($p>0.01$)

**Conclusion**

Best results were achieved in the treatment of musculoskeletal pain, good in headache treatment where the frequency and intensity of attacks was diminished. In neuropathic pain treatment results were poorer because of weak patients' compliance due to side effects of antiepileptics and antidepressants. Regarding the questionnaire used patients and parents satisfaction with analgesia treatment was high 8.9 (range 1-10). Organisation of APS and Pain Clinic is an indicator for improvement of hospital quality as stated by Croatian Ministry of Health Committee for Quality Assurance.
Title: The Prevalence And Impact Of Chronic Pain In Children Aged 5-12 Years Living In Ireland: Results From The Prime-C Longitudinal Study

Poster Number PW0118

Authors

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Aim of Investigation
The PRIME-C study aimed to explore the prevalence, impact and cost of chronic pain among 5-12 year olds and their families living in Ireland.

Results
Approximately 10% of 5-12 year olds reported that they had chronic pain, with patterns of persistent and recurrent episodes of chronic pain emerging over the 3 time points. The prevalence of chronic pain increased with age, with 16.6% of 12-year-old children reporting chronic pain compared to 2.7% of 5-year-olds (Time 1). The most common sites of pain reported were head, abdomen and musculoskeletal. Children with chronic pain reported significantly lower quality of life than those without pain. Persistent chronic pain was associated with impaired family functioning, school functioning and emotional wellbeing.

Conclusion
These findings establish chronic pain as a common health issue among primary school children in Ireland with significant negative effects on child functioning at school, within the family and in terms of emotional well-being.
Title: Comparative Evaluation Of Thoracic Paravertebral And Epidural Analgesia For Postoperative Pain Relief In Patients Undergoing Open Nephrectomy

Poster Number PW0119

Authors
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Aim of Investigation
The aim of this prospective, double-blind, randomized trial was to compare the thoracic paravertebral and epidural analgesia for post-operative pain relief in patients undergoing open nephrectomy.

Results
The two groups were similar with regard to demographic factors. The VAS scores at rest, deep breathing and coughing were similar in the two groups (P>0.05); the incidence of side effects were also similar in the two groups (P>0.05). The mean systolic blood pressures were lower in the epidural group (group 2) as compared to the paravertebral group (group 1); but the difference was not significant (P>0.05).

Conclusion
Post-operative pain relief provided by thoracic paravertebral analgesia was similar to the thoracic epidural analgesia in patients undergoing open nephrectomy.
**Title:** Effectiveness Of Epidural Postoperative Analgesia For Hepatobiliary Surgery: A Retrospective Cohort Analysis In A Malaysian Liver Center

**Poster Number** PW0120

**Authors**
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**Aim of Investigation**
Hospital Selayang is the biggest liver centre in Malaysia with more than 200 liver-related surgeries performed annually. Epidural analgesia has been shown to provide excellent post-operative pain relief in upper abdominal surgery and is used as the standard analgesic regime for hepatobiliary surgery in our center. We aimed to determine the factors that affect the effectiveness of epidural post-operative analgesia in these patients.

**Results**
A total of 410 patients were included. The mean age was 54.9 years (range 12-89) and 56.2% were males. 34.9% of patient had liver surgery, 30.5% pancreatic surgery and 25.5% biliary and gall bladder surgery. More than two thirds of patients had a right subcostal incision. The mean duration under APS care was 3.4 days (SD1.8), and mean epidural infusion rate on POD1 was 8.0 ml/h (SD 2.2, range 4-16). 87.9% of patients had no complications related to the epidural; the most common complication was dislodgement of the epidural catheter which occurred in 4.2% of patients. On POD1, static PS <4 was achieved in 89.7% of patients but only 64.7% of patients had dynamic PS <4; this increased to 94.6% and 73.7% respectively on POD3. Univariate analysis showed that of all the factors studied, only epidural infusion rate was significantly associated with high dynamic pain score on POD1; this factor still remained significant when analysed using multiple logistic regression (p = 0.040 for duration of APS and p<0.001 for rate of epidural infusion).

**Conclusion**
Our study showed that the success of postoperative epidural analgesia for hepatobiliary surgery was
influenced only by the epidural infusion rate. Standardized protocols with clearly defined epidural infusion rates may result in more effective postoperative analgesia in this cohort of patients.
Title: Analgesia With Dexketoprofen, But Not With Opioid Prevent Immunosuppression In Patients After Kidney Surgery Due To Cancer

Poster Number PW0121

Authors
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Aim of Investigation
The main causes of death in cancer patients are the development of metastasis and recurrence after primary treatment. Surgical treatment of cancer remains the basic. Postoperative analgesia with opioids may cause impairments function of immune cells including depressing NK cells and cytotoxic T lymphocytes (CTLs) and stimulates angiogenesis. Recent studies have shown that NSAIDs possess the ability to enhance apoptosis of tumor cells and inhibit angiogenesis. The goal of our study was to investigate the influence of perioperative analgesia with omnopon (opioid) or dexketoprofen (NSAID) on the immune system in patients after surgery due to kidney cancer.

Results
After the surgery the average pain intensity (VAS) in the movement through 12 hours in patients Gr. 1 was 3.6 ± 0.9 and in patients Gr. 2 - 3.4 ± 1.1 (p = 0.5799). Twenty-four hours after the surgery the average pain intensity during the movement in patients Gr. 1 was 4.1 ± 1.1 and in patients with Gr. 2 - 3.5 ± 0.9 (p = 0.245). In Gr. 1 before the surgery (Ph.2) the number of CD3+ decrease in 5% and at the end of the surgery by 16% compared with the value before premedication (p = 0.143), whereas in Gr. 2 before surgery it was increased by 8%, but decreased by 11% by the end of the surgery, p = 0.068. The number of CD4+ in Gr. 1 decreased by 9% in Ph. 2, 27% in Ph.3 and 20% in Ph.4, (p = 0.012). In Gr. 2, it was seen decreasing of CD4+ by 6% in Ph.2 and by 23% and 15%, respectively in Ph.3 and Ph.4 (p = 0.101). Cytotoxic T lymphocytes in Gr.1 decreased by 14% in Ph.2, 7% in Ph.3 and 34% in Ph.4, p = 0.007. In Gr. 2 cytotoxic T lymphocytes increased by 2% in Ph.2 and reduced in Ph.3 only by 9% and 10% in Ph.4, p = 0.258. The number of NK cells (CD16+) in Gr.1 decreased by 7% in Ph.2 - Ph.3 and by 48% in Ph.4, p = 003. In Gr. 2 the amount of CD16+ increased by 67% in Ph.2 and 38% in Ph.3 with returned to baseline in Ph.4, p = 0.0014. The IFN-γ secretion by CD3+ lymphocytes was significantly reduced in Gr.1 by 10-15% at all stages of the observation, while in Gr. 2 the secretion of IFN-γ by CD3+ lymphocytes increase by 15-20% in all phases of the study.
Conclusion
The administration of dexketoprofen for premedication and postoperative pain relief in patients with kidney cancer prevented immunosuppression in comparing with opioid analgesic omnopon and save higher IFN-γ production by T-lymphocytes, increase the number of natural killer cells and increase cytotoxic activity of T-lymphocytes.
Title: The Relationship Between Minimum Nociceptive Threshold And Postoperative Opioid Requirements

Poster Number PW0122

Authors
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Aim of Investigation
There are individual differences in postoperative opioid requirements for adequate pain relief. Additionally, an appropriate dose of opioid should be administered to avoid life-threatening complications including respiratory depression. However, there are few preoperative ways to predict individual postoperative opioid requirements. If there was a correlation between the minimum nociceptive threshold (MNT) measured before surgery and postoperative opioid consumption, it would be possible to predict the amount of opioid that will be necessary for post-operative analgesia. In this study, we measured the MNT using the PainVisionTM system (Nipro Co., Ltd., Osaka). It delivers current to the electrodes attached to the patient in, gradually increasing amounts. The stimulus current is a pulsed current (50Hz, 150μArms, pulse width 0.3ms). The moment the patient feels the pain, she can stop the stimulus by pushing the hand switch. The amount of current at that time is the MNT. The optimum stimulation frequency is known to be different for each type of sensory nerve fiber. The frequency of the electrodes used in this measuring instrument stimulate mainly Aβ fibers with some Aδ fibers. Postoperative pain is predominantly somatic and visceral pain, and nerves involved in the perception of it are Aδ fibers and C fibers. Therefore, we thought that there might be some degree of correlation between the amount of opioid required for post-operative analgesia and MNT. As we also carried out MNT measurements at the surgical site, it was considered a more accurate correlation could be determined. In this study, we tested two assumptions. 1) There is relationship between MNT and required opioid dose for postoperative analgesia. 2) There is difference in the MNT between body parts.

Results
We registered 38 patients in this study. Five patients were excluded due to severe diabetes and use of antidepressants. Thus, we finally analyzed the results from 33 patients. Average of MNT at the forearm was 7.6±2.4 mA (mean±SD); at abdomen average MNT were 9.8±3.3 mA. Average bolus counts of PCA
was 44±40, average of total fentanyl dose for postoperative analgesia was 2160±1360 μg, and average total days of PCA was four. There was significant negative correlation between MNT in abdomen and PCA bolus counts, total fentanyl dose and total days of PCA. MNT at the forearm, in contrast, was not related to PCA use. There was no significant relation between MNT at the forearm and abdomen.

**Conclusion**
There was significant negative correlation between MNT measured at the abdomen, PCA bolus counts, and total fentanyl dose used for postoperative pain relief in the patients undergoing gynecological cancer surgery. There was no significant relation between MNT at the forearm and the abdomen.
Title: Comparison Of Analgesic Effect Of Ultrasound-Guided Transversus Abdominus Plane Block With Epidural Analgesia In Patients Undergoing Gynecological Procedures

Poster Number PW0123

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Aim of Investigation
We hypothesized that co-administration of sonographically guided TAP block with continuous epidural infusion of local anesthetics as part of a multimodal analgesic technique would result in superior postoperative analgesia (lower pain scores) and better patient satisfaction in patients undergoing total abdominal hysterectomy.

Results
We observed that Group 2 had lower pain scores at rest and on movement at 6, 24 and 48hr post-operatively. Time to first epidural rescue analgesia was prolonged in Group 2 (2.65hrs in Group 1 vs 1.16hrs in Group 2). We did not observe any difference in the total epidural bolus drug consumption, patient satisfaction scores and PONV scores. Also the post-operative pulmonary function tests were not significantly different across both the groups

Conclusion
Sonographically guided TAP block co-administered with epidural analgesia in a multimodal regimen has the potential to be an important tool in the management of post-operative pain control in abdominal hysterectomy. Although TAP block alone may not compare or replace epidural analgesia in this clinical setting, a combined technique has the ability to decrease incidence of known side effects of the epidural technique and improve efficacy of analgesia.
Title: Efficacy Of Transdermal Buprenorphine Patch On Postoperative Pain Relief After Elective Spinal Instrumentation Surgery

Poster Number PW0124

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Aim of Investigation
Pain management after spinal instrumentation is challenging. Adequate pain control reduces postoperative morbidity and mortality. NSAIDS & Opioids are two most commonly used therapeutics in pain management having several adverse effects if used by systemic routes. Buprenorphine, a partial agonist of mu opioid receptor having less adverse effects, found to be more potent than morphine when used by transdermal route, with prolonged duration of analgesia in management of chronic pain. So the aim of our study is to evaluate the clinical efficacy and safety of transdermal buprenorphine in management of acute post-operative pain after elective spinal instrumentation.

Results
Time of requirement of rescue analgesia (inj. Tramadol 2mg/kg) was average 11.87 hr. in the postoperative period in transdermal buprenorphine group (TDB) and was 90min in placebo group which was statistically significant (p < 0.001). Rescue analgesic requirement was much higher in control group (p < 0.001). Overall VAS score remained significantly low in buprenorphine group than that of placebo group. In buprenorphine group, five patients (4-male, 1-female) weighing 50-55kg did not require any rescue analgesics, ten patients required twice and rest of patients required single dose throughout the study period. In contrast patients of placebo group required more frequent tramadol administration. Total dose of tramadol consumed in postoperative period was also much higher in placebo group than the TDB group which was highly significant. It was observed that patients of TDB group maintained their hemodynamics (HR, SBP , DBP, MAP, RR,SPO2) better than that of placebo group & did not receive any additional doses of fentanyl intraoperatively. But patients in placebo group received additional doses of fentanyl (mean-27.40mcg).
Conclusion
Transdermal buprenorphine patch may be considered as a suitable alternative for post-operative pain management.
Title: Identification Of Neuropathic Pain Component In Patients Of Various Age With Knee Osteoarthritis

Poster Number PW0125

Authors
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Aim of Investigation
Osteoarthritis-induced pain is a result of nociceptor stimulation, associated with local tissue damage and inflammation. Recent data suggest the presence of neuropathic pain symptoms in patients with osteoarthritis. The aim of this study was to estimate the structure of pain syndrome, reveal the presence of neuropathic pain (NP) component, symptoms and signs of NP in patients suffering from knee osteoarthritis.

Results
72.7% of patients with knee osteoarthritis examined by painDETECT were unlikely to have the NP component, 22.7% might possibly, 4.6% – probably. LANSS scale: 25% were probably to have NP. DN4 scale: 31.2% probably had NP. Moderate to significant correlations were found between intensity of pain by VAS data and Neuropathic Pain Scales (painDETECT, LANSS, DN4) data (p<0.05). It was established than higher results of screening by painDETECT and DN4 positively correlate with a disturbance of physical function tested by WOMAC (p<0.05). PainDETECT data have moderate to significant correlations with EuroQol-5D questionnaire (p<0.01). Verbal descriptors as pins and needles, tingling, numbness and alldynia, pain from light touch which are revealed by 3 screening scales can significantly contribute to the likely neuropathic component in patients with knee osteoarthritis (p<0.05). Burning pain (p<0.01), pins and needles (p<0.05) can be associated with a more severe pain in patients with knee osteoarthritis.

Conclusion
Thus, in patients with osteoarthritis the pain syndrome may reveal NP features. Identification of these would promote a targeted treatment strategy.
Title: Characterization Of Behavioral And Histopathological Changes In A Mia Model Of Osteoarthritis Of The Rat Ankle Joint

Poster Number PW0126

Authors
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Aim of Investigation
Osteoarthritis (OA) is a complex disease of the whole joint, and in humans it commonly manifests itself as mechanical hypersensitivity in the knee, ankle, hip and shoulder joints. To this day, there is no satisfying method of relieving osteoarthritic pain, which affects over 27 million American adults, and 3 million Canadian adults. Mechanisms of osteoarthritic pain have been studied in the rat knee joint by intra-articular injections of the chondrocyte glycolytic inhibitor Mono-Iodoacetate (MIA). MIA-induced pain indicates that this method is clinically relevant and will continue to be useful for the development of better therapeutic strategies. However, most measures that confirm the pain behavior in the osteoarthritic knee joint do so by applying mechanical and thermal stimulus to the paw, an area remote from the knee joint. We suspect that this practice detects secondary hyperalgesia, which is due to sensitization of neurons in the central nervous system (CNS) rather than the local release of inflammatory mediators. The present study characterizes the behavioral changes and histopathological changes of cartilage necrosis and degeneration that occur in a new model of MIA-induced OA in the rat ankle joint, which we believe will more closely replicate the clinical symptoms of the human disease.

Results
In this characterization experiment, we determined that a dose of 2.4 mg of MIA in 40 µl of saline administered via intra-articular injection in the right ankle joint generated significant mechanical hypersensitivity starting at 4 weeks post-injection as detected by the Von Frey Filament test. Additionally, the mechanical hypersensitivity was accompanied by cold allodynia starting at 5 weeks post-injection as tested by the Acetone Test. Cold allodynia had not been previously reported in the rat osteoarthritic knee joint. Safranin histological staining of the cartilage pathology assessment showed significant cartilage loss matching the pathologic features of the clinical disease, best shown at a dose of 2.4 mg of MIA in 40 µl saline. In future experiments, x-ray microtomography scans (micro CT) of the
ankle joint will be performed to confirm that bone fragmentation and remodeling associated with the clinical disease are replicated in our osteoarthritis ankle joint model.

**Conclusion**

The present study showed sensitization of the joint, as measured by Von Frey filaments and acetone direct application to the affected osteoarthritic ankle joint. Detection of cold allodynia has previously not been reported in other models of MIA-induced OA. We are confident that these measures are detecting primary hyperalgesia, and predict that the proposed model will more closely replicate the clinical symptoms than the existing knee joint model, as cold pain is often reported in human patients. To further characterize our model, we will investigate peripheral changes in innervation of the joint and skin surrounding the affected ankle joint, along with corresponding central changes in the superficial lamina of the dorsal horn of the spinal cord following OA.
Aim of Investigation
To assess the reliability and validity of Foot Function Index Thai Version (FFI-TH).

Results
A total of 97 patients were enrolled. Most participants were female (80.47%), with an average age of 45.74 years and an education level of at least bachelor's degree (81.40%). The most common diagnoses were plantar fasciitis (41.0%), ankle sprain (28.0%), and hallux valgus (16.0%). Median time to onset of problem was 5.5 months. Reliability testing for internal consistency and stability demonstrated satisfactory results. Three domains revealed acceptable Cronbach's alpha coefficient values, as follows: pain subscale (0.94), disability subscale (0.96), and activity limitation subscale (0.72). Moreover, intraclass correlation coefficient (ICC: 0.92) indicated high stability. The test for construct validity demonstrated significant correlation between the total and subscale of FFI-TH scores when compared to VAS-pain and SF36-TH for bodily pain, as determined by moderate correlation from Pearson's correlation coefficients that ranged from 0.5 to 0.7. Average time to complete the FFI-TH was significantly lower than time to complete VASFA-TH (4.67 min vs. 6.63 min).

Conclusion
FFI-TH demonstrated good reliability and validity, similar to that of VASFA-TH. Patients were able to complete the FFI-TH questionnaire within 5 minutes. FFI-TH is suitable to be included as one of the Thai PRO measures that provide clinical benefit in musculoskeletal medicine, especially in patients with painful foot/ankle problems. In rehabilitation medicine, FFI-TH can be used as a clinical tool for evaluation of disease severity and outcome of treatment.
Title: Pain Catastrophizing Has A Major Impact On Both Subjective And Composite Outcomes In Patients With Rheumatoid Arthritis: Results From A Longitudinal Study Of Patients Starting BDMARDs

Poster Number PW0128

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Aim of Investigation
Patient reported outcomes (PROs) are important for the evaluation of treatment response in patients with rheumatoid arthritis (RA). The degree of pain catastrophizing (conceptualized as a negative cognitive–affective response to anticipated or actual pain) may influence the patient's scoring of disease activity. Ultrasound (US) is a sensitive method for assessing inflammation, including grey scale synovitis (GS) and vascularization (power Doppler (PD)). The present aim of investigation was to explore the impact of pain catastrophizing on subjective outcomes and composite scores in comparison with objective outcomes, such as US-defined synovitis, during one-year follow-up of patients with RA starting treatment with biologic DMARDs (bDMARDs).

Results
209 patients were included and 152 patients (72.7%) continued their bDMARD for the whole 12 months study. All variables, including pain catastrophizing, decreased significantly (p<0.001) during follow-up. Pain catastrophizing was highly correlated with patient reported outcomes (r=0.51-0.65, p<0.001), moderate with DAS28/CDAI (0.43/0.32, p<0.001) but not with CRP (r=0.1), SJC (r=-0.01) or GS (r=-0.06) / PD (r=-0.04) scores. All the subjective and composite scores were much higher (p<0.001) in patients with higher levels of pain catastrophizing. Using a mean cut-off of 1.5 for level of pain catastrophizing, there were almost double levels of patient's level of symptoms (PROs), while there were no differences for CRP, SJC or US scores. All subjective and composite scores had increasing levels with increased quintiles of pain catastrophizing (p<0.001), while this was not found for CRP, SJC or US.

Conclusion
It is generally assumed that the tendency to catastrophize plays a causal role in the pain experience which may influence the PROs. Pain catastrophizing was presently found to have a major impact on all
the subjective as well as composite scores, but not on inflammatory variables like CRP, SJC or US assessments. This emphasises the importance of taking into account the degree of pain catastrophizing when evaluating disease activity in RA patients.
Title: Post-Operative Prevention And Management Of Persistent Pain After Knee Replacement: The Star Program

Poster Number PW0129

Authors

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Aim of Investigation
Current estimates suggest that 10-34% of people who undergo total knee replacement report persistent pain at three or more months post-operatively. Our previous research in the UK found that referral for assessment and care is patchy, and people with persistent pain after knee replacement do not necessarily seek or receive care. STAR (Support and Treatment After Replacement) is a five year, UK-based programme of multidisciplinary research funded by the NIHR. The aim of the programme is to conduct a series of linked projects to inform care for people with persistent pain after total knee replacement.

Results
All work packages within this Programme are ongoing. Preliminarily results are available for two projects. In Work Package 1, the systematic review of interventions for persistent pain after diverse surgeries identified 36 randomised trials, most of which evaluated pharmacological interventions; no trials evaluated a care pathway. In Work Package 3 the finalisation of the care pathway has involved 28 health professionals rating the appropriateness of components of the care pathway. Consensus was achieved on most aspects, and an additional component (physiotherapy) was included. The preliminary care pathway comprises clinical assessment to identify potential causes of pain and then onwards referral to appropriate existing services, such as a surgeon, physiotherapist, general practitioner or pain specialist. Ongoing follow-up will be available if appropriate.
**Conclusion**
This Programme will provide high quality evidence about how to provide best care for people with persistent pain after total knee replacement. Acknowledgements This abstract summarises independent research funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research programme (RP-PG-0613-20001). The views expressed in this abstract are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. The STAR research team acknowledge the support of the NIHR, through the Clinical Research Network.
Title: Effects Of Multifactorial Intervention Program For Community-Dwelling Overweight Older Adults With Knee Osteoarthritis: A One-Year Follow-Up

Poster Number PW0130

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Aim of Investigation
The purposes of our phase II study were to: 1) determine participant adherence to an intervention related to health behavior after completion of a 8-week intervention program; and 2) examine whether a 8-week intervention program can reduce knee pain and improve knee function and weight loss in community-dwelling overweight older adults with knee osteoarthritis (OA) after the termination of the intervention program.

Results
Results revealed that >60% of the participants adhered to the program, and the participant's dropout was found only 5%. In the intervention group there was a significant improvement of knee range of motion at 6 and 12 months compared with baseline, and a significant reduction in knee pain, time spent in the Timed-Up-and Go test, and body weight compared with baseline. These study variables, except body weight, between the intervention group and control group were significantly different.

Conclusion
Evidence from this study shows the benefit of a multicomponent intervention on knee pain, knee function, and weight loss among community-dwelling overweight older adults with self-reported knee OA. The effect of quadriceps exercise along with weight reduction/control programs (dietary and walking exercise programs) appeared to last throughout a year follow-up, but a health education and a home visit programs given to the intervention group at the phase I would also be helpful to promote continued participation and adherence to health behaviors with a low dropout rate.
Title: Total Knee Replacement Followed By Non-Surgical Treatment Reduces Localized And Spreading Sensitization At 12 Months In Knee Osteoarthritis: A Predefined Analysis From A Randomized Controlled Trial

Poster Number PW0131

Authors
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Aim of Investigation
The purpose of this pre-defined exploratory analysis from a randomized controlled trial was to compare the 12-month effects of total knee replacement (TKR) followed by a 12-week non-surgical treatment program with the non-surgical treatment alone in reducing pain sensitization and pain intensity in patients with knee osteoarthritis (OA). Trial registration: clinicaltrials.gov NCT01410409.

Results
1,470 patients seen in secondary care by an orthopedic surgeon were assessed for eligibility, 1,348 were ineligible, and 27 did not want to participate. The primary reasons for ineligibility for the study were ineligibility for a TKR (n = 544), OA not severe enough (Kellgren-Lawrence score < 2; n = 197), not able to participate in the intervention (n=180), and unable to come to treatment site (n=145). The 100 patients included had a mean (SD) age of 66.4 (8.7) and 62% were women. Out of the 100 patients randomized 46/50 (92%; one patient did not undergo TKR) in the TKR + non-surgical group and 49/50 (98%; 13 patients underwent TKR during the 12 months) in the non-surgical group completed both baseline and 12-month follow-up. 39 randomized to TKR + non-surgical treatment and 42 randomized to non-surgical treatment alone had available PPT-data from both baseline and the 12-month follow-up. There was a statistical significant mean difference (95% CI) in change in PPTs from baseline to 12 months between groups of 65 kPa (7-123), favoring the group randomized to TKR (p=0.03). There were non-significant mean (95 % CI) between-group differences in change in peak pain intensity of 14 (-0.4-29) and pain intensity after 30 min of walking of 14 (-0.7-29) from baseline to 12 months, favoring the group randomized to TKR (p=0.06). In the as treated analysis, the differences in change in pain intensities
became significant with larger improvements in patients receiving a TKR (p=0.001-0.006). Both groups improved in PPTs and pain intensities (P<0.05).

**Conclusion**
At 12 months, TKR followed by non-surgical treatment is more effective in reducing localized and spreading pain sensitization than non-surgical treatment alone. The long-term improvements in pain intensities showed a tendency towards larger improvements in the group randomized to TKR that was significant only when analyzing the patients by the treatment they actually received. Acknowledgments Supported by the Obel Family Foundation, the Danish Rheumatism Association, the Health Science Foundation of the North Denmark Region, Foot Science International, Spar Nord Foundation, the Bevica Foundation, the Association of Danish Physiotherapists Research Fund, the Medical Specialist Heinrich Kopp's Grant, and the Danish Medical Association Research Fund.
Title: Long-Term Effects Of A Combined Non-Surgical Treatment Program On Pain And Sensitization In Knee Osteoarthritis: A Predefined Analysis From A Randomized Controlled Trial

Poster Number PW0132

Authors
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Aim of Investigation
The purpose of this pre-defined exploratory analysis from a randomized controlled trial was to compare the 12-month effects from a 12-week non-surgical treatment program compared to usual care in reducing pain sensitization and pain intensity in patients with knee osteoarthritis (OA). Trial registration: clinicaltrials.gov NCT01535001.

Results
654 patients seen in secondary care by an orthopaedic surgeon were assessed for eligibility, 553 were excluded and one was not willing to undergo randomization. The primary reasons for ineligibility for the study were being eligible for TKA (n=192), not radiographic OA (Kellgren-Lawrence score<1; n=87), and inability to comply with study protocol (n=159). The 100 patients included had a mean (SD) age of 66.0 (8.9) and 51% were women. Out of the 100 patients randomized 47/50 (94%; three patients underwent TKR during the 12 months) in the MEDIC group and 44/50 (88%; five patients underwent TKR during the 12 months) in the usual care group completed both baseline and 12-month follow-up. 39 randomized to MEDIC treatment and 36 randomized to usual care had available PPT-data from both baseline and the 12-month follow-up. There were non-significant mean (95 % CI) between-group differences in change in PPTs from baseline to 12 months between groups of 29 kPa (-11-69), favoring the group randomized to MEDIC treatment (p=0.16). In the per protocol analysis, this difference in change in PPTs became significant with larger improvements in patients receiving the MEDIC treatment (p=0.007). There were statistical significant mean (95 % CI) between-group differences in change in peak pain intensity of 14 (0.5-28) and pain intensity after 30 min of walking of 27 (14-41) from baseline to 12 months (p=0.001-
0.04). Both groups improved in PPTs and peak pain intensity, while only the MEDIC group improved in pain intensity after 30 min of walking (P<0.05).

**Conclusion**

At 12 months, a non-surgical treatment program is more effective in reducing pain compared to information and treatment advice. The long-term improvements in localized and spreading pain sensitization showed a tendency towards larger improvements in the group receiving non-surgical treatment that was significant only when excluding patients who had a TKR during the follow-up from the analysis. Acknowledgments This trial was partially funded by The Danish Rheumatism Association and The Association of Danish Physiotherapists Research Fund. The authors do not have any potential conflict of interest relevant to this study.
Title: Initial Results Of A Pilot Study Comparing Modulation Of Pain Mechanisms By Tapentadol Pr Or Oxycodone Cr In Osteoarthritis Knee Pain: A Mechanism-Based Approach

Poster Number PW0133

Authors
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Aim of Investigation
The impairment of descending pain inhibition is assumed to play an important role in widespread sensitization of patients with chronic osteoarthritis knee pain. In this single center, mechanistic, exploratory study, we investigated quantitatively the effect of oxycodone CR and tapentadol PR on the descending pain pathways, widespread hyperalgesia, clinical pain, and side effects. Oxycodone is a µ-opioid receptor agonist (MOR), tapentadol targets descending pain inhibition with two mechanisms of action – MOR and noradrenaline reuptake inhibition – which may generate a differentiated effect on the different pain mechanisms and clinical outcomes. The study objectives were to assess and compare pain response patterns using a mechanism-based approach in addition to clinical outcomes (effect and side effects).

Results
Recruitment for the study was difficult with a screen failure rate of 38%; 40 patients could be randomized. Twenty-two (55%) completed the study, seven oxycodone and 15 tapentadol subjects. The drop-out rate was 2.6 times higher for oxycodone (65% vs. 25%). Main reasons for study withdrawal were adverse events (AE) such as nausea and vomiting. The majority of patients reported treatment-related AEs (tapentadol 80%, oxycodone 90%). Markedly more oxycodone than tapentadol subjects experienced nausea (65% vs. 10%) and vomiting (55% vs. 0%). Twenty-six patients (tapentadol 16, oxycodone 10) for whom at least one post-baseline pain assessment was available were included in the full analysis population (69.5±7.4 years of age, 69% female). Data analyzed by the time of presentation will be presented.

Conclusion
There are significant problems in obtaining a sufficient patient sample for a randomized, double-blind
trial with an oxycodone treatment arm due to the markedly higher drop-out rates compared with the tapentadol group making such comparative studies difficult to complete. First data using the mechanism-based study approach will be presented.
Title: A Multi-Center, Randomized, Double-Blind, Active-Controlled, Parallel Group Study To Evaluate The Dose Effect Of Intradermal Injections Of Honeybee Toxin Versus Histamine Control In Patients With Pain And Inflammation Of Osteoarthritis Of The Knee

Poster Number PW0134

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Aim of Investigation
To evaluate the safety and pain reduction of honeybee toxin (purified <i>Apis mellifera</i> toxin) injections given on a single day to patients with osteoarthritis (OA) of the knee.

Results
Most patients (33/40, 82.5%) reported at least one treatment-emergent adverse event (TEAE). The majority of TEAEs were related to the injection sites, and none caused discontinuation. Injection site reactions, including discomfort, edema, induration, pain, pruritus, urticaria and warmth, were generally mild to moderate. Two subjects (100 μg and 300 μg dose groups) reported severe reactions. All injection site reactions resolved by Day 14. There were no SAEs associated with use of honeybee toxin, and there were no changes in laboratory parameters, vital signs, or electrocardiograms. For the WOMAC pain subscores, at Day 7, all three honeybee toxin dose groups showed an improvement in pain relative to control that was numerically similar across the doses but not significant; i.e. least square mean (LSM) difference from control: -2.23, -2.27 and -2.11, respectively, for the 100 μg, 300 μg and 1000 μg doses; p=0.2880. Physical function subscores, however, showed significant improvement versus control at Day 7: -11.27 (p=0.0374), -11.38 (p=0.0308) and -10.35 (p=0.0541), respectively, for the 100 μg, 300 μg and 1000 μg honeybee toxin doses. Further, at Day 7, a significant majority of all honeybee toxin treated patients (66.5%; p=0.0177) assessed their condition (PGA) as being 'very good or good' whereas 90% of subjects in the control group perceived their condition as being 'fair or poor.' The PhGA was generally consistent with the PGA, >90% of patients in the control group were considered to have an OA condition that was 'fair or poor' while 55.2% of honeybee toxin treated patients were considered to be 'good' or 'very good'; no honeybee toxin treated patient had 'poor' assessment by either PGA or PhGA. Regarding
Day 14 efficacy assessments, most were consistent with Day 7, however, the improvements among the doses were not as significant.

**Conclusion**
In this Phase 2 study, the honeybee toxin injection regimens at a single visit resulted in consistent improvement in pain, physical function, and global health perceptions in patients with knee OA that appeared to peak by Day 7 post-treatment. The safety results raised no concerns or issues related to honeybee toxin treatment. The results of this trial provide sufficient clinical evidence to justify investigating the safety and efficacy of honeybee toxin for treating patients with OA pain and inflammation in a Phase 3 trial.
Title: The Effect Of Current Modalities Of Physiotherapy In Reducing Pain Of Patients With Knee Joint Osteoarthritis

Poster Number PW0135

Authors
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Aim of Investigation
Osteoarthritis (osteoarthrosis) or degenerative joint disease is the most joint affection and is popular problem in elderly persons. Knee is the most common joint affected with clinical manifestation of joint pain, stiffness and limitation of motion led to decreased activity and dependency of patients.

Results
The subject’s age ranged between 48-83 years (Mean 62.4) and duration of disease was between 0.5-20 years (mean4.6). Seventy four patients were female and 29 male. Abnormal clinical signs were detected as genu-varum in 36.9%, genu-valgum in 2.9%, flexion contracture in 54.3%, and bony hypertrophy in 57.2% of patients. Radiography were graded as, G0 = 7.76%, G1 = 10.6%, G2 = 82.4%, G3 = 19.4%, and G4 = 9.7%. Combination of hot pack (HP), transcutaneous electrical nerve stimulation (TENS) with isometric exercise were highly effective in 10.3%, moderately effective in 61.8% and ineffective in 10.3%.

Conclusion
There were higher proportion of women with symptomatic knee OA. The study shows that the prevalence of knee OA increased with age throughout the elderly life. Low cost physical modalities and isometric quadriceps exercise are effective at short time in reducing pain, decreased knee deformities, increased function and even decreased radiological findings of knee OA.
Title: Lysophosphatidic Acid Is Implicated In The Establishment Of Joint Neuropathic Pain

Poster Number PW0136

Authors
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Aim of Investigation
Emerging evidence indicates that peripheral neuropathy contributes to osteoarthritis (OA) pain in some patients. The molecular mechanisms responsible for joint neuropathic pain are unknown, but could involve the lipid mediator lysophosphatidic acid (LPA). Subcutaneous injection of LPA has been shown to cause peripheral neuropathy and neuropathic pain-like symptoms in skin. The present study tested the effect of LPA on joint nerve morphology and pain generation in rats.

Results
Injection of LPA into rat knees caused a significant increase in G-ratio (P<0.05) indicative of demyelination. Similarly, LPA treatment caused a heightened expression of ATF-3 in ipsilateral nerve cell bodies. In animals assessed for pain, all 3 doses of LPA elicited a dose-dependent pain response. The pain persisted after a single LPA injection out to 51 days post injection. All histopathological and nociceptive responses were inhibited by Ki16425 pre-treatment.

Conclusion
Intra-articular injection of LPA caused joint nerve injury and neuropathic pain in rat knees. These effects were blocked by an LPA receptor antagonist indicating that pharmacological blockade of LPA receptors could be an efficacious means of controlling joint pain in neuropathic OA patients.
**Aim of Investigation**
Chronic joint pain is the cardinal symptom of all forms of arthritis, and is the underlying cause of disability in individuals afflicted by this disease. Although joint pathology is an underlying factor, some patients with severe joint pathology report little to no pain, while others with minor joint pathology experience debilitating and unremitting pain. This discordance between pain severity and peripheral pathology of the arthritic joint suggests the extent of joint damage is not necessarily a direct predictor of ensuing chronic pain. Thus, the association between the progression of osteoarthritis and the development of joint pain remains unresolved. This study focused on the central mechanisms involved in modulating chronic osteoarthritis pain signaling. Specifically, we examined the importance of microglia and ATP-gated P2X7 receptors (P2X7R) in chronic arthritis pain.

**Results**
The onset of mechanical allodynia and thermal hyperalgesia occurred as early as day 3 post-MIA injection, with allodynia persisting to at least day 28. On day 7 post-MIA, we detected an increase in expression of microglial markers, Iba-1 and CD11b, in the ipsilateral spinal dorsal horn and an increase in P2X7R expression on CD11b positive cells. Given that P2X7Rs have a peripheral and central mechanism of action, and are a locus through which microglia contribute to chronic pain, we asked whether spinal P2X7Rs are causally involved in the development and expression of MIA-induced arthritic pain behaviours. We implanted an intrathecal osmotic pump that delivered continuous A740003, a selective P2X7R antagonist, for 7 days and found that A740003 attenuated the development of mechanical allodynia and thermal hyperalgesia in MIA-injected rats. In addition, we showed that an acute intrathecal injection of A740003 in animals with established MIA-induced arthritis pain transiently reversed both the mechanical and thermal hypersensitivity.
Conclusion
Collectively, our results suggest that spinal P2X7Rs are causally involved in the development and tonic ongoing expression of arthritis pain. In particular, cellular adaptations mediated by microglial-P2X7R signaling within the spinal cord critically underlie joint pain associated with arthritis.
Title: Connexin Inhibition Attenuates Cancer-Induced Bone Pain

Poster Number PW0138

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Aim of Investigation
Pain is a common and highly debilitating complication for cancer patients significantly compromising their quality of life. The severe pain often associated with advanced cancer is challenging to treat, and current treatments leave one third of the patients with inadequate pain relief. Cancer-induced bone pain involves a complex interplay between multiple cellular components, and involves processing and modulation at both peripheral and central sites. Connexins, a key protein in cell-cell communication, have the potential to affect bone cancer pain at multiple levels, including nociceptive signaling, bone degradation and tumor progression. The aim of the investigation was to test the analgesic potential of connexin inhibition, modulated through a novel triple-action approach for the treatment of bone cancer pain.

Results
20mg/kg and 40mg/kg carbenoxolone significantly attenuated pain-related behavior. Compared to sham animals, the cancer vehicle group displayed significant decrease in limb use score and weight-bearing ration from day 14. In contrast the cancer groups treated with carbenoxolone did not display significant decrease in pain-behavior until day 18, demonstrating a delay in onset of pain-related behavior in the carbenoxolone-treated animals. In addition, both carbenoxolone-treated cancer groups demonstrated significant higher limb use scores compared to the vehicle-treated group on day 14 and 18, indicating attenuation of pain-behavior. This was supported by a significant increased weight-bearing ration in the 20mg/kg carbenoxolone-treated group compared to the vehicle treated group. The delayed onset and attenuated pain-related behavior observed in the carbenoxolone-treated cancer group were reflected in time to reach humane endpoint, as both treatment groups displayed significant longer time to reach humane endpoint compared to the vehicle treated group. Carbenoxolone did not affect the bodyweight in any of the groups, and had no effect in sham-operated animals. Analysis of carbenoxolones effect on tumor burden and bone degradation is in progress.
Conclusion
Overall, the data demonstrate an analgesic effect of connexin inhibition in this osteosarcoma model of cancer-induced bone pain.
Title: Comparative Evaluation Of Retrocrural Versus Transaortic Neurolytic Celiac Plexus Block For Pain Relief In Patients With Upper Abdominal Malignancy: A Retrospective Observational Study

Poster Number PW0139

Authors
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Aim of Investigation
Neurolytic celiac plexus block (NCPB) is known to provide good pain relief in patients suffering from upper abdominal malignancy. However, there is lack of evidence regarding the technique which is most effective for NCPB. In the present study we wished to comparatively evaluate Retrocrural versus Transaortic Neurolytic Celiac Plexus Block for pain relief in patients with upper abdominal malignancy.

Results
Patients in group R had significantly reduced VAS pain scores and morphine consumption as compared to patients in groups T at day1, week 1, 2 and 3 (P <0.05). Quality of life was comparable between the groups, and no major complications were noted.

Conclusion
Retrocrural NCPB provides superior pain relief along with reduction in morphine consumption as compared to Transaortic NCPB in patients with pain due to upper abdominal malignancy.
Title: Intrathecal Catheter Insertion And Analgesia Is A Safe And Effective Method Of Pain Control In Patients With Advanced And Intractable Cancer Pain

Poster Number PW0140

Authors
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Aim of Investigation
Background Cancer is a major cause of morbidity and mortality worldwide and also in Singapore. Cancer pain management is an increasingly important aspect of Chronic Pain and Palliative Care management. The WHO step ladder approach to management of cancer pain leads to successful treatment of majority of patients. However, a small percentage of patients suffer from intractable pain requiring the insertion of intrathecal catheter. Study Aim To evaluate the safety and efficacy of intrathecal catheter insertion and analgesia for adequate pain control in patients with advanced cancer who have failed other forms of analgesia.

Results
44 patients (male 24; mean age 54.5 +/- 14.4) were included from February 2005 to December 2015. Majority of patients had a primary intra-abdominal malignancy (50%), followed by breast (25%) and lung (9%). 86.4% of patients had metastatic disease. Commonest indication for intrathecal catheter insertion was uncontrolled pain (56.8%). 16/44 (36.4%) patients were started for adverse effect, with 27.3% of patients experiencing nausea. Remaining patients were started for both indications. Mixed pain was the most commonly reported mechanism (43.2%), followed by somatic pain (31.8%) and visceral pain (11.4%). Catheter entry was predominantly at the lumbar level (59.1%). Pain score was significantly reduced from 6.7 to 1.6 after intrathecal catheter insertion and analgesia (p < 0.001). 2/44 (12.5%) required readjustment of intrathecal catheter, 3/44 (6.8%) developed fever post-insertion, and 1 patient (2.3%) had local pruritus at the insertion site. Fewer patients experienced drowsiness (5/44; 11.4%, p = 0.059). 5/44 (11.4%) patients had lower limb weakness after intrathecal analgesia. There was no difference in incidence of nausea.

Conclusion
The insertion of intrathecal catheter for analgesia is effective in difficult-to-control cancer pain when
systemic opioids have failed. Systemic side effect of drowsiness was decreased with intrathecal analgesia. However, there is also a risk of lower limb weakness with this method of pain control.
Aim of Investigation
Damietta Cancer Center (DCC), is one of the comprehensive cancer institutes located in Damietta City. The institute was found in 1999 to provide medical services to oncology patients in the Delta region of Egypt. The Quality Council in DCI started planning for a Pain Management Program based on: 1. Organization’s Strategic Goals: as one of the Institute’s strategic goals is to help cancer patients suffering the misery of pain to relief their complaints. 2. Customer Needs: The pain clinic is the request of cancer patients resident in Delta region as well as oncologists who prefer to follow up their patients near their institute. 3. A Governmental Mandate for compulsory accreditation. It was intended to be placed into effect by the 1st JANUARY 2015 aiming to achieve the following GOALS: 1- Safe and effective pain management service for cancer and end of life patients 24 hours/7 days a week. 2- Customer complaint is markedly decreased with Zero% complaints. 3- Patient and Family education about the proper use and safety precautions of modalities used in their pain treatment to achieve 100% misuse. 4- Educational Programs to paramedics and junior medical staff to reach about 100% of Educational goals they must know. 5- Guidelines of policy and procedures used, that must be matched to 100% of evidence – based documented practices. 6- Cost – reduction by about 50% as a result of decreased average length of stay (LOS), and physician visits.

Results
After 15 months of implementation of this new program and through doing regular quality control processes using survey studies and using different sensors, the following results was achieved: 1. Patients and families satisfaction rises from 12% at the start up to 52%. 2. Patients and families education was improved from 22 to 78%. 3. Educational goals to stakeholders (other than patients and families) were raised from 35 up to 88% with 95% adherence to updated guidelines. 4. Cost reduction by 38% was achieved
Conclusion
A quality planning process is very important in organizing and establishing any new chronic pain program in an established organization. The ultimate goals are safety, efficacy and cost reduction. The planning must be tailored to each organization putting in mind its goals, manpower, financial resources and the type of patients. Putting proper indicators and sensors is vital for measurement of performance to detect defects and do improvements.
Date: 09/28/2016 09:30:00 AM

**Title:** Mr Imaging Analyses Between Spinal Cord Injury Symptoms And Locations Of The Spinal Metastasis

**Poster Number** PW0142

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**Aim of Investigation**
Spinal cord injury (SCI) due to cancer metastases greatly impairs the quality of life in advanced cancer patients. Subsequent to advancements in cancer treatments, which can successfully improve the cancer prognosis, numbers of patients with spinal metastases who suffer various serious symptoms caused by the SCI in years are increasing. The present study aimed to investigate the relationship between location of spinal metastases and clinical symptoms of the SCI in cancer patients.

**Results**
Spinal metastases were identified in total 66 vertebrae and 174 axial slices. The patients with more Squares in the posterior part of the vertebral body and the anterior part of the spinal canal were significantly affected in the patients with the muscle weakness. At-level-pain patients demonstrated spinal metastases more frequently in the vertebral arch or intervertebral foramen. Further, the patients with metastatic vertebral fracture were affected more in the center of the vertebral body.

**Conclusion**
The present findings demonstrated that the respective SCI symptoms are caused by specific locations. Lesions of the posterior part of the vertebral body would impair the anterior horn of the spinal cord in patients with motor dysfunction. Metastases near the intervertebral foramen would injure a nerve root, resulting in neuropathic at-level pain. Lesions of the center of the vertebral body would induce vulnerability to the vertical mechanical load, leading to the fracture. Metastases locations might predict
the functional prognosis of advanced cancer patients and be of some help to determine therapeutic strategy to treat spinal metastases.
Aim of Investigation
Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) have significant scientific support for their use as tissue protectors. Preliminary studies suggest that their angiotensin-II type 2 receptor (AT2R)-blocking properties have a beneficial profile in the treatment of neuropathic pain. The purpose of the current study was to quantify the extent of the somatosensory effects of ACEI and ARB in cancer patients with chemotherapy-induced peripheral neuropathy.

Results
Of the 209 patients available for analysis, 145 met inclusion criteria. Baseline characteristics of patients included were generally similar. We identified 29 patients who were receiving AT2R inhibitors prior to starting chemotherapy. Touch thresholds were significantly lower in the thenar aspect of hand in the study group (patients who received AT2R inhibitors) than in the control group [mean (± SD) 3.03 g (± 11.05), median 0.56 g and 6.75 g (± 18.28), 0.56 g, respectively (P = 0.0441)]. Similarly, the cold pain threshold was significantly higher at the thenar area for the study group [mean (± SD), median 13.23°C (± 8.02), 11.73°C] than for controls [9.89°C (± 6.62), 10.05°C (P = 0.0369)].

Conclusion
AT2R inhibitors offer partial and selective neuroprotective qualities of the myelinated fibers A-β and A-δ in cancer patients who receive neurotoxic chemotherapy.
Title: Lumbar Radicular Pain In A Patient With Sacral Metastases: A Case Report

Poster Number PW0144

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Aim of Investigation
Pain in cancer patients can also be due to non cancer etiologies and should always be kept in mind, especially if the pathology is in the same place.

Results
There was more than 70% relief after the procedure till 3 months follow up. Oswestry disability index (ODI) has also improved from 78% to 40% 2 week after the procedure and the patient was able to resume her normal activities.

Conclusion
Our patient was unique with respect to the fact that she has metastases to sacrum and L5 nerve root pain could have easily been misdiagnosed as metastatic bone pain. Careful history taking and systematic neurological examination along with radiological findings have helped us to arrive at this treatable condition.
Title: Factors Related To Subjective Pain In Cancer Patients During Daily Activities

Poster Number PW0145

Authors

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Aim of Investigation
Even if pain and ability to perform activities of daily living are improved by medical treatment and rehabilitation in cancer patients, some patients continue to present with an incapacitating pain. This fact shows that cancer patients have higher subjective pain. In such a case, their quality of life (QOL) is difficult to improve. However, it is unclear what factors influence the subjective pain in cancer patients. In this study, we investigated the influences of physical and psychological symptoms on subjective pain during daily activities and QOL in cancer patients.

Results
Physical function was assessed by handgrip strength, isometric knee extension force, physical activity, 10 MWT, and mFIM. There were no significant differences between the 4 groups. Additionally, pain intensity (NPRS) did not differ between the 4 groups. By contrast, fatigue (CFS), anxiety, and depression (HADS) in the group IV were significantly higher than those in the groups I and II. QOL in the group IV was the lowest among all groups. A decline in cognitive functioning scale of EORTC QLQ-C30 was especially noticed in the groups III and IV.

Conclusion
In this study, cancer patients were grouped according to their subjective pain during daily activities. There were no significant differences in physical function or pain intensity among the four groups. Thus, the subjective pain during daily activities is not due to physical function or pain intensity. It is possible that the subjective pain during daily activities relates to fatigue, anxiety, and depression; all of these factors together lead to a decline in the QOL. Additionally, patients who complain of subjective pain during daily activities also showed cognitive dysfunction when assessed by the functioning scale of EORTC QLQ-C30. Therefore, assessment and treatment of psychological symptoms and cognitive
function are required in order to improve QOL in cancer patients who present with subjective pain during daily activities.
Title: Influence Of Cancer Pain Beliefs On Taiwanese Cancer Patients’ Pain-Related Experiences

Poster Number PW0146

Authors
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Aim of Investigation
Background: Early evidence shows that patients’ cancer pain-related beliefs may be a contributing factor to cancer pain experience and remains insufficient understanding in Taiwanese cancer outpatients.

Purpose: To explore the contribution of these beliefs on pain experience in Taiwanese cancer outpatients.

Results
The majority (>55%) agreed that cancer pain was chronic but also unpredictable, with negative emotional representation. They mostly believed (64%) that treatment could palliate pain but less endorsed that they had personal control to influence pain (47% agreed). Most (64%) agreed that analgesics were necessary for managing pain but also held concern beliefs about analgesics (51% agreed). Participants who diagnosed with colorectal cancer reported higher scores of positive cancer pain beliefs (treatment control beliefs, personal control beliefs, and coherence beliefs) than lung cancer ones did (p<0.05). Participants with advanced disease had less personal control beliefs comparing with ones with stage II/III had (p<0.05). Significant Contributors to pain interference included more serious consequence beliefs and more negative emotional representation, patients with advanced stage disease, and worst pain intensity (β=0.28, 0.22, 0.16, and 0.22, respectively, p<0.05) in hierarchical linear regression. Together all of independent variables explained 55% of the variance in pain interference (R²=0.55, F=10.0, p<0.001).

Conclusion
The results of this study highlight the independent contribution of a comprehensive set of cancer pain-related beliefs to pain experience in cancer outpatients. Future development of interventions targeting
clinician and patient pain assessment and education should incorporate these beliefs on pain experience.
Title: Oral Decoction Containing Herbal Medicine Yuanhu Reduces Pain And Adverse Reactions Of Morphine Treatment In Patients With Bone Cancer Pain

Poster Number PW0147

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Aim of Investigation
Treating cancer pain continues to possess a major challenge and clinical approaches are limited. We investigated analgesic effect of combination of herbal medicine decoction (HMD) containing Yuanhu and morphine and the effects of Yuanhu on the adverse reaction of morphine in treating bone cancer pain.

Results
Oral administration of HMD (200 ml, bid, for 7 consecutive days) alone greatly reduced cancer pain. Repetitive treatment with a combination of HMD and morphine (15 mg and 30 mg, respectively) produced significant synergistic analgesic effects. Meanwhile, HMD greatly reduced the adverse reactions associated with cancer and/or morphine treatment. In addition, HMD treatment significantly reduced the proinflammatory cytokines interleukin-1β and tumor necrosis factor-α as well as increased the endogenous anti-inflammatory cytokine interleukin-10 in blood.

Conclusion
These findings demonstrate that HMD can effectively reduce bone cancer pain probably mediated by the cytokine mechanisms, facilitate analgesic effect of morphine, and prevent or reduce the associated adverse reactions, supporting a use of HMD, alone or with morphine, in treating cancer pain in clinic.
Title: Methadone-Induced Hypoglycemia In A Hemodialysis Patient With Cancer-Related Pain: A Case Report

Poster Number PW0148

Authors
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Aim of Investigation
Methadone is an important drug in palliative care for management of intractable pain. A recent cohort study has shown an increased risk of hypoglycemia for patients with cancer pain treated by more than 40mg per day of oral methadone (Flory HF, Wiesenthal AC, Taler HT et al, 2016). However, it is still little-known and underreported. We describe a french palliative care unit experience.

Results
An 80-year-old man was hospitalized in a palliative care unit for intractable pain. His main comorbidities were renal insufficiency with hemodialysis three times a week, mellitus diabetes and pulmonary adenocarcinoma in a palliative state. He was treated by acetaminophen, oxycodone, pregabalin and amitriptyline with intense pain still reported. Oral methadone was introduced. A six days titration was done and led to 10mg per day with 1mg of breakthrough dose. Pregabalin and amitriptyline were stopped, as methadone had an efficacy on neuropathic component. From the beginning of titration period, several hypoglycemas (blood glucose level between 0.5 and 0.6g/l) were reported without neurological symptoms. They generally occurred during the morning fasting period, and it also happened one time before and after evening meal. Timing of hypoglycemas was not related to days of hemodialysis. No hypoglycemia was reported at home before hospitalization. The first hypothesis was poor oral nutritional intakes. Insulin was stopped, and oral intakes were adapted. Patient went back home, and methadone was progressively raised to 20mg per day because of increasing pain. He was hospitalized one month later for general health degradation and intractable pain again. Methadone was increased to 40mg per day with 5mg of breakthrough dose. Breakthrough dose was taken four to five times in a day. Hypoglycemas were still persistent, hepatic failure has been excluded. As oral intake was impossible due to nausea and dyspnea, methadone was switched to intravenous oxycodone (intravenous methadone is not available in France). A second switch was made to sufentanil for better...
safety and efficacy in this hemodialysis patient. Four days after the methadone interruption, glycemies were normal while caloric intakes still very poor. As general health was worst, hemodialysis were stopped. This occurred after glycemies normalization. Therefore, we concluded to methadone-induced hypoglycemias.

**Conclusion**

Methadone-induced hypoglycemia risk seems to be more important for patients with cancer. Nevertheless, it is a recent and underknown data. This case was particular because of associated hemodialysis. Furthermore studies are probably necessary, and maybe recommendations about blood glucose monitoring could be discussed.
Title: Lidocaine Topical Patch 5% For The Treatment Of Chronic Refractory Neuropathic Pain In Cancer Patients: A Prospective Open-Label Study

Poster Number PW0149

Authors
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Aim of Investigation
To determine the effectiveness of Lidocaine topical patch 5% in the treatment of refractory peripheral neuropathic pain among cancer patients

Results
Mean VAS scores were, at baseline (6.0±1.7), at day7 (3.3± 1.6), and at day30 (2.4±1.6). There was a significant reduction in VAS scores (p<0.01) after 7 and 30 days. Treatment with lidocaine topical patch helped relieve various characteristics of pain, including burning, electrical shock-like pain and allodynia. No adverse events were reported with lidocaine patch

Conclusion
Lidocaine topical patch 5% have potential benefits for treatment of refractory neuropathic pain in cancer patients; controlled clinical trials is suggested to further evaluate the efficacy and also assessment in a larger study is recommended.
Date: 09/28/2016 09:30:00 AM

**Title:** The Effect Of Repeated Exposure To Visual Body Illusions In Complex Regional Pain Syndrome

**Poster Number** PW0150

**Authors**
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**Aim of Investigation**
People with Complex Regional Pain Syndrome (CRPS) dislike the appearance of their painful limb, a characteristic feature of body perception disturbance. Growing evidence suggests that an illusionary change to the painful body part appears to reduce pain. We wished to establish whether repeated exposure to a body illusion that subjectively improves the appearance of the affected body part would enhance the therapeutic effect.

**Results**
Twenty participants with a mean age of 52 (SD 11) and disease duration mean of 44(36) months experienced a significant reduction in hand pain (p = 0.048) following repeated illusionary exposure when compared to controls (n=18, mean age 54(16), mean disease duration 60(62)). The overall between group reduction in pain following repeated exposure was -1(2) compared to -0.5 (1) after single exposure to the illusion.

**Conclusion**
Repeated rather than a single exposure to illusions that visually altered hand appearance provided greater pain reduction. These findings support the need for further research to determine the optimum dose for therapeutic use.
Title: Understanding Experimentally-Induced Body Image Distortions

Poster Number PW0151

Authors
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Aim of Investigation
A distorted body representation is common in chronic pain patients. Experimentally inducing these distortions in healthy volunteers helps us understand how they occur and how we can correct them. One method of inducing these distortions is via vibration of tendons. Recent research that the vibration of two antagonist tendons leads to the 'telescoping effect' reported in some pain disorders, raised an exciting new possibility, but important questions remained unanswered. This study aimed to answer those questions and therefore verify this experimentally induced telescoping effect.

Results
Experiment 1: the Triceps vibration induced the largest mislocalisation of the target finger towards the body along the x-axis (D $p=.011$, B $p<.001$, N $p<.001$). A significant shift in the same direction was also induced by the Dual vibration (B $p<.001$, N $p=.002$). A significant upward bias was found for the Triceps vibration condition (B $p<.001$, D $p=.002$, N $p<.001$) and a significant downward bias was found for the Biceps vibration condition (D $p=.001$, N $p=.012$) along the y-axis. Experiment 2: hand perceived length was not significantly different between conditions ($p=0.073$). The forearm perceived length during dual vibration was not significantly different from Triceps or Biceps vibration ($p>.005$).

Conclusion
The present research does not support the idea that tendon vibration can induce a telescoping limb effect, commonly reported by people with pathological pain problems, in healthy volunteers. Instead, the vibration of antagonist tendons was shown to involve a displacement of the entire forearm, possibly due to an illusory involvement at the shoulder level induced by Triceps (but not Biceps) vibration and
creating an imbalance between the two tendon-induced illusory movements. Our study corroborated the utility of tendon vibration to induce distorted body representations but alternative designs will be needed in order to elucidate the relationships between pain and distorted body image.
Title: Experimental Modelling Of Neglect-Like Aspects Of Crps In Humans

Authors
L. Moseley\textsuperscript{,2}, V. Bellan, T. Stanton\textsuperscript{,2}, H. Gilpin\textsuperscript{1}, A. Gallace\textsuperscript{,6}

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Aim of Investigation
Neglect-like symptoms have been identified in Complex Regional Pain Syndrome. The relevance of spatial cues coming from sensory modalities other than touch in localising one’s own limb can be crucial in understanding these problems. We developed an experimental approach to investigate self-localisation in states of abnormal multisensory input and, here, we sought to clarify the importance of spatial processing and explicit knowledge that sensory input is erroneous. If spatial weighting contributes to perceived localisation, we would see an effect of non-informative spatial cues. We therefore hypothesised that auditory cues coming from one side of space would not impact self-localisation, but explicit knowledge of sensory incongruence would. Specifically, we expected a more rapid shift in relative weighting from visual to proprioceptive input after disconfirmation of the perceived location of the hand.

Results
Location of auditory cue did not modulate the accuracy of the localisation judgements: repeated measure ANOVA revealed no significant effect of Tone (p=0.134). Reaching across to touch the disappeared hand before starting the localisation task increased the accuracy of the localisations. A paired sample t-test showed significantly more accurate localisation when participants were aware of the sensory incongruence than when they were not (p=0.012).

Conclusion
In healthy population, self-localisation ability is not affected by the manipulation of weight given to different portions of the space, but the shift in relative weighting from visual to proprioceptive input is
more rapid once the perceived location of the participant's hand is disconfirmed by tactile input of the sensory incongruence. These results shed light on the primary role of vision and proprioception over differential weighting of space in self-localisation, and suggests that differential spatial weighting may not contribute to self-localisation problems in CRPS. Future research will focus on whether and how this model of self-localisation can be disrupted.
Title: Clinical Symptoms In Complex Regional Pain Syndrome

Poster Number PW0153

Authors
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Aim of Investigation
The aim of this study was to analyze a large cohort of patients with Complex regional pain syndrome (CRPS) regarding epidemiological data and clinical phenotype using different established and validated questionnaires.

Results
Data of 1822 patients (mean age 50.3 ± 13.7 years; 1302 (71.5 %) female; 520 (28.5 %) male) with diagnosis of CRPS was analyzed. 460 (31.6 %) patients had an onset of disease within one year, 68.9 % had a disease duration longer lasting than one year. Pain intensity was rated on a visual analogue scale (VAS, 0-100) judging current (49.7 ± 24.6), maximum (79.3 ± 18.5) and average (57.4 ± 19.4) pain. 584 (48.2 %) of the patients demonstrated moderate, 380 (31.4 %) severe stage of chronification by MPSS. According to PD-Q score 871 (54.0 %) patients had a likely, 366 (22.7 %) an unlikely neuropathic component. The most severe symptom reported upon PD-Q was pressure-induced pain. One out of three patients described allodynia, which might be interpreted as a hint for central sensitisation. 957 (70.1 %) patients showed functional limitations in activities of daily living, of these 52.6 % had a clinically relevant impairment. In comparison to male, female showed higher pain intensities (current: 50.7 vs. 47.2; p = 0.015; average: 58.3 vs. 55.1; p < 0.01; maximum: 80.4 vs. 76.3; p < 0.001), higher functional impairment (FFbH, 64.5 vs. 69.2; p < 0.0001) and had higher graded depressions (10.2 vs. 9.5; p < 0.05). There were no differences in PD-Q final score, stage of chronification and sleep behaviour between genders.

Conclusion
Results demonstrate that (A) more than half of the patients have evidence for a neuropathic pain component, (B) in gender comparison female patients had a higher disease burden regarding pain,
functional impairment and depression, but (C) without a difference concerning the prevalence of neuropathic pain.
Title: Acute Inflammation Does Not Contribute To The Development Of Complex Regional Pain Syndrome

Poster Number PW0154

Authors
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Aim of Investigation
To test whether greater acute pro-inflammatory immune activity after a fracture increases the risk for development of CRPS.

Results
At the follow-up, 13 participants (2.3%) met the Budapest criteria for CRPS, and a further 60 participants (10.6%) met the IASP criteria for CRPS. In both primary and secondary analyses, there were no statistically significant associations between the expression of any cytokine and risk of development of CRPS. Compared to controls, individuals with CRPS (Budapest) were more likely at baseline to have reported severe pain (p<0.001), depression (p<0.001), anxiety (p<0.006) and stress (p<0.007), and were more likely to have sustained an intra-articular fracture (p<0.004).

Conclusion
We found no evidence to support the theory that cytokine expression significantly contributes to the development of CRPS, whether individuals were diagnosed using the Budapest or the IASP criteria. Therefore we provisionally reject the hypothesis that acute inflammation plays a key role in the development of CRPS after an acute upper extremity fracture. Acknowledgments/Disclosures: Dr. Luke Parkitny is supported by a project grant from the Fetzer Institute and was previously supported by an International Association for the Study of Pain Fellowship funded by the Scan|Design Foundation and an NHMRC scholarship (ID 1017607). Dr. James H McAuley reports no disclosures. Dr. Robert D Herbert reports no disclosures. Dr. Flavia Di Pietro is supported by an NHMRC C.J. Martin Early Career Fellowship (ID 1091415) and previously by an Australian Postgraduate Award Scholarship. Dr. Patrick Kelly reports
no disclosures. Dr. G. Lorimer Moseley is supported by an NHMRC Fellowship (ID 1061279). This project supported by a project grant from the NHMRC (ID 630431).
Title: Leaving The Wheelchair Behind

Poster Number PW0155

Authors
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Aim of Investigation
Aims The aims of the present study were to increase function in individuals with CRPS by targeting immobilisation and cortical reorganisation, using cognitive behavioural (e.g. exposure in vivo), sensory (e.g. sensory re-training), and motor (e.g. mirror visual feedback) strategies.

Results
Characteristics
Before treatment
After treatment
A Female, 34 years with CRPS II after a left foot trauma, 2009. Before, never putting any weight on the affected limb, using wheelchair outside and walking on crutches inside. After, walking without any mobility aids.
B Female, 21 years with CRPS II after a right foot trauma, 2008. Before, walking on crutches. After, walking without any mobility aids indoors.
C Female, 56 years with CRPS II after a left knee trauma, 1995. Before, never touching the ground with the affected limb, using wheelchair all the time. After, walking without any mobility aids for shorter walks outdoors, using crutches for longer walks.
D Female, 44 years with CRPS II after a right foot operation, 2011. Before, limping, never touching the ground with the forefoot. After, walking without limping, putting weight on the forefoot.

Conclusion
Conclusions Two out of four patients with longstanding CRPS type II showed substantial improvements in function after treatment and were able to truly leave the wheelchair behind.
Aim of Investigation

Novel responder definitions for fibromyalgia (FM) clinical trials have been proposed by the Outcome Measures in Rheumatology (OMERACT) FM subcommittee. These definitions add key symptom and functional domains relevant to FM patients, in addition to traditional pain assessments. Development of these responder approaches were validated using outcome data from 12 previous registration trials of 4 other candidate treatments for fibromyalgia (Arnold L et al, Arth Rheum 64:885, 2012.) TNX-102 SL (TNX)* is a proprietary sublingual formulation of cyclobenzaprine designed for rapid absorption and bedtime use. In a 12-week, randomized, double-blind, placebo-controlled trial conducted at 17 US sites, TNX-102 SL showed improvements in pain and other symptoms. 205 participants were randomized in this study (TNX=103; placebo=102). This current presentation is a retrospective analysis of the trial results using the two preferred response definitions proposed by the OMERACT committee.

Results

TNX improved multiple domains of FM. Results below compares a pain responder analysis (≥30% improvement in pain based on daily diary scores) to the alternative composite responder definitions proposed by OMERACT.

<table>
<thead>
<tr>
<th>Definition</th>
<th>Physical Function</th>
<th>#Additional Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result/p Value</td>
<td>30% Pain Responder</td>
<td>34.0% vs. 20.6%; p=0.033 FM30 Short Ver 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SF-36 physical function</td>
</tr>
<tr>
<td>Function 1</td>
<td></td>
<td>23.3% vs. 11.8%; p=0.038 FM30 Short Ver 2</td>
</tr>
<tr>
<td>FM30 Short Ver 2</td>
<td>SF-36 PCS score</td>
<td>25.2% vs. 11.8%; p=0.015 FM30 Long Ver 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SF-36 physical function</td>
</tr>
<tr>
<td>Function 2</td>
<td></td>
<td>21.4% vs. 9.8%; p=0.031 FM30 Long Ver 2</td>
</tr>
<tr>
<td>SF-36 PCS score</td>
<td></td>
<td>23.3% vs. 9.8%; p=0.011</td>
</tr>
</tbody>
</table>

Physical function improvement defined as ≥10% improvement
in measure shown. Additional Measures: 1: ≥ 30% improvement in either FIQ sleep or FIQ energy; 2: ≥ 30% improvement in any 2 out of FIQ sleep, FIQ energy, FIQ depression or FIQ anxiety. Additional improvements noted over placebo included: FIQ-R total score (-17.2 vs. -9.1, p = 0.015), PGIC response rate (30.1% vs. 16.7%, p = 0.025), PROMIS sleep (-9.5 vs -6.1, p = 0.004), sleep based on daily diary (change from baseline to week-12, 1.9 vs. -1.0; p<0.001) and FIQ-R sleep item (-2.9 vs. -1.2; p<0.0001). Systemic adverse events reported were similar to placebo. The most common local adverse event was transient tongue or mouth numbness occurring in 44% of TNX patients.

**Conclusion**

Bedtime TNX improved multiple domains of FM. Analysis by a composite responder criteria developed by OMERACT suggests that the improvements in FM symptoms seen with TNX are not limited to an analgesic response, since these composite criteria require improvement in other somatic and functional symptoms. *TNX-102 SL is an Investigational New Drug and has not been approved for any indication. Sponsored by Tonix Pharmaceuticals, Inc.*
Aim of Investigation

Fibromyalgia is a well-known disease of clinical chronic pain. It causes significant functional impairments for patients and a heavy socio-economic burden for society. Its pathophysiology is complex. Previous studies using QST (quantitative sensory testing) in fibromyalgia patients have already found sensory perturbations suggestive of small nerve fiber dysfunction. In our study, we aimed to investigate a putative correlation between QST, pain intensity and functional impact in fibromyalgia patients.

Results

1. An important component of neuropathic pain (NPSI) was observed in fibromyalgia patients. The intensity of neuropathic pain (NPSI) and the importance of functional disability (PDI, FIQ) appeared to be correlated to the degree of cold allodynia in the upper limb in patients with fibromyalgia.

2. A previous observation of more evident thermal hypoesthesia in the lower limb in patients with fibromyalgia was confirmed, providing further evidence in support of the concept of impaired small fiber function.

Conclusion

Our results highlight the complexity and heterogeneity of pain in fibromyalgia patients. The data obtained may contribute to the understanding of the pathophysiology underlying this disease. We want to highlight the importance of quantitative sensory testing in the clinical evaluation of fibromyalgia.
Title: Eeg-Neurofeedback Targeting Amygdala Activity Reduces Pain And Improves Sleep In Patients With Fibromyalgia

Poster Number PW0158

Authors
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Aim of Investigation
Fibromyalgia syndrome (FMS), a condition characterized by widespread pain and chronic fatigue, has been suggested to represent a prototype of central nervous system hypersensitivity (central sensitivity-CS). While the mechanisms underlying CS remain incompletely understood, a role for limbic dysregulation has been argued. The aim of the current study was to examine the feasibility of fMRI-inspired Electrical Finger Print (EFP) of the amygdala as a probe for NeuroFeedback (amyg-EFP NF) training for FM patients. We expected improved pain symptoms and sleep quality among trainees successful in downregulating amygdala activity.

Results
Following NF Training, patients displayed an improved clinical status as indicated by reduction in FM symptoms (SSS+WPI, T=2.43 P=0.037. FIQ, T=2.55 P=0.031). Improvements in self-reported pain (SF 36, R=0.805, p=0.004) and physiological function (SF 36, R=0.806 ,p=0.004) were correlated with measures of amygdala down-regulation. Affective and anxiety scores (STAI-T, beck depression inventory) remained unchanged. Moreover, patients demonstrated reduced sleep latency following treatment (T=2.71, P=0.02), albeit with unchanged subjective sleep scores (Pittsburgh sleep quality).

Conclusion
Amy-EFP NF improves disease-specific symptoms, widespread pain and sleep latency in FM patients. Interestingly, this was not accompanied by a change in affective measures. Apart from demonstrating an important role for the Amygdala in CS, this study presents a novel, non-invasive, non-pharmacological, brain-directed treatment for FM.
Title: The Effect Of Pain Chronification On Placebo Analgesia: Lower Placebo Responses After Long-Term Exposure To Fibromyalgia Pain

Poster Number PW0159

Authors

Aim of Investigation
Knowledge about placebo effects in patients with chronic pain is scarce. Fibromyalgia syndrome (FM) is associated with dysfunctions of the central pain inhibitory network, and there are negative effects of FM duration on brain volume in key areas for pain inhibition. As placebo analgesia is activated through central endogenous pain inhibitory mechanisms, we hypothesized that long-term exposure to FM pain would negatively affect placebo analgesia.

Results
Patients who reported a positive treatment response on PGIC were significantly improved in almost all outcomes from before treatment to follow-up (FM impact p=.001, clinical pain intensity p=.001, pain drawing p=.003), except for P50, p=.865. Conversely, placebo non-responders did not improve in any outcomes (FM impact p=.160, clinical pain intensity p=.495, pain drawing p=.780, P50 p=.485). In the non-responder group there was a negative correlation between FM duration and baseline P50 (r=-0.496, p=.019) as well as baseline clinical pain variability (r=-0.345, p=.037), but not among the responders (r=-0.070, p=.805 vs. r=-0.348, p=.112). However, the duration of FM correlated with the P50 change after treatment among placebo responders (r=0.689, p=.004), indicating that a long FM duration was associated with low P50 improvement, but not among non-responders (r=-0.348, p=.112).

Conclusion
This study suggests that FM duration influences endogenous pain regulation, as pain levels and placebo
analgesia were negatively affected. Our results point to the importance of early FM interventions, as endogenous pain regulation may still be harnessed and chronification avoided at that early time. Also, placebo-controlled FM trials should take pain duration into consideration when interpreting results.
Title: Does The Ability To Filter Information Differ Between People With Fibromyalgia And Healthy Controls?

Poster Number PW0160

Authors
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University of South Australia, Adelaide, Australia, Clarkson University, Potsdam, NY, Neuroscience Research Australia, Sydney, Australia

Aim of Investigation
Fibromyalgia (FM) is characterised by chronic widespread pain and hypersensitivity to noxious (hyperalgesia) and non-noxious (allodynia) stimuli including heat, pressure, and touch. In addition, FM is associated with a range of debilitating symptoms such as fatigue, cognitive impairment (the 'fibro fog'), altered bowel habits and altered mood. Converging evidence from neurophysiological studies of people with FM suggests abnormal processing of somatosensory stimuli may contribute to the underlying pathophysiology. Brainstem-level filtering of somatosensory information flow to the brain can be probed using a robust paradigm – prepulse inhibition (PPI) and prepulse facilitation (PPF) of the auditory blink response to a startling sound. Our aim was determine whether people with FM show abnormal auditory sensory filtering compared with healthy controls. We examined the auditory blink response to threshold level startle pulse, PPI and PPF in people with FM and healthy controls. We hypothesised that people with FM have a lower threshold, less inhibition and more facilitation of the auditory blink response than healthy controls.

Results
Data for 16 FM (mean (SD) age = 46.8 (11.3) years) and 16 matched controls (mean (SD) age = 46.3 (11.9) years) were analysed. Women with FM had a lower startle threshold than controls (more responses to 80 dB than controls) and a greater PPF response than controls (amplitude of response to PPF mean (SD) FM 55.22 (34.59) microVolts, HC 30.61 (31.27) microVolts; p = 0.04). Analysis of the data in people with FM is complicated by an unexpected blink response in 12 participants. This response occurred 50ms after the prepulse but prior to the startle.

Conclusion
Women with FM show abnormal auditory sensory filtering, as assessed by the auditory blink response to
threshold level startle pulse, prepulse inhibition (PPI) and prepulse facilitation (PPF) of the auditory blink response. Blink response threshold is lower in those with FM, the PPF response is larger and the majority show an unexpected and currently unexplained blink response 50ms after the prepulse.
Aim of Investigation
Chronic widespread pain (CWP) is a complex pain condition which is difficult to treat. The prevalence of CWP is about 10% in the general population and is more common among women compared to men. The molecular mechanisms behind CWP are not fully elucidated and so far few studies have been investigating biomarkers for CWP in plasma. In this study we aim to analyze the protein pattern, and potential new biomarkers in plasma samples from CWP patients compared to healthy pain-free controls (CON).

Results
Multivariate statistical analysis (OPLS-DA) of quantified proteins showed twenty-two proteins, including several different isoforms, with a VIP-value>1.0 that were considered to be important for group separation and significantly altered among women with CWP compared to controls (R2=0.84; Q2=0.60; CV-ANOVA p-value=2.31e-6). Many of the identified proteins are previously known to be involved in iron hemostasis, metabolic-, immunity- and inflammatory processes e.g. Vitamin-D binding protein, haptoglobin, transthyretin and Alpha-2-HS-glycoprotein. Vitamin D-binding protein was further verified and significant altered concentrations in women with CWP compared to controls was found (median ± min-max; CWP: 121.8 ± 73.7-232.4 ng/µl; CON: 103.5 ± 67.0 -160.7 ng/µl, p-value=0.035).

Conclusion
In this present study we found significant alterations in both inflammatory-, immunity- and metabolic proteins in plasma samples from women with CWP compared to healthy pain-free controls. The findings
from this proteomic approach in combination with multivariate statistics illustrate the potential use of proteomics for identifying systemic protein changes associated with CWP.
Aim of Investigation
The aim of the study is to objectively determine the pain modulation effects of low frequency repeated transcranial magnetic stimulation (rTMS), in FM patients.

Results
RIII latency increased in response to cold noxious stimulus during pain modulation paradigm in FM-rTMS group during rTMS week 4 and post-rTMS week 2 (131.1±15.03 ms and 134.3±12.72 ms, respectively) as compared to basal value of 102.2±13.65ms (p<0.001) indicating long term beneficial effect of rTMS. However, in the FM–Sham group the RIII latencies were 99.0±11.58 ms and 96.6±12.69 ms at rTMS week 4 and post-rTMS week 2, respectively. This was not statistically significantly different from each other (p<0.073). The scores were significantly lower at each time point in FM-Sham group in comparison to FM-rTMS group (p<0.073)

Conclusion
The objective assessment of chronic pain showed a significant decrease in pain and associated symptoms following rTMS treatment which was sustained till week 4 of follow up as supported by subjective assessments.
Title: Increased Reaction To Monetary Rewards In Fibromyalgia Patients With Co-Morbid Depression: A [11C]-Raclopride Pet Study

Poster Number PW0163

Authors

University Hospital Zurich, Zurich, Switzerland, University Hospital Zürich, Zürich, Switzerland, University Zurich, Zürich, Switzerland, University Bern, Psychiatric University Hospital, Bern, Switzerland, University Hospital Zurich, Department of Psychiatry and Psychotherapy, Zurich, Switzerland, University Hospital Zurich, Zürich, Switzerland, University Fribourg, Fribourg, Switzerland

Aim of Investigation
Aim of investigation: Dopamine (DA) has been shown to be involved in the processing of pain and reward. Fibromyalgia syndrome (FMS), characterized by chronic widespread pain, is frequently associated with depression. Reduced dopamine function and reduced responses to reward have also been demonstrated in depression. Primary evidence suggests that chronic pain might impair reward processing. Therefore, a reduced dopamine reaction to reward could be involved in the depressive and pain symptoms observed in fibromyalgia syndrome. We tested whether striatal dopamine responses to monetary rewards would be impaired in FMS compared with healthy controls and whether this reduction would be stronger in FMS patients with co-morbid depressive disorder (MDD).

Results
Results: Significant reductions in D2/3 receptor binding potential were found in the reward vs. control condition in the right nucleus accumbens and caudate nucleus. This reduction in binding potential in the right nucleus accumbens was more prominent in FMS patients with co-morbid depression (41.1%) compared with healthy controls (23.3%; p < 0.01). Among FMS patients, the reduction in the right caudate nucleus was significantly higher in those with co-morbid MDD (24.6%) relative to those without MDD (13.4%), (p < 0.02).

Conclusion
Conclusions: This study showed that fibromyalgia syndrome patients had an increased reaction to rewards that was more accentuated in patients with depression, suggesting that these patients exhibit...
altered dopamine responses to monetary rewards relative to healthy controls. These results are important for the understanding of depression associated with chronic pain conditions and for development of specific treatment strategies according to depressive symptoms.
Title: Higher-Order Multimodal Brain Networks And Associated Primary Sensory Disturbances In Migraine

Poster Number PW0164

Authors

Bostom Children's Hospital, Harvard Medical School, Boston, MA, Department of Psychiatry, Harvard Medical School, Boston, MA, Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Boston, MA, Boston Children's Hospital, Harvard Medical School, Boston, United States, Department of Oral and Maxillofacial Surgery, Massachusetts General Hospital, Boston, MA, Harvard Medical School, Boston, MA, Boston Children's Hospital, Waltham, MA, Boston Children's Hospital, Boston, MA

Aim of Investigation
Cutaneous allodynia, photophobia, phonophobia, and osmophobia are clinical symptoms that accompany most migraine attacks. These sensory events may vary in intensity, but are usually related, as the heightened sensitivity in one sensory modality is often associated with the heightened sensitivity in the other sensory modalities. The mechanisms proposed to underlie this phenomenon include the activation and sensitization of neurons along the trigemino-cortical pathway. However, little is currently known about the involvement of higher-order multisensory regions and integrative mechanisms in migraine. The aim of this investigation was to explore the effects of convergence and interactions of the primary sensory systems at the brain connectivity level. We also compared the self-reported (retrospective) migraine symptoms, including the prevalence of sensory symptoms across the different phases of the migraine cycle. We hypothesized that migraineurs would show abnormalities with respect to the networks and regions that are involved in making the complex connections between the primary sensory and higher-order multisensory distributed systems of the human brain.

Results
Migraine symptom profiles: As expected, migraine patients reported a high incidence of sensory abnormalities. Photophobia was the most commonly reported symptom, but the occurrence of phonophobia and osmophobia was not uncommon. Further evidence of central sensitization in the trigeminal-cortical pathway was revealed through the presence of expanding cutaneous allodynia (CA)
Multimodal brain networks: The use of resting-state intrinsic functional connectivity enabled us to map the network interactions in the migraine brain relating to the principal primary sensory systems. Following comparisons between the migraineurs and controls, we revealed that migraineurs have reduced anti-correlations to distinct cortical regions of the PCC/PCu, mPFC/DLPFC, and LPC, best known as the cortical hubs of default-mode network (DMN). In the opposite direction, migraineurs showed decreased positive correlations to areas of the MCC and operculo-insular cortex, which have been described as key hubs of the salience network.

**Conclusion**

Migraine is a multifactorial disorder that is associated with abnormalities in sensory processing, including nociceptive and non-nociceptive processing. Accumulating evidence suggests that the neural basis of multisensory integration begins in early sensory processing. Here we describe a novel mechanistic search for a common pathway in migraine symptomatology. Our results support the notion that migraineurs are characterized by abnormal interictal functional connectivity between networks involved in linking external and internal information. This effect may involve both multisensory and integrative mechanisms. These findings offer a potential new framework for understanding clinical features and associated symptoms of migraine.
Aim of Investigation
Posttraumatic headache is a common physical manifestation of traumatic brain injury (TBI) [1,2] and patients with preexisting headache syndromes often experience worsening of their prior symptoms [3,4,5]. PTH as currently defined by the International Classification of Headache Disorders, second edition (ICHD-2)[6], is a secondary headache disorder that must start within seven days of injury or after regaining consciousness following TBI. PTH can occur after mild, moderate, or severe TBI, usually resolving within the first 3 months, although a minority develop chronic headaches. An acute PTH becomes chronic if headaches persist beyond three months after injury. Current therapy includes Topiramate [7,8]. Stellate ganglion blockade [9,10] and occipital nerve blocks [11] have been considered a useful technique in patients with severe PTH when conservative measures failed. The aim of this study was to investigate changes in measures of self-report pain and disability measures following pulsed radiofrequency of superior cervical sympathetic ganglion under a novel ultrasound guided approach in individuals with chronic posttraumatic headache. The null hypothesis was that reducing sympathetic innervation to the face and head would not result in changes in self-report pain or changes in disability measures.

Results
From January and February 2016, 6 patients were included in the study: 40% males aged 36-64 (Median 52 +8.7 SD). Median HIT-6 at baseline: 68, and 4 weeks after procedure: 62. Median NRS at baseline: 7/10, and 4 weeks after procedure: 5/10. Median pain interference with daily activities at baseline: 8/10, and 4 weeks after procedure: 5/10. 16 % of patients rated PGIC 6 = much improved, and 66% of patients rated 5 = slightly improved, and 16% rated 4 = no change.
Conclusion
The superior cervical sympathetic ganglion (SCG) is the most cranial part of the sympathetic chain and provides sympathetic innervation to the face and head [17,18]. It is the largest of the cervical ganglia, fusiform in shape, and located in the prevertebral fascia anterior to the longus capitis muscle and dorsal to the internal carotid artery. Sympathetic blocks in the SCG are been described for a variety of diagnostic and therapeutic purposes. Treggiari et al [19] performed SCG blocks to improve cerebral perfusion in patients with cerebral vasospasm after aneurysmal subarachnoid hemorrhage. Koning et al performed radiofrequency lesion of the SCG to patients with non-traumatic neck pain not responding to conventional therapy [20]. Spacek and Elsner have injected buprenorphine next to the SCG to provide pain relief in patients suffering from different kinds of neuropathic facial pain conditions [21,22]. A blind transoral approach has been described contraindicated because the potential risk of carotid artery puncture [23,24]. Siegenthaler et al [25] described a simulated ultrasound guided approach to the SCG. Because the very close proximity of the SCG and the common carotid artery bifurcation, Wisco et al [26] suggest makes this artery a good landmark for the ganglion's localization for ultrasound guided blocks. We designed the novel posterolateral approach to SCG based on landmarks suggested by Wisco et al [26] using real-time ultrasound guidance. The precise mechanisms responsible for analgesic effects of PRF of superior cervical sympathetic ganglion are not yet clearly understood. According to Wang et al [27] the analgesic mechanism underlying the effects of stellate ganglion block may involve a reduction in the neuroinflammatory process. Vallejo et al [28] observed that the mechanical allodynia, induced by spared nerve injury (SNI) pain model, was reversed to control values within 24 hours post-PRF therapy. Hagiwara et al [29] suggest that the analgesic action of PRF could involve the enhancement of noradrenergic and serotonergic descending pain inhibitory pathways. We speculate that PTH and CRPS share similar neural mechanisms of neuroinflammation, which is maintained by a dysfunctional prefrontal cortex-amygdala relationship, characterized by hypoactive prefrontal cortex (PFC) and a hyperactive amygdala, as we proposed recently [30]. Recently Alkire et al [31] found out that stellate ganglion block was associated to reduction of right amygdala hyperactivity with rapid and sustained relief of symptoms in post-traumatic stress disorder (PTSD) patients. According to our preliminary results, PRF of SCG could represent a novel approach for the treatment of intractable PTH and, to our knowledge, such treatment has not previously been performed. Despite limitations in this study because of low sample size, decreased 2.0 and 3.0 points in NSR and BPI ratings should be considered a clinically important improvement [32].
Title: Place Of Osteopathy And Cranial Osteopathy In The Multidisciplinary Management Of Chronic Headache: Experience With Twelve Patients At The Nantes Multidisciplinary Pain Center

Poster Number PW0166

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Aim of Investigation
The majority of headache sufferers (62 to 73%) are managed by complementary therapies. The objective of this study was to assess the value of one such complementary therapy: cranial osteopathy.

Results
Four patients were lost to follow-up during the study. Evaluations after the first consultation showed a benefit in 7 out of 11 patients. Three months after the last consultation, 6 out of 8 patients reported a benefit, with a benefit rated as major in 3 cases and complete in 2 cases. Patient satisfaction with management was also globally excellent.

Conclusion
In the light of these results, cranial osteopathy appears to be a beneficial complementary therapy in the multidisciplinary management of chronic headache and could be usefully integrated into a multidisciplinary pain centre. This study allowed us to establish recommendations for future studies.
Title: Migraine And Complex Regional Pain Syndrome: A Case-Referent Clinical Study

Poster Number PW0167

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Aim of Investigation
Untreated migraine is considered to be a risk factor for the development of Complex Regional Pain Syndrome (CRPS). The aim of this study was to evaluate clinical phenotype differences among migraineurs who developed CRPS and those who did not.

Results
A total of 30 Mig+CRPS cases (13% males, mean age of 48 years) and 38 Mig-CRPS referents (17% males; mean age of 51 years) were included. IRR revealed a Cohen's $\kappa$ of 0.85. Sex differences amongst the two cohorts was not associated with CRPS occurrence (Odds Ratio of 1.30, 95% CI 0.33, 5.11). Thirty-three % of the Mig+CRPS cohort exhibited Episodic Migraine while the remaining 66% had Chronic Migraine. Similarly, 38% of the Mig-CRPS cohort exhibited Episodic Migraine (EM) while the remaining 62% suffered from Chronic Migraine (CM); this revealed that migraine frequency was not associated with CRPS occurrence (Odds Ratio of 0.98, 95% CI 0.36, 2.67). Age at first migraine attack was mostly around early school years and was found to be comparable between the two cohorts of Mig+CRPS and Mig-CRPS. Migraine onset preceded CRPS onset among all cases of Mig+CRPS with a median of 18.5 years (IQR 10-25). Median duration of CRPS was 3 years (IQR 3-5) among the EM+CRPS (Episodic Migraineurs with CRPS) cohort and 6 years (IQR 4-12) among the CM+CRPS (Chronic Migraineurs with CRPS) cohort (Mann-Whitney test, $p < 0.02$). EM+CRPS cohort exhibited observably higher prevalence of CRPS type 2 (60%) compared to CM+CRPS cohort (12%) (Odds Ratio of 0.22, 95% CI 0.03, 1.73). Mig+CRPS (57%) cohort carried higher burden of psychological problems compared to the Mig-CRPS cohort (6%). Past or current medical comorbidities were also more common among the Mig+CRPS cohort compared to Mig-CRPS cohort. Sixteen % of the Mig+CRPS cohort were on current or previous opioid-containing pain medications use to manage their headache compared to 3% of the Mig-CRPS cohort.
Conclusion
Migraine frequency was not associated with CRPS occurrence; however, higher migraine frequency was associated with longer CRPS duration. Migraine-to-CRPS progression occurred in about 2 decades. Migraineurs who develop CRPS had higher prevalence of psychological and medical disorders. Managing migraine by reducing its frequency can lessen CRPS duration and may have important implications for future treatment options. Alleviating migraineurs' psychological and medical comorbidities can help lower CRPS occurrence.
Title: The Hypothalamus As The True Motor Of Migraine Attacks: Continuous Scanning Of The Migraine Cycle Over 30 Days

Poster Number PW0168

Authors
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Aim of Investigation
Functional imaging using PET and later fMRI revealed a particular brainstem area which is believed to be specifically activated in migraine during, but not outside of the attack and consequently has been coined the migraine generator. However, the pathophysiological concept behind this keyword is not undisputed and typical migraine premonitory symptoms such as fatigue and yawning but also a typical association of attacks to circadian and menstrual cycles all make the hypothalamus a possible regulating region of migraine attacks. Neuroimaging-studies investigating native human migraine attacks however are scarce and for methodological but also clinical reasons there are currently no studies investigating the last 24 hours before headache onset. Here we aim at identifying the specific motors of the different phases of spontaneous human migraine attacks and their specific functional connectivity by daily fMRI over a period of 30 days.

Results
We found that hypothalamic activity is altered during the last 24 hours prior to pain onset, i.e. increases towards the next migraine attack. More importantly, the hypothalamus shows altered functional coupling with the spinal trigeminal nuclei and the region of the 'migraine generator' i.e. the dorsal rostral pons during the premonitory day and the pain phase of native human migraine attacks.

Conclusion
These data suggest that although the brainstem is highly linked to the migraine biology, the real motor of attacks are the functional changes in hypothalamic activity and hypothalamo-brainstem connectivity.
Date: 09/28/2016 03:15:00 PM

Title: Case Report On Management Of A Ventral CSF Leak In The Lumbar Region In A Pediatric Patient Resistant To Standard Management Algorithms

Poster Number PW0169

Authors
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Aim of Investigation
We present a case of an 11yo male with a history of hypogammaglobulinemia and a previous history of Post Dural Puncture Headache (PDPH) successfully managed with an epidural blood patch, who developed a second PDPH that was refractory to conventional management.

Results
In follow-up one month later the patient remains symptom-free and has returned to regular activities.

Conclusion
A residual posterior defect in the dural sac is usually the underlying lesion that results in leakage of CSF and intracranial hypotension following a lumbar puncture. It is generally accepted that the headache is due to the leak of cerebrospinal fluid (CSF), resulting in diminished hydraulic support for intracranial structures. Tension on cerebral structures results in headache. In addition, it has been postulated that compensatory vasodilatation of cerebral vessels contributes to PDPH. Epidural blood patch in the region of the presumed leak is a commonly used management technique for intracranial hypotension. In this case, 3 posterior lumbar epidural blood patches failed to provide complete or durable symptom relief. Radiologic imaging identified the CSF leak to be in the ventral region of the spinal canal. After partial response to the transforaminal injection, symptom relief became complete with a high-volume saline infusion. One explanation for the beneficial effect of epidural saline is that the increased epidural pressure may have resulted in approximation of the dura and arachnoid at the puncture site, thus sealing the defect. This may be an oversimplification, however, and there may be other mechanisms at play. This case report illustrates management of a PDPH secondary to a ventral epidural CSF leak, an unusual occurrence, and the failure of posterior epidural blood patches to treat such a dural leak. Ineffectiveness of blood patches performed posteriorly should lead the clinician to pursue radiographic confirmation of a CSF leak, and definition of its location in order to best direct further blood patches.
Aim of Investigation
The definition of medication overuse headache (MOH) implies headache on 45 or more days per 3 months in combination with regular medication overuse for at least 3 months. The aim of this study was to compare health-related quality of life of patients with medication overuse headache (MOH) after completion of a specific inpatient headache program with normative population-based data.

Results
Fifty-one patients (72.5% female, mean age 47.3 years) were included with an average headache duration of 25.3 years. Average headache was 6.51 (SD=2.04) on the MIDAS VAS (0-10) and SF-36 bodily pain was 40.3 (SD=20.3, norm=59.0, p<0.001). All other SF-36 scales showed significant (p≤0.041) impairments with levels far from the expected scores, e.g., general health 48.7 vs 62.1=norm , social functioning 56.8 vs 82.1 and mental health: 59.7 vs 68.5. Physical functioning was not affected on the SF-36 when compared to the norms (means: 78.4 versus 81.8, p=0.663). Depression and anxiety on the HADS were much higher than expected on the SF-36 when compared to the norms (means: 78.4 versus 81.8, p=0.663). Depression and anxiety on the HADS were much higher than expected from the normative levels: 67.6 vs 78.1, p=0.016 and 63.3 vs 76.5, p<0.001. The same was true for the obsessive/compulsive symptoms scale (74.1 vs 87.4) and, somewhat less, for the interpersonal sensitivity scale (79.9 vs 89.6) of the SCL-90-R. In contrast to that, patients were not more schizotypic (84.4 vs 88.8, p=0.807) but less schizophrenic (nuclear symptoms: 94.4 vs 95.1) than expected.

Conclusion
Pain and psycho-social impairment levels were moderate to high and higher than expected from the norms. However, physical functioning on the SF-36 was not affected. High expectancies to functional ability may be a reason for this discrepancy. This corresponds to substantially affected mental health in
many important dimensions, which are known to reduce ability to cope with pain. Prospective studies will refine insight into processes of treatment.
Title: Establishment Of A Rat Model Of Mechanical Low Back Pain

Poster Number PW0171

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Aim of Investigation
The lifetime prevalence of low back pain (LBP) is high at ~84%, resulting in a socioeconomic burden estimated at USD$100 billion per annum. Despite this high burden, knowledge on the pathobiology of chronic mechanical LBP is limited. Hence, our aim was to establish an optimized rat model of chronic mechanical LBP devoid of a potentially-confounding neuropathic pain component.

Results
Mechanical hyperalgesia developed in a temporal manner in the deep axial tissues at L4/L5 (primary hyperalgesia) and L1 (secondary hyperalgesia) in LBP-rats but not sham-rats. Importantly, PWTs remained unaltered in the bilateral hindpaws for the 49-day study period. Preliminary histological analysis of the IVD tissue sections from LBP-rats showed an apparent loss of sharp/straight junctions in the cranial and caudal posterior aspects as well as a loss of sharp junctions between the nucleus pulposus and the annulus fibrosus in the dorsal and ventral aspects. There was also evidence of degeneration in the nucleus pulposus and disruption of the annulus fibrosus that presented as wavy, non-parallel fibers and vertical clefts in IVD sections from LBP-rats. These histological changes were not evident in the corresponding IVD sections from sham-rats.

Conclusion
We have established successfully a rat model of mechanical LBP devoid of a neuropathic component that will be invaluable in future investigations of the pathobiological mechanisms underpinning this chronic pain condition that is difficult to alleviate with clinically available analgesic medications.
Title: Intraosseous Blockades In The Treatment Of Low Back Pain, Caused By Modic Type 1 Changes In The Lumbar Vertebrae

Poster Number PW0172

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Aim of Investigation
Low back pain is one of the most common causes of long-term physical disability in the world. Modic type 1 changes in the lumbar vertebrae have been identified as an important subgroup among patients with low back pain. We assume that intraosseous receptors take part in the development of low back pain, caused by Modic type 1 changes in the lumbar vertebrae. The aim of our study was to prove the efficacy of intraosseous blockades in the treatment of low back pain and to show the important role of intraosseous receptors in pathogenesis of low back pain, caused by Modic type 1 changes in the lumbar vertebrae.

Results
After the treatment with intraosseous blockades pain syndrome according to VAS had decreased on an average from 7.8 to 2.5. As a result of this treatment 9 (30%) patients reported about full regression of pain, 14 (47%) patients - about reduction of pain for more than 50%, another 7 (23%) patients - about reduction of pain for less than 50%. The values according to MPQ had decreased as follows: number of words - from 11.6 to 4.7, pain rating index - from 21.8 to 8.2. There was no side effects or complications.

Conclusion
Intraosseous blockades are highly effective in the treatment of low back pain, caused by Modic type 1 changes in the lumbar vertebrae. The high efficacy of intraosseous blockades confirms the important role of intraosseous receptors in the pathogenesis of low back pain, caused by Modic type 1 changes in the lumbar vertebrae.
Title: Interdisciplinary Management Of Low-Back Pain In Primary Care: Interim Evaluation Of A Novel Program In Quebec

Poster Number PW0173

Authors
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Aim of Investigation
Patients who do not respond to conventional back pain management algorithms six weeks after the onset of acute pain present an opportunity to identify barriers to recovery, and to implement treatment aimed at preventing the development of chronic low back pain (LBP). We present one component of the evaluation of a novel interdisciplinary approach to LBP implemented in a primary care setting. In this paper we examine the impact of the program on pain intensity and disability after six months.

Results
Up to 4 February 2016, 463 patients had been enrolled and consented in the study (mean age 52.4y (SD 15.1); 60% female). Mean baseline pain was moderate (VAS pain intensity 4.9 (SD 2.0); VAS pain interference 4.7 (SD 2.4)). Mean Oswestry score was 34.1 (SD 15.8) Moderate to severe risk of chronicity was present in 65% of patients. For the 186 who have completed six months of follow up to date, significant improvement was noted in pain intensity (VAS 2.7; p<0.001) and pain interference (VAS 2.1; p<0.001), and ODI (20.6; p<0.001).

Conclusion
The program is ongoing and these data suggest that improvements in a broad range of outcomes are being observed. Ongoing program evaluation with respect to primary healthcare practice and patient satisfaction will help inform further program development and wider implementation.
Title: Pain Thresholds In Patients With Lumbar Radicular Pain (Sciatica)

Poster Number PW0174

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Aim of Investigation
Quantitative sensory testing (QST) is commonly used to study sensory alterations in patients with neuropathic pain (NP). In patients with sciatica, several studies revealed elevated sensation (i.e. heat, cold, pressure) thresholds. In contrast, the evidence regarding pain thresholds in these patients is less unequivocal: while some studies found differences between the affected and unaffected areas, others found no such differences. The aim of the current study was to compare thermal and mechanical pain thresholds between the affected and the unaffected legs in a cohort of patients with sciatica, and by that to assess their contribution for diagnosing NP (according to the new IASP criteria) in these patients. Our working hypothesis was that pain thresholds will differ between legs.

Results
Mean clinical pain intensity and pain duration were 65.6±17.4 (NPS, 0-100) and 69 ± 73.3 (months), respectively. Mean pain thresholds measured in the affected leg and the unaffected leg were: 9.5±9.9°C and 7.5±8.9°C for cold pain threshold; 45.7±3.89°C and 46.1±3.36°C for heat pain threshold; 63.3±17.4gr and 70.5±70.9gr for mechanical pain threshold. No significant differences between the legs were found in any of the three measured pain thresholds (p>0.05, paired sample t-test), thus refuting our hypothesis. In addition, no correlations were found between pain thresholds and pain intensity or pain duration.

Conclusion
(1) Thermal and mechanical pain thresholds do not differ between the legs in patients with sciatica. This lack of differences can be attributed to preservation of evoked pain thresholds in the affected limb regardless of the sciatic nerve root injury/irritation. Alternatively, it is possible that pain thresholds on both legs are equally altered (segmentally), thus showing no differences. (2) In any case, assessing pain
thresholds by QST does not seem useful in establishing the diagnosis of NP (according to the new IASP criteria) in patients with sciatica.
**Title:** Effect Of Betametasone Injection On The Spontaneous Regression Of Intervertebral Disc Herniation

**Poster Number** PW0175

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**Aim of Investigation**
Local inflammatory response and the body's autoimmune response at the intervertebral disc hernia site play a key role in its decrease. The use of a betamethasone epidural leads can decrease and in some cases, probably, a complete cessation of autoresorption processes. It also increases the chances of transforming this into a chronic ailment as a result of continuous alternation between suppression and resumption of the inflammatory and autoimmune processes. This may in turn lead to the need for immediate surgical intervention, with the alternative being disability. The aim of our study is to determine the role of betamethasone as opposed to placebo in decreasing intervertebral disc hernias.

**Results**
Group A - Two females, from Group A had to leave the study due to the fact that they developed gastropathy. Group B - 3 patients left the study (2 males and 1 female). This was due to the development of severe pain requiring constant medication. At the end of 28 days, all patients received a second MRI. Results showed a decrease in the size of the intervertebral hernias. Group A - average decrease from 9.2 mm to 9.00 mm (0.2mm decrease). (p ≤ 0,05) Group B - average decrease from 9.3 mm to 7.0 mm (2.3 mm decrease). (p ≤ 0,05) At the beginning of the study, the VAS scale showed that Group A recorded a more rapid decrease in pain in comparison to Group B. By the end of the study both groups recorded similar responses to pain stimulation.

**Conclusion**
Initial findings already show that the role of betamethasone must be reconsidered in the treatment of certain types of intervertebral hernias, in particular, those that are subject to relatively fast resorption. Such hernias can be supported with alternative pain medication that does not include the use of
steroids which only suppress the inflammatory process, which seems to be a requisite for effective resorption and therefore, recovery.
Title: Isometric Back Exercise Induces A Decrease In Pressure Pain Sensitivity In Healthy Men And Women: A Pilot Study

Poster Number PW0176

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Aim of Investigation
Exercise-induced hypoalgesia (EIH) describes a decrease in pain sensitivity in healthy subjects after different types of exercises. EIH after isometric exercise is greater at local compared to remote assessment sites, and seems to be more pronounced in women. Further, previous studies showed dysfunctional EIH in different chronic pain populations. Existing isometric EIH paradigms use exercises at the extremities including hand grip, knee extensions, and elbow flexions. Considering a potential involvement of peripheral processes in EIH, a need for paradigms which target the lower back muscles arises in order to improve the study of EIH in patients with low back pain (LBP). Therefore, the primary aim of this study was to assess pressure pain sensitivity at local and remote assessment sites, before and after an isometric back exercise in healthy men and women.

Results
After exercise, pressure pain sensitivity at the hand decreased in women, but not men (p<.05, partial η2=.17). Pressure pain sensitivity at the leg decreased in both women and men (p<.05, partial η2=.27) and at the lower back, there was a trend towards a decrease in both women and men (p=.07, partial η2=.12).

Conclusion
These results indicate that local EIH is produced after performance of the BS test in men and women supporting peripheral mechanisms as part of the EIH response. Remote EIH was only demonstrated in women, supporting the influence of sex in EIH. The effect of the BS test on pain sensitivity in patients with low back pain should be investigated in future studies.
Aim of Investigation
Chronic low back pain (CLBP) is one of the most important pain disorders with increasing social and economic implications. CLBP is thought to be a multidimensional process associated with comorbidities such as depression and pain catastrophizing. Advancement of in vivo brain imaging technologies has revealed increasing insights into the etiology and pathogenesis of chronic pain; however, the exact mechanisms of chronification of LBP remain still unclear. The purpose of the current study was to analyze the psychometric alterations and the characteristics of brain images in CLBP.

Results
Scores of PDAS, HADS and PCS were statistically significantly higher in the CLBP group compared with the control group. On the other hand, EQ-5D was significantly lower in the CLBP group compared with the control group. On MRS, NAA/Cho in PFC was significantly lower in the CLBP group compared with the control group. On VBM, significant regional atrophy was observed at left supramarginal gyrus, right precuneus, left precentral gyrus, left angular gyrus, and right parietal operculum in the CLBP group compared with the control group.

Conclusion
It was confirmed that the cases of CLBP showed disability, anxiety, depression, and lower QOL. Pain catastrophizing is thought to be an important factor in the development of chronic pain. Pain catastrophizing might be related to CLBP from the results of the current study. Since pain is realized in brain, functional brain imaging is important to clarify the pathogenesis of CLBP. The current study showed that functional change occurred in the PFC which is an affective-cognitive-evaluative area. Also, brain morphometric changes were seen in CLBP. These changes might be related to the chronification...
of LBP. However, the current study was a cross-sectional study. A further longitudinal study is needed to better clarify the pathomechanisms of CLBP.
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Aim of Investigation
We examined increase of the bone mineral density and a correlation of the pain control. We considered that increase of the bone mineral density could become the index of the pain control. We perform lumbar epidural block in elderly women with low back pain to improve activities of daily living (ADL), with the aim of enhancing QOL, in our clinic. We are convinced that pain control in elderly patients can extend healthy life expectancy. We performed pain control in patients with low back pain and found that a significant increase in bone mineral content correlated with ADL improvement. Increased bone mineral content after treatment also correlated significantly with the pain relief effect.

Results
In Group A, the JOA score was 7.26 ± 1.45 before the start of treatment and 19.39 ± 1.21 after the 6-month treatment, and the respective bone mineral contents were 1459.26 ± 13.03 m/s YAM 61.04 ± 6.07% and 1478.00 ± 12.00 m/s YAM70.22 ± 5.99%. In Group B, the JOA score was 11.33 ± 1.25 before the start of treatment and 15.50 ± 1.26 after the 6-month treatment, and the respective bone mineral contents were 1466.00 ± 14.52 YAM64.08 ± 6.46% and 1463.33 ± 22.86 m/s YAM 63.5 ± 11.29%.

Conclusion
The JOA scores demonstrated the high efficacy of lumbar epidural nerve block treatment, in terms of ADL improvement, in elderly people. However, JOA scores are primarily based on subjective symptoms and self-assessed ADL improvement. Bone mineral content measurements before and after treatment are considered to be effective for quantifying the pain relief effect.
Title: Chronic Low Back Pain, Cognitive Performance, And Opioids: The Role Of Plasma Cytokine Concentrations

Poster Number PW0179

Authors

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Aim of Investigation
Cognitive functioning has been found to be impaired in people with chronic pain. However, much of the research has lacked control for opioid therapy and sleep disturbance and has not considered the array of biological, psychological and social variables involved in the pain experience. Therefore this cross-sectional, clinical, exploratory, pilot study was undertaken to provide a comprehensive picture of chronic low back pain by quantifying the independent contributions of pain and the impact of opioid therapy on cognitive performance, whilst taking into account sleep status, psychosocial variables and plasma cytokine concentrations.

Results
The performance on tasks of memory, attentional processing and executive working memory were significantly lower in OP and NO when compared to HC's. There were no significant differences (P>0.05) in the level of pain severity, pain interference and catastrophising thoughts associated with pain for both OP and NO. Opioid therapy appeared to further impair attentional processing, numeric scanning ability and self-efficacy beliefs. In addition, insomnia disorder, depression, anxiety and stress were significantly greater (P<0.05) in OP and NO and thus may also independently contribute to the decrease in cognitive performance. Mean plasma cytokine concentrations were not significantly different (P>0.05) between OP, NO and HC for all cytokines measured. The anti-inflammatory cytokine, IL-13, was chosen for further analysis because of its reasonably linear co-efficient and since all concentrations were within
the range of detection. However, IL-13 did not significantly correlate (P<0.05) with self-efficacy beliefs or attentional processing.

**Conclusion**
This study provides insight into the independent contribution of pain in reducing cognitive performance in patients with chronic low back pain. Those receiving opioid therapy performed worse on attentional aspects of the cognitive tests. The implications of co-existing variables with potentially independent associations to decreased cognition may have clinical implications that support a multidisciplinary biopsychosocial approach to pain management.
Title: Application Of Prolo Scale And Eq-5D-5L Questionnaire In Spine Surgery Outcome Assessment

Poster Number PW0180

Authors
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Aim of Investigation
During the past decades, several scoring systems have been developed to assess the functional status of patients with spine related problems. Degenerative spine diseases are the most frequent cause of disability and work incapacity, which represents large social and economic problem in developing countries. There are surgical and non-surgical treatments and concurrently growing demand for outcome measurement and quality assurance. According to this we used economic and functional rating score (Prolo scale) and VAS pain scale before and after spine operation, as well as EQ-5D-5L (Euroqol Health Questionnaire) after more than 6 months of surgery. This observational study is the first step in creation of national strategy for prevention and treatment such conditions.

Results
There were 24 men and 24 women who participated in the study, age from 29 to 63, mean 47 years. Comparing VAS pain scale before and after surgery (VAS I and VAS II) with T-test for independent samples we found statistically significant differences among groups: 9.1 vs. 3.4, p=0.000. Differences between Prolo rating scale was statistically significant too, 5.1 vs. 6.4, p=0.0074. Multiple regression statistics was used to assess relationship between anxiety/depression and mobility, self-care, usual activities, pain/discomfort as well as between self-rated health records and these dimensions. Anxiety/depression and self-rated health records were significantly in correlation with mobility, self-care, usual activities, pain/discomfort, p<0.05, but not with employment status, p= 0.71.

Conclusion
Despite a small sample size of patients the results show complex connections between health and functional, economic, and social status. The use of Prolo scale and EQ.5D-5L questionnaire could
contribute to better assessment of spine and any pain related problems which require operative or conservative treatment.
Title: Manage Backs: An Early Intervention Group For People With Low-Back Pain (Plbp)

Poster Number PW0181

Authors
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Aim of Investigation
The first point of contact for PLBP is often physiotherapy outpatients where traditionally appropriate care is assumed to require biomedical assessment and communication of biomedical maintaining factors. Research evidence shows a biopsychosocial approach should be at the centre of management decisions, by addressing PLBP's unhelpful beliefs and enhancing their activation. This shift from the LBP in itself, to the pain cognitions and behaviours that maintain disability and distress offers the potential to improve quality of life, resilience and anxiety. Manage Backs (MB) was designed through transformative co-production to integrate these findings into primary care physiotherapy where a Group Intervention (GI) changed the care pathway entry point from a traditional 1:1 physiotherapy assessment. This GI allowed the physiotherapist to engage PLBP in shared decision making about pain self-management based on an enhanced understanding of biopsychosocial maintaining factors and potential for activation self-efficacy. MB Aims: Engage PLBP in collaboration about decisions and self-management strategies; Enhance physiotherapists' attitudes and beliefs to support this heightened patient engagement; Reduce waste of healthcare resources.

Results
85 GI's were delivered by 12 physiotherapists to 611 PLBP (Mean: 7 per GI) across 6 hospital sites. The qualitative and quantitative evaluation measures confirmed MB's acceptance on the primary care LBP pathway. Clinically, PLBP completing GI's demonstrated improvements in activation (PAM), function (PSFS) and quality of life (EQ-5D). The percentage of PLBP attaining significant improvements was greatest in the GI model for activation (confidence to engage in decisions and self-management strategies) at 52.1%, followed by function (48.7%) and quality of life (28%). The level of significant change was determined through comparison with reported levels from the literature. MB saved healthcare resources as GI attendees demonstrated lower new patient non-attendance, lower new patient to follow-up ratio and also exhibited increased confidence to self-manage which supported them
to exit the pathway earlier. A lower re-referral rate for those who completed the GI also occurred. In total pathway delivery cost savings were potentially up to 28%.

**Conclusion**

The clear impact and value, both clinically and economically, that has been achieved through this pathway transformation in primary care which shifts the focus from LBP itself, to the pain cognitions and behaviours that maintain disability and distress have been identified. Developing the physiotherapy teams' attitudes and beliefs through mentoring was vital for heightened patient engagement within the GI and allowed PLBP to effectively make decisions about self-management strategies. The pathway cost savings of the MB model of care appear clear. This study provides an early indication of the potential value of this co-produced, patient centred and prudent model of care.
Title: Clinical Phenotypes Of Injured Workers With Chronic Low Back Pain: A Latent Class Analysis

Poster Number PW0182

Authors
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Aim of Investigation
To determine a) clinical phenotypes of injured workers with chronic low back pain using physical and psychological indicators, b) predictors of class membership and c) to assess associations of the classes with work status.

Results
A 3-class model was chosen based on fit statistics, along with consideration of theoretical and clinical knowledge of this population. The resultant 3 classes represented low, moderate and high levels of all indicators demonstrating increasing severity of clinical presentation. The variables of depression, pain catastrophizing, disability, negative affective, resilience and fear avoidance beliefs had the greatest influence on class formation and demonstrated distinct mean values based on 95% confidence intervals across the classes. Pain intensity was not well discriminated between classes. The highest means for negative psychological factors were observed in the most severe group, which also had the lowest means for resilience and pain self-efficacy. The opposite was observed in the least severe class.

Predictors of being in the high severity group compared to the low severity group were < high school education [OR= 3.06, 95% CI (1.47, 6.37)] and comorbidity total [OR=1.28, 95% CI (1.03, 1.59)]. Moderate severity group membership was associated with male sex [OR= 2.26, 95% CI (1.03, 4.97)] compared to the low severity group. Being in the high severity class was associated with ~ 4x increased risk of being off work compared to those in the low severity class [OR=3.98, 95% CI (1.61, 6.34)]. This estimate decreased to ~1.5x increased risk for those in the moderate severity group [OR= 1.60, 95% CI (0.73, 2.47)].

Conclusion
Three clinical phenotypes with distinct psychological and physical profiles were identified. To our knowledge, this is the first study of clinical phenotypes in a cohort of injured workers with chronic low
back pain, who are known to have a different clinical course than people with low back pain in the general population. These profiles are useful in aiding clinicians to identify injured workers of high clinical severity who are at greater risk for being off work. Further the class structure highlights the distinct contribution of positive and negative psychological constructs and that pain severity is indiscriminate.
Title: Correlated Cortical Thickness: Static And Dynamic Fmri Connectivity Changes In Chronic Low-Back Pain Patients

Poster Number PW0183

Authors
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Aim of Investigation
This study aims to (1) understand the relationships between psychophysical measures of heat pain, whole brain cortical thickness, and static functional connectivity (sFC) changes in chronic low back pain (CLBP) patients, and (2) to determine whether temporal dynamic functional connectivity (dFC) analysis of resting state fMRI signals reveals additional changes in the brain's functional circuits.

Results
Psychophysical analysis showed that the CLBP group rated significantly higher (p < 0.05) than the CON group for mild and moderate pain in comparable temperature range. Although both groups gave comparable ratings for severe pain, the mean temperature reported for severe pain was significantly lower for CLBP patients (p < 0.05). The range of temperatures reported for moderate pain was significantly larger across three repeated measures in CLBP patients (p < 0.05). Compared to CON, 27 cortical regions in the CLBP group exhibited cortical thickening and thinning (p < 0.01, multiple comparison corrected). Among all the possible pairs of the 27 ROIs, five of the ROI pairs (i.e., superior-parietal_L – inferior-temporal_L, inferior-temporal_L – caudalmiddel-frontral_R, superior-parietal_L – inferior-parietal_R, superior-parietal_L – pre-central_R, inferior-temporal_L – pre-central_R) showed altered FC (p < 0.01). The secondary level dynamic analysis of the five ROI pairs using SW and FFT methods found that the lowest-frequency range had the highest FFT amplitude, the CLBP group has relatively larger amplitude than CON, and the max between-group differences occurred in 0.002 – 0.006 Hz range. Compared to CON across the above five ROI pairs, the CLBP group showed significant amplitude differences for window sizes of 30, 60 and 120 s compared to that of 240 s.
Conclusion
CLBP patients showed altered pain sensitivity in all three levels (mild, moderate and severe) of pain, rated more pain at the lower heat temperature, and reported severe pain at significantly wider range of temperatures. Widespread cortical thickness changes were identified in CLBP patients. Pair-wise resting state FC changes occurred only in a subset of these regions (five ROI pairs; p < 0.01), and varied in connectivity strengths (r values). These regions also showed dFC differences between CLBP and CON groups.
Distorted Body Perception Mediates The Relationship Between Pain And Disability In People With Low-Back Pain: A Cross-Sectional Study

Poster Number PW0184

Authors

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Aim of Investigation
Chronic low back pain (LBP) is often associated with perceptual dysfunction. Moreover, several studies indicate that perceptual dysfunction might offer a potential target for rehabilitation. The Fremantle Back Awareness Questionnaire (FreBAQ) was designed to assess back specific disruption in self-perception in people with low back pain. When completing the scale patients are asked to endorse items related to neglect like symptoms, reduced proprioceptive acuity and perceived body shape and size. Scores on the questionnaire are associated with pain intensity, disability, fear of movement, and catastrophizing in people with LBP. However, the mechanisms underlying this association are not well understood. Self-efficacy, psychological distress, and fear of movement are thought to mediate the relationship between pain and disability in people with back pain, but it is unclear whether distorted body perception might also play an intermediate role in how pain leads to disability. We investigated whether distorted body perception mediates the relationship between pain and disability in people with chronic LBP.

Results
Full data were available for 100 participants (64 Female, mean (SD) age =56.0 (16.4) years). The total effect (relationship between pain and disability) was significant ($c = 0.059$, $p < 0.001$). Direct effect of total pain on RDQ was significant ($c' = 0.047$, $p = 0.002$). The indirect effect of pain on RDQ through FreBAQ ($a1 \times b1 = 0.011$, 95% CI = 0.001 - 0.030) was significant. Overall, 18.6% of total effect was mediated by FreBAQ in the relationship between pain and disability.
Conclusion
Distorted body perception contributes to the relationship between pain and disability in people with chronic LBP. Improving body perception, for example via sensory and motor discrimination tasks, may reduce disability in people with chronic LBP.
Aim of Investigation
Voxel-Based Morphometry (VBM) is a diagnostic imaging technique to analyze brain morphology. The purpose of this study was to examine characteristic morphological changes in the brain in patients with chronic low back pain (cLBP) using VBM.

Results
In patients with cLBP, VBM analysis showed gray matter volumes were significantly decreased in the amygdala (Z-score mean±SD; Right 3.44±1.61 Left 3.05±1.40), the posterior entorhinal cortex (BA: Brodmann area-28) (Right 2.75±1.53 Left 2.22±1.38) and the anterior entorhinal cortex (BA-34) (Right 3.00±1.54 Left 2.85±1.55) on both sides after adjusting age and total intracranial volume. It was also observed that gray matter volumes were significantly decreased in the amygdala(P-value=0.0038) and the posterior entorhinal cortex (BA-28) (P-value=0.0001) on right hemisphere than left hemisphere. On the other hands, it was not observed significant difference in decrease of gray matter volumes in the anterior area (BA-34) (P-value=0.1738) on both sides.

Conclusion
In the present study, we detected that gray matter volumes in the amygdala, the posterior entorhinal cortex (BA-28), and the anterior entorhinal cortex (BA-34) were significantly decreased in patients with cLBP. There also were lateral differences in the volume reduction of the amygdala and BA-28 in patients...
with cLBP. Volume reductions of gray matter and lateral differences in specific area in patients with cLBP might be associated with the cLBP mechanisms.
Title: Which Factors Of Disturbed Body Perception Are Related To Motor Imagery And Pain Intensity?

Poster Number PW0186

Authors
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Aim of Investigation
There is a growing interest in the role of perceptual dysfunction, such as distorted body image, decreased tactile acuity, impaired proprioceptive acuity, reduced trunk motor imagery performance, and neglect-like tactile dysfunction, in individuals with chronic low back pain (CLBP). The Fremantle Back Awareness Questionnaire (FreBAQ) has been recently developed as a simple and quick method of assessing disturbed perceptual awareness of the back in individuals with CLBP. The total score of FreBAQ is associated with pain intensity, maladaptive belief, and disability. FreBAQ comprises three subscales, 'neglect-like symptoms', 'reduced proprioceptive acuity', and 'body shape and size'. However, the mechanisms underlying these three subscales remain unclear. The laterality judgment task involves individual judgment as to whether a model is rotated or laterally flexed to the left or right in a series of images. This task could be used to evaluate body representation and schema. Some studies have demonstrated that chronic back pain is related to disruption of the motor imagery of the trunk. However, to date, no study has simultaneously evaluated body perception and motor imagery. This study aimed to investigate the relationship among disturbed body perception, impaired laterality judgment ability, and pain intensity.

Results
The 'neglect-like symptom' subscale of FreBAQ was significantly correlated with VAS at rest ($r = 0.38, p < 0.01$), during motion ($r = 0.40, p < 0.01$), and RDQ ($r = 0.53, p < 0.01$). The 'body shape and size' subscale significantly correlated with accuracy ($r = -0.31, p = 0.03$), RT ($r = 0.29, p = 0.04$), and RDQ ($r = 0.30, p = 0.03$). There was no significant correlation between the 'reduced proprioceptive acuity' subscale and pain intensity, RDQ, accuracy, and RT.
Conclusion

Only the 'body shape and size' subscale of FreBAQ was associated with accuracy and RT. This result suggests that a disrupted body image leads to impaired motor imagery. In contrast, only the 'neglect-like symptom' subscale was correlated with pain intensity. Moreover, the 'reduced proprioception' subscale was not associated with laterality judgment ability or clinical symptoms. These results suggest that each subscale of FreBAQ could differently contribute to clinical symptoms.
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Title: Study Protocol For A Multicentre Double-Blind, Randomised, Controlled Trial To Assess The Clinical And Cost-Effectiveness Of Facet-Joint Injections In Selected Patients With Non-Specific Low-Back Pain: A Feasibility Study (Facet Feasibility Study)

Poster Number PW0187

Authors
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Aim of Investigation
Pain of lumbar facet-joint origin is a common cause of low back pain in adults, and may lead to chronic pain and disability. At present, there are no diagnostic criteria for lumbar facet-joint pain, and no definitive research to support the use of targeted lumbar facet-joint injections to manage this pain. There is no standardised technique for facet-joint injection, and no consensus of what would constitute a suitable sham procedure. Due to the lack of high quality clinical evidence, the National Institute for Health and Care Excellence (NICE) guidelines published in the UK in 2009 did not recommend injections of therapeutic substances into the back for non-specific low back pain, despite their potential to reduce pain intensity and rehabilitation, and NICE called for further research to be undertaken. The aim of this pilot study is to examine the feasibility of undertaking a definitive fully powered double-blind randomised controlled trial to evaluate the clinical- and cost-effectiveness of facet-joint injections compared to a sham procedure, in participants with non-specific low back pain of more than 3 months' duration. Specific objectives are to: ensure the standardisation of the method of injection and sham procedure, check the study design is acceptable to patients and clinicians, and ensure sufficient patients can be recruited and retained. The pilot study will also be used to inform the development of a suitable framework to assess cost-effectiveness in a future definitive trial.
Results
Diagnostic test for facet-joint disease: all patients enrolled into the study will receive 4 medial branch nerve blocks at 2 bilateral lumbar levels with 0.5ml 1% lidocaine per injection, under fluoroscopic guidance. Those who achieve 50% or greater pain reduction lasting for more than 30 minutes will be considered to have a 'positive' test i.e. their low back pain is likely to be of facet-joint origin, and will be randomised to receive either lumbar facet-joint injections or a sham procedure. Facet joint injections: a spinal needle will be placed within the facet-joint under fluoroscopic guidance, and 0.5ml 0.5% bupivacaine with 20mg methylprednisolone injected per joint. Four facet-joints will be injected, at 2 bilateral lumbar levels. Sham procedure: a spinal needle will be placed in the peri-articular space surrounding the facet-joint under fluoroscopic guidance, at each of the 4 painful areas at 2 bilateral lumbar levels, and 0.5ml normal saline will be injected through each needle.

Conclusion
The results of this ongoing pilot trial will inform us of the feasibility of conducting a definitive trial in terms of: successful standardisation of the methods of injection, acceptability of the study design to patients and clinicians, and ability to retain and recruit sufficient participants.
Title: Kinesiophobia And Anxiety Mediate The Relationship Between Pain And Life Satisfaction In People With Low-Back Pain

Poster Number PW0188

Authors

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Aim of Investigation
Assessing quality of life (QOL) is important in clinical practice when rehabilitating patients with chronic pain because the goal of rehabilitation is to improve activity of daily living (ADL) and QOL, as well as to decrease pain intensity. The concept of life satisfaction, which is a subjective component of QOL, focuses on the individual’s perception of the differences between their subjective reality and their needs or wants in several important domains of functioning and activity/participation. Recent studies have shown that people with chronic musculoskeletal pain have lower life satisfaction than the general population, and that low life satisfaction is associated with psychological factors, such as anxiety and depression. However, these findings do not elucidate the process by which pain leads to low life satisfaction or identify specific targets for interventions to improve life satisfaction. Therefore, this study aimed to investigate whether psychological factors mediate the relationship between pain and life satisfaction in people with low back pain (LBP).

Results
The total effect of the relationship between pain and life satisfaction was significant (c = −0.007, p = 0.03). The direct effect of pain on LiSat-11 after controlling for mediator and confounding variables was not significant (c' = −0.001, p = 0.75). The indirect effect of pain on LiSat-11 through TSK (a×b = −0.0022, 95% CI = −0.0055—−0.0004) and HADS-anxiety (a×b = −0.0015, 95% CI = −0.0041—−0.0001) was significant. Overall, 52.8% of the total effect was mediated by TSK and HADS-anxiety in the relationship between pain and life satisfaction.
Conclusion
Our data shows that pain did not relate directly to life satisfaction and that fear of movement and anxiety may play an intermediate role in the development of life satisfaction. These results suggest that interventions targeting fear of movement and/or anxiety might improve life satisfaction in people with LBP rather than interventions only targeting pain intensity reduction.
Title: Motor Imagery And Catastrophizing Are Related To Postoperative Pain After Rotator Cuff Repair

Poster Number PW0189

Authors
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Aim of Investigation
Pain after rotator cuff repair (RCR) has been reported to adversely affect postoperative outcomes and patient satisfaction. Therefore, it is important to clarify factors that affect postoperative pain. Recently, there have been reports indicating that motor imagery and catastrophizing are related to pain. However, there are few reports investigating these factors for pain after RCR. The aim of the present study was to investigate factors related to pain after RCR based on postoperative physical and mental functions, including motor imagery and catastrophizing, in addition to preoperative physical characteristics.

Results
Multiple regression analysis indicated the following items were variables that significantly related to the NRS: age (β=0.18), active ROM (β =-0.23), KI (β=-0.26), and rumination (β=0.38) (R=0.34, p<0.00).

Conclusion
The results of the present study clarified that in addition to the physical characteristics and functional factors of age and active ROM, KI, which is a process that internally simulates movement, and the condition of rumination, in which the patient fixates on the pain, also were related to postoperative pain after RCR. Therefore, in addition to shoulder joint functional training, neurorehabilitation, which intervenes in the movement simulation process, and patient education to ensure the patient does not fixate on the pain, are essential to reduce postoperative pain.
Title: Expression Of Nmda-Receptors And Substance P In Healthy Human Muscle Tissue

Poster Number PW0190

Authors
A. Alhilou, N. Christidis, B. Cairns, M. Ernberg

Aim of Investigation
Glutamate has been shown to evoke nociceptive responses and muscle pain through the activation of peripheral N-methyl-D-aspartate (NMDA) receptors (NR). Substance P (SP) plays a role in processing nociceptive information. This study aimed to investigate the frequency of nerve fibers that express NR2B-receptors alone or in combination with SP in masseter and tibialis anterior muscles of healthy, pain-free subjects. Another aim was to compare the frequency of expression in men and women and in the two muscles.

Results
There was a significantly higher frequency (P<0.016) of nerve fibers in the healthy tibialis (87.0%) than the healthy masseter (64.3%) muscle that expressed NR2B-receptors. In the masseter, the majority of these fibers (69.1%) were found in the connective tissue (P<0.05) whereas in the tibialis the majority were found in association with myocytes (72.0%; P<0.05). Co-expression of NR2B and SP was found in 28.6% and 46.4% of masseter and tibialis nerve fibers, respectively. In the masseter, most of these fibers (68.2%) were found in connective tissue (P=0.056), while in tibialis most of these fibers (68.6%) were found in association with myocytes, but this difference was not significant (P=0.087). In men, significantly more fibers in the tibialis muscle were found in association with myocytes than with connective tissue (P<0.001) while significantly fewer fibers in the masseter muscle were found in association with myocytes than with connective tissue (P<0.001). No other sex differences were found.

Conclusion
These findings indicate that NR2B-receptors are highly expressed in the masseter and tibialis muscles of healthy individuals. Since it is thought that NR2B-SP co-expressing nerve fibers participate in
nociception, changes in the number of these fibers could prove useful as a potential biomarker of muscle pain.
Title: Sleepiness, Insomnia, And Pain Amongst Nurses

Poster Number PW0191

Authors

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Aim of Investigation
Disturbed sleep and pain are commonly associated, but it is not known whether pain is more related to sleepiness or to insomnia. The aims of this study were to explore cross-sectionally which sleep problem (i.e. daytime sleepiness, insomnia, overall sleep quality) is the most important predictor of musculoskeletal and gastrointestinal pain, when controlling for other work factors and demographics.

Results
According to standardized cutoffs, 17.3% had daytime sleepiness (ESS > 10), 49.8% had insomnia (BIS > 2 in one of questions 1-4 and BIS > 2 in questions 5-6), and 47.6% had poor sleep quality (PSQI > 5). The most commonly reported types of pain were headache (87.79%), back pain (86.25%), and neck pain (73.85%), while the less frequently reported symptoms were pain in left forearm (8.37%) and vomiting (1.83%). Daytime sleepiness (β=0.164, p<.001) and insomnia (β=0.223, p<.001) were significant predictors of musculoskeletal pain severity, while overall sleep quality was not (β=0.064, p>.05), after accounting for the aforementioned work factors and demographics. Age (β=.146, p<.001), exercising to treat musculoskeletal conditions (β=0.113, p<.01) and working in a strenuous environment (β=0.141, p<.001) were also significant predictors of musculoskeletal pain. The impact of daytime sleepiness (t (804) = 4.86, p<.001) and insomnia (t (804)= 4.84, p<.001) in terms of predicting musculoskeletal pain was almost the same. Daytime sleepiness (β=0.100, p<.01) and overall sleep quality (β=0.117, p<.05) were significant gastrointestinal complaints severity predictors, while insomnia was not, after accounting for the aforementioned work factors and demographics. Exercise of high intensity (β=−0.070, p<.05), influence over the work schedule (β=−0.128, p<.001), working from a standing position (β=0.114, p<.01) and having to physically lift unexpected loads (β=0.074, p<.05) were also significant predictors of
gastrointestinal complaints severity. Daytime sleepiness \( (t (804)= 2.87, p<.01) \) had a somewhat greater impact than overall sleep quality \( (t (804)= 2.41, p<.05) \) in predicting gastrointestinal complaints.

Conclusion
The results suggest that, for the present population of nurses, daytime sleepiness is associated with both musculoskeletal and gastrointestinal complaints while insomnia and overall sleep quality are only associated with musculoskeletal pain and gastrointestinal complaints, respectively. Hence, sleep complaints seems to influence somatic symptoms in a differential way. This reflects that it could be important which sleep problems are asked for when investigating the relationship between sleep complaints and pain.
Title: Sex Differences In Experimental Mechanical Allodynia After Injections Of Nerve Growth Factor Into The Human Masseter Muscle

Poster Number PW0192

Authors
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Aim of Investigation
Because it can produce some features of temporomandibular disorders (TMD) myalgia, intramuscular injection of algesic substances is frequently used to induce experimental masseter muscle pain. Unlike hypertonic saline and glutamate, an intramuscular injection of nerve growth factor (NGF) does not induce spontaneous pain, but causes profound and long-lasting mechanical allodynia in human skeletal muscles, which suggests that NGF injection might be a useful experimental model for mechanical muscle alldynia. However, it is not known if there are sex differences in the effects. In this study, NGF was injected into the masseter muscle of healthy participants with the purpose of 1) to study if there are sex differences in mechanical allodynia after NGF-injection and 2) if mechanically induced hyperalgesia by NGF-injection is associated with up-regulation of the expression of pain receptors.

Results
PPT values in the masseter muscle on the experimental side on Day 10 significantly decreased by 58.1 ± 23.4 % (P < 0.001, paired t-test), compared to baseline on Day 7, whereas PPT values on the control side did not change (P = 0.932). Interestingly, decrease of PPT after NGF injection was significantly greater in females than males (females: 65.4 ± 19.9 %, males: 51.3 ± 24.7 %, P = 0.016, t-test). Temporal summation in the masseter on the experimental side was not observed at baseline on either Day 7 or Day 10. Significantly higher scores of both pain intensity (P < 0.001, paired t-test) and fatigue level (P < 0.001, paired t-test) after the chewing test, as well as JFLS scores, were reported on Day 10, compared to Day 7 (P < 0.001, paired t-test). Furthermore, female participants scored significantly higher scores than male participants in the masticatory part of JFLS on Day 10 (females: 23 ± 10, males: 14 ± 11, P = 0.047, t-test). Expression of biomarkers in the biopsy samples involved in pain signaling is currently being analyzed.
Conclusion
The results of this study showed a more profound mechanical allodynia in healthy women than men after NGF-injection into the masseter muscle, which corroborates clinical findings in TMD patients. Analyses currently being performed will reveal if the mechanical allodynia induced by NGF is associated with up-regulation of pain biomarkers and if there are sex differences in their expression.
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Title: Effects Of Intranasal Oxytocin On Heart Rate Variability In Chronic Neck And Shoulder Pain

Poster Number PW0193

Authors
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Aim of Investigation
Chronic neck-shoulder pain (CNSP) is a common musculoskeletal disorder in working populations (1). Previous studies have demonstrated that persons with chronic CNSP display autonomic imbalance (i.e., an imbalance between the sympathetic and parasympathetic nervous systems; 2). Heart rate variability (HRV) refers to the variability in the interval between successive heart beats and is a non-invasive tool for measuring autonomic modulation of the heart. Reduced HRV is associated with a plethora of poor long-term health outcomes (3). Chronic pain patients have been shown to have reduced HRV compared to healthy controls, particularly with respect to the vagally-mediated high-frequency (HF) HRV (4). Oxytocin (OXT) is a hormone primarily synthesised within the hypothalamus (5), and was initially known for its role in the contraction uterine muscles during childbirth (6). However, in the central nervous system OXT acts as a neurotransmitter in regions such as the hypothalamus and amygdala (7), two regions involved in the control of autonomic activity (8) and the perception of pain (9). Therefore it may be possible that centrally released OXT plays a role in the modulation of autonomic activity in persons with chronic pain. The aim of this study was to investigate the effects of intranasal OXT on HRV in persons with CNSP.

Results
Participants had significantly lower lnHF after OXT (M = 5.44, SD = 1.08) during the paced breathing task compared to PLB (M = 6.09, SD = 0.52; p = .038, d = .81). Participants also had a significantly lower LF/HF ratio during the paced breathing task (M = 0.95, SD = 0.20) compared to the SST (M = 1.27, SD = 0.15) following OXT administration (p = .006, d = 1.82). No other significant differences between OXT and PLB were observed for the paced breathing task, and there were no effects of OXT on HRV during the SST.
Conclusion

These preliminary findings suggest that OXT may modify the autonomic imbalance associated with CNSP. A more accurate determination of the effect will become clear when this study completes recruitment of the full sample. OXT may ultimately have utility as a therapeutic agent to aid chronic pain management, either to target autonomic imbalance or as a potential novel analgesic.
Title: Increased Fatty Infiltration In The Right Sternocleidomastoid Muscle In Individuals With Extensive Neck Disability Due To Chronic Whiplash Associated Disorders

Poster Number PW0194

Authors

Aim of Investigation
The aim of the study was to investigate muscle fatty infiltration of anterior neck muscles in patients with chronic WAD compared to age and gender matched healthy controls. Another aim was to investigate the correlation between fatty infiltration and pain intensity/neck disability/physical measures of the neck. Both the flexors and extensor neck muscles are important for functional movement and postural control of the neck. Increased fatty infiltration in the longus colli (Lco)/capitis (Lcap) and Sternocleodomastoid (SCM) muscles in women with chronic whiplash-associated disorders (WAD) has been quantified, however, the precise mechanisms underlying muscle degeneration and their influence on pain-related disability and WAD recovery are largely unknown. It is plausible such degenerative changes could contribute to persistent pain-related deficits in movement and postural control common to WAD.

Results
Individuals with extensive disability (NDI ≥40%) had significantly (p=0.02) higher content of fatty infiltration on the right SCM compared to healthy controls. Otherwise there were no statistical differences between the three groups. Except for a moderate correlation between left SCM and NDI (r=0.51, p=0.02) and a low correlation between right Lco and pain intensity (r=0.43, p=0.05), there were no significant correlation between fatty infiltration and pain intensity/NDI/physical measures.

Conclusion
Individuals with extensive pain-related disability following whiplash demonstrated a higher fatty
infiltration in the right SCM, which may have implications for altered biomechanics of the neck and postural stability. Only a few low/moderate correlations between fatty infiltration and pain/NDI/physical measures were found. A prospective study comparing men and women with varying levels of WAD-related disability and to healthy age-matched controls matched is warranted.
Title: Pain And Disability Changes With Manual Therapy In Whiplash And Mechanical Neck Pain Patients: An Experimental And Clinical Study

Poster Number PW0195

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Aim of Investigation
Manual therapy and exercise are often proposed as treatments for neck pain, and numerous systematic reviews support that. There is evidence supporting that whiplash (WAD) patients shows more signs of sensitization than mechanical neck pain (MNP) patients, and this could lead to different responses with manual therapy treatment. The aim of this experimental and clinical study was to compare the effect of 1 as well as of 6 standardized manual therapy (MT) treatment in patients with MNP and WAD.

Results
51 patients (23 MNP and 28 WAD) were included in the study. The WAD group had at baseline (before 1st treatment) the lowest (p=0.012) PPT at tibialis anterior, the lowest flexion ROM (p=0.038), and the highest NDI (p=0.012); no other significant difference were found at baseline. The 2 study groups showed a significant difference for improvement in NPRS between baseline and post-1st treatment assessment (p=0.005), between baseline and post-2nd treatment assessment (p=0.000), between pre-2nd treatment assessment and post-2nd treatment assessment (p=0.004), between baseline and post-6th treatment assessment (p=0.004), and between pre-6th treatment assessment and post-6th treatment assessment (p=0.029), with the MNP group having a larger improvement in NPRS at all time points. Furthermore, the 2 study groups showed a significant difference in NDI changes between baseline and post-6th treatment assessment (p=0.027), with the MNP group having most improvement in NDI. Thus, the most sensitized group (WAD) showed lower improvement in NPRS and NDI as compared to MNP group: this support the idea that once widespread hypersensitivity develops, it may represent a limit to MT efficacy.

Conclusion
The WAD group had the most pronounced widespread hyperalgesia (lowest PPT at tibialis anterior) at
baseline, and in general benefitted less in terms of pain and disability by the standardized MT. WAD patients may require a different and more complex approach to manage their pain (due to the generalized hypersensitivity), and even extended MT will not help, as suggested by previous studies, indicating that short and long treatment period in WAD gives the same results.
Title: Evaluation Of Pain-Related Factors In Adults With Cerebral Palsy With Chronic Neck Pain

Poster Number PW0196

Authors

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Aim of Investigation
Adults with cerebral palsy (CP) have a significantly higher prevalence of chronic disabling pain than that in the general population. Neck pain is one of the most common musculoskeletal complaints in adults with CP. Although compensatory increased cervical lordosis and compensatory movements in the spine were reported, no significant correlation was found between pain and motor impairment, postural asymmetries, or spasticity; therefore, the mechanism underlying neck pain in adults with CP remains unclear. Recent studies have shown that chronic neck pain is associated with maladaptive beliefs, such as pain catastrophizing and fear of movement; perpetual dysfunction, such as subjective sense of expanded or shrunken body image; and decreased tactile acuity. However, none of these studies included adults with CP. The purpose of the present study was to examine whether maladaptive beliefs and body perception are different between adults with CP with and without neck pain.

Results
Participants were distributed across the following gross motor function classification levels: level I, n = 1; level II, n = 1; level III, n = 2; level IV, n = 3; and level V, n = 4 as the pain group and level I, n = 2; level II, n = 1; level III, n = 2; level IV, n = 2; and level V, n = 2 as the no pain group. Differences were identified between the pain and no pain groups in PCS (26, 21–35 vs 8, 3–3.5), TSK (40, 35–44 vs 29, 27–37), and FreNAQ (10, 7–19 vs 3, 0–5) (all p < 0.05). Although the TPD distance in cheek were not significantly different between the pain and no pain groups (15, 12.5–20 vs 15, 10–21.2), the TPD distance threshold in the neck was significantly larger for the pain group than for the no pain group (40, 37.5–45 vs 35, 30–40.6) (p < 0.05).

Conclusion
Our results suggest that PCS, TSK, and FreNAQ scores and TPD distance threshold in neck are higher in
the pain group than in the no pain group in adults with CP. Cognitive behavioral therapy for maladaptive beliefs and sensory motor retraining for distorted body perception may be used for chronic neck pain in adults with CP as well for patients with chronic neck pain without CP.
Title: Prognostic And Prescriptive Clinical Prediction Rules For Neck Pain Require Further Validation And Impact Analysis: A Systematic Review

Poster Number PW0197

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Aim of Investigation
To identify prognostic and prescriptive clinical prediction rules (CPRs) relevant to the conservative management of adults with neck pain and appraise stage of development, quality and readiness for application in clinical practice.

Results
A total of 8,837 records were retrieved and screened for eligibility, of which 33 studies reporting on 27 CPRs were included in the review. Most CPRs (n = 17) were at the derivation stage of development. Four prognostic CPRs using neck disability, work disability and self-perceived recovery as outcome measures in acute whiplash (n = 3) and non-specific neck pain (n = 1) populations, have been successfully validated. No studies supported the validity of any of the identified prescriptive CPRs (n = 11). No impact analysis studies were identified. The quality of included studies varied considerably. Insufficient sample size (n = 18), incomplete reporting of statistical analyses and model performance (n = 11), and use of an inappropriate study design for the type of CPR being developed (n = 7) were identified as prominent methodological issues.

Conclusion
Most CPRs reported in this review are not yet ready for clinical application because of their early stage of development and moderate methodological quality. Four validated prognostic CPRs may be considered for use with caution where clinical setting and patient population is comparable to that of the development studies. It is recommended that these models be used in combination with other assessment techniques and/or clinical decision-making strategies until further validation and impact analyses are completed.
Title: Effects Of Manual Home Cervical Traction In Chronic Neck Pain

Poster Number PW0198

Authors
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Aim of Investigation
To find out the effects of manual home cervical traction on the patients with chronic neck pain.

Results
Base lines characteristics of the patients in both the group were identical. In group –A, there were 73 patients initially, but 12 patients were dropped out from the study because of their irregularities to take treatments. So, there were 61 patients participated in the clinical trial and they took treatments and all suggestions properly. There was marked improvement of the condition of the patients in response to treatment for 6 weeks. The numerical data of pre-treatment and after treatment assessment scores were compared statistically (paired student’s ‘t’ test) and found highly significant (P = 0.007. 95% CI =7.09 to 8.80). So, home cervical traction was found significantly effective to reduce the sign & symptoms of chronic neck pain. In group – B, there were 72 patients initially, but 8 patients were dropped out from the study because of their irregularities to take treatments. There were 64 patients participated in the clinical trial. There was improvement of the condition of the patients in response to treatment for 6 weeks. The numerical data of pre-treatment and after treatment assessment scores were compared statistically (paired student’s ‘t’ test) and found highly significant (p = 0.01, 95% CI= 5.21 to 6.81). So it was also found effective to reduce the sign & symptoms of cervical spondylosis. Overall comparative improvement between two groups: At the time of first visit, there was no significant improvement between two groups (P= 0.36, 95% CI= -0.56 to 1.51) but on the other hand there was significant improvement in Group-A than Group-B after six weeks treatment (P= 0.003, 95% CI= -2.40 to -0.51). This results indicates that the improvement of the patient with chronic neck pain was seen more in home cervical traction group than other group who received some rehabilitation treatment without cervical traction.

Conclusion
It may be concluded that home cervical traction is beneficial for the patients with chronic neck pain.
Date: 09/28/2016 03:15:00 PM

**Title:** Distinct Spinal And Supraspinal Pain Modulation After Spinal Cord Injury

**Poster Number** PW0199

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**Aim of Investigation**
Accompanying neuropathic pain (NP) symptoms at and below the level of spinal cord injury (SCI), studies adopting quantitative sensory testing have reported evidence of altered sensation in otherwise intact dermatomes. While above level changes have been postulated as a function of chronic activation of descending inhibitory control pathways responding to the presence of neuropathic pain (i.e., conditioning stimulus), few studies have explicitly examined endogenous pain modulation. The present study aimed to address endogenous pain modulation in individuals with SCI. The primary objective of the study was to reveal if the endogenous pain modulation above the lesion level is altered by the presence of NP. Applying TENS as a conditioning stimulus, utilizing segmental homotopic (i.e., ipsilateral) and heterotopic (i.e., contralateral) stimulation locations to discern spinal and supraspinal modulation. Individuals with SCI (with and without NP) and healthy control individuals (without NP) participated in a crossover-designed study. Perception to non-noxious and noxious afferent stimuli was examined before and after homotopic and heterotopic TENS. Our primary hypothesis was that individuals with SCI and NP would have an altered capacity to modulate perception to noxious afferent stimuli above the level of injury, which was associated with the severity of NP.

**Results**
In total, we enrolled 15 healthy control individuals (mean (SD) 46.07 (9.5) years; gender: 1 female, 14 male) and 34 individuals with traumatic SCI (47.0 (11.0) years; gender: 2 female, 27 male). Two individuals with SCI had to be excluded due to incomplete dataset (i.e., drop-out). Lesion level included cervical (n=5), thoracic (n=22), and lumbar injuries (n=5). According to the ISNCSI impairment classification, 16 of 32 individuals with SCI had complete (1 tetraplegic, 15 paraplegic) and 16 incomplete (4 tetraplegic, 12 paraplegic) injury of the spinal cord. From the individuals with SCI, 19 individuals (18 with paraplegia, 1 with tetraplegia) suffered from neuropathic pain (SCI-NP). The mean and maximal pain intensities were 4.2 ± 2.2 and 6.5 ± 1.9, respectively, and the duration of ongoing pain ranged from
3 to 35 years (mean 10.5 +/- 7.8 years). In individuals with SCI and NP, behavioral responses to capsaicin and contact heat pulses were significantly lower compared to pain-free individuals (i.e., SCI and healthy controls). Briefly, healthy control individuals and pain-free individuals with SCI reported significantly higher ratings (NRS Controls=4.9±2.1; NRS Pain-freeSCI =4.7±2.6) than individuals with SCI-NP (NRS SCI-NP =3.7±1.8). Homotopic TENS significantly reduced capsaicin-evoked pain in all individuals with SCI and healthy individuals (all p<0.001). Pain-free individuals and healthy control individuals also experienced pain-relief in response to TENS applied heterotopically. In comparison, individuals with SCI-NP did not demonstrate significant modulation in response to heterotopic TENS (p=0.053). The reduction of capsaicin-evoked pain was correlated with the intensity of reported neuropathic pain. Homotopic TENS also resulted in significant relief of thermally evoked contact heat pain in the area of capsaicin application across all three groups (all p<0.001). Notably, the NRS was decreased relative to pre-TENS values (i.e., after 30 minutes of capsaicin). Similarly, segmental heterotopic TENS had modulatory effects on thermally evoked pain in healthy control individuals and pain-free individuals with SCI (all p<0.001). In contrast, heterotopic TENS resulted in no significant thermally evoked pain relief in individuals with SCI suffering from NP (p=0.59).

**Conclusion**

In response to homotopically applied TENS, healthy controls and individuals with SCI (i.e., NP and pain-free) demonstrate robust modulation of experimentally modeled thermal hyperalgesia. However, when applying heterotopic TENS (i.e., contralateral to the test site) a significant modulation of noxious test stimuli occurred only in individuals not suffering from pre-existing NP (i.e. controls and SCI). The distinct responsiveness between heterotopic (non-effective) and homotopically (effective) applied TENS suggests different mechanisms underlying modulation. Homotopically applied TENS may be considered to have an immediate effect onto spinal pain modulation. In contrast, heterotopic TENS is rather relying on supraspinal descending control mechanisms that might be already engaged in SCI patients suffering from chronic NP. Collectively, our results indicate that the supraspinal modulation of noxious input is reduced after SCI in individuals with NP. This may be the result of engagement by below-level NP. In contrast, spinal modulation remains fully intact. To our knowledge, this is the first time a clear distinction between homo- and heterotopic TENS mechanism has been demonstrated in humans.
Title: Involvement Of Adrenomedullin In The Development Of Bone Cancer Pain And Neuropathic Pain

Poster Number PW0200

Authors
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Aim of Investigation
Adrenomedullin (AM) is a member of the calcitonin gene-related peptide (CGRP) family and has been demonstrated to be a pain peptide. This study investigated the possible involvement of AM in the pathogenesis of bone cancer pain and neuropathic pain and its underlying mechanisms.

Results
The mRNA or protein levels of AM and the AM receptor components calcitonin receptor-like receptor (CLR) and receptor activity-modifying protein 2 (RAMP2) were increased in the spinal cord and DRG in bone cancer pain. AM protein was also increased in the injured L5 and uninjured L4 DRG neurons in SNL animals. The intrathecal administration of AM22-52 significantly attenuated mechanical allodynia in the both models. The administration of AM22-52 also abolished the increase of AM and nNOS expressions in the DRG of cancer pain animals and the increase of AM in the L4 DRG and the decrease of CGRP in the L5 DRG of SNL rats.

Conclusion
Enhanced AM receptor activity recruited the pronociceptive mediator nNOS or CGRP contributing to the pathogenesis of bone cancer pain and neuropathic pain.
Title: Hyperactivity Of Spinothalamic System Around Cerebro-Vascular Lesion On The Sensory Thalamus In The Genesis Of Central Post-Stroke Pain

Poster Number PW0201

Authors
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Aim of Investigation
We studied the essential factors in the genesis of CPSP, particularly functional changes of thalamo-cortical system, based on the data of intraoperative thalamic microrecording and microstimulation. We also studied the effectiveness of thalamic ventralis intermedius (Vim) - ventralis caudalis parvocellularis (Vcpc) or Vim-Vcpc-centralis lateralis (CL) stimulation for pain relief in cases with central post-stroke pain (CPSP).

Results
SEPs (N13, N20) were flat or markedly decreased in all examined cases. From the data obtained by electrophysiological study on the thalamus during surgery, we could classify these patients into 3 groups. In group A (3 cases), we encountered irregular long-duration burst discharges frequently and no SR in the sensory thalamus. The perceptive field to microstimulation was not compatible with the receptive field to peripheral natural stimulation. In group B (3 cases), we encountered burst discharges frequently, which were recognized around decreased or voided areas of thalamic neural activity. We found SR in the limited area of the thalamic sensory nucleus. In group C (3 cases), we rarely encountered bursts and found SR frequently in the wide area of the thalamic sensory nucleus. Long-lasting good pain relief was achieved in group B (3 cases), moderate in group A (3 cases), and fair in group C (3 cases), depending on the level of functional change of sensory thalamus. Pain relief was recognized during chronic thalamic stimulation on the rostroventral part of surrounding area of the CVD lesion, where irregular burst discharges were frequently found. In group B, sensory responses were encountered on the ventral part of this area, where corresponds to thalamic Vim-Vcpc nucleus.

Conclusion
We found both severe dysfunction of the lemniscal system and moderate to severe functional change of the spino-thalamo-cortical system on the thalamus in cases with diffuse type CPSP. It has been
suggested that these functional changes, which were focal hyperactivity or electrical unstability around the CVD lesion in the affected sensory thalamus, affect perception or conduction of sensory impulses in the lateral sensory thalamus, resulting in the genesis of CPSP. Sufficient and long-term pain relief was obtained using thalamic Vim-Vcpc-CL stimulation in cases with CPSP.
**Title:** Subgroup Perspectives On Living With Chronic Pain After Spinal Cord Injury

**Poster Number** PW0202

**Authors**
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**Aim of Investigation**
The present study is part of a larger mixed-methods study concerning positive (facilitators) and negative (barriers) contributors to living with chronic pain after a spinal cord injury (SCI). Commonly endorsed themes based on qualitative interviews were rated in a large online survey including people with SCI living with chronic pain. Based on these data common facilitator dimensions (i.e., Information regarding pain and treatments [Info]; Resilience [Res]; Coping [Cope]; Medication use [Med]) and barrier dimensions (i.e., Poor communication from provider [Poorcomprov]; Pain impact [Imp]; Poor ability to communicate about my pain [Poorcom]; Difficult nature of pain [Diffpain]; Treatment concerns [Treatcon]) were defined. Due to the variability in perspectives among individuals, the primary purpose of the present study was to: (1) Define subgroups based on cluster analysis of the facilitator and barrier dimensions, and (2) Characterize the subgroups with respect to pain-related variables.

**Results**
The cluster analysis resulted in 3 significantly different (p<0.001) subgroups: 

- **Group 1** (50.1%) had the highest factor scores on Info, Cope, Med and Imp, Poorcom, Diffpain. This group had more intense pain (7.15±1.56), more pain with neuropathic characteristics, greater pain impact, affective distress, and lower life control than the other subgroups. Thus, people experiencing severe pain with substantial life impact utilize multiple ways to cope with pain in addition to medication. They also perceive that information about pain and its management is critical, but feel that they are not able to communicate adequately about their pain.

- **Group 2** (28.8%) had high factor scores on Info, Res, Cope, Treatcon, and low factor scores on Med and Poorcom. Their average pain intensity was in the high moderate range (6.45±1.59) with moderate levels of pain impact, affective distress, and life control. They utilize multiple...
ways to cope with pain, carry on despite pain, use less medication due to concerns about side-effects and addiction, and perceive that information about pain and its management is critical. Group 3 (21.1%) had the lowest factor scores on Info, Cope, Poorcomprov, Imp, Poorcom, and Diffpain. This group also had the lowest pain interference, difficulty dealing with pain, affective distress, and neuropathic pain characteristics. Despite a moderately high average pain intensity (5.91±1.64), people in this group experienced less impact on life and perceived information about pain and its treatments to be less important compared to the other groups. Communication between them and their providers was also less of an issue in this group.

Conclusion
This study shows that people with more severe pain have different perspectives on pain, and its management, compared to those with less severe pain. This is possibly due to a number of factors including the presence of more persistent neuropathic pain types and greater overall difficulty in dealing with this type of pain. This study suggests that treatment approaches need to be individually tailored, not only to type of pain, but also to personal factors and preferences.
Title: Serious Complication Of Spinal Cord Stimulation For Intractable Pain Relief: Case Report

Poster Number PW0203

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Aim of Investigation
Spinal cord stimulation (SCS) is an effective therapy for different types of chronic pain. It is a reversible method. Although it is believed to be safe, adverse effects by SCS is high. Serious complication is very rare. We experienced such a case and discuss a preventive way.

Results
Adverse effects after operative procedure for spinal cord stimulation can be divided into two categories, hardware-related complications and biological complications. The former includes electrode displacement, electrode fracture, hardware malfunction, insulation damage, electrical leak, etc. The latter includes infection, hematoma (subcutaneous, epidural or intraspinal) and CSF leakage. Injuries to the nerve root or spinal cord are rare. Severe neurological complications can result from intraoperative root or spinal cord injury or spinal cord compression by intraspinal clot or epidural hematoma. Recently it has been reported that epidural fibrosis or scar tissue can develop spinal cord compression. In our case, test stimulation dramatically decreased the intractable pain and increased muscle power. Although stable paddle electrode was implanted, tetraplegia occurred postoperatively against expectation. Epidural hematoma or laceration of dura mater were not recognized on re-operation. The exact cause of cervical cord compression is speculative. The size of paddle electrode are larger than that of cylindrical electrode. Previous cervical operation may aggravate stenosis of cervical canal. Epidural electrode may rotate after change of body position.

Conclusion
We have to check the condition of spinal stenosis no matter how transient or permanent. We have to be very careful for exchange of epidural electrode from cylindrical type to paddle type. We had better avoid this change when cylindrical electrode is successful.
Title: Motor Cortex Stimulation: Our Experience With Seven Patients

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Aim of Investigation
Motor cortex stimulation (MCS) was first used in 1988, and published by Tsubokawa et al. in 1991. Although several case series and studies have been published, the indications vary considerably, and there is not a consensus about the effectivity of the therapy. Despite an important relief of pain during the first months, there is a significant percentage of patients losing pain relief over time, according to the medical literature. Our group, like some others, believes that this therapeutic option continues to be perfectly valid.

Results
Our group of 7 patients is composed by 4 patients with pain related to deep intracerebral hemorrhage and 3 patients with thalamic ischemic stroke. The best pain relief was found in the first group, with a pain relief of 85-90% in the VAS scale (from a mean value of 9-10 pre-implant to 0-2, one year later) while the pain relief in the second group were 10-15%.

Conclusion
Based on our results, we conclude that the MCS is a good therapeutic option for a selected type of patients with pain refractory to other treatments.
Title: Outpatient Intravenous Ketamine Infusion For Management Of Central Neuropathic Pain: An Observation Study

Poster Number PW0205

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Aim of Investigation
Central neuropathic pain is caused by a lesion or disease of the central somatosensory nervous system. Central pain can be spontaneous or stimulus-evoked and may involve dynamic mechanical allodynia, cold allodynia, paresthesia and dysesthesia. The pain can occur immediately at disease onset or can be delayed for several months & can be present from a small area to a large area. It is also associated with emotional distress and lower health-related quality of life. Central sensitization and ongoing discharges in central pain pathways contribute to the development of central pain. Other important mechanisms of chronic (neuropathic) pain development include phosphorylation and upregulation of the N-methyl-D-aspartate receptor (NMDAR), loss of descending inhibition, plastic changes in the spinal cord and activation of immune cells in the spinal cord with the release of pro-inflammatory cytokines. Treatment includes antiepileptic drugs (e.g., gabapentin or pregabalin), antidepressants (e.g., amitriptyline, imipramine, or duloxetine), and other drugs. Nonpharmacological approaches include cognitive-behavioral therapy, hypnosis, and neurostimulation therapies. Irrespective of treatment, efficacy is limited with just 30-40% of patients showing adequate to good pain relief. In chronic pain states prolonged nociceptive stimulation causes activation and upregulation of the NMDAR at dorsal horn synapses resulting in enhanced and amplified trafficking of pain signals to the brain (central sensitization). Ketamine produces strong analgesia in neuropathic pain states, by blocking the NMDAR. It is able to halt the excessive barrage of nociceptive input to the brain and also enhances the central descending inhibitory pathway. Ketamine has potent antidepressant qualities and hence has a positive effect on depressive symptoms. In this study we were aiming to find out the effectiveness and the safety of IV ketamine infusion in case of central neuropathic pain who have failed conservative treatment. We would also like to find out the appropriate dosing for IV ketamine infusion in such patients.
Results
The VAS Score of 5, 20 & 45 days showed significant reduction (decreases of 2) in 82.5% patients, no significant reduction in 15% pts and no reduction 2.5% pts. The disability score showed reduction in 80% pts. The physiological scores showed improvement in 90% pts. No significant adverse drug reaction was reported by any patient.

Conclusion
Intravenous ketamine infusion is a good modality for providing significant pain relief along with improvement in the disability and physiological well-being of the patient. Considering the small sample size and short duration of the study further multi-centric studies with long-term follow-up is required for it to be accepted as standard modality of treatment. Until definite proof is obtained ketamine administration should be restricted to patients with therapy-resistant severe neuropathic pain.
Title: Anxiety Affecting Disability And Quality Of Life In Patients With Painful Diabetic Neuropathy

Poster Number PW0206

Authors
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Aim of Investigation
Painful Diabetic Neuropathy (PDN) is known to negatively affect psychosocial functioning as expressed by enhanced levels of anxiety and depression, leading to disability and suboptimal glycemic control. The aim of this study was to specify diabetes and pain related fears and to identify predictors for disability and quality of life (QoL).

Results
This study included 159 patients (99 male, 62%). Mean age was 66.4 years (SD=6.4). Pain intensity (β=0.23; p<0.01), HFS (β=0.25; p<0.01) and FES-I (β=0.44; p<0.01) showed to be predictors for QOL-DN and accounted for 65% of the variance (R =0.65). Pain intensity (β=0.26; p<0.01) and FES-I (β=0.51; p<0.01) were predictors for PDI and accounted for 60% of the variance (R =0.60).

Conclusion
Pain intensity and fear of falling are important predictors for QoL and disability in patients with PDN. Interestingly, also fear of hypoglycemia showed to be a predictor for disability. Unraveling fears in PDN enables clinicians to identify specific targets for behavioral interventions (e.g. Graded Exposure in vivo) in order to improve the physical and psychosocial well-being in patients with PDN.
Title: X-Linked Adrenoleukodystrophy And Pain In Sons And Mothers

Poster Number PW0207

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Aim of Investigation
X-linked adrenoleukodystrophy is the most frequent peroxisomal disease. It is caused by mutation of the gene ABCD1, which encodes the protein ALDP, an ATP-binding cassette transporter located in the peroxisomal membrane. ALDP deficiency impairs peroxisomal β-oxidation of very long chain fatty acids (VLCFA), which remain in the cytoplasm and become the substrate for their further elongation by the enzyme ELOVL1. An excess of VLCFA in plasma and tissues is toxic, with the main damage affecting both the central and peripheral nervous systems and in some cases also the adrenal cortex (Addison’s disease). Although X-ALD mostly affect males, carrier mothers can also show some symptoms.

Results
For several of these parameters there was a generally worse condition, both emotionally and physically, in the mothers than in the sons. In particular, they reported painful symptoms more than their sons: 6/18 sons reported a painful condition while 8/10 mothers reported pain. Pain was present mostly in the lumbar region and lower legs. Pain features were very different among subjects, both in the mother and son groups. Regarding the POMS data, the two groups showed different (pathological) levels, with most of the parameters being worse in the mothers. A similar result was found for the SF-26 data, with sons having better scores than their mothers.

Conclusion
X-ALD is considered a male pathology, the mothers being considered only carriers. However it is increasingly evident that the disease also affect the mothers and for some aspects (pain) to a greater degree than their sons. The variability found among patients of the same and different sex is probably due to the absence of correlation between the X-ALD genotype and phenotype.
Title: Neural Regeneration Capacity In A Human Model Of Neuropathic Pain

Poster Number PW0208

Authors
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Aim of Investigation
Peripheral neuropathies are characterised by neuronal dysfunction, but often involve frank axonal degeneration. Specifically, the presence of small fibre degeneration and its role in neuropathic pain conditions has gained increasing interest in the past decade. The regeneration capacity of small nerve fibres has been extensively studied in animal models, but remains elusive in humans. A better understanding of neural regeneration in patients with peripheral neuropathies would facilitate the development of novel treatment strategies. We have recently identified structural degeneration of small diameter neurones in patients with carpal tunnel syndrome (CTS). CTS is one of the rare neuropathic pain conditions which can be treated surgically and therefore provides a unique model that allows the prospective evaluation of neural regeneration.

Results
At 6 months post surgery, 77% of patients rated their symptoms as at least 'a great deal better' compared to only 30% of patients without surgery. Concomitantly, postsurgical recovery of median nerve neurophysiology was apparent (p<0.0001), but remained incomplete in most patients. No significant neurophysiological changes were found in patients without surgery (p=0.125). QST revealed a significant postoperative improvement in both small and large fibre function as determined by a normalisation of thermal and vibration detection thresholds (p<0.004). Without surgery, the somatosensory phenotype either remained unchanged (p>0.460) or deteriorated (e.g., cold detection p=0.027). This was accompanied by a progressive decline in IENFD in patients who did not undergo surgery (p=0.007). In contrast, epidermal small fibres regenerated at least partly 6 months after surgery (p=0.043). Interestingly though, most patients failed to reach normal IENFD and there was substantial variation in the extent of small fibre regeneration between patients.
Conclusion
Using CTS as a model to study small fibre regeneration, we identified a significant postoperative improvement in small and large fibre function. Structural regeneration of small fibres was also apparent, but failed to reach normal levels even at 6 months post surgery, when symptoms of most patients have vanished. We are currently searching for molecular signatures which correlate with small fibre regeneration in the context of peripheral nerve injury. A better understanding of nerve regeneration in humans may lead to the identification of therapeutic targets.
Title: Oxaliplatin-Induced Neuropathy: Axonal Excitability Changes And Acute Symptoms

Poster Number PW0209

Authors
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Aim of Investigation
The chemotherapeutic agent oxaliplatin induces a dose-limiting acute neuropathy characterized mainly by paresthesia and cold-evoked symptoms. The aim of this study was to examine multiple sensory and motor excitability parameters in patients with acute oxaliplatin-induced neuropathy and to correlate these to sensory symptoms and signs in order to investigate the underlying pathophysiological mechanisms.

Results
The most frequent symptoms after oxaliplatin treatment were tingling paresthesia in the hands (100%), feet (42%) and orofacial area (50%), and throat discomfort (100%). Patients experienced significantly more pain (p=0.004), unpleasantness (p=0.004) and pricking (p=0.003) after holding a cold metal cylinder at the post-infusion examination than at the recovery examination. Nine patients presented electrophysiological signs of motor afterdischarges and repetitive firing at the post-infusion examination, which resolved at recovery examination. The most prominent axonal excitability changes were seen in the motor recovery cycle where we found significantly decreased superexcitability at the post-infusion examination compared to the recovery examination and healthy controls. There was a correlation between the decrease in motor superexcitability (percentage) and pain intensity from holding the cold metal cylinder (Spearman Rho: 0.60, p=0.041) as well as the average intensity of abnormal sensations (Spearman Rho: 0.78, p=0.0031). The strength duration time constant was significantly decreased with a corresponding increase in rheobase in both motor and sensory axons at the post-infusion examination in comparison with recovery examination and healthy controls. In
contrast, threshold electrotonus and I/V relationship were normal in both sensory and motor nerves and sensory recovery cycle parameters were normal.

**Conclusion**
Paresthesia/dysesthesia and cold allodynia were the most pronounced acute symptoms after oxaliplatin treatment. We found no changes in sensory nerve excitability parameters. Changes in motor nerve excitability parameters are probably caused by repetitive activity. Axonal excitability tests suggest that oxaliplatin neurotoxicity involves terminal axons rather than the nerve trunk.
Title: Study Of Modulating Microglia Activation And Neuropeptide Expression In The Cuneate Fasciculus After Multiple Cervical Root Transection

Poster Number PW0210

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Aim of Investigation
Study how adipokines modulating inflammation after multiple cervical roots transection

Results
Our preliminary data showed adipokines may play an important role in neuronal peptides induction, which in turn causes neuropathic pain after cervical root injury. In this study, we examined it's expression in the cuneate fasciculus, which involved in neuropathic pain pathway, after multiple cervical roots transection (MCT) in SD rats, B6 mice, and mutant mice. Sham operations with laminectomy alone without root transection were used as control. Our results demonstrated that there was almost no CGRP immunoreactivity detected in the cuneate fasciculus of the sham-operated rats. In contrast, there was a significant increase immunoreactivity in cuneate fasciculus of the lesion side of both SD rats and B6 mice in the MCT group; most of the immunostaining cells colocalized with activated microglia. The expression of CGRP was also increased in the cuneate fasciculus, which most of these neuronal peptides-positive fibers co-localized with it's receptor. To the contrary, MCT in the mutant mice caused neither microglia activation nor CGRP expression in the cuneate fasciculus, but these phenomenons reversed by combination of MCT with exogenous treatment.

Conclusion
Our data suggested that adipokine plays an important role in modulating microglia activation after MCT, which in turn increases neuropeptides expression. Since neuropeptide expression has long been thought
to be associated with abnormal sensory perception, we therefore suggested that adipokine might be a potential therapeutic target for the treatment of neuropathic pain in patients with MCT in the future.
Title: Vc1.1, An A-Conotoxin, Reverses Mechanical Allodynia And Inhibits Ectopic Discharge In Neuropathic Pain Models

Poster Number P0211

Authors
F. Zhao, H. Wei, A. Whyment, N. Michael, A. Robinson, D. Adams, D. Spanswick

Aim of Investigation
It has been suggested that the α-conotoxin Vc1.1 exerts its analgesic effect via an action at nicotinic acetylcholine receptors (nAChR) and/or via GABAB receptors coupled to N-type voltage-gated calcium channels (VGCC). To further explore the utility of Vc1.1 for various pain conditions and the site and mechanisms of action of this compound, we have examined the effects of Vc1.1 on mechanical allodynia and ectopic discharge (ED) of peripheral nerves in rat models of neuropathic pain (chronic constriction injury, CCI and Chung models). We have also examined the cellular/ionic mechanisms of action of Vc1.1 in spinal cord slice preparations and acutely isolated dorsal root ganglion (DRG) neurones from neuropathic pain models.

Results
In behavioural studies, i.m. injected Vc1.1 dose-dependently reversed the mechanical allodynia in CCI rats. At a dose of 0.1 mg/kg, Vc1.1 increased the PWT from the baseline level of 2.38 ± 0.26 g to 4.75 ± 0.37 g, 5.75 ± 0.41 g, 7.75 ± 1.26 g, 5.25 ± 0.70 g and 4.75 ± 1.08 g at 1, 2, 4, 6 and 24 hours post-dosing (P < 0.05 to 0.01). In vivo electrophysiology revealed that following i.v. Vc1.1 dosing at 0.1mg/kg, ED of neuroma and DRG-origin was reduced to 39% and 37% of control level, respectively (P < 0.05 and 0.01, compared to the saline group, n=3-4). In lamina I/II dorsal horn neurons, Vc1.1 (300 nM) induced a membrane hyperpolarisation of -6.4 ± 1.1 mV (n=5) associated with a reduction in neuronal input resistance. Voltage-current relations indicated membrane hyperpolarisation induced by Vc1.1 was associated with activation of an inwardly rectifying potassium conductance. Whole-cell patch clamp
recordings from DRG neurones revealed no obvious change in passive membrane and subthreshold active conductances in these neurones in the presence of Vc1.1. However, a distinct reduction in the action potential duration and repolarisation phase of action potentials was observed in a subset of DRG neurones.

**Conclusion**
Vc1.1 significantly reverses mechanical allodynia in neuropathic rats and reduces ectopic discharge in peripheral nerve. This effect is partly mediated via a reduction in ectopic discharge associated with injured peripheral nerves. The analgesic mechanism of action of this compound involves activation of receptor-signal transduction pathways consistent with activation of an inwardly rectifying potassium channel at the level of the dorsal horn and inhibition of a conductance contributing to action potential firing at the level of the DRG.
Correlation Between Corneal Confocal Microscopy And Quantitative Sensory Testing Parameters In A Multicentre, Mixed Aetiology Neuropathy Cohort

Aim of Investigation

Corneal confocal microscopy (CCM) is a non-invasive method for early detection of diabetic polyneuropathy (1,2). The cornea is innervated by small Aδ and C fibres, therefore previous studies focused on CCM in the diagnosis of small fibre neuropathies, showing a good correlation between both intra-epidermal nerve fibre density and reported symptoms with corneal nerve fibre (CNF) architecture (3,4), and a reversal of CNF pathology after causal therapy (5,6). In contrast to skin biopsy, assessing the small fibre morphology invasively, quantitative sensory testing (QST) examines the function of both small Aδ and C fibres, as well as large Aβ fibres, but is time consuming (7). Whether abnormal CCM findings are specific for small fibre loss or rather a marker for neuropathy itself, has not been studied yet. This study aims to analyse the correlation between CCM measures and QST-identified large and small fibre function in patients with suspected polyneuropathy of different origin.

Results

150 patients were recruited (n=23 ChT, n=63 DIAB, n=22 HIV, n=42 IPN; mean age 55±13 years, male: female=1.9:1). In the pooled cohort, we observed a significantly decreased CNFL, CNFD or CNBD in 33%, abnormal small fibre function (cold and warm detection threshold (CDT, WDT)) in 33% and abnormal large fibre function (tactile mechanical and vibration detection threshold (MDT, VDT)) in 43%. For CCM and small fibre QST, abnormal findings were most frequent in ChT (39%/30%), followed by diabetes (37%/27%), IPN (31%/26%) and HIV (18%/23%). Abnormal findings for large fibre QST were most frequent in ChT (63%), followed by IPN (45%), HIV (41%) and diabetes (35%). Overall, thermal thresholds and CCM parameters did not correlate, and there was only a weak correlation between VDT and CNFL (r=0.25). Strongest correlations were identified in ChT for VDT (vs CNFL r=0.40, vs CNFD r=0.54, vs CNBD
VDT correlated with CNFL also in diabetes and IPN (r=0.25, r=0.35). CNFL correlated with CDT and WDT also in ChT (r=0.25, r=0.35). In HIV there was a negative correlation between both VDT and CDT and CNBD. No consistent association was seen between disease duration and CCM parameters.

Conclusion
Changes in CNF architecture seem to depend on the aetiology. Interestingly, strongest correlations were seen with CCM parameters and Aβ function although the cornea is thought to be innervated by small fibres. This may indicate that CCM parameters correlate with neuropathy, rather than small fibre loss only, as neurotoxic mediators, responsible for large fibre damage, may also affect vulnerable CNF exposed to the same mediators in tear fluid, whilst peripheral small fibres are preserved. Pathophysiology of spinal and trigeminal nerve territories may also differ. A stronger correlation to thermal thresholds might have been expected, particularly in diabetes, as previously shown, however this may become apparent with larger group sizes. Although some subgroups are small, this study highlights heterogeneity in CNF architecture between disease entities and demonstrates that a multicentre validation process can be utilised to collect large cohorts in profiling studies involving CCM.

Title: Effect Of Minocycline On The Neuropathic Pain: Molecular Study

Poster Number PW0213

Authors
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Aim of Investigation
Neuropathic pain arises after injury to peripheral nerves, inflammation or infection. So far, there has not been effective treatment for this type of pain. It has been shown that some proteins like brain Derived neuropathic factor (BDNF), GABA-A receptor and potassium-chloride co-transporter 2 (KCC2) may play a key role in the pathogenesis of neuropathic pain. Minocycline (microglia inhibitor), was reported to reduce chronic pain. This study was performed to assess the effect of minocycline on the expression of these proteins in the chronic constriction injury (CCI) model of neuropathic pain in rat.

Results
Minocycline when administered before nerve damage, decreased Iba1, BDNF and increased KCC2, GABAA/2 protein expression.

Conclusion
Although minocycline, administered before nerve ligation, could change in the expression of proteins of interest but was not able to make any change when used 7 days after nerve injury.
**Title:** Effect Of Paroxetine On The Neuropathic Pain: Molecular Study

**Poster Number** PW0214

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**Aim of Investigation**
Neuropathic pain due to damage to the peripheral nerve has influenced millions of people life all over the world and there is not effective treatment for this type of pain. Paroxetine, an Antidepressant, has been shown that can relieve neuropathic pain. Recently role of some proteins like brain Derived neuropathic factor (BDNF), GABA-A receptor and potassium-chloride co-transporter 2 (KCC2) in the pathogenesis of neuropathic pain has been well known. In the present study, effect of paroxetine on the expression of these proteins was evaluated.

**Results**
in the preventive and post injury paradigm, paroxetine decreased BDNF and increased KCC2 protein expression compared to the control group.

**Conclusion**
it seems that, paroxetine with change in expression of two important proteins involved in neuropathic pain, can attenuate this type of chronic pain.
Title: Evaluation Of IL-6 Concentration In Macrophage And Microglial Cells Under The Influence Of Nimesulide In CCI Model Of Neuropathic Pain In Rat

Poster Number PW0215

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Aim of Investigation
The pathogenesis of neuropathic pain involves interactions between neurons, inflammatory peripheral and central immune cells. Inflammatory mediators have an important role in inducing neuropathic pain. It has been shown that cyclooxygenase products can exaggerate neuropathic pain. In this study, we assessed the effect of pain reducing properties of nimesulide in chronic constriction injury (CCI) model of neuropathic pain on interleukin-6 (IL-6) concentration in cultured macrophage and microglia cells in rat.

Results
Nimesulide (2.5, 5 mg/kg) attenuated pain behavior and a decrease in IL-6 concentration was observed in macrophage and microglial cells. Conclusion: pain behavior was reduced and a decrease in IL-6 concentration was observed in macrophage and microglial cells by nimesulide.

Conclusion
pain behavior was reduced and a decrease in IL-6 concentration was observed in macrophage and microglial cells by nimesulide.
Title: Efficacy Of Duloxetine On Pain In Elderly Patients With Stroke And Painful Diabetic Neuropathy

Poster Number PW0216

Authors
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Aim of Investigation
The aim of this study is to assess the effect of duloxetine on pain in diabetic neuropathy elderly patients. The pain is a common complication after stroke and is associated with the presence of depression, cognitive dysfunction, and impaired quality of life. Painful diabetic neuropathy affects 16-20% of patients with diabetes. After stroke a lot of people still their life with moderate or severe stroke consequences. Painful diabetic neuropathy in stroke patients is frequently ignored and untreated. Post-stroke neuropathic pain. Central poststroke pain (CPSP) is known as thalamic pain syndrome of Déjerine and Roussy. It is a central neuropathic pain manifested in patients affected by stroke. It is one manifestation of central pain, which is broadly defined as central neuropathic pain caused by lesions or dysfunction in the central nervous system. CPSP is characterized by constant or intermittent pain and is associated with sensory abnormalities, thermal dissensation, spontaneous dysesthesia and the stimulus-evoked sensory disturbances of dysesthesia, allodynia and hyperalgesia. Other types of post-stroke pains are: Post-stroke shoulder pain (PSSP) has a prevalence between 5% -84% and increases with post-stroke time. PSSP correlated with motor deficit of affected side, severity of impairment and living at home. Pain may present as neuropathic, spastic and somatic. Complex Regional Pain Syndrome may develop also. Prescribing in the elderly The pharmacokinetics and pharmacodynamics of most drugs are altered to an important extent in the elderly. Altered pharmacokinetics may include absorption, distribution, metabolism and excretion. The elderly often have a number of concurrent illnesses and may require treatment with several drugs. This leads to a greater chance of problems arising because of drug interactions and to a higher rate of drug-induced problems in general. It is reasonable to assume that all drugs are more likely to cause adverse effects in the elderly than in younger patients.

Results
Duloxetine treated patients have 32% improvement on VAS and 28% better results on NPIS even on the day 30 than NSAIDs treated. On the 90 day VAS shows 50% better and NPIS shows 43% better results.
compared with the control group. CPSP patients results show 80% improvement and PSSP patients show 85% improvement on the 90 day.

Conclusion
Diagnosis of different pain symptoms in elderly post-stroke patients is further complicated by cognitive and speech limitations that may occur following stroke, as well as by depression, anxiety and sleep disturbances. Identification, assessment and therapy of post-stroke pains presents an ongoing management problem for patients, caregivers, and physicians. The present results suggest that duloxetine, 60 mg/day, is effective in treatment for some pain symptoms in patients age ≥65 years. The dual action of duloxetine on 5-HT and norepinephrine reuptake inhibition may explain its efficacy in treating the different central and peripheral pain symptoms. Our results also suggest that duloxetine, 60 mg/day, is well tolerated in elderly patients. Collectively, the present results indicate that duloxetine, 60 mg/day, may represent a first choice pain treatment option for elderly patients with painful diabetic neuropathy and other post-stroke pain syndromes: post-stroke shoulder pain and central post-stroke pain.
Title: Epidermolysis Bullosa Is A Primary Dermatological Condition Associated With A High Prevalence Of Neuropathic Pain Due To Small Fibre Neuropathy

Poster Number PW0217

Authors
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Aim of Investigation
Small fibres that innervate the skin are especially susceptible to damage in systemic diseases such as diabetes mellitus. However, their role in the development of neuropathic pain (NP) is still unclear. We are investigating pain in Epidermolysis-Bullosa-Dystrophic, (EBD) a rare disorder in which mutations of proteins of the dermo-epidermal junction lead to blistering. The somatosensory system in these patients is intact, except from the probable damage that occurs in their skin fibres. The aim of this research is to investigate if EBD-patients present NP and if this is due to intraepidermal fibre damage.

Results
We interviewed 27 healthy volunteers and 29 EBD patients. Both populations showed no difference in age (p=0.13). There were more females in EBD group than in the control group, but it was not statically significant (p=0.3). The prevalence of NP (DN4 score 4 or higher) was 75.9% in EBD patients. The actual VAS score of EBD patients was 4.21 ± 0.54, while the worst was 7.45 ± 0.61. The mean of the PainDetect score was 13.5 ± 1.6. The NPSI questionnaire revealed that 61% of patients had burning sensations, 52% has electric shock sensations, 48% had pin and needles, 56% had tingling, 72% has stabbing sensations. The QST revealed that EBD patients presented with a unique somatosensory profile with exclusive loss in thermal detection thresholds. This dysfunction presented a length dependant distribution: 50% patients had no sensations up to the knee, 71.4% had no sensations up to the ankles, 80.1% had no sensations up to the metatarsophalangeal joint, and only 19.2% were normal. Only 17.2% present with dynamic allodynia. Nerve conduction studies (sural and motor peroneal CV and amplitude) were normal. Testing of the autonomic system (blood pressure and heart rate response to standing, heart rate response to deep breathing and Valsalva ratio) revealed no dysfunction. Quantification of IENFD of 18 EBD patients showed a significant decrease in fibre density (2.6 ± 1.2) compared with healthy volunteers (14.1 ± 0.6, p<0.0001).
Conclusion
These data show for the first time that EBD patients with pain of neuropathic characteristics have a small fibre neuropathy. We are now investigating the mechanisms involved using an animal model of the disease.
Title: The Pain In Neuropathy Study (Pins): A Cross-Sectional Observational Study Determining The Somatosensory Phenotype Of Painful And Painless Diabetic Neuropathy And The Role Of Ion Channels

Poster Number PW0218

Authors
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Aim of Investigation
Diabetic peripheral neuropathy (DPN) is one of the most frequent complications of diabetes mellitus and affects between 28 and 49% of patients. Between 25% and 50% of patients with DPN develop neuropathic pain (NeuP) - defined as pain arising as a consequence of a lesion or disease of the somatosensory nervous system. Although analgesic agents exist for the symptomatic treatment of NeuP treatment is often inadequate and NeuP has a subsequent major deleterious impact on quality of life. Our objectives were: 1) to compare those patients with and without NeuP to identify sensory abnormalities that were specific to NeuP, 2) To compare some of the existing commonly used screening tools for NeuP in these populations, and 3) To relate sensory phenotype to measures of DPN severity and HbA1c in order to investigate the relationship of NeuP to the underlying disease process 4) to determine whether polymorphisms, known to be associated with neuropathy and pain, within voltage gated sodium channels and the transient receptor potential cation channel (TRPA1) are associated with diabetic NeuP

Results
1) The DN4 questionnaire demonstrated excellent sensitivity (88%) and specificity (93%) in screening for NeuP. 2) Hierarchical and k-clustering performed using the Neuropathy Pain Symptom Inventory revealed distinct sub-groups of participants with NeuP. 2) There was a positive correlation between greater neuropathy severity (r= 0.39, P < 0.01), higher HbA1c (r= 0.21, P < 0.01), and the presence (and severity) of NeuP. 3) DPN sensory phenotype is characterised by hyposensitivity to applied stimuli that was more marked in the moderate/severe NeuP group than the mild NeuP or no NeuP groups. 4) Brush
evoked allodynia was present in only those with NeuP (15%), the paradoxical heat sensation did not
discriminate between those with (40%) and without (41.3%) NeuP.  5) The 'irritable nociceptor'
subgroup could only be applied to a minority of patients (6.3%) with NeuP.  6) Preliminary analysis has
not shown an association between sodium channel and TRPA1 polymorphisms and the presence and
severity of NeuP.

**Conclusion**
PiNS has provided evidence in a well characterised DPN cohort that neuropathic pain is related to
neuropathy severity. The sensory profile of DPN patients with NeuP was distinct from those patients
without NeuP showing greater hyposensitivity to sensory stimuli across a range of sensory modalities.
The sensory profile was not uniform in the NeuP group and a minority of patients demonstrated positive
sensory signs such as dynamic allodynia, however very few patients would meet the criteria for the
'irritable nociceptor' group. This study provides a firm basis on which to rationalise further phenotyping
of painful DPN, for instance to optimise clinical trial outcomes. Future prospective studies will be
needed to evaluate how sensory phenotype evolves over time in relation to DPN and NeuP.
Title: Phenotyping Non Freezing Cold Injury

Poster Number PW0219

Authors
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Aim of Investigation
Non Freezing Cold Injury (NFCI) is a clinical syndrome resulting from prolonged exposure to temperatures of close to 0°C. Under such conditions a constellation of typical symptoms is seen in the hyperacute phase affecting the distal extremities, including skin colour changes, numbness, dysaesthesia and pain. This phase is usually self-limiting after a period of up to three months. However, a proportion of subjects develop chronic, disabling pain. NFCI is described almost exclusively in soldiers. The underlying pathogenesis is not fully understood and there are no evidence based diagnostic criteria. The aim of this study was to determine the sensory phenotype of NFCI and determine whether there was objective evidence of sensory axonal injury. This will facilitate accurate, expeditious diagnosis in the future. We hope that insights gained from this study may have broader implications for our understanding of the mechanisms involved in the initiation and establishment of neuropathic pain. In turn this may aid in the development of more efficacious, personalised therapeutics.

Results
All patients had ongoing moderately severe pain involving the hands and feet, with severe intermittent exacerbations caused by cold. DN4 (mean score 6.6) and PainDetect Questionnaires suggested neuropathic characteristics. Neurological exam showed loss of thermal sensitivity and pinprick sensitivity in the hands and feet. Mean MRC sensory sum score was 7 (n=6, range 2-14). The TCSS mean value was 6.83 (n=6, range 5-9). QST results were variable with an overall loss of sensation across a number of sensory modalities. Negative Z score values were obtained for cold and warm detection thresholds in the foot (Mean -1.98 and -1.055, respectively) and hand (Mean -3.433 and -2.77, respectively). Negative Z scores were obtained for mechanical modalities (e.g. Mean Z score for VDT - 2.31 for the foot and -2.20 for the hand). There was no allodynia in any of the patients. Three patients had paradoxical heat sensation when a cold stimulus was administered. Nerve conduction studies were normal. IENFD, normalised for age and gender, were reduced (n=5, Mean 4.3 fibres/mm +/- SD 1.344).
Conclusion
The data support the hypothesis that NFCl is associated with a small fibre neuropathy. There is a symmetrical, distal loss of pinprick and temperature sensation, reduced intra-epidermal nerve fibre density of the distal leg and normal nerve conduction studies. We are currently recruiting and assessing more patients to confirm our initial findings.
Date: 09/28/2016 09:30:00 AM

Title: The Prevalence And Impact Of Diabetic Peripheral Neuropathy In A Malaysian Community Clinic Facility

Poster Number PW0220

Authors
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Aim of Investigation
To determine the prevalence of painful diabetic peripheral neuropathy (PDPN) in a population based sample and to estimate it's severity and impact

Results
There was a 89.1% response with 64.2% subjects reporting pain. 21.9% had PDPN, 35.7% non neuropathic pain, 9.1% mixed pain and the rest had no pain (33.3%). 83% of patients with PDPN complained of moderate to severe pain and reported poorer quality of life. Pain and neuropathic score are strongly associated with quality of life.

Conclusion
Our study showed a prevalence of PDPN of % which has a significant effect on the quality of life. The gradual development of neuropathy appears to be a strong indicator to the risk of developing PDPN.
Title: Periodic Limb Movement Syndrome In Subjects With Chronic Neuropathic Pain

Poster Number PW0222

Authors
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Aim of Investigation
To evaluate the sleep architecture using polysomnographic records in subjects with chronic non-oncologic neuropathic pain

Results
We selected 75 subjects and we collected data from 20 patients with chronic non-oncologic neuropathic pain due painful diabetic polyneuropathy (mean DN4 = 6 points, SD: 0.9). 55 subjects were mobilized. Mean age was 63 years old (SD: 14.29), 60% were female, and the mean pain intensity using the VAS was 4 (DS: 2). Using the PSQI six subjects obtained less than 5 points (good sleepers) and 14 obtained 5 points or more (bad sleepers). Mean Total Sleep Time (TST) was 6 hours (DS: 0.8), mean number of awakenings during sleep was 16 (DS: 13). Sleep phases I and II (light sleep) represented 74% of the TST, the phases III and IV (delta sleep) represented 8.9% of the TST, the rapid eye movement (REM) phase represented 16% of the TST. Periodic limb movements presented a mean value of 45 movements per hour (DS: 32).

Conclusion
This study evaluated sleep architecture in patients with chronic non-oncologic neuropathic pain due painful diabetic polyneuropathy. We observed that: (i) the proportion of light sleep increased, (ii) the delta sleep decreased, (iii) periodic limb movements increased when those values were compared to normal values. Pain intensity had not any correlation with analyzed values. The sample size shall increase to have more statistical power and a control group needs to be included in further analysis. Latino population had never been solely evaluated in studies of pain and sleep even though there are variations in the sleep architecture related to this specific population. More studies and new lines of investigation are needed.
Date: 09/28/2016 03:15:00 PM

**Title:** Pain And Sensory Disturbances Before And After Pulsed Radiofrequency Treatment

**Poster Number** PW0223

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**Aim of Investigation**
Postmastectomy pain (PMPS) is a neuropathic pain syndrome caused by damage of intercostal nerves during breast cancer surgery [1]. Pulsed radiofrequency (PRF) is a treatment option for neuropathic pain that may be effective in relieving PMPS [2] [3]. The pain relieving mechanisms of PRF are unknown. It may modulate molecular pathways of hypersensitivity and descending inhibitory pathways [4] [5]. This retrospective study aims to identify the effects of PRF on pain and sensory nerve function by means of quantitative sensory testing (QST).

**Results**
Before PRF treatment, QST revealed severely reduced thermal and tactile sensitivity. Detection thresholds to cold (CDT), warmth (WDT), alternating cold/warmth (TSL), touch (MDT) and vibration (VDT) were increased (2-3 SD; all p<0.0001) and thermal pain sensitivity was also reduced by 1 SD, p<0.01. Increased pain sensitivity in deep tissue was observed (hyperalgesia to blunt pressure; PPT) (gain 1.5 SD, p<0.0001). Pain summation (wind-up ratio WUR) was enhanced (= 1.5 SD, p<0.05). Patients exhibited subtle signs of dysesthesia (DMA) and paradoxical heat sensation (PHS). After PRF, average pain intensity reduced significantly by 60% (NRS 5 (0-9) to 2 (0-5); p<0.001. The extent of sensory loss or gain did not change significantly, although non-nociceptive detection thresholds improved marginally (NS) and pain summation returned to normal reference values.

**Conclusion**
PMPS was accompanied by severe sensory loss affecting A-β, A-δ, and C-fibers. Paravertebral PRF reduced the intensity of PMPS pain by 60%. PRF did not increase nerve damage. On the contrary, limited sensory improvement in thermal and mechanical detection thresholds was observed. These findings
confirm that PRF is a non-neurodestructive, effective treatment of neuropathic pain. The modulation of descending inhibition might be a mechanism of PRF.
Title: Systemic Administration Of A Gaba Transporter 1 Inhibitor Attenuates Established Paclitaxel-Induced Neuropathic Pain In Mice

Poster Number PW0224

Authors
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Aim of Investigation
The use of paclitaxel in the treatment of breast cancer and other solid tumours is sometimes limited due to the development of dose-limiting painful peripheral neuropathy in some patients. Recently, we found that during paclitaxel-induced neuropathic pain (PINP) there is significant increase in gamma-aminobutyric acid transporter-1 (GAT-1) expression in the anterior cingulate cortex, an area in the brain involved in both pain perception and modulation. These findings suggested that GAT-1 might be a potential therapeutic target for managing PINP. Thus, our aim was to evaluate if systemic administration of a GAT-1 inhibitor ameliorates PINP.

Results
Administration of paclitaxel reduced reaction latency time to thermal stimuli (thermal hyperalgesia) at day 7 after treatment with paclitaxel, similar to our previous findings. Treatment with NO-711 produced antinociceptive effects against thermal nociception in mice with paclitaxel-induced thermal hyperalgesia in a dose dependent manner. Three doses of NO-711, 3, 5 and 10 mg/kg, significantly increased the reaction latency of mice with paclitaxel-induced hyperalgesia on day 7 from 6.3 ± 0.3 to 10.1 ± 0.6 s, 6.2 ± 0.3 to 16.5 ± 2.1 s and 6.9 ± 0.3 to 20.7 ± 2.4 s, respectively (p < 0.01 for all doses; n = 8-10) at 30 minutes after administration. Two doses of NO-711 (3 and 5 mg/kg) that had antinociceptive activity were tested in the rotarod test. No motor deficits were observed with NO-711 at a dose of 3 mg/kg, 265 ± 35 s at 30 minutes after administration versus baseline value of 300 ± 0 s (p >0.05; n = 8), whereas a higher dose 5 mg/kg caused motor impairment and reduced mean time spent on the rotarod from 300 ± 0 s at baseline to 123 ± 52 s (p <0.01; n =8) at 30 minutes after administration.

Conclusion
These results show that systemic administration of the GAT-1 inhibitor NO-711 can attenuate paclitaxel-induced thermal hyperalgesia at lower doses without impairing motor activity, whereas higher doses
cause motor impairment. Thus, low doses of GAT-1 inhibitors could be useful for the management of PINP.
Aim of Investigation
In recent years, numerous studies have noted that substrate topography has a significant influence on neuronal morphology, but the extent of morphological changes depends on the type of neurons as well as geometry and physical properties of the substrate. Our study focuses on characterization of dorsal root ganglion (DRG) neurons cultured on silicon micro-pillar substrates (MPS), as directly related to the design of micro-electrode arrays (MEAs).

Results
We showed that MPS provide a permissive environment for growth of adult and neonatal DRG neurons, equally well as control glass surfaces. Better alignment and length of the neurites was observed on MPS relative to the control glass surfaces, for both adult and neonatal neurons. On MPS areas of particular spacing-range (0.6–1.4 µm), more DRG neurons were present; neurites were longer and more aligned. Furthermore, MPS architecture influences growth directionality of all main DRG neuronal subtypes: large myelinated neurons, peptidergic and nonpeptidergic neurons. In the above mentioned micro-pillar spacing, neurites preferentially oriented along three directional axes at 30°, 90° and 150°. We also noticed that further increase in spacing between the pillars on MPS reduce the topographic guidance and orientation of all DRG neuronal subtypes.

Conclusion
Our results indicate that micro-pillar substrate topography affect the morphology of DRG neurons. The knowledge gained by this research will allow us and other researchers in this field of interest to fabricate MEA with precisely defined physical features for successful electrophysiological recordings of DRG neurons.
**Title:** Cutaneous Allodynia In Subjects With Atypical Odontalgia

**Poster Number** PW0226

**Authors**
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**Aim of Investigation**
To estimate the occurrence of cutaneous allodynia (CA) in subjects with atypical odontalgia (AO) and its correlation with anxiety and depression symptoms, sleep quality, healthy related quality of life (HRQoL) and results of quantitative sensory testings (QSTs).

**Results**
Median score of ASC-12 was 3.5 of 24 [interquartile range (IR)= 6]. The presence of CA by any severity was observed in 55% of AO sample. High scores of ASC-12 were positive correlated only with high scores of BAI (rho=0.682; p=0.001), and BDI (rho=0.523; p=0.018).

**Conclusion**
Most patients with AO present CA, suggesting the relevance to evaluate this symptom. The severity of CA was correlated with anxiety and depression symptoms.
Title: Neurochemical Changes In The Dorsal Root Ganglion, Spinal Cord, And Sciatic Nerve After Chronic Fluoride Exposure In Rats

Poster Number PW0227

Authors
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Aim of Investigation
To elucidate the cellular changes that may contribute to increased peripheral sensory responses induced by chronic sodium fluoride (NaF) exposure in female Wistar rats.

Results
Mechanical allodynia and thermal hyperalgesia thresholds were significantly decreased in NaF-treated rats as compared to control rats. Expression of GFAP in L5 DRG satellite cells as well as the expression of CGRP in L5 DRG neurons and peripheral nerves was significantly increased in NaF-treated rats as compared to control group. There were no significant changes in the expression of ATF3 and CD68 in L5 DRG and sciatic nerve no one changes in the expression of CGRP, ATF3 and GFAP in the lumbar spinal cord from rats treated with NaF were observed.

Conclusion
These results taken together suggest that, increased mechanical and thermal hypersensitivity is associated to neuropathological changes in the DRG and sciatic nerve.
Title: Specific Jaw Exercises Can Change Jaw Movement Patterns During Chewing: A Possible Mechanism For The Management Of Pain Associated With Temporomandibular Disorders

Poster Number PW0228

Authors
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Aim of Investigation
Temporomandibular disorders (TMD) are the most prevalent orofacial pain condition of non-dental origin and the second most common musculoskeletal condition that results in pain and disability after chronic low back pain (CLBP). Jaw pain along with limitations and/or deviations of mandibular movements are common signs and symptoms of TMD which impact on an individual's ability to chew. Therapeutic exercise is a common treatment modality used in the management of many painful musculoskeletal conditions, including TMD, although the mechanism of action in the case of TMD is relatively unknown. However musculoskeletal pain is often associated with biomechanical deficiencies of altered patterns of muscle activation and therapeutic exercises have changed motor activity and restored normal muscle activity and resolved pain. Such motor activity changes have not been demonstrated in TMD and our aim is to determine if exercise modifies jaw movement. We hypothesise that an isometric resistance exercise task modifies masticatory movements of the human jaw.

Results
Five principal components of a total of 123 principal components explained 92.1% of the total variance in the chewing cycles of all participants. Furthermore, in asymptomatic individuals, isometric resistance exercise applied against a lateral jaw movement resulted in masticatory movement paths significantly (p < 0.001) more horizontally orientated in the coronal plane and more protruded in the sagittal plane.

Conclusion
These results suggest that isometric resistance exercise which uses a simple and discrete task can modulate the muscle activation pattern of more complex and repetitive motion such as mastication. Changes in jaw movement patterns may reflect changes in the central motor control of mastication.
brought about by the application of the exercise task. Restoration of normal joint kinematics associated with earlier muscle activation has been demonstrated in other joints and in patients with CLBP after completion of specific therapeutic exercise regimens. In particular, earlier onset of transversus abdominis in recurrent LBP patients was associated with reorganisation of the motor cortex representation of transversus abdominis. Future studies investigating the activation patterns of the muscles of mastication and the potential reorganisation of their cortical representations would further elucidate the mechanisms whereby therapeutic exercise affects these muscles. Applying the findings from this study to a population of patients diagnosed with painful TMD with limitations and/or deviations of mandibular movements also warrants further investigation in a clinical setting utilising appropriately matched controls. This may help determine the effectiveness of therapeutic exercise in the management of pain associated with TMD.
Title: Somatosensory Abnormalities In Chinese Patients With Painful Temporomandibular Disorders

Poster Number PW0229

Authors
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Aim of Investigation
Patients with TMD pain are not sufficiently and adequately diagnosed or treated, this study aimed to evaluate the somatosensory abnormal phenotypes of temporomandibular disorder (TMD) patients by use of contemporary techniques and guidelines.

Results
For patients, 82.5% had somatosensory abnormalities in the painful facial region, while 60.0% had abnormalities confined to the right hand, compared with 31.2% in facial and 24.3% in hand regions of the reference population. The most frequent abnormalities were somatosensory gain to suprathreshold pinprick (35.0%) and pressure (35.0%) stimuli, somatosensory loss to suprathreshold pinprick (25.0%), cold (22.5%), and heat (15.0%) nociceptive stimuli. The most frequent loss/gain score was L0G2 (no somatosensory loss combined with a gain of mechanical somatosensory function) for both the facial (40.0%) and hand (27.5%) regions. Involving side-to-side differences in the evaluation increased the diagnostic sensitivity by 2.5-25.0% across different parameters.

Conclusion
Somatosensory abnormalities were commonly detected in TMD pain patients both within and outside the primary painful region, strongly indicating disturbances in the central processing of somatosensory stimuli. This information may be an important step in the development of individualized mechanism-based management.
Title: Lymphotactin (Xcl1) Modulates Markers Of Central Sensitization In The Trigeminal Subnucleus Caudalis (Vc) In Vitro

Poster Number PW0230

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Aim of Investigation
A link between pro-inflammatory cytokines, sensitization and chronic pain is established. The contributions of lymphotactin (XCL1) and its cognate receptor XCR1 to central sensitization in the trigeminal subnucleus caudalis (Vc), an area linked to oro-facial pain, is unknown. In this study, we investigated XCL1 and XCR1 expression in the adult rat trigeminal brainstem using Western blotting and immunohistochemistry, respectively.

Results
XCL1 protein was expressed within trigeminal brainstem, as assessed by Western blotting. XCR1 immunolabelling was observed in Vc superficial layers where it co-localised extensively with the vesicular glutamate transporters 2 (VGlut2) in superficial layers. The vesicular glutamate transporters 1 (VGlut1) staining was distributed to deeper regions with little evidence of colocalisation with XCR1. Incubation of trigeminal brainstem slices with XCL1 (2h) increased activation of c-fos, p-P38 and p-ERK in the superficial layers of Vc, as assessed by semi-quantification of immunostaining (p < 0.05). c-fos, p-P38 and p-ERK activation was blocked by the XCR1 antagonist vMIP-II.

Conclusion
Our findings suggest that XCL1 through XCR1 can activate specific markers of central sensitization within Vc that is involved in modulation of nociceptive signals in the oro-facial region. Acknowledgments: Research funded by BBSRC as an Industrial Partnership award with Pfizer, UK.
Title: Relationship Between Activity Electric Of Temporal Muscles And Length Coronoid Process In The Orofacial Pain Subjects

Poster Number PW0231

Authors
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Aim of Investigation
This was a cross-sectional exploratory study that included quantitative data and random sampling of patients who were seen and/or who had been referred by Health Services to the outpatient Odontology Clinic at Tuiuti University of Paraná Curitiba, Brazil. The project was approved by opinion CAAE: 37870114.9.0000.0103. All participants provided signed informed consent. The sample consisted of 46 patients between 18 and 77 years of age (X = 41.5). Of these patients, 80.1% were females and 19.9% were males. Patients were examined by two calibrated and trained dental surgeons (k = 0.81), according to the Research Diagnostic Criteria/Temporomandibular Disorders (RDC/TMD) tool [Dworkin and LeResche, 2011; Truelove et al., 1992]. The examiners did not have prior access to patient records. Based on the criteria for RDC/TMD, the patients were classified with myofascial pain group. They had unilateral pain, independent of limitations of mouth opening (N = 46). Digital panoramic radiographs were taken for all patients and data were obtained directly from digital JPEG image files without amplification during the acquisition. To mark the anatomical landmarks, a protocol was used for the acquisition of panoramic images in occlusion and the median sagittal plane perpendicular to the ground (Fig. 1). The anatomical points for the gonion (Go), most superior point on the condyle (Co), most superior point on the coronoid process (Cr) and inferior-most point of the sigmoid notch (Sn) were marked by the same dental surgeon radiologist, who did not know the diagnosis (Fig 2). All patients underwent surface electromyography of the anterior temporal muscle. The exams were performed by a single operator who did not know the diagnosis. In total, 3 acquisitions were performed at rest and 3 at the habitual maximum intercuspal position for 15 seconds each. The mean of each of the exams was used. The skin was aseptically cleaned, and the electrodes were attached to the anterior temporal muscle region in area 9 (Fig.3). The values used for this study were the result of the square root of the quadratic mean of the values - RMS (Root Mean Square). The results were subjected to statistical analyses, were performed using Tukey’s HSD test. When the differences and variances were
heterogeneous was used the Games-Howell test. A student’s t-test was used for paired and independent samples. Differences were identified in the mean measurements between side A and side B. There was a Pearson’s correlation coefficient. There was a level of significance of 5% (p ≤ 0.05).

Results
The sample found 45 patients (90 TMJs) which was compared by vertical measurements on panoramic radiographs side A (pain) and side B (no pain) between the coronoid process of the mandible (Cr) and points in the angle of the mandible (Go) and sigmoid notch (Sn). The results were subjected to statistical analyses, comparing the mean values of the different variables from side A and from side B. A student’s t-test was used for paired and independent samples. Differences were identified in the mean measurements between side A and side B. There are no statistically significant difference between EMG R-L and EMG Clench R-L but there is a statistically significant difference between CrSnA and CrSnB tending side A is larger than the B (P = 0.0189) and there is a statistically significant difference between CrGoA and CrGoB, tending right side A is larger than the side B (P = 0.0480). There was a correlation between all the variables using Pearson's correlation coefficient for parametric samples with n > 30 and with continuous variables. There was a level of significance of 5% (p ≤ 0.05). There was a Pearson's correlation between all the variables CrSnA/CrSnB (r=0.650) and CrGoA/CrGoB (r= 0.559).

Conclusion
Based on the analysis of the results and the limitations of the present study, the following conclusions can be reached: When patients presented with unilateral pain, there was a significant correlation between the mean of morphological changes from the coronoid process (Cr) to the sigmoid notch (Sn) and from the coronoid process (Cr) to the gonion (Go) when both sides of the mandible were compared. However, it was not possible to confirm, using the methods applied here, that the electrical activity of the anterior bundle of the temporal muscle was responsible for these morphological changes. It suggests new studies using computed tomography exams.
Title: Jaw Pain After Whiplash Trauma In Relation To Neck Pain, Non-Specific Physical Symptoms, And Depression

Poster Number PW0232

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Aim of Investigation
There is a relationship between pain in the jaw and neck regions and orofacial pain is commonly reported after whiplash trauma. The pathophysiology of the development of orofacial pain following whiplash trauma is unclear. Intensity of neck pain in the acute stage has been identified as one of the strongest prognostic factors for poor outcome after whiplash trauma. It may be that post-traumatic pain in the jaw region is associated to the intensity of neck pain as well as to psychosocial factors. The aim of the present study was to analyze jaw pain after a recent whiplash trauma in relation to neck pain, non-specific physical symptoms and depression.

Results
Individuals with a recent neck trauma reported higher intensity of neck pain (33.3 CPI, P < 0.0001) and jaw pain (15.1 CPI, P < 0.0001) compared to controls (6.4 and 3.1). Individuals with a recent neck trauma also had higher scores for physical symptoms (1.0, P < 0.0001), non-pain physical symptoms (0.7, P < 0.0001) and depression (0.9, P < 0.0001) compared to the control group (0.3, 0.2 and 0.4, respectively). For the cases, there was a moderate positive correlation between jaw pain and neck pain (r = 0.46, P < 0.0001), physical symptoms (r = 0.60, P < 0.0001), and non-pain physical symptoms (r = 0.60, P < 0.0001). There was a low correlation between jaw pain and grade of depression (r = 0.32, P = 0.001).

Conclusion
These findings indicate that orofacial pain following whiplash trauma is related to intensity of neck pain, non-specific physical symptoms as well as to psychosocial factors.
Title: Advanced Retrograde Fluorescence Labeling Of Dental Primary Afferent Neurons Innervating Rat And Mouse Maxillary Molars

Poster Number PW0233

Authors
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Aim of Investigation
Pain in the oral and craniofacial system like odontogenic pain and dentine hypersensitivity represents a major medical problem with high prevalence. Reported pain intensities are often severe and pain is frequently resistant to currently available analgesics which in addition have unpleasant side effects. We successfully translated a method of retrograde fluorescent labeling of dental primary afferents (DPA) innervating molar teeth from rats to mice. Tooth pulp afferents are a highly enriched and specialized population of nociceptors. Because dialkylcarbocyanine dyes do not interfere with cell viability or basic physiological characteristics, the mouse model with DiI-labeled DPAs is suitable to study the physiological and pathophysiological properties of this nociceptor population and to access transgenic mouse models.

Results
The NeuroTrace<sup>®</sup> Dil tissue-labeling gel has superior staining characteristics in comparison to the crystalline application of Dil, because labeled cells appear in higher fluorescence intensity, which allows a better distinction of the cells from background and thereby leads to a more constant labeling result in rats. A dye transport time of 120 h led to the highest amount of fluorescent cells in the rat per TG: in comparison to all shorter timeframes there was a 3-fold increase in the amount of labeled cells. In mice we found satisfying fluorescence intensity only with the Dil gel but not with crystalline Dil. We confirmed the same retrograde transport time of 120 h as ideal. Using cell cultures of TGs, we found labeled DPAs to be viable and 25% of them expressed TRPM8.
Conclusion
We transferred and optimized a model of retrograde labeling of DPA neurons with Dil from rats to mice, enabling us to study the molecular specialization of the nociceptive detection apparatus in molar teeth and to evaluate physiological and pathophysiological properties of tooth pulp nociceptors by using transgenic mouse models. Likely, this model will help to find potentially unique pharmacological targets for the treatment of tooth pain.
Title: Dental Implants: Assessment Of Pain, Discomfort, And Altered Sensations

Poster Number PW0234

Authors
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Aim of Investigation
The purpose of this observational study is to establish the estimated point prevalence and putative risk factors for post-dental implant sensory disturbances (PISD) in the community of patients served by the UNC School of Dentistry. Dental implants have become an increasingly common method for replacing missing dentition. However, some implant recipients experience PISD characterized by persistent discomfort, pain, and inflammation, symptoms which are commonly associated with peri-implantitis. To date, no scientific assessment of the prevalence of PISD and its contributing putative demographic, clinical, and biopsychosocial risk factors has been conducted. This presentation reports our initial findings from an ongoing observational study.

Results
The study is ongoing; thus, the results should be viewed as preliminary. Current findings suggest that the estimated prevalence of self-reported PISD is 28.6% in this cohort. The demographics of participants with PISD compared to those without did not differ. While trapezius muscle pressure-pain thresholds did not differ, several psychosocial factors such as perceived stress, anxiety, and depression were elevated in participants with PISD. Initial assessments of clinical markers of inflammation around implant sites, such as frequency of gingival inflammation and bleeding on probing, did not differ between PISD cases and non-cases. At this time, few distinctions have been made between cases and non-cases in relation to implant manufacturer, post-implantation time, or previous dental treatments.

Conclusion
In this ongoing observational study, we obtained preliminary evidence that PISD is highly prevalent and associated with multiple biopsychosocial factors. Whether these factors are antecedent and predictive of future destructive peri-implantitis, which also impacts a high percentage of implant patients, requires further investigation.
Title: Severe Refractory Chronic Orofacial Pain Managed With Noninvasive Neuromodulation Technique: The Scrambler Therapy

Poster Number PW0235

Authors
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Aim of Investigation
To present our experience in managing severe refractory orofacial pain patients adding noninvasive neuromodulation with the MSA device- the scrambler therapy (ST), to our current routine; neuropathic pain can be extremely difficult to manage in some patients, trigeminal neuralgia can be disabling and other orofacial neuropathic pain syndromes significantly alter vital functions like speech, swallowing and dental hygiene. Some patients experience medication induced side effects, limiting the benefits of pain control.

Results
Case 1- 61 years old male patient with disabling trigeminal neuralgia, glossopharyngeal nerve hyperalgesia and allodynia impairing swallowing, 12 kg weight loss in two months, nonresponder to carbamazepine, pregabalin. 12 ST treatments significantly improved pain and functioning. RF ablation was performed at VAS 2-3/10 with sustained pain relief at 24 months. Case 2 - 72 years old female patient, with severe trigeminal neuralgia, major depression, not responding to carbamazepine. Mouth mucosal hyperalgesia made food and liquid ingestion impossible, requiring parenteral hydration and nutrition. Liquids ingestion became possible after 2 ST treatments. After 10 ST treatments she accepted RF ablation, with partial relief but increased functioning and QoL. Case 3 - a 52 years old female patient with disabling painful temporomandibular joint disorder was primarily referred to us by her GP. Pain improved after the first 4 ST treatments, but aggravated thereafter; simultaneous head MRI and ENT consultation referral revealed a cavum carcinoma and the patient was sent to the oncology multidisciplinary team. She required palliative pain management using ST to reduce opioid therapy side effects (constipation, hallucinations) and control the neuropathic component as tumor growth involved the ipsilateral trigeminal nerve. Case 4- 64 years old male patient with severe refractory phantom tooth syndrome (3 consecutive tooth extractions from the upper left dental maxillary bone). Pain improved with 8 ST treatments. Dental implant surgery went well, but severe pain reappeared after 14 days, with
numbness and tingling of the face and partial relief during ST treatments. An X ray exam revealed a bone cyst filled with liquid and we asked for dental surgeon reassessment.

**Conclusion**

ST improved our pain management protocols for severe refractory orofacial pain with neuropathic component, hastening better pain control with less medication side effects, improved functioning and QoL, especially in elderly patients with significant comorbidities. We used it as a bridge to RF ablation in trigeminal neuralgia, in palliative care- in malignant and non malignant pain syndromes. Inconsistent pain relief in cases 3 and 4 raised suspicions of an added nociceptive component and urged further investigations, thus enabling proper diagnose and treatment. The lack of side effects and very few contraindications enTitle its use in severe refractory neuropathic pain syndromes and in palliative care.
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. The Norwegian Ministry of Health commissioned a program comprising multidisciplinary evaluation of TMD/TMJD patients. The aim of the program was to systematically assess refractory TMD-associated pain, characterize the patient group and propose an individualized treatment plan for each patient. The program has previously been presented as a preliminary report.

Results
Results The results from the questionnaire showed that the typical TMD patient in this project is a female (51:9), 45 years of age (range 20-67) has 12 years of schooling or a Bachelor degree. She works in sales, service or a care profession and has an average or poor economy. She is married and has 2 children. She reports severe pain, but has no opinion on how it started or why she has pain. Forty five percent of patients reported previous trauma, while 25 % reported general joint hypermobility. Commonly reported comorbidities were neck, shoulder and back pain (88%), headache (75%), muffled hearing (57%), otalgia (42%), allergy (33%) and asthma (15%). The clinical examinations revealed that almost all patients had moderate to severe jaw muscle pain and 85% had raised scores on the mandibular function impairment questionnaire. Fifteen patients had posterior open bite due to long-term use of an anterior mandibular repositioning splint. MR revealed that 52% had anterior disk displacement and 10 % severe arthritis with degenerative joint changes. On referral 8 patients had a fibromyalgia diagnosis, 10 had migraine and 4 chronic fatigue. Thirteen patients had Vitamin D deficiency (S-25-Hydroxy Vit. D3 < 50 nmol/L). More than 2/3 of patients had palpable trigger points,
while 50% had impaired ability to relax. The majority reported sleep disturbances, 50% had raised anxiety and/or depression scores, and almost all had elevated catastrophizing scores. The majority of patients were advised conservative TMD treatment including jaw exercises and occlusal splints. Seven patients needed surgery. Lifestyle factors (sleep, physical activity and diet) and medication were addressed. Fifty percent of patients required referral for psychological treatment. A small number of patients required further investigation to exclude underlying medical conditions.

Conclusion
Conclusions All patients had a long history of pain. Females dominated and a majority had impaired mandibular function, in addition to pain. Chronic, widespread pain and muscular trigger points were common, as was an impaired ability to relax. Almost all patients had elevated catastrophizing scores. In the majority of cases conservative treatment was advised. Refractory pain in TMD patients requires a multidisciplinary approach.
Title: Trigeminal Neuralgia: A Biopsychosocial Approach To Management

Poster Number PW0237

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Aim of Investigation
Determine the role of a psychosocial approach to management of trigeminal neuralgia

Results
An 89% response rate was obtained: 11 by the telephone and 5 postally. The overall rating of the program on a scale of 0 to 5 was 4.6. Sessions that were particularly popular were 'thoughts and feelings', 'mindfulness including mindful breathing' and 'problem solving'. Confidence in coping with attacks of TN was rated on average 4.5 (scale of 0-6). Participants reported improved confidence in a variety of areas including eating foods they had avoided, taking part in more activities, return to work. One of the most useful outcomes was meeting fellow sufferers and all remarked how it reduced their isolation. Advise to new sufferers included remaining positive, getting better educated so as to loose fear and going on a pain management course. Patients reported on their ability to adjust their doses as needed or called the clinical nurse specialist. None had attended an emergency clinic to get help. It was noted that fewer younger patients and males were present due to work commitments. When asked if the service can be run by patients as a local support group, most patients believed a clinical psychologist is needed, 'to act as a leader to prevent everyone from simply catastrophizing'. However, the consensus seems to be that a patient-run service would be better than no service at all in cases where there are not enough resources. Follow up sessions would be useful. The telephone consultations that patients had with the CNS were principally related about use of drugs. The 15 patients who have provided feedback found the service very good or excellent but would have liked a faster response, the service only runs half a day a week and 80% considered the time they for the consultation was sufficient.

Conclusion
Conclusions
The evaluation by the independent observer reduces bias
The TN Pain
Management Programme is an effective programme to reduce fear and anxiety in TN patients whose quality of life is severely affected by the condition. The programme content was well rated and future programme should continue to include the 3 sessions most highly rated. Where resources are available, a clinical psychology-led programme is preferred. A clinical nurse specialist with an interest in TN can provide considerable support about medication use and cut down on appointments with medical staff.

Title: Role Of Endothelins In Evoked And Ongoing Pain In A Model Of Facial Carcinoma In Rats

Poster Number PW0238

Authors
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Aim of Investigation
Pain represents a frequent symptom of cancer patients, affecting 1 out of 3 people undergoing treatment. Cancer pain occurs in many ways, and many patients report not only episodes of evoked, but also ongoing pain with very poor analgesic management. Thus, studies aimed to evaluate new targets and pharmacological strategies to control ongoing pain are clearly warranted. There is mounting evidence that endothelins participate in the development of some types of cancer, promoting angiogenesis and cell proliferation, and contributing to the development of sensory changes, such as allodynia and hyperalgesia. In spite of their well characterized role in trigeminal nociceptive transmission, the involvement of endothelins in evoked and non evoked pain related to facial cancer has not yet been investigated. In light of these considerations, the current study aimed to evaluate the participation of endothelins in thermal and mechanical hypersensitivity as well as, ongoing pain, in a model of facial cancer.

Results
Heat and mechanical hypersensitivity related to facial tumor was unchanged by oral treatment with Bosentan at 100 mg/kg. On the other hand, a single administration of Bosentan at 300 mg/kg abolished heat, but not mechanical hypersensitivity on day 6 after tumor cell inoculation, up to 5 h after the treatment. Interestingly, the mixed endothelin ETA/ETB receptor antagonist treatment, at 100 mg/kg, reduced the spontaneous grooming induced by the inoculation of tumor cells. To confirm this ongoing pain reduction, CPP was assessed and the data demonstrate that tumor-bearing rats, but not control group, demonstrate preference to the Bosentan 100 mg/kg paired- chamber.

Conclusion
This study provides evidence that endothelins, acting through ETA and ETB receptors, may participate
on the development of heat hypersensitivity and ongoing pain associated with facial cancer. A lower dose of Bosentan was able to control non evoked pain compared to evoked pain, suggesting a better efficacy of the drug on ongoing pain management, which increases the relevance of this pharmacological target.
Title: The Effect Of Impaired Central Processing Mechanisms On Pain Outcomes In Patients With Orofacial Pain

Poster Number PW0239

Authors
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Aim of Investigation
Orofacial pain has been defined as 'pain perceived in the face and/or oral cavity'. (IASP) The American Academy of Orofacial Pain definition also includes symptoms related to cervical musculoskeletal pain, headaches, and systemic disorders that cause pain located in the orofacial area. (AAOP website) The prevalence of orofacial pain is estimated to be 10% in the adult population, increasing to 50% among older adults. (Shinal 2007) Psychosocial factors have been shown to contribute to the development and prolongation of orofacial pain. (Aggarwal 2011) Numerous psychosocial mechanisms to explain the persistence of orofacial pain have been reported. Several promising theories propose that alterations in central pain regulating mechanisms caused by acute pain result in the perpetuation of chronic pain at an intensity that is no longer consistent with the underlying tissue damage. Conditioned pain modulation is a normal process in which an individual perceives less pain when exposed to two noxious stimuli applied simultaneously to remote body areas, when compared with the situation in which only one noxious stimulus is applied. Sustained concurrent noxious stimuli have been shown to activate descending analgesic systems, thereby inhibiting pain. Impairments in this pain modulation response have been associated with the transition from acute to chronic pain. (Pavlakovic 2010) Numerous tests to indirectly quantify the efficacy of this pain modulation system have been proposed. These tests involve application of a noxious stimulus followed by the application of two noxious stimuli simultaneously. If pain perception is decreased with the application of two noxious stimuli when compared with a similar application of one noxious stimulus, then the inhibitory pain system is working normally, whereas if the patient does not experience this decrease in pain, the system is deemed impaired. We aimed to investigate this phenomenon in a sample of patients with orofacial pain being seen for an initial examination in a specialized orofacial pain clinic. We hypothesize that the presence and extent of an
impairment in the conditioned pain modulation system would predict changes in pain at 6 to 8 weeks follow-up.

**Results**
Conditioned pain modulation had a significant effect on change in 7-day least pain, increasing the predictive capabilities of the regression model by fully 12%. Nevertheless, conditioned pain modulation did not significantly predict 7-day or 24-hour worst pain. The data also suggest that female gender may have a small negative effect on change in 7-day worst pain.

**Conclusion**
These results suggest that testing for impairments in conditioned pain modulation might predict changes in 7-day least pain at 6 to 8 week follow-up, although the effects of this impairment on 24-hour and 7-day worst pain is less evident. Further exploration of these findings in a different population of patients with orofacial pain is warranted.
Title: A Novel Method For Intraoral Access To The Superior Head Of The Human Lateral Pterygoid Muscle

Poster Number PW0240

Authors

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Aim of Investigation

The uncoordinated activity of the superior and inferior part of the lateral muscle (LPM) has been suggested to one of the causes of temporomandibular joint (TMJ) disc displacement. A therapy for this muscle disorder is the injection of botulinum toxin (BTX), of the LPM. However, there is a potential risk of side effects with the injection guide methods currently available. In addition, they do not permit appropriate differentiation between the two bellies of the muscle. Herein, a novel method is presented to provide intraoral access to the superior head of human LPM with maximal control and minimal hazards.

Results

A novel method was developed to produce an injection guide for intraoral access to the superior head of the human LPM, using medical image processing programs and rapid prototyping technology. Upon the manipulation of the 3D virtual images obtained from a CT scan and the identification of the infra temporal crest of greater wing of the sphenoid bone, the virtual guide was meticulously designed to fit the upper and lower dental a, the direction of the injection has been gotten and the guide was built in a rapid prototyping machine. To preliminary access the clinical reliability of the guide, 2cc of lidocaine hydrochloride 2%, without vasoconstrictor was infiltrated in the left superior head of the LPM of a volunteer. The guided injection abolished the signs and symptoms of TMJ clicking, without interfering in the mandibular movements, thus proving to be a reliable and safe method.

Conclusion

The efficacy of BTX in the LPM to treat anterior TMJ disc displacement has been reported in the literature. However, the LPM access is challenging and there are risks associated with the procedure.
The goal of such therapy is to abolish spasm of superior head of LPM. This spasm could provide a uncoordinated disc-condyle kinematic. The traction of the superior head could retain the disc anteriorly, the thin upper ligament of bilaminar zone composed of elastin, would not support the tension provide by the upper LPM spasm, resulting in disc dislocation and clicking sound during its reduction to normal disc-condyle relationship. Up to now, electromiography is the most common technique applied to access LPM in vivo. Notwithstanding it permits the localization of the LPM, but it doesn't provide the proper differentiation between the superior and inferior parts of the muscle. This characteristic is extremely relevant given that BTX injection in the inferior head of LPM is invariably associated with temporary limitation of the lateral mandibular movement to the contralateral side and jaw deflection during maximum mouth opening. The use of a patient specific guide to orient the direction of the needle allows the proper differentiation between the tow heads of LPM, avoiding any potencial side effects. The prototype guide presented in this study is a reliable tool for accurate and safe intraoral injection in the superior head of the LPM. Further studies will be necessary to test the efficacy and validate the method.
Title: Posterior Disc Displacement Of The Tmj: Systematic Review Of The Literature And A Very Rare Case Report

Poster Number PW0241

Authors
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Aim of Investigation
Aim of this study was to review the literature systematically to look into the prevalence of the posterior disc displacement (PDD) of temporo-mandibular joint (TMJ), which is a very rare finding and the associated radiographic features and management protocol of the condition. Thereafter we discuss a very rare case of posterior disc displacement.

Results
Initial search resulted in total of 1833 Titles matched. Finally 17 papers were included after a two-step (abstract and full-text revision) screening process, for qualitative data synthesis. Prevalence of PDD reported varies from 0 - 2.9%. Associated osseous changes when reported were change in morphology of condyle, disc and articular eminence and osseous abnormalities (like erosion, osteophytes etc.) and joint effusion. Concurrent sideways displacement of the discs was also reported. Due to paucity of the literature and heterogeneity of the data it is difficult to say conclusively about the other aspects like the cause, risk factors and ideal treatment of PDD. The case report is about a female 71 years old with the chief complaint of lack of bite on the right side. Patient gave history of sub-luxation and joint noise on the right side from past 30 years and then on August 1st, 2015 she noticed the jaw was deviated to the left side and she was not able to chew from right side. Clinical examination revealed tenderness in masseter on both side, maximum mouth opening 41mm, deviation to the left on opening. Intraoral examination findings were midline deviation- 2 mm to the left, lack of occlusal contact in right premolar region. MRI showed right side PDD in both open and closed mouth position. Based on Research Diagnostic Criteria for Temporo-mandibular disorders RDC/TMD, diagnosis of bilateral myofascial pain (Group I a) and osteoarthritis right side (Group III b) with right side PDD and joint effusion was made. Patient was managed conservatively by following physical therapy, avoidance of tooth contact during
the day time and massage. When improvement in muscle pain was observed after 2 months a night time maxillary stabilization splint was given to provide occlusal contact. Joint injection was proposed which patient denied as her pain had subsided. Composite restorations were planned to give occlusion. On follow up visit patient was able to chew normally and occlusion was improved.

**Conclusion**

Within the limitation of this study it can be concluded that PDD is a definite entity with an overall very low prevalence. More number of databases and non-English language literature may be explored to procure more number of relevant articles and to reach on definitive conclusion related to the cause, risk factors and treatment of PDD. Based on the experience of our clinical case a conservative treatment should be the first choice of management. A long follow up may be required to monitor the function and treatment outcome.
Title: Thalamic Gaba Concentration In Chronic Neuropathic Orofacial Pain

Poster Number PW0242

Authors

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Aim of Investigation
To determine whether there is a difference in thalamic inhibitory (gamma-aminobutyric acid; GABA) neurotransmitter concentration between chronic neuropathic orofacial pain patients and a healthy control sample.

Results
Ten patients (mean age 47.9 years; 3 males) and 10 healthy controls (mean age 45.2 years; 3 males) were included in the current investigation. Median pain duration in the patients was 25 months, and mean pain intensity score was 3.2/10 (Numerical Rating Scale). No significant difference in GABA:Cr was found between the patients and the healthy controls (U = 44; p = 0.65). There was no correlation in the patient group between GABA:Cr and pain duration (p = 0.34) or pain intensity (p = 0.3).

Conclusion
We found no evidence of a difference in GABA concentration in chronic neuropathic orofacial pain patients when compared with healthy, pain-free controls. This is in contrast to recent work (Henderson et al., 2013), which reported a significantly lower GABA concentration in neuropathic pain patients than in controls, but no difference when comparing non-neuropathic pain patients and controls. Our sample here was small, but given that we found no evidence of a trend it is possible that there are significant differences in the clinical presentation of our patient group and that of the past work, specifically in the diagnosis of neuropathic pain. These preliminary findings will be more definitive with a larger sample and with interpretation of the data alongside other neuroimaging outcomes. References: Henderson, L.A., et al. (2013). Chronic pain: lost inhibition? Journal of Neuroscience 33, 7574-7582. Mullins, P.G., et al. (2014). Current practice in the use of MEGA-PRESS spectroscopy for the detection of GABA. Neuroimage 86, 43-52.
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Title: Purinergic P2Y2 Receptors On Satellite Glial Cells As New Potential Targets For The Pharmacological Control Of Trigeminal Pain

Poster Number PW0244

Authors
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Aim of Investigation
The trigeminal ganglion (TG) is involved in inflammatory, neuropathic and other painful conditions of the head and facial districts. Within the trigeminal ganglion, neuronal functions are modulated by surrounding resident glial cells, the so-called satellite glial cells (SGCs). SGCs react to painful conditions by releasing pro-inflammatory and pro-algogenic mediators and signalling molecules, thus contributing to neuronal sensitization and to the development of pain. TG-related pain is extremely intense, highly disabling and often lacks satisfactory pharmacological control. Since ‘classical’ analgesic drugs mostly act on neurons, innovative targets for the development of more effective analgesics could emerge from a better understanding of the molecular cross-talk between TG neurons and SGCs. We have already demonstrated that G protein-coupled P2Y purinergic receptors (P2YRs) activated by extracellular nucleotides and expressed by SGCs are upregulated in vitro by pro-algogenic molecules, such as bradykinin (BK) and CGRP (Ceruti et al., 2011, J Neurosci 31:3638-49). The overall aim of the present study is to identify the specific glial P2YR subtypes potentiated by CGRP in the TG, and to determine whether their role is pro- or anti-algogenic.

Results
First, we have identified the P2YR subtypes specifically modulated by algogenic conditions in vitro as the P2Y1R (activated by ADP) and the P2Y2R (activated by UTP), and demonstrated the contribution of prostaglandins to their upregulation. Next, we have translated our data to the in vivo model of TG pain, and demonstrated development of mechanical allodynia, activation of SGCs, together with upregulation of P2Y1R and P2Y2R expression in the ipsilateral TG. Pharmacological treatments showed that the P2Y2-selective AR-C118925 compound completely inhibited SGCs activation, exerted a potent anti-allodynic effect that lasted over time, and was still effective when its administration was started 6 days post
induction of allodynia, i.e. under sub-chronic pain conditions. Conversely, the P2Y1-selective antagonist MRS2179 had no effect on facial allodynia. Similarly to ASA and Sumatriptan, the P2X/P2Y-non selective antagonist PPADS was only partially effective, and completely lost its activity under sub-chronic conditions (Magni et al., 2015, Glia 63:1265-69).

**Conclusion**

Taken together, our results highlight the P2Y2R subtype as a new potential 'druggable' target for the successful management of TG-related pain. The present study has been supported by Italian Telethon Foundation (Grant #GGP10082A) and Cariplo Foundation (Grant #2011-0505). The authors have no financial relationship with the manufacturer/supplier of any commercial products or services related to the work reported in the abstract.
Title: Sex Differences In Oestrogen-Dependent Macrophage-Fibroblast Interaction In Cardiac Inflammation

Poster Number PW0245

Authors
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Aim of Investigation
Sex hormones directly act on the immune system via hormone receptors. Most of the autoimmune diseases are more prevalent in women than in men, which has been attributed to the immune stimulatory effects of oestrogen (E2). Mice with myocarditis in the oestrus phase showed significantly lower amounts of inflammatory cells. IFN-γ-positive CD4 cells and activated T-cells were decreased in the oestrus phase, while the amount of regulatory T-cells was increased, suggesting the pivotal role of oestrogen in the development and chronicity of myocarditis. We propose sex differences in the macrophage differentiation and activation in myocarditis. We also expect cross-talk between macrophages, fibroblasts and adaptive immune cells that might be involved in impaired wound healing, leading to fibrosis.

Results
Human male macrophages express both oestrogen receptor (ER)α and ERβ. E2 treatment significantly induces monocyte proliferation as well as differentiation into macrophages in male human U937 cells (p< 0.01 or p< 0.001). Female and male M1 and M2 differentiated macrophages showed differences in the cell structure. In addition, E2 treatment changed the morphology in female and male activated macrophages. Treatment with E2 and ICI in combination increased the expression of the M-CSF receptor in female M2 macrophages (p<0.05), however E2 alone did not increase the expression of the receptor (p>0.05). E2 treatment did not influence the expression of the M-CSF receptor or GM-CSF receptor in female M1 macrophages (p>0.05). E2 treatment increased the expression of the GM-CSF receptor in female M2 macrophages after 24 h treatment (p<0.05). Furthermore, ICI inhibited the effects of E2 in M2 macrophages (p> 0.05). In addition, E2 treatment increased the expression of the chemokine receptors CCR2 and CCR3 in female M1 and M2 macrophages (p< 0.01 and p< 0.001). IL-1β
RNA expression is decreased in male but not in female undifferentiated human macrophages after E2 treatment (p< 0.001 and p> 0.05, respectively).

**Conclusion**
Our preliminary results show sex-differences in the effects of E2 in the morphology of macrophages, leading to sex-specific phenotypes. Furthermore, E2 enhances chemotaxis of female monocytes. In addition, E2 modulates the expression of pro-inflammatory cytokines, potentially promoting the modulation of the immune response in the heart during inflammation, which may be directly involved in cardiac tissue remodelling.
Title: Comorbid Fibromyalgia In Systemic Lupus Erythematosus Is Associated With Worse Health-Related Quality Of Life And Increased Perceived Disease Severity

Poster Number PW0246

Authors
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Aim of Investigation
Systemic lupus erythematosus (SLE) is a rheumatic disease that can result in significant morbidity and mortality. Pain and fatigue are common symptoms with anywhere from 5 to 25% of patients with SLE also meeting criteria for fibromyalgia. Participants with comorbid fibromyalgia tend to have greater symptom severity and worse quality of life, but what is not clear is how comorbid fibromyalgia impacts measures of disease activity. The objective of this evaluation was to assess the prevalence of fibromyalgia within a well-phenotyped SLE cohort, assess the relationship between the presence of fibromyalgia and clinical outcomes including health-related quality of life (HRQoL) and to explore these relationships in the context of self-reported measures of SLE disease activity.

Results
The MILES Cohort is comprised of 462 SLE participants and 192 controls. At enrollment, 75.5% of SLE participants rated their level of general pain as ≥4 using a VAS of 0-10 indicating the presence of at least moderate pain, compared to 45.8% of our population-based controls (p=0.000). In addition, significantly more SLE participants (41.1%) met the 2011 survey criteria for fibromyalgia, compared to 13.0% of controls (p=0.000). Frequency of comorbid fibromyalgia was similar among black SLE participants (38.6%) and white SLE participants (42.8%), but more common in black controls (20.5%) compared to white controls (7.4%; p=0.038). Moreover, across all eight domains of the RAND SF-36 HRQoL measure, the fibromyalgia-positive SLE participants (n=190) scored significantly worse compared to fibromyalgia negative participants on all scales including energy/fatigue (p<0.001). Also, SLE participants with comorbid fibromyalgia reported worse pain (98.4% vs 59.6% with pain ≥4; p=0.000) and were more prone towards pain catastrophizing (11.7 vs 5.3 CSQ; p=0.000) compared to those who did not meet criteria. Lastly, we found that patient-reported lupus disease activity scores measured by the SLAQ were
2 times higher among SLE participants with comorbid fibromyalgia than in those without comorbid fibromyalgia (18.6 [0.5] vs 9.0 [0.4], respectively; p<0.0001).

**Conclusion**
Fibromyalgia, assessed by the 2011 survey criteria, was found to be more common in SLE in this population-based study than previously reported. Those who met fibromyalgia criteria reported greater pain and fatigue and worse quality of life. Moreover, the SLAQ, a validated measure of SLE disease activity for use in epidemiologic research, was associated with a doubling in the presence of comorbid fibromyalgia. The clinical implications are that participants with comorbid fibromyalgia may present as more symptomatic and describe features consistent with greater lupus disease severity, which in fact might be attributable, at least in part, to underlying fibromyalgia.
Title: Prediction Of Disease Activity And Temporomandibular Joint Involvement In Patients With Juvenile Idiopathic Arthritis

Poster Number PW0247

Authors
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Aim of Investigation
There is a need of better diagnostic procedures and markers of disease activity in the temporomandibular joint (TMJ) in patients with Juvenile Idiopathic Arthritis (JIA). This is due to an often clinically silent development of TMJ involvement and the high incidence of severe and life-long consequences of the TMJ-involvement in patients with JIA, such as micrognathia, pain as well as functional and aesthetic impairments. An early and more accurate diagnosis of disease activity in the TMJ would improve the possibility for early treatment and decrease the risk for future impairments. The aim of this study was to identify diagnostic methods and predictive factors for disease activity in TMJ involvement in JIA.

Results
Baseline data from 61 patients, 45 girls and 16 boys with a mean age of 10.6 years and a mean diagnosis of 4.2 years (median 3.5, range 0-13 years) are reported. According to ILAR two patients had monoarthritis, 22 oligoarthritis, 24 polyarthritis, 3 psoriatic arthritis and 10 was diagnosed as unspecified arthritis. 15 had no medication, 26 NSAID:s, 24 MTX, 15 Biologics and 2 were treated with Prednisolon. On the question: 'Do you ever experience pain in the jaw?', 42% of the children answered that they previously had had jaw pain and 36% that they had it at present. On the question: 'Do you feel pain when open wide or when biting as hard as you can?', 18 % answered muscle pain, 34% TMJ pain and 13% muscle and TMJ pain. The radiographic examination by CBCT and Panoramic x-ray showed hard tissue changes of the TMJ in 72% of the children at baseline. According to RDC/TMD 37% was diagnosed with myofacial pain, 3% with myofascial pain with reduced mouth opening, 8.5% disc displacement with reduction, 17% arthralgia, 32% osteoarthritis and 54% osteoarthrosis. ANOVA test showed that patients
with osteoarthritis have significantly smaller mouth opening without pain compared to patients with either arthralgia or osteoarthrosis (p = 0.001)

**Conclusion**
Conclusions: The results of this study indicate that there is a high frequency of self-assessed orofacial pain and impaired jaw function in children with JIA and that increased jaw opening could be a predictor for active TMJ arthritis in JIA
Title: A Pilot Study Of Wrist Pain After Childbirth In Hong Kong Mothers

Poster Number PW0248

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Aim of Investigation
To examine the prevalence and associations of wrist pain among mothers after childbirth, and the implications of future antenatal education and postpartum care.

Results
259 mothers (89.3% response rate) participated in this telephone survey, with 149 mothers (57.5%) developed wrist pain after childbirth. 124 mothers (84%) had persistent wrist pain at 2 months after delivery, with 43.5% suffered from moderate and 21% from severe degree of pain. 43.2% of the mothers had unilateral wrist pain and 56.8% had bilateral wrist pain. 56.8% of the pain was located on the radial side of the wrist, followed by dorsal wrist pain (13.2%) and generalized wrist pain all around the wrist (13.2%). Nulliparity appeared to be the risk factor associated with the development of wrist pain after childbirth; and the pain intensity was found to have negative correlation with baby's birth weight. The mean PREW-pain score and PRWE-function score was 22.8 and 15.6 respectively. Wrist pain was also found among 19.5% of the helpers involved in taking care of the newborns.

Conclusion
Wrist pain is prevalent among mothers after childbirth, with majority of them suffered from moderate to severe pain intensity. More studies are needed to find out the reasons for the development of the wrist pain, the possible ways to prevent its happening and the long term consequences of it on maternal health.
Title: Regulation Of Trpv1 Activities By Serotonin-Mediated Sexually Dimorphic Mechanism

Poster Number PW0249

Authors
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Aim of Investigation
We hypothesized that 5-HT releases a 'soluble factor' from female human biopsies but not male biopsies and this factor sensitizes capsaicin-sensitive peripheral nerve fibers.

Results
1. CM only from female dental pulp treated with 5-HT sensitized I<sub>CAP</sub> responses; 2. The soluble factor is a peptide and not a lipid; 3. Proteomics revealed that the soluble factor is complement C3a (C3a); 4. C3a receptor antagonists and anti-C3a antibody block CM-induced sensitization of I<sub>CAP</sub>.

Conclusion
Collectively, these novel data suggest that 5-HT triggers a peripheral sexually dimorphic pain mechanism in women via release of complement peptides that leads to enhanced activity of capsaicin-sensitive trigeminal nociceptors. Acknowledgements: Barker Foundation and Owens Medical Research Foundation
Title: Characterization Of Pain, Psychology, And Sleep During Pregnancy

Authors

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Aim of Investigation
Pain during pregnancy is poorly studied or characterized. It may be associated with anxiety, depression and impaired sleep, all of which can put women at a higher risk of persistent post-operative pain after surgical delivery. As part of the Oxford Persisting Post-Operative Pain Study (OxPPOPS), a longitudinal prospective trial investigating the incidence of chronic post-surgical pain (CPSP) after caesarean section (CS), we explored pain, sleep and psychological factors in pregnant women awaiting planned CS.

Results
Data were available from 588 of the 728 women who gave informed consent to participate in the study. The majority of women experienced some pain during pregnancy (71%), most commonly in the back (39%) or pelvis (37%). Approximately 40% of the women reported pain persisting for more than 3 months during pregnancy, thus achieving the IASP criteria for chronic pain. The intensity of pain in the last week, also reported by 40% of women, had a median [IQR] of 29/100 [13-46]. A fifth of women (20%) required analgesia in the last seven days, whilst 4% required analgesia every day. Only five patients (<1%) had a likely neuropathic component to their pain. Depression, anxiety and impaired sleep were statistically higher for the women who experienced chronic pain that began during pregnancy (CES-D: Z=3.43, p<0.01; trait anxiety: Z=2.86, p<0.01; sleep - PSQI global: Z=3.52, p<0.001) when compared with pain-free women. This was also the case in women who experienced pain late in pregnancy (CES-D: Z=4.76, p<0.001; trait anxiety: Z=2.91, p<0.005; state anxiety: Z=2.72, p<0.01; sleep - PSQI global: Z=5.39, p<0.001). Additionally, the intensity of the pain experienced in the last week positively correlated with both state anxiety (R=0.182, p<0.05) and PSQI global sleep scores (R=0.33, p<0.01). In contrast, women who experienced some pain during pregnancy had significantly increased depression (Z=3.04, p<0.005) and impaired sleep (Z=3.549, p<0.001) levels but were not found to be more anxious when compared to pain-free women.
Conclusion
This study indicates that pain during pregnancy is commonly experienced and can become chronic in duration. It is generally associated with increases in anxiety, depression and impaired sleep, although the directionality of the relationships is difficult to establish. We are currently addressing the impact of these factors on CPSP following CS and exploring novel analytical techniques with a view to predicting the individuals at-risk of developing CPSP.
**Title:** An Investigation Of Associations With Dysmenorrhoea In Adolescents And Young Women: A Twin Family Case-Control Study

**Poster Number** PW0251

**Authors**
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**Aim of Investigation**
Dysmenorrhoea has been identified as affecting up to 90% of young females, 10-20% of whom report their pain and suffering as severe. Recent investigations have demonstrated neurobiological abnormalities in response to noxious stimuli at all phases of the menstrual cycle in dysmenorrheic, but otherwise healthy, women. Dysmenorrhoea has been found to co-occur frequently with a number of primary chronic pain conditions, particularly those associated with visceral pain such as irritable bowel syndrome and with fibromyalgia. Family history of dysmenorrhoea has also been identified as being associated with menstrual pain. An investigation of associations between dysmenorrhoea, primary pain conditions, and conditions with established primary pain associations such as restless legs syndrome (RLS), iron deficiency (ID) and anxiety or depression may serve to elucidate knowledge regarding the aetiology and potential risk factors for the development of chronic pain conditions. Utilising a twin family case-control design, our aims were to investigate genetic influence and to determine associations between dysmenorrhoea and primary pain disorders.

**Results**
Significant heritability was found for lifetime prevalence of bothersome dysmenorrhoea symptoms (h² ± s.e = 0.58 ± 0.29), measure of current menstrual pain intensity (0.66 ± 0.06), but not lifetime prevalence of bothersome period pain (0.39 ± 0.28). Generalised estimating equation regression analyses revealed multivariate associations between lifetime prevalence of period pain with migraine (β=0.66, p<0.01) and RLS (β=0.81, p<0.01). Lifetime prevalence of bothersome associated symptoms was multivariately associated with RLS (β=0.68, p<0.01) and LBP (β=0.60, p<0.01). Highest pain intensity rated on a current cycle was multivariately associated with headache (β= -1.31, p<0.01), and iron deficiency (β=1.78, p<0.01).
**Conclusion**

The results of within twin analyses suggest that the experience of symptoms associated with dysmenorrhea in addition to pain intensity suggest heritability and are consistent with genetic influence. Correlational analyses support previously reported associations between period pain and migraine in older populations. The associations observed between dysmenorrhea measures, RLS and iron deficiency are consistent with an hypothesised role of iron in pain experiences. These associations in particular demonstrate further similarities between dysmenorrhea and primary pain conditions, although with fewer associations observed.
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Title: Cyclicity Is Rarely Assessed Or Accounted For In Chronic Pelvic Pain Trials In Women

Poster Number PW0252

Authors
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Aim of Investigation
Chronic pelvic pain (CPP) is a common and often disabling condition affecting up to 15% of women, that is frequently difficult to treat. A significant body of evidence suggests that women with CPP syndromes experience variation in symptom severity across the menstrual cycle, whatever the aetiology. This variation could confound results if not properly assessed and accounted for in clinical trials, which in turn may hinder translational efforts. We therefore performed a systematic review to assess the extent to which cyclicity is assessed and accounted for in trials of interventions for CPP in women, and the methods by which this is undertaken.

Results
9248 unique results were identified by the searches. Of these, 612 were selected for inclusion. Only 16 studies assessed cyclicity. Assessment methods included measurement of serum hormones (e.g. oestradiol and follicle stimulating hormone) and monitoring of uterine bleeding patterns. No studies expressly accounted for cyclicity in trial design. Although several trials did commence therapy at a specific point in the menstrual cycle, follow-up assessments were performed at 4-weekly intervals rather than at the same point of the menstrual cycle.

Conclusion
Despite good basic science and epidemiological evidence of the influence of sex hormones and/or menstrual cycle phase on pelvic pain severity, only 3% of the studies we identified made any assessment of cyclicity. The majority of studies assessing serum hormones used these an endpoint rather than for cycle timing. Surprisingly, no studies stated a plan to account for cyclicity in trial design, even if the pathology of interest was 'gynaecological.' We suggest cyclicity may be an important confound in trials assessing CPP, and therefore recommendations are needed for how this should be assessed and accounted for in the design of future trials.
Title: Association Of Acute, Subacute, And Chronic Postoperative Pain With Prospectively Assessed Psychosocial And Psychophysical Variables In Women Undergoing Breast Cancer Surgery

Poster Number PW0253

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Aim of Investigation
Aim of Investigation: Breast cancer is the most common form of female cancer, the treatment of which often involves either partial or total mastectomy. Previous reports cite persistent postmastectomy pain (PPMP) incidence around 30%, with putative risk factors including younger age, type of surgery, axillary dissection, anesthetic technique, genetics, negative affect (psychosocial factors) and increased pain sensitivity (psychophysical factors). However, most previous studies of PPMP have been retrospective and cross sectional in design. In the current study, a broad array of potential risk factors were assessed in women prospectively before surgery, in order to determine whether the prediction of subsequent acute, subacute and chronic pain differentially depends on these factors.

Results
Patients undergoing more extensive surgery reported higher acute pain (postoperative day 0 and 1), with severity correlating with surgical extent (bilateral mastectomy> unilateral mastectomy> lumpectomy), as well as younger age, and higher preoperative psychosocial dysfunction (high catastrophizing, anxiety, depression). Subacute postoperative pain (postoperative day 14) also correlated with younger age and preoperative psychosocial dysfunction, but not surgical extent and duration. By 90 days after surgery, PBI was no longer associated with age or surgical factors, but remained correlated with preoperative psychosocial factors, as well as heightened baseline sensory processing (higher temporal summation of pain and painful aftersensations).

Conclusion
Conclusions: These findings suggest that the factors influencing acute pain after surgery may differ somewhat from those that predict more persistent pain. By more extensively phenotyping individual
differences in pain processing in the preoperative period, we may be able to identify those at greater risk of acute vs chronic postsurgical pain, and design preventive therapies accordingly.
Title: Acute Postoperative Pain And Persistent Postsurgical Pain: Incidence, Risk Factors, And Risk Groups In Austria

Poster Number PW0254

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Aim of Investigation
Acute postoperative pain has been identified as a predictor for persistent postsurgical pain (PPSP). Surprisingly, this evidence has been derived mostly from clinical trials and other studies performed for different reasons. Prospective observational studies focused on identifying incidence, risk factors and risk groups are surprisingly rare and data concerning the Austrian population is scarce. The aim of this study was to investigate the influence of acute postoperative pain on PPSP and establish incidence, magnitude, and risk factors for perioperative pain in a variety of patients.

Results
Overall 326 patients were included for the analysis of acute perioperative pain (pre-operative, PACU and POD1) and 246 patients were included in the long-term (one-year) follow-up period, with a follow-up rate of 81.7% at three months. The most commonly performed procedures were hernia repair (22%), laparoscopic cholecystectomy (18%), thyroid surgery (14%) and resections of the colon (11%). Preoperative pain was reported by 33.3% of patients, with a mean pain intensity (at the moment) of 4.2 (±2.5). Pain at the PACU was surprisingly low with an average maximum pain intensity of 2.9 (±1.4). On POD1 27.3% of patients reported a pain intensity of 4 or higher at the moment, 44.7% had suffered from pain of 4 or higher on average since the operation, and 34.2% had experienced intense pain (NRS 7-10) at some point since the day before. At three months, 51 people (25.4%) reported pain in the area of surgery, more women reported PPSP than men (37 vs. 14, p = 0.031). PPSP rates were 21.3% for hernia repair surgery, 22.9% for laparoscopic cholecystectomy, 12.5% for thyroid surgery, and 7.1% for colon surgery. Patients who developed PPSP suffered from more intense pain preoperatively (p < 0.001), at the PACU (p = 0.068), and reported more intense pain on POD1 at the moment (p < 0.0001), on average since the day before (p < 0.0001), and maximum pain since the day before (p < 0.0001). Patients reporting on POD1 that they had experienced moderate to intense pain at any point since the day before had a relative risk of 4.7 (2.0-11.3, 95%CI) for developing PPSP.
Conclusion
Patients undergoing elective abdominal surgery suffering from more intense perioperative pain are at higher risk for developing PPSP. The incidence of moderate to severe acute postoperative pain is high, despite the availability of a dedicated pain service. About one quarter of operated patients suffer from PPSP three months after the operation.
Title: Ultrasound Guided Transversus Abdominis Plane Block: Useful To Prevent Chronic Pain After Laparoscopic Cholecystectomy?

Poster Number PW0255

Authors
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Aim of Investigation
There are multiple risk factors involved in the transition from acute to chronic pain after surgery, but the severity of acute postoperative pain is the most important independent predictor of chronic pain (CP) after surgical intervention, there are multiple risk factors and mechanism involved in this transition. Regional anesthesia and analgesia techniques has been shown o reduce the incidence of CP in many kind of surgery. Conventional laparoscopic cholecystectomy (CLC) is regarded as the gold standard for cholecystectomy, however even this techniques carry a 5% risk of developing a CP. Regional anesthesia and analgesia techniques has been shown o reduce the incidence of CP in many kind of surgery. The Transversus abdominis plane block (TAP) have been shown to be an effective technique for cholecystectomy, in terms of good post operative analgesia, reduced opiates consumption and side effects. However, even if regional anesthesia and analgesia techniques has been shown to reduce the incidence of CP in many kind of surgery when compared to intravenous analgesia (IV), there is a lack of data regarding the role of TAP in the prevention of chronic pain, and we are going to investigate on this topic.

Results
During the period we included 45 patients in Group A and patients 43 in Group B. All the procedure were performed under total intravenous general anesthesia with propofol. The Group A did not require intraoperative opioid but the bolus used for the induction of general anesthesia. Demographic data didn't show statistically significant differences between the 2 groups. CP never occurred in Group A, while occurred in 3 patients in Group B (7.0%), this difference is not statistically significant (p=0.112, Fisher's exact test). The mean NRS for the patients at the end of the procedure was 2.05 ± 1.03 in Group
A and 4.30 ± 1.71 in Group B, this difference is statistically significant (p< 0.0001, Unpaired student's t test)

**Conclusion**
A modern approach to pain control should consider the reduction or elimination of pain and suffering together with the consideration that reduced morbidity, length of stay and hospital costs markedly improve when pain management is successful. Conventional laparoscopic cholecistectomy has a low incidence of chronic pain but the Transverse abdominal plane blockade seems to reduce it even if in this paper there is not a statistically significant difference most probably because of the small number of patients included. The TAP did show a significant reduction of the NRS at the end of the intervention but regarding this issue even the IV seems to be a good choice as the pain scores are low in both groups. TAP block could be promising in reduce the opioids related side effects because less opioids were used during surgical act.
Title: Ultrasound-Guided Pulsed Radiofrequency Treatment On The Saphenous Nerve For Persistent Postoperative Pain After Total Knee Arthroplasty

Poster Number PW0256

Authors

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Aim of Investigation
Persistent postoperative pain (PPP) has been defined by the International Association of the Study of Pain (IASP) as pain that develops after surgery and has been present for at least 3 months, which is beyond the time for normal healing. It is known that almost 40% of patients undergone total knee arthroplasty (TKA) are affected with PPP, which is often refractory to conventional treatment. We present two patients with PPP after TKA who were treated successfully by ultrasound-guided pulsed radiofrequency (PRF) on the saphenous nerve.

Results
Case 1: After the procedure, the pain and restricted knee ROM immediately improved. The effect lasted for 12 months. Case 2: The allodynia was immediately improved after PRF. The effect lasted for 12 months.

Conclusion
The ultrasound-guided PRF on saphenous nerve can be useful for the management of PPP after TKA, and it supports functional return.
**Title**: Risk Factors For Neuropathic Pain After Thoracic Surgery

**Poster Number** PW0257

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**Aim of Investigation**
Postoperative neuropathic pain following thoracic surgery is common. Although video-assisted thoracic surgery (VATS) is considered less invasive, neuropathic pain even after total VATS can still occur. This study aims to clarify the risk factors for neuropathic pain after thoracic surgery including after total VATS.

**Results**
Forty-eight patients (25.9%) suffered neuropathic pain after surgery. Median onset time was seven days (range 1-30 days) and median offset time was 50 days (range 14-365 days). They had significantly acute pain (P < 0.005), frequent analgesic use (P < 0.0001), and long postoperative hospitalization (P < 0.0001). Nine of 48 patients (18.8%) have had neuropathic pain even one year after surgery. Multivariate logistic regression analysis revealed that preoperative use of sleeping drugs [odds ration (OR), 5.04; 95% confidence interval (CI), 2.32-11.33, P < 0.0001] and operation duration (≥2 hours) (OR, 2.61; 95%CI, 1.05-7.20; P = 0.0387) were risk factors for neuropathic pain after thoracic surgery, while total VATS decreased the risk (OR, 0.23; 95% CI, 0.09-0.55; P = 0.0008).

**Conclusion**
Preoperative sleeping drugs, thoracotomy and an operation time extending beyond two hours were associated with neuropathic pain after thoracic surgery. Total VATS appears to decrease the incidence of it.
Title: A Retrospective Study Of Acute And Persistent Postoperative Pain Following Thoracic Surgery

Poster Number PW0258

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Aim of Investigation
In our outpatient pain clinic, all patients who underwent thoracic surgery at Osaka University Hospital were evaluated their status of pain from the acute to the chronic phase. This retrospective study aims to determine the prevalence of persistent postoperative pain (PPP) after thoracic surgery and to compare the pain intensity and other pain-related indicators between acute and chronic phase.

Results
There were forty-two patients who fulfilled the criteria. The number of patients applicable for PPP was 28 (66.7%), and those who had moderate to severe pain (NRS 4 and more) was 7 (16.7%). All the indicators of PPP group were significantly worse than those of NP group in acute phase. The NRS and pain-related indicators of PPP group remains worse from acute phase, and no significant change between acute and chronic phase. There were no differences about background data of the patients.

Conclusion
PPP occurs frequently after thoracic surgery in our hospital. As a result, assertive intervention to control the pain from acute phase would play a significant role in decreasing PPP.
Title: Preoperative Opioid Use Is Independently Associated With Increased Costs And Worse Outcomes Following Major Abdominal Surgery

Poster Number PW0259

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Aim of Investigation
Opioids are increasingly used to manage chronic pain, and chronic opioid users are challenging to care for perioperatively. Given the epidemic of opioid-related morbidity and mortality, it is critical to understand how preoperative opioid use impacts surgical outcomes. The aim of this investigation was to explore the clinical and financial implications of preoperative opioid use in major abdominal surgery. We hypothesized that preoperative opioid users would have higher hospital costs, longer hospital length of stay, higher morbidity, increased discharge to nursing and rehabilitation facilities, and increased hospital readmission.

Results
2413 patients met inclusion criteria. 502 patients (21%) used opioids preoperatively. After multivariate covariate adjustment, opioid users (compared to opioid-naïve) had higher mean costs ($26,520 vs. $24,266, P=0.006), longer mean LOS (5.9 vs 5.2 days, P=0.007), higher complication rates (20% vs. 16%, P=0.016), higher rates of non-home discharge (14% vs. 11%, P=0.050), and increased readmission rates (10% vs 6%, P=0.005). Significant univariate differences in morbidity were found for surgical site infection (14.9% vs 8.3%, p<0.001), sepsis (3.8% vs 1.6%, p=0.004), postoperative unplanned intubation (2.6% vs 1.3%, p=0.04), postoperative myocardial infarction (1.0% vs 0.3%, p=0.038), and postoperative transfusion (7.2% vs 3.5%, p=0.001).

Conclusion
Opioid use is common prior to abdominopelvic surgery and is independently associated with increased postoperative healthcare utilization, morbidity, and poor postoperative outcomes. Preoperative opioids represent a potentially modifiable risk factor and a novel target to improve quality and value of surgical
care. Future studies are needed to determine whether preoperative opioid weaning and/or cessation can improve postoperative outcomes.
Title: Development Of A Risk Score For Persistent Postoperative Pain Following Breast Cancer Surgery

Poster Number PW0260

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Aim of Investigation
Persistent postoperative pain concerns 30-50% of patients following breast cancer surgery. Multiple studies have already identified numerous risk factors. Studies testing preventive measures, however, have so far failed to produce consistent positive results. If preventive measures could be targeted to a subgroup of patients at high risk of persistent pain, positive results would be more likely. Therefore, we studied known risk factors for persistent pain in patients scheduled for breast cancer surgery in order to construct a risk score simple enough to select high-risk patients in future prevention studies.

Results
At 4 months, data from 127 patients were available. In univariate analysis, the following factors were significantly associated with 'clinically significant pain': history of depression, pre-existing pain at the surgical site, high acute pain expectation, younger age, and state anxiety. Age and state anxiety score deviated from log-linearity. Age was consequently dichotomized in age groups of ≤50 or >50 years, for state anxiety no meaningful cut-off was found and this variable was not further used in the analysis. The coefficients of the logistic regression model were 2.42 for pre-existing pain, 1.32 for history of depression, 1.51 for high expected acute pain, and -1.22 for age above 50 years. The area under the curve of this model is 0.851, after correction for overfitting 0.816. Using the significant parameters, a risk score was constructed identifying patients with a predicted risk of clinically significant persistent pain at 4 months. Pre-existing pain at the surgical site adds 2 points, and history of depression, high acute pain expectation (>6/10), and age ≤50 years each add 1 point to the score. Patients with a score of ≥2 points have a predicted risk of persistent pain of >30% (the actual risk in this group was 57.6%).

Conclusion
A simple risk score with 4 parameters (pre-existing pain, history of depression, high acute pain expectation, and age) may allow to identify patients with high (>30%) risk of persistent pain already before breast cancer surgery, and thus enable the study of targeted preventive interventions. Other
parameters (such as questionnaires) may identify high risk patients with higher precision, but simple scores have a higher chance to be used in clinical practice. However, the risk score developed in this study needs to be validated in different settings.
Title: Improving Post Surgical Neuropathic Pain (Psnp) Relief In Cancer Patients Using High Concentration (8%) Capsaicin Patch

Poster Number PW0261

Authors

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Aim of Investigation

Many cancer patients experience post-surgical neuropathic pain. Current Pharmacological treatments bring only partial relief with tolerance issues. The capsaicin 8% patch is an approved treatment for localized peripheral neuropathic pain. We report here our experience with this agent in a cohort of patients with PSNP.

Results

20 patients with post-surgical complex cancer pain with areas of focal neuropathic pain, aged 38-68 years, were treated with a 60 minute application of a capsaicin 8% patch on the area with alldynia. All patients had loco regional block analgesia before capsaicin application to prevent pain worsening during procedure. Neuropathic pain in our cohort was related with several cancers: carcinoma (n=10); sarcoma (n=6); lymphoma (n=2); neurofibromatosis (n=1); ependymoma (n=1). All patients were resistant to a well-conducted neuropathic pain treatment according to French recommendation. All patients reported significant pain relief during the first month after capsaicin use. At 6 months, pain scores were reduced by <30% in 2 patients (10%), 30-50% in 2 patients (10%), 50-70% in 8 patients (40%), 70-90% in 5 patients (25%), and >90% in 3 patients (15%). Capsaicin patch was well tolerated. This procedure was repeated in case of pain recurrence: 8 patients received 1 applications, 6 patients 2 applications, 4 received 3, 1 received 4 , for 1 patient procedure was repeated 11 times. The median delay between two consecutive applications was 6 months in our cohort.

Conclusion

Capsaicin 8% patch appears to be effective and well tolerated for patients with PSNP, with a prolonged effect, allowing discussing its use earlier in the management of patients with painful PSNP.
Aim of Investigation
Epidural injection of various medications has been established as one modality for management of chronic pain. Proper identification of the epidural space is the first step in such procedure. The present study was conducted to compare and evaluate the common loss of resistance (LOR) syringe technique (subjective method) and the drip infusion technique (objective method) for identifying the epidural space in patients with failed back surgery.

Results
First attempt success rate for epidural space localization was higher in Group II (100%). The mean time taken for epidural space localization was significantly shorter (P < 0.01) in Group II when compared with Group I. Number of attempts for space localization was less in the majority of patients of Group II, but the difference was found to be statistically nonsignificant. Group II showed better ease and satisfaction scores than Group I with statistical significance. There was one case of unintentional dural puncture in Group I.

Conclusion
The time taken to localize the epidural space was less in the drip infusion technique. Both techniques are comparable as regard the number of attempts and rate of complications. Being an objective method, the drip infusion technique is considered a safe and feasible technique for epidural space localization in patients with failed back surgery.
Title: Is There A Key Role For MMP-12 In The Visceral Pain Of Crohn’s Disease In Pediatrics?

Poster Number PW0263

Authors
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Aim of Investigation
Visceral pain is a cause of significant morbidity in Crohn’s disease. It can frequently be of moderate to severe intensity and persists within remission in the majority of patients. Pain in Crohn’s disease is triggered by the activation of pain sensing nerves which innervate the gut (nociceptors) by substances released from the inflamed bowel. Traditional inflammatory mediators such as prostaglandins, and cytokines such as TNF-alpha or IL-1-beta are implicated in this process. The aim of current study was to investigate the mechanisms of nociceptor activation in Crohn’s disease using biopsy samples taken from inflamed mucosa, following the informed parental consent (ethical approval REC# p/01/023) with Crohn’s disease and abdominal pain, undergoing endoscopy as part of their standard clinical treatment.

Results
Supernatants from Crohn’s disease patients produced a significant increase in serosal nociceptor activity compared to control supernatants (p<0.001). This increase in nociceptor activity was comparable between drug treated (e.g. prednisalone, infliximab or azathioprine) and drug naïve Crohn’s patients, despite the clear reduction in IL-8 levels in samples from drug treated patients (122.2 ± 43.1 vs 8.2 ± 3.8 pg/ml, respectively; p<0.001). Further analysis of transcript levels revealed striking reductions in the expression of TNF-alpha, IL-1 beta, IL-6, and COX-2 in biopsies from drug treated patients, suggesting that these mediators are unlikely to be responsible for supernatant-driven nociceptor activation. By contrast, expression of tryptase, MMP-9 and MMP-12 remained elevated in drug treated and drug naïve patients; and a significant correlation was found between MMP-12 expression and nociceptor activation (p<0.01, r\textsuperscript{2} = 0.44).

Conclusion
This study suggests that MMP-12 plays a key role in the production of visceral pain in Crohn’s disease.
Title: Evidence For Reduced Nociceptor Activation With Increased Disease Severity In Pediatric Ulcerative Colitis

Poster Number PW0264

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Aim of Investigation
Introduction and Aims. Visceral pain is a cause of significant morbidity in patients with Ulcerative Colitis (UC) who experience abdominal pain (~60%). The activation of pain sensing nerves which innervate the gut (nociceptors) by mediators released from the inflamed bowel is an important trigger for pain in UC. However, mediators which inhibit nociceptors are also produced in the bowel of UC patients e.g. opioids, and so the level of pain experienced is a balance between the production of pro- and anti-nociceptive mediators. The aim of the current study was to investigate the effects of mediators produced by the mucosa of UC patients on visceral nociceptor activity.

Results
Supernatants from UC patients contained significantly more IL-8 than control supernatants (p<0.01) and elicited a significant increase in serosal nociceptor activity compared to control supernatants (p<0.01). Interestingly, nociceptor responses were significantly reduced (p<0.05) in UC supernatants with high IL-8 levels (>100 pg/ml) compared with UC supernatants with low IL-8 levels (<75 pg/ml) suggesting an inverse correlation between nociceptor activation and the level of tissue inflammation in UC. This observation was further supported by transcript expression, which demonstrated significantly greater levels of COX-2, IFN-gamma, MMP-1/-3/-9/-12, and IL-6, in biopsies with high IL-8 supernatants compared with biopsies of low IL-8 levels (p<0.05). Analysis of nociceptor activation against transcript expression across all biopsies revealed a significant inverse correlation of firing with expression of tryptase, histidine decarboxylase, IL-6, COX-2, MMP-1 and MMP-9 (p<0.05). Consistent with the hypothesis that nociceptor firing decreases with increased mucosal inflammation in UC.

Conclusion
We speculated that the increase in mucosal inflammation coincides with the production of an inhibitor
mediator, which is responsible for preventing the activation of nociceptors by pro-nociceptive inflammatory mediators produced in UC.
Title: The Impact Of Opioid Treatment On Regional Gastrointestinal Transit

Poster Number PW0265

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Aim of Investigation
To employ a human experimental model of opioid-induced bowel dysfunction (OIBD) in healthy volunteers, and evaluate the impact of opioid treatment compared to placebo on gastrointestinal (GI) symptoms and motility, assessed by questionnaires and regional GI transit times.

Results
GI symptom scores increased significantly across all applied questionnaires during opioid treatment. Oxycodone increased median total GI transit time from 22.2 to 43.9 hours (P<0.01), segmental transit times in the cecum and ascending colon from 5.7 to 9.9 hours (P<0.05), rectosigmoid transit time from 2.7 to 9.0 hours (P<0.05), and colorectal transit time from 18.6 to 38.6 hours (P<0.01). No association between questionnaire scores and segmental transit times were detected.

Conclusion
Self-assessed adverse GI effects and increased GI transit times in different segments were induced during oxycodone treatment. This detailed information about segmental changes in motility has great potential for future interventional head-to-head trials of different laxative regimes for prevention and treatment of OIBD.
Title: Case Series Of Perioperative Analgesia For Pancreatectomy & Autologous Islet Cell Transplant Patients

Poster Number PW0266

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Aim of Investigation
Congenital/hereditary pancreatitis is a lifelong debilitating condition for patients. A number of these patients have intractable abdominal pain and are started on analgesic therapy, including opioids, from a young age. Pancreatectomy and autologous islet cell transplantation offers the possibility to reduce pain, however, the procedure itself can be challenging for patients given that is invasive and many are opioid-tolerant requiring long-term follow-up to avoid complications. Our primary goals were to facilitate perioperative analgesia, avoiding potential complications, reducing opioid consumption, in order to meet our goals of reducing, if not eliminating opioid use in the long-run, e.g. months after surgery. A team consisting of transplant surgery, anesthesiologist/pain physician, nursing, social work, developed a perioperative pathway to smoothen the transition of these patients through their transition into and out of their surgery.

Results
Data still being analyzed. 80% of patients had a significant reduction in the consumption of their opioids after surgery as compared to prior to surgery. 40% of the patients were able to taper off all of their opioid medications and currently are not taking any opioids.

Conclusion
This is a small descriptive analysis of peri-operative pain management in a complex cohort of patients with lifelong visceral and inflammatory pain undergoing a potentially ameliorating surgery. Surgery itself can be a risk for significant and persistent pain, therefore, a system attempting to address this in a multi-modal and interdisciplinary manner was necessary to provide the best outcomes for our patients. This surgery is unique, not only for its novelty and rarity, but also for its goal in reducing pain and opioid consumption for patients. While this analysis does not compare individual modalities, nor does it
compare it to a cohort of patients not receiving aspects of therapy, we used data and experience to
determine our pathway and hope to continuously improve on it as we learn more about our patient
population and applications from other preoperative pathways.
Aim of Investigation
Among the mediators present in IBS patient colons, proteases able to signal to enteric neurons are of major importance. However, lack of knowledge on the origin and nature of these proteases has hampered further research and development. We made the hypothesis that the intestinal epithelium is an important source of proteases that are inducing neuronal signaling, and potentially hypersensitivity symptoms associated with IBS.

Results
We showed that stimulated intestinal epithelial cells released trypsin-like activity specifically on the basolateral side. This activity was able to activate cultured sensory neurons. In IBS patient colons, increased trypsin-like activity was associated with the epithelium. We identified that Trypsin-3 was the only form of trypsin up-regulated in stimulated intestinal epithelial cells and in IBS patient tissues. Trypsin-3 was able to signal to human submucosal enteric neurons and sensory neurons through a Protease-Activated Receptor-2 (PAR2)-dependent mechanism. Trypsin-3 was also able to induce visceral hypersensitivity in vivo, when delivered into mouse colon.

Conclusion
Our data demonstrated in IBS, that the intestinal epithelium produces and releases the active protease Trypsin-3, which is able to signal to enteric neurons and to induce visceral hypersensitivity.
Title: Sublimed Tens: A Connected And Wearable Transcutaneous Electrical Nerve Stimulation (Tens) Innovative Device For The Relief Of Back Pain

Poster Number PW0268

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Aim of Investigation
Based on 5 patents, the SUBLIMED TENS, is a new device for low back chronic pain assessment and therapy. Wearable, miniaturized and smartphone controlled, the SUBLIMED TENS brings key innovations for both patients and therapists. It allows to follow patient pain evolution and history of use, in order to achieve a better therapy efficiency control.

Results
All patients wearing a conventional TENS complain of discomfort directly related to the device: clutters of the device, length of the wires, difficulty to carry them under clothes, to stretch and to take off the electrodes, difficulties to target the stimulation areas. Caregivers interviews pointed out these issues and also the difficulties to teach the patients how to better use the device and thus to improve observance. Both patients and caregivers emphasize a great interest in the SUBLIMED TENS presented at the end of the interviews.

Conclusion
The conventional TENS therapy is a worldwide developing chronic pain treatment. However, 30% of patients drop out because of the constraints and difficulties of the current available devices. The SUBLIMED TENS lets avoid the physical and psychological discomfort usually encounter with classical TENS devices. After an education session, the patient will be totally independent and will be able to return to an everyday life. The SUBLIMED smartphone application collects, analyzes and synthesizes the patient data: history of use, pain on VAS score, global improvement through physical activity evolution, sleeping time duration, number of micro awakenings. Presented in a user friendly way, charts allow the practitioner to see the trends at a glance. Thus, the practitioner will be easily informed whether the therapy is beneficial for the patient or not and he will be able to better personalized the treatment
based on the results recorded in the long term. While discreetly supporting the patient in daily activities and relieving pain in any circumstances, SUBLIMED makes the TENS therapy enter in a new era of connected medicine giving more tools to physician to accompany patient. SUBLIMED TENS is also relevant to treat many neuropathic chronic pains, as an ongoing multi-centric study will confirm.
Title: Effects Of Stimulation Site Of Transcutaneous Electrical Nerve Stimulation On Pressure Pain Threshold In Healthy Human Subjects

Poster Number PW0269

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Aim of Investigation
Transcutaneous electrical nerve stimulation (TENS) is a noninvasive technique used for pain management. While the effects of TENS are influenced by stimulation site, the optimal stimulation site for pain management remains elusive. Previous studies have shown that hypoalgesic effect is produced when TENS is applied ipsilaterally, bilaterally and contralaterally to the site of pain. However, the investigations compare the effects of these stimulation sites are little. Further, the hypoalgesic effects of bilateral stimulation may be increased by increased charge amounts as additive stimulation from contralateral site. The purpose of this study was to compare the hypoalgesic effects of ipsilateral, bilateral, contralateral stimulation at the same charge amounts.

Results
B-2channel showed significant increase in PPT at 10 and 20 minutes compared to R-1channel (p < 0.05), L-1channel (p < 0.01) and control (p < 0.01) and at 30 minutes compared to R-2channel (p < 0.05), R-1channel (p < 0.01), L-1channel (p < 0.01) and control (p < 0.01). R-2channel showed significant increase in PPT at 10 and 20 minutes compared to R-1channel (p < 0.05), L-1channel (p < 0.01) and control (p < 0.01) and at 30 minutes compared to L-1channel (p < 0.01) and control (p < 0.01). R-1channel showed significant increase in PPT at 10 and 20 minutes compared to R-1channel (p < 0.05), L-1channel (p < 0.01) and control (p < 0.01) and at 30 minutes compared to L-1channel (p < 0.05) and control (p < 0.01). L-1channel showed significant increase in PPT at 10, 20 and 30 minutes compared to control (p < 0.01).

Conclusion
In spite of much the same charge amounts, B-2channel showed significant increase in PPT at 30 minutes compared to R-2channel. These data indicate that bilateral stimulation produces greater hypoalgesic effect compared to ipsilateral stimulation. Although contralateral stimulation produced
lower hypoalgesic effect compared to ipsilateral stimulation, contralateral stimulation may be effective when TENS cannot be applied to same side as trauma or disease.
Title: Tai Chi Significantly Modulates The Impaired Resting State Functional Connectivity Of The Cognitive Control Network In Fibromyalgia

Poster Number PW0270

Authors
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Aim of Investigation
A substantial body of literature suggests that pain and cognition on interact reciprocally, i.e., pain can negatively influence cognitive performance, while cognition on can significantly modulate our pain experience. Previous studies suggest that Tai Chi, a mind-body exercise, has clinically important benefits for pain and may also modulate individuals' cognitive function. We conducted the first pilot brain imaging study to systemically determine whether Tai Chi can influence the top-down modulation of pain among fibromyalgia (FM) patients. We first compared the resting-state functional connectivity (rsFC) of the cognitive control network (CCN) of FM patients to that of the matched healthy controls, and then further examined how Tai Chi practice can modulate the CCN rsFC in relation to clinical outcomes.

Results
Twenty-one FM patients and 20 healthy controls completed the study. The mean age of subjects was 51.5 ± 11.6 (mean ± SD). One FM patient and 1 healthy control were excluded from the rsFC analysis due to excessive head movement during scan. There were no significant differences in age and gender between the FM and healthy control groups. After Tai Chi interventions, there was a significant decrease in the general FIQR score (mean ± SD, Pre: 45.7 ± 18.3, post: 36.4 ± 21, p < 0.001) and the three FIQR domains: Function (pre: 12.2 ± 6.1, post: 8.5 ± 6.4, p< 0.001), Overall Impact (pre: 8.9 ± 6.2, post: 7.0±5.7 p<0.05), and Symptom (pre: 25.4 ± 8.3, post: 20.9 ± 11.7, p< 0.02). Analysis of CCN rsFC showed that compared to matched healthy controls, FM patients were found to have significantly greater rsFC between DLPFC and bilateral rostral anterior cingulate cortex (rACC) / medial prefrontal cortex (MPFC), and the left precentral gyrus. In addition, we found significant increase in the DLPFC rsFC at left rACC / MPFC. There was a significant association between the changes in cluster Fisher z values at rACC/MPFC and corresponding changes in cognitive performance after Tai Chi practice, measured by the FIQR overall Impact subscores after controlling for age (p = 0.002).
Conclusion
Our results suggest that in FM patients, Tai Chi practice can significantly modulate the impaired CCN rsFC over 12 weeks. Our study implies that Tai Chi may achieve clinical improvement in FM patients by modulating the rsFC between the CCN and rACC / MPFC. Future studies in randomized populations to validate these findings are needed.
Title: Efficacy Of Multidisciplinary Pain Treatment At The End Of Treatment And Two Years Follow Up

Poster Number PW0271

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Aim of Investigation
Investigate how opioid treatment, pain sensitivity and Health quality of life, is different between patients, who respond to multi disciplinary treatment. investigate how changes in opioid treatment, pain sensitivity and health quality of life is maintained at 2 years follow up.

Results
Opioid dose at baseline are associated with pain score (P=0.042). Significant larger amount of opioid users in the responder group compared to the non-respond group at baseline (P=0.024). At follow up there was strong significant tendency to difference between the responder and non-responder group (P=0.058). There was no significant difference in health related quality of life between the two groups at follow up.

Conclusion
High dose of opioids are associated with high pain score. When patients are tapered or reduced in opioids their pain is reduced and their health related quality of life is improved. At 2 years follow up the positive effect is reduced, but they are still better compared to baseline.
Title: The Art Of Analgesia: A Pilot Study Of Specialized Art Museum Tours To Decrease Pain And Social Disconnection Among Individuals With Chronic Pain

Poster Number PW0272

Authors
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Aim of Investigation
Pain is widely recognized as a complex biopsychosocial phenomenon.[1-3] Yet, treatment primarily targets the physiological or psychological components of pain, with little attention given to its social dimension. This practice endures despite a recent body of literature demonstrating that social disconnection may contribute as much to the pain experience as nociception.[4] An appreciation for the social determinants of health[5-8] has created new opportunities for organizations outside of the clinical enterprise, such as museums, to become public health partners. Art museums can be restorative environments[9,10] that foster a sense of social inclusion.[11,12] The Integrative Pain Management Program at University of California, Davis (UCD) has initiated an innovative program for individuals suffering from chronic pain called Art Rx. Based on the findings that social connection may be analgesic,[4] Art Rx seeks to encourage positive experiences that reduce the burden of chronic pain through specialized tours and facilitated discussion at the Crocker Art Museum, Sacramento, CA USA. The aims of this pilot study are to evaluate the feasibility of Art Rx and provide preliminary data on its effectiveness to decrease perceived social disconnection and pain among individuals with chronic pain.

Results
Forty-six individuals participated in this study (average age 59; SD 15, 18-93). The majority of participants were female (65%) and white (78%). Twenty-two percent designated their health status as 'poor' or 'fair', 35% as 'good' and 28% as 'very good' or 'excellent.' A majority of participants identified as having pain for >1 year (82%) and brought at least one guest (74%). Program satisfaction was high. Between 87-96% of participants indicated satisfaction on indicators such as knowledge of staff, registration process, activities conducted, content covered, attentiveness of staff, ability to keep engaged, and the quality of the overall experience. In addition, 94% of participants agreed with the statement, 'I would come on another Art Rx tour.' A majority of participants (54%) stated they
experienced pain relief during the tour. Of those who experienced pain relief, the average pain relief reported was 46%. Participants experienced a significant decrease in social disconnection from immediately before the tour to immediately after the tour [-0.3 (95%CI 0.1-0.5); p<.01].

Conclusion
Results from this pilot study suggest that specialized docent led tours of an art museum for individuals with chronic pain are a feasible intervention that may provide short-term relief from pain and perceived social disconnection. These compelling findings warrant future experimental studies that explore the mechanisms and durability of sociogenic analgesia. Art Rx represents a novel public health partnership between an academic tertiary care pain clinic and a public art museum that targets the long acknowledged, but seldom addressed, social disconnection experienced by individuals with chronic pain.

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**Title:** Yokukansan, A Japanese Traditional Herbal (Kampo) Medicine, Prevents The Development Of Morphine Tolerance Through The Inhibition Of Glial Cell Activation In Rats

**Poster Number** PW0273

**Authors**
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**Aim of Investigation**
Animal models have shown that glial cells (microglia and astrocytes) in the spinal cord undergo activation following peripheral injury associated with chronic pain, suggesting the involvement of these cells in pain diseases. We have previously reported that Yokukansan (YKS), which is a Japanese traditional herbal (Kampo) medicine, is effective against chronic pain through the suppression of spinal glial cell activation. Morphine is a widely-used opioid analgesic used for relieving severe pain, but its repeated administration leads to the development of antinociceptive tolerance. The development of morphine tolerance is also reported to be caused by spinal glial cells activation. In the present study, we investigated the inhibitory effects of YKS on the development of morphine tolerance and the activation of the spinal microglia and astrocytes using a rat model.

**Results**
The pre-administration of YKS (started 3 days before the morphine injection) prevented the development of morphine tolerance. The repeated administration of morphine increased Iba-1 and GFAP immune reactivities in the spinal cord; however, these activations were inhibited by the pre-administration of YKS.

**Conclusion**
These results suggest that the pre-administration of YKS attenuates the development of antinociceptive morphine tolerance and the suppression of spinal glial cell activation may be one mechanism underlying this phenomenon. The authors declare that they have no conflict of interest.
Title: Comparison Of Analgesic Effects Of Resveratrol And Cyclo-Oxygenase (Cox) Inhibitors (Diclofenac And Rofecoxib)

Poster Number PW0274

Authors
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Aim of Investigation
AIMS AND OBJECTIVES The aim of this study is to investigate the analgesic effect and the neuromodulatory role of resveratrol and compare it with those of Diclofenac and Rofecoxib (COX-Inhibitors) SPECIFIC AIM To evaluate the analgesic effects of Resveratrol OBJECTIVES 1. To compare the analgesic effect of Resveratrol with Diclofenac 2. To compare the analgesic effect of Resveratrol with Rofecoxib 3. To assess the side effects if any of Resveratrol as compared with Diclofenac and Rofecoxib

Results
Administration of rofecoxib produced minimal antinociception at either formalin concentration. In contrast, diclofenac and resveratrol produced a dose-dependent antinociceptive effect in the second phase of both 1% and 5% formalin test. The peripheral antinociception produced by diclofenac or resveratrol was due to a local action. Results indicate that rofecoxib does not produce peripheral antinociception in formalin-induced inflammatory pain. In contrast, selective COX-1 and non-selective COX inhibitors (resveratrol and diclofenac, respectively) are effective drugs in this model of pain.

Conclusion
The analgesic properties are confirmed and resveratrol might become a useful addition to clinical pain management approaches-especially in patients with acute post operative pain and chronic, severe pain. The results add to other recent experimental evidence suggesting that resveratrol can maintain the pain-relieving effect of morphine.
Title: The Analgesic Effect Of Light Emitting Diode Irradiation On Incised Wound Is Associated With The Decreased Expression Of IL-6 And Cyclooxygenase-2

Poster Number PW0275

Authors
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Aim of Investigation
Light emitting diode (LED) phototherapy has been reported to reduce pain and induce tissue repair through several mechanisms. In recent years the role of cytokine-mediated neuroimmune interactions in the development and maintenance of pain has been studied extensively. Moreover, the preemptive analgesic effect of LED therapy on surgical pain has not been examined. In this study, we examined the analgesic effect of LED therapy on incised pain and the change of cytokines and cyclooxygenase-2 (COX-2) after LED therapy.

Results
Thermal hyperalgesia was attenuated in the three groups received LED phototherapy compared with the incision only group. The expression of IL-6, COX-2 and prostaglandin E2 were significantly decreased in the three LED-treated groups compared with I group. No significant difference in the expression of IL-1b and TNF-alpha were noted in LED treatment group and I group.

Conclusion
We concluded LED therapy could relieve thermal hyperalgesia on incised wound and the analgesic effect is associated with the decreased expression of IL-6 and COX-2.
Title: Therapeutic Efficacy Of Hai Hua® Technique In Acute And Chronic Neck, Shoulder, And Low-Back Pain: A Prospective Preliminary Study

Poster Number PW0276

Authors
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Aim of Investigation
To research the analgesic efficacy of Hai Hua® technique in acute and chronic cervical, shoulder and lumbar pain in adult patients.

Results
Eight patients, 7 female and 1 male, 20-59 y, were included. Two of them had acute shoulder and neck pain from noncomplicated local trauma, 2 had acute nonradicular low back pain, 1 had chronic shoulder and neck pain from noncomplicated degenerative disease and 1 had chronic nonradicular low back pain. Mean pain intensity scores, 5 min before and 30 min after the 1st, 2nd and 3rd interventions, were 7.0±3.2 and 3.62±3.01; 3.25±2.58 and 1.62±2.06; 1.75±2.05 and 0.87±1.12, respectively. Statically, there was a significant reduction of pain scores 30 min after the 1st intervention. Comparing the 1st and 2nd procedures, pain scores were also significantly reduced at 5 min before the 2nd intervention. The same results were obtained when comparing the 5 min values before the 1st and 3rd procedures. There were no side effects recorded, except for mild tenderness at the site of introduction of the electrodes in some patients.

Conclusion
According to preliminary data, Hai Hua® technique is apparently a safe and feasible therapeutic option for some pain conditions. Considering the scarce literature about this method, it deserves further clinical investigation.
Title: The Efficacy Of Acupuncture Pain Treatment Between Male And Female On Acute And Chronic Pain

Poster Number PW0277

Authors
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Aim of Investigation
We previously showed that acupuncture effectively and acutely attenuate pain by inducing a steep increase of extracellular purines and subsequent activation of adenosine A1 receptor at the acupuncture point (Goldman et al. Nat Neurosci 2010). Therefore, acupuncture therapy triggers a local analgesic biological mechanism beside the placebo effects that often believed to play a major role. Our previous study was conducted with adult male mice. In fact, many basic research of pain using laboratory animals were conducted exclusively with male gender, for the purpose of simplicity and stability of the data. However, some chronic pain conditions such as osteoarthritis are more prevalent in women than men. Therefore, we here compared the efficacy of acupuncture and adenosine receptor-mediated analgesia between male and female mice.

Results
For chronic osteoarthritis pain induction, the rate of pain development was noticeably slower in female, which took about a month to reach the maximum pain level while the male group peaked at 9 days. No such differences were observed in CFA-induced acute pain. At any rate, the acupuncture effectively attenuated mechanical allodynia in both male and female animals in both acute and chronic joint pain. We found no significant differences between the male and female groups. The effect of CCPA mirrored the acupuncture, with equal potency to male and female.

Conclusion
Both the acupuncture therapy and the pharmacological local adenosine receptor activation was equally effective toward immediate pain relief in both male and female groups. Our data indicated that acupuncture was a viable option for pain management, especially when other medications were inappropriate. Since women during pregnancy are subjected to severely limited options for medications,
it is particularly important that both doctors and female patients are aware of this pain management option.
Title: Transdermal Capsaicin 8% May Improve Trophic Properties, Mobility, And Blood Flow Of Painful Neuropathic Scar Tissue: A Case Series Of Three Patients

Poster Number PW0278

Authors
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Aim of Investigation
Transdermal capsaicin 8% is regularly included into the treatment protocol of painful neuropathic scar tissue following surgical intervention, for example after spondylodesis of the cervical spine. Depending on the extent of the surgical procedure and the length of the scar, this not only can lead to distinct neuropathic pain with pinprick hyperalgesia, and dynamic allodynia, but to profound changes of the skin, with adherence to the deeper tissue and successive immobility. In order to treat the neuropathic pain component, we employed transdermal capsaicin 8% within the area of hyperalgesia an allodynia. This not only led to a distinct improvement of neuropathic pain but, as a very interesting side-effect, to an improvement of skin mobility, blood perfusion and trophical properties of the scar.

Results
All three patients reported of pronounced burning sensations within the application site, which was very well tolerated. This burning pain Sensation persisted for an average of 8 hours. Over the following 2 days pinprick-hyperalgesia and alldynia disappeared in two patients, and was reduced by 50% in the third patient. The pronounced 'dimpling' of the scar in one of the patients was distinctly reduced with a depth reduction of the cavity of more than 50%. Moreover, the mobility of the scar tissue relative to the deeper layers was considerably improved. The skin itself showed signs of increased blood perfusion, with an increase of the skin temperature compared to the surrounding unaffected skin. Further inspection of the neck showed an increased rotational mobility compared to pre-treatment.

Conclusion
The treatment of the neuropathic scar tissue with transdermal capsaicin 8% expectedly resulted in the reduction of pinprick-hyperalgesia and alldynia. Besides these obvious results, capsaicin 8% was able to distinctly reduce the 'dimpling' of the scar tissue, and to improve the mobility of the skin adhering to the
spinal processes, and respectively, to an improvement of the mobility of the head and the neck. This allowed the patients to participate in physical therapy more compliantly. These findings are so far preliminary, and need further investigation in order to find the mechanisms involved in the described effects on the scar tissue.
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**Title**: Effect Of A Mindfulness Based Stress Reduction Course On Pain And Quality Of Life In Patients With Painful Diabetic Peripheral Neuropathy

**Poster Number** PW0279

**Authors**

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**Aim of Investigation**
Painful diabetic peripheral neuropathy (PDPN) is a prevalent type of neuropathic pain that will increase with the increasing incidence of diabetes mellitus (DM) and an aging population. It is known that pharmacologic therapy rarely provides sufficient relief from chronic neuropathic pain and therefore effective psychosocial treatments are desirable to maintain quality of life. Mindfulness based stress reduction (MBSR) courses consist of psycho-education and mindfulness exercises that serve to increase awareness of sensations, thoughts and emotions. With this awareness participants develop the ability to practice self-regulation strategies and choose healthy and adaptive responses to various stressors, including chronic pain. We wished to determine the effect of MBSR on pain, function and quality of life in patients with PDPN. We are not aware of any published study investigating a mindfulness intervention in a cohort of patients with neuropathic pain.

**Results**
Of 81 consenting patients 66 were randomized, 60 have completed 3 month follow-up, 2 are in progress, 3 have dropped out and there was 1 late exclusion. N for this analysis is 60. Median age was 59 (range 35 -79) with 57% females. Fourteen (23%) were type 1 DM and 46 (77%) were type 2 DM. Median pain duration was 5.5 years (range 1- 31). Nine (15%) were employed and 44 (73%) had post-secondary education. Outcomes are presented below as mean (SD) before randomization and change score (3 months minus pre-randomization) (SE, P change = 0). Brief Pain Inventory (BPI) Interference Score: 4.82 (2.35), -0.66 (0.29, .02). Twenty-six (43%) had a decrease of one or more in pain interference. Pain Intensity on BPI: 5.16 (1.92), -0.66 (0.27, .02). Pain Catastrophizing Scale: 22.9 (12.1), -4.4 (1.56, .007). PHQ-9 depression 11.3 (5.65), -2.53 (0.74, .001). SF-12 PCS (physical...
composite scale): 32.3 (8.9), 3.64 (1.04, .001). SF-12 MCS (mental composite scale): 44.0 (8.9), 1.79 (1.12, .12).

**Conclusion**
Improvements were documented in several domains three months after completion of the MBSR course. A decrease of one or more in the BPI interference score is considered clinically significant (IMMPACT) and 43% of patients met this criterion. There were significant improvements in mean BPI pain intensity scores as well. Pain catastrophizing total score which is an important prognostic variable in chronic pain, decreased significantly (by approximately 10 percentiles). Depression scores fell from a mean in the moderate category to the mild category. The SF-12 PCS increased indicating improved physical health status, congruent with the improvement in BPI interference. The MCS did not change, perhaps surprising as the PHQ-9 depression score decreased significantly. Examination of the SF-12 subscales may reveal the underlying mechanisms of these changes. These data suggest that MBSR can improve pain, functioning and health related quality of life of patients suffering with painful diabetic peripheral neuropathy.
Title: Predicting Of Opioid Analgesia Using Electroencephalography And Machine Learning

Poster Number PW0280

Authors
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Aim of Investigation
Opioids are popular analgesics, but response is often lacking and dependent on the individual opioid. Biomarkers are therefore needed to select the appropriate drug for each patient, a concept known as personalized medicine. Quantitative sensory testing (QST) and clinical parameters can provide some guidance for response, but objective biomarkers are preferable. Electroencephalography (EEG) may be suitable since it assesses the central nervous system where opioids mediate their analgesic effects. The aim of the study was to investigate if EEG can be utilized as an objective biomarker for analgesic response to opioids.

Results
Eighty-one patients were included. Group-wise statistics showed a connection between the pre-existing chronic pain grade and response to opioid treatment (P=0.04). Hence, more severe chronic pain prior to surgery increased the chance for insufficient postoperative analgesia. Preoperative EEG analysis was able to predict responders with an accuracy of 65%; P=0.009), but only during tonic pain.

Conclusion
Chronic pain grade before surgery is associated with postoperative analgesia. Furthermore, EEG can be used as an objective biomarker to predict postoperative opioid analgesia.
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**Title**: Electroacupuncture For Patients With Painful Diabetic Neuropathy: A Three-Armed, Randomized, Controlled, Clinical Trial

**Poster Number** PW0281

**Authors**
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**Aim of Investigation**
The aims of this study were (1) to assess the effectiveness and safety of electroacupuncture (EA) in treating PDN for pain, sleep disturbance, depression, health-related quality of life (HRQoL) and adverse events as compared to sham electroacupuncture (SEA) and the usual care (UC) and (2) to identify the feasibility of a large-scale clinical trial.

**Results**
For the confirmatory analysis, the mean change from baseline in the PI-NRS was -2.65 (95% CI -3.81 to -1.49) in the EA group, -1.54 in the SEA group (95% CI -2.33 to -0.74) and -0.25 in the UC group (95% CI -1.20 to 0.70) at 9th weeks (p < .003). There was a statistically significant difference in the PI-NRS between the EA with UC group (-2.34; 95% CI -3.65 to -1.02), but not with the SEA group (-1.13; 95% CI -2.45 to 0.18). In subgroup analysis, the PI-NRS of patients with no pain medicine in the EA group were significantly different with that in the SEA (-2.05; 95% CI -3.61 to -0.50) and UC group (-3.32; 95% CI -4.92 to -1.72), but the PI-NRS of patients with pain medicine in the EA group were not with that in the SEA (0.16; 95% CI -2.16 to 2.49) and the UC group (-1.03; 95% CI -3.28 to 1.18). The effect of EA did not last until 17th weeks. For the secondary analysis, the EA group showed significant improvement over the UC group in the SF-MPQ, sleep disturbance and bodily pain in the SF-36 at 9th and 17th weeks. There was no statistically significant difference in sleep disturbance, depression and HRQoL between the EA with SEA group. Minor adverse events related with acupuncture treatment were reported in EA (6 times) and SEA group (2 times).

**Conclusion**
In conclusion, EA significantly improved pain, sleep disturbance and HRQoL and was safe for patients with PDN. However, the benefits of real EA were only greater than those of SEA in patients with no pain
medication. Further rigorous large-scale trial for patients with no pain medication and interaction study between EA and pain medication is needed to determine the efficacy of EA in patients with PDN.
Title: An Exploratory Study On The Effectiveness Of Calmare Therapy In Patients With Cancer-Related Neuropathic Pain: A Pilot Study

Poster Number PW0282

Authors
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Aim of Investigation
Calmare therapy (CT) has been suggested as a novel treatment for managing chronic pain. Recently, it was reported to show a positive therapeutic outcome for managing neuropathic pain condition. We performed an exploratory prospective study on the effectiveness of CT in patients with various types of cancer-related neuropathic pain (CNP).

Results
CT significantly decreased NRS pain score at one month from baseline (p < 0.001) in 20 patients with chemotherapy-induced peripheral neuropathy (n = 6), metastatic bone pain (n = 7), and post-surgical neuropathic pain (n = 7). It also improved overall BPI scores, decreased consumption of rescue opioid (p = 0.050), and was found satisfactory by a half of patients (n = 10, 50.0%).

Conclusion
Our preliminary results suggest that CT may be considered for cancer patients with various types of CNP. Large studies are necessary to confirm our findings and ascertain which additional CNP show positive response to CT.
Title: Effectiveness Of Rikkosan For Intraoral Intractable Pain

Poster Number PW0283

Authors

Aim of Investigation
Our study aims to investigate the effectiveness of Rikkosan (RKS, Zhan-Xiao-San), one kind of Japanese traditional herbal medicine, in treatment of intraoral pain. RKS is a powdered, freeze-dried water extract, which comprises five decocted medicinal herbs: Asarum heterotropoides root, Saposhnikovia divaricata root, Cimicifuga simplex Rhizome, Gentiana scabra, and Glycyrrhiza uralensis Rhizome. This RKS is effective for pain after tooth extraction, and toothache, mainly due to the local anesthetic properties of Asarum heterotropoides root. At our department we mainly treat patients with intractable pain of the oral and maxillofacial areas, in most cases of which NSAIDs are ineffective. We often treat burning mouth syndrome (BMS) and atypical odontalgia (AO) using RKS. There are several reports of the effectiveness of RKS on trigeminal neuralgia, glossopharyngeal neuralgia, and intraoral neuropathic pain. In the present study, we aimed to retrospectively examine the effectiveness of RKS in our department.

Results
RKS was effective for BMS, AO, atypical facial pain, trigeminal neuralgia, neuropathic pain (other than trigeminal neuralgia), odontogenic toothache, dysgeusia, and dry mouth disease in 237 cases. Among these, BMS was present in 82 patients and AO was present in 111 patients. The relationship between the presence or absence of pain while eating and the efficacy or no of RKS on both BMS and AO was analyzed using the $\chi^2$ test ($P < 0.05$).
Conclusion
According to the current results, RKS is effective for BMS and AO. Furthermore, RKS is not only effective for nociceptive pain, but also for neuropathic pain. Therefore, the analgesic mechanisms of RKS may differ from those of NSAIDs. In addition, although BMS and AO are not usually considered painful while eating we have encountered many atypical cases in which increased pain while eating was reported, suggesting different pathophysiology. The relationship between the presence or absence of pain while eating and the presence or absence of the effectiveness of RKS on each of BMS and AO was statistically significant. Therefore, RKS should be prescribed according to the presence or absence of pain while eating.
Title: Morphine Treatment Facilitates Interactions Between The Mu-Opioid And 5-HT[Sub]1A[/Sub] Serotonin Receptors: In Vitro Cellular Study By Methods With Single-Molecule Sensitivity

Poster Number PW0284

Authors
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Aim of Investigation
The usefulness of long-term opioid treatment is seriously hampered by the development of opioid induced hyperalgesia and tolerance. In animal studies serotonin (5-HT<sub>1A</sub>) receptor agonists can prevent and reverse opioid induced hyperalgesia/tolerance<sup>1,2</sup>, although the underlying cellular and molecular mechanisms are still not well understood. In this study, we investigated the interactions between the mu-opioid (MOP) and serotonin (5-HT<sub>1A</sub>) receptors in live cells and assessed the effect of morphine on these interactions. Our aim was to understand whether these two signaling pathways are integrated at the cellular level via direct binding between the MOP and 5-HT<sub>1A</sub> receptors and to quantitatively characterize the effect of morphine and serotonin on these interactions.

Results
MOP and 5-HT<sub>1A</sub> receptors do not form heterodimers under normal cell culture conditions. Prolonged (18 h) treatment with morphine (250 nM; 500 nM and 750 nM) facilitates MOP heterodimerization with 5-HT<sub>1A</sub> in a dose-dependent manner – the higher the concentration of morphine, the larger is the number of observed heterodimers. Combined treatment with MOP and 5-HT<sub>1A</sub> agonists (750 nM morphine and 1 µM serotonin, 18 h treatment) abolishes heterodimerization.

Conclusion
MOP and 5-HT<sub>1A</sub> receptor interactions were potentiated by exposure to morphine. Hypothetically, altered cellular signaling due to receptor heterodimer formation may contribute to neuroplastic changes that, eventually, lead to sensitization of pronociceptive pathways. Combined treatment with opioid and serotonin receptor agonists diminished receptor heterodimer formation by reducing the surface density of 5-HT<sub>1A</sub> receptors. Our results indicate interactions between
MOP and 5-HT<sub>1A</sub> receptors at a cellular level. <b>References</b>


Aim of Investigation
Introduction: To evaluate the new chemical identities in different pain areas, various animal pain models are known as classical pain tests and models in different pain areas such as acute and tonic pain, neuropathic pain, inflammatory pain, post-operative pain, and visceral pain. The aim of this study was to set up an in vivo High Throughput Screening tool (ALGOGram™) and to validate this tool with reference compounds.

Results
Results: Buprenorphine, morphine and tramadol are active in 11 different pain models. In contrast, gabapentin is active in several hypersensitive pain models. Diclofenac and acetaminophen presents antinociceptive effects in some inflammatory pain models. These activities were compared with results obtained with appropriate reference compounds used in classical pain studies (from our historical database).

Conclusion
Conclusion: ALGOGram™ permits to provide a rapid and cost-effective evaluation of new chemical entities in different pain indications. This tool can provide a user-friendly pharmacological compound profile, facilitating the crucial 'GO / NO GO' decisions routinely faced by pharmaceutical companies.
Title: Nav1.7 Inhibitors Modulate Evoked Activity Of Spinal Neurons And Spontaneously Active Aδ Fibers In The Rat

Poster Number PW0286

Authors

Authors
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Aim of Investigation
Pain is a frequent debilitating feature reported in peripheral neuropathies with involvement of small nerve (Aδ and C) fibers (Faber et.al., J. Peripher. Nerv. Syst.; 2014). Voltage-gated sodium channels are responsible for the generation and conduction of action potentials in the peripheral nociceptive neuronal pathway where voltage-gated sodium channel 1.7 (NaV1.7) has a critical role. Human loss-of-function (LOF) mutations in the SCN9A gene, which encodes NaV1.7, result in congenital indifference to pain (Ruitenberg et. al., Channels; 2012). To test the ability of small molecule inhibitors of NaV1.7 to recapitulate the expected human phenotype of a reduction in nociceptive signaling, we examined the efficacy of two Merck NaV1.7 inhibitors (Compound A and B) in electrophysiological in vivo assays for acute nociception. We examined the modulation of spinal cord wide dynamic neurons (WDR) and nociceptive specific (NS) neurons in naïve rats and ectopic firing in rats after chronic constriction injury (CCI).

Results
At the maximum dose tested, the Compound A inhibited WDR thermal evoked responses (75±20%; iv. infusion at 20 mpk/30 min.) but had a weaker effect on mechanical evoked responses (30±21%, same dose). However, the same Compound had a better inhibitory effect on mechanical evoked responses in NS neurons (45±24%, same dose). Compound B regularized and fully inhibited Aδ ectopic firing activity (i.v. 10 min infusions: 40±20% inhibition at 0.3 mpk, 65±8 % at 1 mpk and 100% at 3 mpk) in CCI induced animals.

Conclusion
These results demonstrate that small molecule selective inhibitors of NaV1.7 can replicate the expected
physiological reduced activity of nociceptors in human Nav1.7 LOF patients. Our findings corroborate the critical role of NaV1.7 channels in acute nociception and neuropathic spontaneous pain.
Title: Mazindol Induces Antinociception In A Mouse Model Of Unilateral Knee Arthritis

Poster Number PW0287

Authors

Aim of Investigation
To determine whether the systemic administration of mazindol has an antinociceptive, anti-inflammatory effect and affects bone density and microarchitecture in a mouse model of CFA-induced arthritis.

Results
Acute mazindol decreased the spontaneous CFA-induced pain-like behaviors in a dose dependent manner, but not modified the CFA-induced knee edema. Chronic administration of 3 mg/kg mazindol has an antinociceptive effect without modifying the locomotor activity. The administration of D2 receptor antagonist (Haloperidol) or an adrenergic antagonist (fentolamine), but not the administration of an opioid antagonist (naloxone) or D1 receptor antagonist (R(+)-SCH 23390 HCl) diminished the antinociceptive effect by mazindol. The chronic administration of mazindol did not significantly modify the density and microarchitecture of periarticular bone (femur and tibia) of the arthritic and non-arthritic knee joints.

Conclusion
Our results suggest that mazindol has an antinociceptive role in mice with CFA-induced knee arthritis, through the activation of D2 and adrenergic receptors and does not modify negatively the bone density and microarchitecture of femur and tibia.
Title: Phα1β Acts As A Trpa1 Antagonist With Antinociceptive Effects In Mice

Poster Number PW0288

Authors

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Aim of Investigation
Peptides from venomous animals have been important tools for understanding pain mechanisms and for the discovery of pain treatments. Phα1β is a peptide purified from the armed spider Phoneutria nigriventer venom that exhibits antinociceptive properties in several pre-clinical pain models. It is known that ion channels are important in the development and processing of pain. The transient receptor potential ankyrin 1 (TRPA1) channel, a nonselective cation channel activated by reactive endogenous and exogenous substances and noxious cold, is now considered to represent a major pain transduction pathway. Here, we hypothesized that Phα1β, a peptide purified from the armed spider Phoneutria nigriventer venom, produces analgesia by blocking the TRPA1 channel.

Results
Phα1β selectively and potently blocked calcium response evoked by TRPA1 agonist allyl isothiocyanate (AITC) on DRG, IMA90 and TRPA1-HEK293 transfected cells. Moreover, intrathecal (i.t.) and intraplantar (i.pl.) administration of Phα1β attenuates acute nociception as well as mechanical and cold hyperalgesia evoked by the TRPA1 agonist, AITC (given i.t or i.pl), but not by TRPV1 or TRPV4 agonists capsaicin (CPS) or hypotonic solution (0.27% NaCl), respectively, given i.pl.. Notably, Phα1β reverted TRPA1-dependent hyperalgesia in a model of neuropathic pain induced by chemotherapeutic agent bortezomib. Finally, the effects produced by the native form of Phα1β were fully reproduced when a recombinant version of the peptide was used.

Conclusion
In summary, we have identified Phα1β as a selective and potent TRPA1 antagonist with antinociceptive
effects and antihyperalgesic action in a relevant neuropathic pain model. The analgesic action of Phα1β on TRPA1-mediated pain predicts a similar effect on pain in humans.
Aim of Investigation
Active pharmaceutical ingredient (API)-API co-crystals represent a new approach by virtue of the unique crystalline structure formed via non-covalent interactions between both molecules, resulting in improved physicochemical (PC) properties. In our proprietary pain relief platform, we apply a series of criteria in the development of New Product Concepts. If the criteria are met (including molecular mechanisms of action, sites of action, synergy in pain relief, enhanced PC characteristics, no deleterious metabolic, pharmacodynamic, or safety interactions), the co-crystal technology is applied to determine: i) if a co-crystal can be formed, ii) if the co-crystal is formed in a therapeutically relevant molecular ratio, iii) if the structure modifies the PC properties favorably, iv) if the conferred PC properties result in an optimization of the in-vivo profile of each component (i.e. co-crystal mechanistic effect), and v) if each of the APIs contribute in a complementary manner to the proposed therapeutic benefit. In our platform we identified two APIs, tramadol (rac-tramadol.HCl; a centrally acting weak μ-opioid receptor agonist as well as an inhibitor of the re-uptake of serotonin and norepinephrine) and celecoxib (a non-steroidal anti-inflammatory molecule, preferentially inhibiting cyclo-oxygenase-2) to apply the co-crystal technology.

Results
A new API-API co-crystal, formed by tramadol.HCl and celecoxib in an intrinsic 1:1 molecular ratio, was identified and structurally characterized. Co-Crystal of Tramadol-Celecoxib (CTC), under development by Esteve/Mundipharma Research (as E-58425/MR308), contains the two enantiomers of tramadol (dextrorotatory isomer [higher affinity for μ-opioid receptors and inhibitor of serotonin reuptake] and levorotatory isomer [more potent inhibitor of norepinephrine reuptake]), its HCl counterpart, and celecoxib. CTC is the first API-API co-crystal of tramadol and celecoxib and was shown to be a unique crystalline entity with a sharp melting event observed by DSC (164 °C), between those of celecoxib (161
°C) and tramadol.HCl (181 °C). Its crystal structure showed a 3D network where the three moieties are linked via hydrogen bonding and where chloride ions establish three key intermolecular contacts with the adjacent molecules. Aqueous oversaturation studies of the co-crystal vs a mixture of the individual components indicated no saturation effect in the case of tramadol, a result expected in view of its high solubility. However, in the case of the highly insoluble celecoxib, a saturation effect was observed, but it occurred at a higher concentration in the case of the co-crystal. Comparative IDR studies indicated that the release of celecoxib was faster (3-fold) from the co-crystal than from celecoxib alone, suggesting a potential for increasing its rate of absorption. The release of tramadol, however, was slower (7-fold) from the co-crystal than from tramadol alone, which was seen as a potential advantage, since it could lead to a more sustained release, resulting in a reduction of the peak effects of tramadol.

**Conclusion**
The first-in-class CTC, formed by tramadol.HCl and celecoxib in a 1:1 molecular ratio, exhibits an advantageous dissolution profile over the individual components. This, together with the synergistic effects observed in its pharmacological characterization in several pain models, support differentiation and its clinical development for the treatment of moderate and severe pain.

Acknowledgments/disclosures: This research has been funded by Laboratorios del Dr. Esteve, S.A.U. Support with editing of the abstract was provided by Louise Niven, DPhil (Aspire Scientific Ltd, Bollington, UK) and was funded by Mundipharma Research GmbH & Co.KG.
**Title:** Administration Of Tramadol And Celecoxib In A 1:1 Molecular Ratio Produces Synergistic Antinociceptive Effects In Postoperative Pain Models: Preclinical Rationale For Clinical Development Of Co-Crystal Of Tramadol-Celecoxib

**Poster Number** PW0290

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**Aim of Investigation**
Active pharmaceutical ingredient (API)-API co-crystals represent a new approach. By virtue of the unique crystalline structure formed via non-covalent interactions between both molecules, API-API co-crystals can offer distinctive physicochemical and pharmacological profiles. Co-Crystal of Tramadol-Celecoxib (abbreviated as CTC and under development by Esteve/Mundipharma Research as E-58425/MR308) combines two well-known active principles with four different mechanisms of action, namely tramadol (rac-tramadol.HCl), a centrally acting weak μ-opioid receptor agonist and serotonin and norepinephrine reuptake inhibitor, and the preferential cyclooxygenase-2 inhibitor celecoxib. Within the co-crystal structure, these two modalities are combined at an intrinsic 1:1 molecular ratio (1:1.27 weight ratio).

Here we aimed to: i) study the effects and interactions of tramadol and celecoxib in a 1:1 molecular ratio (generated by dissolving CTC in solution), tramadol alone and celecoxib alone in a postoperative pain model (rat plantar incision); ii) compare the efficacy and potency of the 1:1 molecular ratio with those of the strong opioids morphine sulfate and oxycodone HCl, as well as of tramadol plus acetaminophen in a free combination at the authorized 1:8.7 weight ratio (1:17 molecular ratio); and iii) evaluate the risk/benefit profile of the 1:1 molecular ratio by measuring effects on locomotor activity, motor coordination, intestinal transit, and gastrointestinal ulceration potential. Isobolographic analyses were performed to establish the nature of the interactions.

**Results**
Tramadol and celecoxib in a 1:1 molecular ratio exerted synergistic antinociceptive effects in mechanical allodynia (experimental ED$_{50}$ Zt = 2.0 ± 0.5 mg/kg, p<0.05) and thermal hyperalgesia (Zt = 2.3 ± 0.5 mg/kg, Zadd = 9.8 ± 0.8 mg/kg, i.p., p<
0.001) in the postoperative pain model. In contrast, the tramadol and acetaminophen free combination showed antagonistic effects in both mechanical allodynia and thermal hyperalgesia (p<0.05 and <0.001, respectively). No synergies between tramadol and celecoxib in locomotor activity, motor coordination and gastrointestinal transit were observed after administration of tramadol and celecoxib in a 1:1 molecular ratio. Safety ratios related to gastrointestinal transit were 2.5, 5.8, 10.3, and 80 for morphine, oxycodone, tramadol and the 1:1 molecular ratio, respectively.

**Conclusion**

Efficacy data reveal that tramadol and celecoxib in a 1:1 molecular ratio provide synergy (in both readouts of efficacy, i.e. mechanical allodynia and thermal hyperalgesia) in the postoperative pain model, without enhancing adverse effects. Moreover, the 1:1 molecular ratio had similar efficacy, but with a clearly improved safety profile, compared with strong opioids (morphine and oxycodone). The overall pharmacological profile of tramadol and celecoxib in a 1:1 molecular ratio, and in particular its synergistic activity and ability to activate multiple pain-inhibitory pathways, supports the ongoing clinical investigation of CTC for the management of moderate to severe pain. Acknowledgments/disclosures: This research has been funded by Laboratorios del Dr. Esteve, S.A.U. Support with editing of the abstract was provided by Louise Niven, DPhil (Aspire Scientific Ltd, Bollington, UK) and was funded by Mundipharma Research GmbH & Co.KG.
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**Title:** Pharmacokinetic Profile Of Multiple Doses Of Co-Crystal Of Tramadol-Celecoxib: Findings From An Open-Label, Four-Period, Four-Sequence, Crossover, Phase I Clinical Trial In Healthy Male And Female Volunteers

**Poster Number** PW0291

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**Aim of Investigation**
Co-Crystal of Tramadol-Celecoxib (CTC) is a first-in-class co-crystal under development by Esteve (as E-58425) and Mundipharma Research (as MR308). Single-dose administration of CTC in human subjects results in an enhanced pharmacokinetic (PK) profile of each active principle (rac-tramadol.HCl and celecoxib). The main objective of this study was to determine the PK profile of formulated CTC vs the individual reference products (tramadol 100 mg and celecoxib 100 mg) and their free combination (co-administration). The secondary objective was to evaluate safety and tolerability of multiple doses.

**Results**
Overall, 32 subjects (20 male) were randomized. Of these, 29 subjects received treatment-1, 30 treatment-2, 28 treatment-3, and 28 treatment-4. Mean age was 35 years (range: 20-50), mean weight was 73.9 kg (range: 54.2-99.0), and mean height was 169.7 cm (range: 150.0-190.0). <b>Single dose:</b> For treatment-1, -2 and -4, adjusted tramadol PK parameters were: mean C<sub>max</sub> (ng/mL) of 249.7, 330.3 and 331.4; mean AUC<sub>TAU</sub> (ng•h/mL) of 2011.5, 2220.2 and 2299.8; median T<sub>max</sub> (h) of 3.5, 1.75 and 2.0. For treatment-1, -3 and -4, adjusted celecoxib PK parameters were: mean C<sub>max</sub> (ng/mL) of 246.5, 358.2 and 202.3; mean AUC<sub>TAU</sub> (ng•h/mL) of 1287.4, 1929.0 and 1255.8; median T<sub>max</sub> (h) of 2.0, 3.0 and 4.0. <b>Multiple dose:</b> For treatment-1, -2 and -4, adjusted tramadol PK parameters were: mean C<sub>max;SS</sub> (ng/mL) of 551.2, 632.0 and 661.2; mean AUC<sub>TAU;SS</sub> (ng•h/mL) of 4795.5, 4990.2 and 5284.2; median T<sub>max;SS</sub> (h) of 3.0, 2.0 and 2.0. For treatment-1, -3 and -4, adjusted celecoxib PK parameters were: mean C<sub>max;SS</sub> (ng/mL) of
444.8, 536.2 and 396.3; mean AUC<sub>TAU;SS</sub> (ng•h/mL) of 2803.1, 3365.8 and 2897.3; median T<sub>max;SS</sub> (h) of 2.0, 2.0 and 3.0. At least one AE was reported in 45% (treatment-1), 87% (treatment-2), 39% (treatment-3) and 71% (treatment-4) of subjects. Related AEs had a similar frequency among the 4 treatments; 78% of AEs were mild in severity. Most AEs were expected based on tramadol safety profile; fewer of these AEs were reported for treatment-1 than for treatment-2 or -4. There were no deaths or serious AEs.

**Conclusion**

CTC administration in humans led to enhanced PK of each active molecule (tramadol and celecoxib) compared with when marketed tramadol and celecoxib were given in free combination. Specifically, CTC was associated with a reduced tramadol peak plasma concentration (while remaining above levels required for efficacy) and an improved and faster peak plasma concentration of celecoxib. CTC was well tolerated. Acknowledgments/disclosures: This research was funded by Laboratorios del Doctor Esteve, S.A.U. and carried out by Algorithme Pharma. Support with editing of the abstract was provided by Louise Niven, DPhil (Aspire Scientific Ltd, Bollington, UK) and was funded by Mundipharma Research GmbH & Co.KG.
Title: Single-Dose Pharmacokinetic Profile Of Co-Crystal Of Tramadol-Celecoxib: Findings From An Open-Label, Four-Period, Four-Sequence, Crossover, Phase I Clinical Trial In Healthy Male And Female Volunteers

Poster Number PW0292

Authors

Laboratorios del Dr. Esteve, S.A.U., Barcelona, Spain, Algorithme Pharma, Laval, Canada, Algorithme Pharma, Montreal, Canada

Aim of Investigation
Co-crystals are usually composed of an active pharmaceutical ingredient (API) with a neutral guest compound (also referred to as a conformer) in the crystal lattice. An API-API co-crystal is under development by Esteve (as E-58425) and Mundipharma Research (as MR308) that is the first to contain tramadol (rac-tramadol.HCl) and celecoxib. This Co-Crystal of Tramadol-Celecoxib (CTC) contains an intrinsic 1:1 molecular ratio (1:1.27 weight ratio). The main objective was to determine the pharmacokinetic (PK) profile of formulated CTC compared with the individual reference products (tramadol 100 mg and celecoxib 100 mg) and their combination (co-administration). The secondary objective was to evaluate the safety and tolerability of CTC following a single-dose administration.

Results
In total, 36 subjects (28 male) were included. Mean age was 36 years (range: 22-52); mean weight was 72.4 kg (range: 45.7-96.4); and mean height was 171.4 cm (range: 145.0-188.0). For treatment-1, -2 and -4, tramadol adjusted PK parameters were: mean C<sub>max</sub> (ng/mL) of 263.2, 345.8 and 349.4; mean AUC<sub>T</sub> (ng•h/mL) of 3039.2, 2979.0 and 3119.4; median T<sub>max</sub> (hours) of 2.7, 1.75 and 1.75. For treatment-1, -3 and -4, celecoxib adjusted PK parameters were: mean C<sub>max</sub> (ng/mL) of 313.3, 448.9 and 284.4; mean AUC<sub>T</sub> (ng•h/mL) of 2182.8, 3093.4 and 2856.0; median T<sub>max</sub> (hours) of 1.5, 2.3 and 3.0. No clinically relevant AEs were reported. Mild somnolence was reported by four subjects and mild headaches by five; medication was not required to treat these symptoms. No serious AEs or deaths were reported.
Conclusion
Tramadol from CTC has a similar AUC<sub>T</sub> and exhibits a slightly delayed absorption compared with tramadol taken individually or concomitantly with celecoxib. This is associated with a lower C<sub>max</sub> value, and a slightly prolonged T<sub>max</sub> compared with the individual or concomitant preparation. Celecoxib from the CTC formulation has a slightly reduced AUC<sub>T</sub>, a lower C<sub>max</sub> and exhibits a faster T<sub>max</sub> compared with celecoxib taken either alone or in combination with tramadol. The observed AEs were consistent with those expected for both tramadol and celecoxib based on their reference product labels. The PK parameters of each API were optimized by co-crystallizing them in CTC compared with marketed tramadol, marketed celecoxib, or their concomitant administration. This optimization of PK parameters may have clinical implications.

Acknowledgments/disclosures: This research was funded by Laboratorios del Doctor Esteve, S.A.U. and carried out by Algorithme Pharma. Support with editing of the abstract was provided by Louise Niven, DPhil (Aspire Scientific Ltd, Bollington, UK) and was funded by Mundipharma Research GmbH & Co.KG.
**Title:** Co-Crystal Of Tramadol-Celecoxib: Efficacy And Safety Results From A Dose-Finding, Randomized, Double-Blind, Multicenter, Phase II Clinical Trial In Patients With Moderate-To-Severe Acute Pain Due To An Oral Surgical Procedure

**Poster Number** PW0293

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**Aim of Investigation**
Co-Crystal of Tramadol-Celecoxib (CTC) is a pain-relieving co-crystal containing equimolar quantities of tramadol (tramadol.HCl) and celecoxib that is being developed by Esteve and Mundipharma Research (as E-58425/MR308). The crystalline lattice in the co-crystal structure improves the physicochemical properties of constituents tramadol and celecoxib, thereby enhancing the pharmacokinetics (PK) of each active molecule. Our aim was to establish the effective dose of CTC for treating moderate-to-severe acute pain after extraction of ≥ 2 impacted third molar teeth requiring bone removal.

**Results**
A total of 334 patients (142 [42.5%] male) with moderate-to-severe pain within 4 h of oral surgery were randomized and received one of 6 treatments: 222 received CTC (50 mg [55]; 100 mg [53]; 150 mg [57]; and 200 mg [57]), 58 received tramadol 100 mg and 54 received placebo. Mean age was 24.5 years (range: 18–48) and mean body mass index [kg/m²] was 23.5 (range: 16.3–36.8). CTC 100, 150 and 200 mg were significantly better than tramadol and placebo across all efficacy measures: SPID (8 h), mean: 90, 139, 173, and 22 and 71 h*mm, respectively; TOTPAR (8 h), mean: 21, 21, 23, 17 and 15; rescue medication: 62%, 50%, 39%, 74% and 80%; responders (50% pain intensity reduction from baseline): 32%, 43%, 52%, 18% and 13%. The lowest dose of CTC (50 mg) was slightly better than 100 mg tramadol and was better than placebo in terms of efficacy. Intake of 50, 100, and 150 mg of CTC led to markedly fewer adverse events (AEs) compared to 100 mg tramadol, whereas, as expected, the safety and
tolerability profile of 200 mg CTC and 100 mg tramadol were similar. The most common AEs with active treatment were nausea, dizziness and vomiting.

**Conclusion**

CTC (100-200 mg) provided greater efficacy over tramadol 100 mg and placebo in the treatment of acute moderate-to-severe pain. CTC produced dose-dependent pain relief associated with similar (200 mg dose) or better (50-150 mg doses) overall safety and tolerability than tramadol 100 mg alone. The significantly improved benefit-risk with CTC involves: i) an intrinsic 1:1 molecular ratio conferred by the co-crystal structure, ii) enhanced PK of both active principles produced by the co-crystal mechanism, and iii) the recruitment of 4 complementary molecular mechanisms of action in both central and peripheral pain pathways. Acknowledgments/disclosures: This research was funded by Laboratorios del Doctor Esteve, S.A.U. The authors present this work on behalf of the 'CTC phase II dose-finding study team'. Support with editing of the abstract was provided by Louise Niven, DPhil (Aspire Scientific Ltd, Bollington, UK) and was funded by Mundipharma Research GmbH & Co.KG.
Title: Aminophylline Suppresses Stress-Induced Defecation And Visceral Hypersensitivity In A Rat Model Of Irritable Bowel Syndrome

Poster Number PW0294

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Aim of Investigation
Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by chronic and recurrent abdominal pain and discomfort (visceral hypersensitivity). These symptoms are associated with altered bowel habits but not with any detectable structural or biochemical abnormality. Although IBS markedly reduces the patient's quality of life, a therapeutic protocol, including pharmacological therapy, has not been established. In order to find candidate drugs for IBS with diarrhea (IBS-D) based on a drug re-positioning strategy, we screened a compound library of clinically used drugs for their ability to prevent stress-induced defecation and visceral hypersensitivity in rats.

Results
Aminophylline, a traditional medicine that is clinically used as a bronchodilator, was selected as a compound that is able to suppress the visceromotor response to repetitive CRD and wrap restraint stress (WRS)-induced defecation. Oral administration of aminophylline did not affect defecation under normal conditions or the serum level of corticosterone under stress conditions. Aminophylline has both antagonizing activity for adenosine receptors (A1ARs, A2AARs and A2BARs) and inhibitory activity on phosphodiesterases (PDEs). Analysis with a specific inhibitor for each subtype of AR and PDE suggested that both A2BARs and PDE4 are involved in the inhibitory effect of this drug on WRS-induced defecation. Aminophylline suppressed maternal separation- or acetic acid administration-induced visceral hypersensitivity to CRD, an effect that appeared to involve both A2AARs and A2BARs. However, it did not affect visceral sensitivity under normal conditions.

Conclusion
Based on results in this study, we propose that aminophylline is a candidate drug for IBS-D, because its safety in humans has already been confirmed clinically and its ameliorating effect on both of stress-induced defecation and visceral hypersensitivity are confirmed here.
Title: The Effect Of High-Dose Remifentanil On The Reversal Of Neuropathic Pain In Post-Herpetic Patients

Poster Number PW0295

Authors
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Aim of Investigation
Opioids are the gold standard for symptomatic therapy of moderate to severe pain. Now, a previously unrecognized effect has been discovered in animals – the reversal of long-term potentiation (LTP) at C-fiber synapses. This opens the possibility for novel therapeutic strategies which potentially cure chronic pain. The aim of this study was to explore the effects of high-dose remifentanil application in chronic post-herpetic pain patients and generate pilot information in human patients on the hypothesized responsiveness.

Results
21 patients were treated, one patient refused any further assessments after the treatment, thus 20 patients were analyzed. Of 20 patients, 11 responded to treatment (55%), with 8 patients (40%) experiencing a good response (≥50% reduction in pain intensity). The mean overall change in pain intensity was -17.5 (-7.1 – -27.9, 95%CI) one day after treatment and -18 (-7.5 – -28.5, 95%CI) seven days after treatment (F(2,19) = 13.17, p = .0001), with the responders experiencing a mean pain reduction of 61% at day seven. In the responder group there was weak evidence of a normalization of mechanical pain sensitivity after treatment, with less patients showing abnormal MPS (p = .08). Surprisingly, non-responders were more hyperalgesic (MPS) at baseline than responders (p < .05). We did not identify any other predictors of treatment response.

Conclusion
In this pilot study we were able to successfully translate basic science knowledge to patients suffering from post-zoster pain evident by the reduction of pain in over 50% of treated patients. The high number of clinically meaningful, good, and excellent responders suggests that a novel, curative treatment
approach for chronic pain may be at hand. We believe the current level of evidence supports the conduction of a randomized controlled trial.
Title: Postoperative Pain Management In 12,006 Patients Submitted To Major Surgeries In An Oncologic Center In Brazil: A Retrospective Study

Poster Number PW0296

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Aim of Investigation
Despite the efforts and improvements in the pain clinical practice along the last years, the postoperative pain control remains a critical problem. It is estimated that thirty-three percent of the oncological patients experience severe pain after surgical procedures. Due to the lack of studies aimed specifically to the postoperative period of surgeries for tumor and metastasis resections, the objective of our study was to evaluate the effectiveness of the acute pain control and incidence of adverse reactions and complications exclusively in oncological patients who underwent major surgeries at AC Camargo Cancer Center (São Paulo, Brazil).

Results
The average age of the patients studied was 54 years. Surgeries by regions: 44,8% of the patients were submitted to colorectal and urologic surgeries; 17,08% to upper abdominal surgeries; 18,18% to thoracic surgeries, 14,69% to gynecological surgeries. Sixty percent of the patients received an IV PCA, 24% epidural morphine boluses and 16% PCEA. Adverse reactions: 14,33% of the patients presented nauseas; 7,59%, vomits; 9,93%, pruritus and 3,89% arterial hypotension. Patients with PCEA had less nausea and vomits when compared to the other techniques; patients with IV PCA had less pruritus, urinary retention and hypotension when compared to the epidural techniques. We had one case of chronic dorsal pain following epidural catheterization, which rhizotomy and laminectomy were needed.

Conclusion
Despite their physical statuses (post chemotherapy and radiotherapy in many cases), surgery site and complexity, our patients had an acceptable pain control and presented less adverse reactions and complications related to the analgesic medications when compared to the literature.
Title: Opioid Therapy In Japanese Patients With Chronic Non-Cancer Pain And Its Everyday Impact

Poster Number PW0297

Authors
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Aim of Investigation
This study examined the effect of opioid therapy, which included the use of opioid analgesics and mental coping, in the daily life of patients with chronic non-cancer pain.

Results
There were 17 male and 18 female subjects (N = 35), who were patients suffering from pain. The subjects’ average age was 61.3 ± 15.9 years (range: 22–86). The mean duration of pain and opioid administration were 11 ± 9.62 years (range: 0.08–33.0, median: 8.42) and 3.4 ± 2.82 years (range: 0–8.83, median: 1.92), respectively. The subjects evaluated the current opioid therapy as significantly better than the previous non-opioid treatment (Wilcoxon signed rank test, P < .001). Female subjects preferred the current treatment more than did the men (Mann-Whitney test, P < .05). Only the sub-domain of vitality in the SF36 showed a significant gender difference (Mann-Whitney test P < .05). The effects of opioid therapy were positively correlated with age. Sleep disruption, presence or absence of workmen's accidents, and opioid therapy duration and current pain level were negatively correlated with the effects of opioid therapy (P < .05). The effects of opioid therapy were also negatively correlated with the catastrophizing subscale of the CSQ (r = -.508, P < .01). Lastly, the effects of opioid therapy had a low positive correlation with the role-emotional subscale of the SF36 (r = .376, P < .05).

Conclusion
Patients with chronic non-cancer pain evaluated opioid therapy as significantly more effective than the previous non-opioid treatment.
Title: Duloxetine Hydrochloride Is One Of The Most Effective Analgesic Option In The Treatment Of Chronic Pain-Related Spinal Disease

Poster Number PW0298

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Aim of Investigation
The analgesics' treatment is an important method for the treatment of chronic pain-related spinal disease (CPSD), as well as exercise therapy and cognitive-behavioral therapy. Duloxetine hydrochloride (DLX) is the first or second option in the guideline for the treatment of neuropathic pain in many countries. The aim of this study is to investigate whether the combination of duloxetine hydrochloride and another analgesic is more useful than single administration of another analgesic in the treatment of CPSD.

Results
A series of spinal disease in all patients containing lumbar post laminectomy syndrome: 31%, lumbar canal stenosis: 19%, lumbar disc herniation: 9%, lumbar foraminal stenosis: 9%, cervical post operative pain: 8%, cervical spondyloradiculopathy: 8% and others. Processes was CR: 9%, PR: 39%, poor22%, and others. Of the amount of DLX, there was not significant differences between 2 groups (32.6mg versus 31.8mg), however, the amount of Pregabalin in good response groups was higher than that in poor response group (not significant differences, 133.3mg versus 110.0mg). The amount of Tramadol in good response groups was lower than that in poor response groups (not significant differences, 114.8mg versus 151.4mg), conversely. The best period of administrating DLX was at bedtime. The side effects of DLX were shown in 19.6% of the all patients, containing with neurologic symptoms (drowsiness or staggering): 8.9%, vomiting: 7.1% and others. Serotonin syndrome or insomnia was not seen in this study.

Conclusion
An additional treatment of DLX in the combination with another analgesic was one of effective therapy for CPSD. An administrating DLX at bedtime is likely good period for the patients without insomnia.
Title: Risk Factors For Increased Occurrence Of Adverse Drug Reactions With Cox-1/Cox-2 Inhibitor Treatment In Patients With Acute Or Rheumatic Pain

Poster Number PW0300

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Aim of Investigation
Increased risk of adverse drug reactions (ADRs) to non-steroidal anti-inflammatory drugs (NSAIDs) may be associated with factors related to treatment (e.g. dose, duration) and/or patient characteristics (e.g. age, gender). The aim of this analysis was to assess the risk of ADRs in patients who participated in clinical trials with the COX-1/COX-2 inhibitor, lornoxicam.

Results
A total of 6420 patients received treatment with lornoxicam; 4065 patients were treated for acute pain and 2355 for rheumatic pain. Treatment was generally administered for less than one month (85% of patients) with an 8 mg dose the most widely used. ADR incidence by dose was: <8 mg=16% of patients; 8 mg=17%; 12 mg=27%; 16 mg=23% and >16 mg=22%. There tended to be an increased incidence of GI ADRs with increasing dose (<8 mg=7% of patients; 8 mg=10%; 12 mg=20%; 16 mg=16% and >16 mg=16%) and duration of treatment but this was not apparent for non-GI ADRs. The dose-relationship for GI ADRs was more clearly shown in patients treated for rheumatic pain than acute pain. When assessed by age, no significant increase in relative risk (RR) were observed with lornoxicam for total ADRs (RR 0.95, 95% CI 0.80–1.13) or GI ADRs (RR 1.01, 95% CI 0.30–1.23) in elderly patients (≥65 years) compared with patients <65 years old. However, gender had a significant effect, with the risk of total ADRs (RR 0.78, 95% CI 0.69–0.88; p<0.0001) and GI ADRs (RR 0.73, 95% CI 0.63–0.85; p<0.0001) significantly lower in men than women.

Conclusion
There was no increased risk of total ADRs or GI ADRs in the elderly (≥65 years) but an increased RR was observed in women (22% total ADRs and 27% for GI ADRs). Incidence of GI ADRs was clearly related to drug exposure (dose and duration of treatment).
Title: Internal Control And Monitoring Can Decrease Overprescription Of Opioids In The Treatment Of Long-Term Non-Cancer Patients

Poster Number PW0301

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Aim of Investigation
Overuse and dependence of prescribed opioids for pain is a problem in many countries. Different approaches to regulate overprescription have been discussed. Methods to decrease liberal prescription are education of prescribers, opioid risk evaluation, opioid contract, drug testing and computerised monitoring of prescription. In the Multidisciplinary Pain Center of Uppsala we have introduced monitoring methods in order to detect and control overprescription. In a previous study we found that opioids were prescribed in a dose that exceeded the ordination by 110% in 67 of 166 (40%) patients during three months of registration in 2014. The overprescribed opioids were morphine (160%), oxycodone (170%), fentanyl TD (360%), buprenorphine TD (210%) and methadone (320%). Tramadol and codeine were not prescribed over ordinated dose. The summarized overprescribed dose of all opioids together was 5 489,7 MoEq. Those findings resulted in increased attention to the problematic situation and prescribers were informed which substances were overprescribed. The primary aim of this quality control assessment was to analyze the opioid prescription pattern in our pain clinic during 2014 and 2015. This was done by comparing the dose ordained to each patient to the actual amount of prescribed to the same patient during three months each year. The opioid prescription patterns between years 2014 and 2015 were then compared in order to analyze the effect of information of the prescribers. The secondary aim was to compare the spectrum and amount of prescribed opioids both in absolute amount PA (MoEq) and relative PR(related to the ordinated dose) in the same periods of 2014 and 2015.

Results
A total of 149 patients could be analyzed after exclusion of 17 patients from the previous group. In 2014 67 (40%) of 166 patients were overprescribed opioids and in 2015 52 (35%) of 149 patients. The relative overprescription of codeine was 310%, tramadol 170%, morphine 140%, oxycodone 160%,
buprenorphine patch 180%, buprenorphine sublingual 160%, fentanyl TD 140% and methadone 140%.
The absolute overprescription of codeine was 201 MoEq, tramadol 80,9 MoEq, morphine 333 MoEq,
oxycodone 2795 MoEq, fentanyl 113 MoEq, buprenorphine TD 207 MoEq, methadone 54 mg and
buprenorphine SL 4,9 MoE. All together the total absolute overprescription of all opioids is 4 207,9
MoEq in 2015 which is 24% less than the amount in 2014.

Conclusion
Both, absolute and relative overprescription of opioids has decreased. There was a major decrease in
both relative and absolute overprescription of methadone, fentanyl TD and buprenorphine and
overprescription of oxycodone and morphine slightly decreased. On the contrary there was an increase
of overprescription of codeine and tramadol. We conclude then that the increased attention to the
opioid prescription can lead to the decrease of overprescription of opioids and even to changes in
spectrum of used opioids. However, the level of overprescription is still high and introduction and
investigation of further control methods is essential.
Title: Chronic Pain In Patient With Ehlers-Danlos Syndrome: Management With Metamizole, Physiotherapy And Physical Exercising

Poster Number PW0302

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Aim of Investigation
To report the use of metamizole and physiotherapy as a therapeutic option in a patient with chronic pain associated with Ehlers-Danlos syndrome.

Results
One month after treatment began, the patient reported static and dynamic pain intensity as 3 and 5, respectively. Three months later, as 1 and 3. He has been followed regularly by the pain clinic and has taken metamizole 500 mg only on demand. According to the World Health Organization WHOQOL-BREF quality of life assessment, evaluated at the beginning of the treatment and 4 months later, the results have been very positive.

Conclusion
As part of a multiprofessional management, low-dose metamizole, associated with physiotherapy and psychological counseling, have contributed to better pain relief and quality of life to this patient.
Title: Use Of Ketorolac Infusion On Post-Operative Pethidine Consumption After Major Gynaecological Surgery: A Comparative Study

Poster Number PW0303

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Aim of Investigation
Aim of investigation: Total or optimal pain relief allowing normal physiology can not be achieved by a single drug or method without an organized surveillance systems or major side effects. Therefore, a multimodal approach for the treatment of postoperative pain is recommended. The modulatory influences of intravenous ketorolac infusion on postoperative pain are confirmed by several previous studies. Midazolam also has significant opioid sparing effect. The effect of combination of low dose midazolam and ketorolac infusion on postoperative pethidine consumption, and nausea and vomiting was assessed in this randomized clinical study.

Results
Results: Pethidine consumption in the Gr-KM group was significantly lower with 144.67 ± 7.501 mg (mean ± SEM) compared with Gr-K which was 213.67 ± 7.723 mg (mean ± SEM) (p = 0.000). Nausea (16.6% in Gr-KM compared with 33.3% in Gr-K; p = 0.026) and vomiting (3.3% in Gr-KM compared with 20% in Gr-K; p = 0.019) were also significantly lower in this group. Overall satisfaction after 24 hours was significantly higher in Gr-KM (p = 0.027). Sedation and oxygen saturation revealed no significant difference between the groups.

Conclusion
Conclusion: We conclude that ketorolac with low dose midazolam infusion produces a significant reduction in postoperative pethidine requirement, improves patient satisfaction and causes less nausea and vomiting compared with ketorolac infusion alone.
Title: Transdermal Duprenorphine Treatment Is Associated With Pain Relief And Improved Quality Of Life In Patients With Moderate To Severe Chronic Non-Malignant Pain: An Open-Label, Single-Arm, Multicenter Study In Three Asian Countries

Poster Number PW0304

Authors
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Aim of Investigation
This study examined the impact of transdermal buprenorphine treatment on pain relief, sleep, and quality of life in Asian patients with chronic non-malignant pain who were not adequately controlled with non-opioid analgesics. It also evaluated the tolerability of buprenorphine transdermal patch.

Results
One hundred and fourteen eligible patients were included in the analysis. The mean (SD) age was 57.0 (13.4) years. Over 50% of patients were Korean while Chinese and Filipino made up the remaining population (22.8% each). Osteoarthritis (48.3%) and low back pain (37.7%) were the most common causes of chronic pain. Following initiation of transdermal buprenorphine treatment, there was a statistically significant and clinically relevant improvement in BS-11 pain score from baseline to the end of titration (p<0.0001), with a least squares (LS) mean change of -2.27 (95% CI -1.87 to -2.66). This improvement was maintained until the end of the treatment (p<0.0001), with a LS mean change of -2.49 (95% CI -2.11 to -2.87). Five out of six GSQA sleep disturbance measures improved significantly at the end of treatment: trouble falling asleep (p<0.0001), need pain medication to sleep (p=0.001), awakened by pain at night (p=0.004), awakened by pain in the morning (p<0.0001), and affect partner's sleep (p=0.007). There were significant improvements in all EQ5D-3L dimensions at the end of treatment: mobility (p=0.0003), self-care (p=0.001), usual activities (p=0.015), pain or discomfort (p=0.003), and anxiety or depression (p=0.004). Patients' overall health state improved significantly from baseline (p<0.0001), with a mean (SD) increase in EQ visual analogue scale (EQ VAS) score of 7.7 (17.9) units at
the end of treatment. Overall, 78.1% of patients reported adverse events (AEs), the majority of which were mild-moderate in intensity (96.5%). Over 20% of patients withdrew from the study due to AEs. Common AEs leading to discontinuation were nausea (11.4%), dizziness (7.9%), and vomiting (5.3%). No drug-related SAEs or deaths occurred during the study.

Conclusion
This is the first multinational study of transdermal buprenorphine treatment in the Asian setting. Our clinical experience demonstrates that transdermal buprenorphine provides effective analgesia along with improved quality of life in Asian patients with chronic non-malignant pain, with a tolerability profile consistent with other opioids.
Title: Long-Term Safety And Efficacy Of Oxycodone/Naloxone Prolonged Release Tablets (Oxn Pr) Up To A Maximum Daily Dose Of 180/90 Mg: Results From A Phase Iii Multicenter, Multiple-Dose, Randomized, Controlled Study With An Open-Label Extension Phase

Poster Number PW0305

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

Results
A total of 243 patients were randomized (123 Oxn PR and 120 Oxy PR) and 209 patients completed the study (105 Oxn PR and 104 Oxy PR). Significantly greater improvements in BFI from baseline were observed with Oxn PR compared with Oxy PR; mean change at 5 weeks: -33.4 vs -13.8 (p < 0.001). Average pain scores show comparable results between the two treatment arms, with no clinically relevant change from baseline throughout the RCT phase. In the extension phase, 195 of 209 (93.3%) patients who completed the RCT entered the extension phase voluntarily and received Oxn PR. Clinically relevant improvements were observed in the BFI already within the first week of the extension phase, especially in patients who had received Oxy PR in the RCT phase (mean change in BFI -25.9). The improved bowel function was also maintained during the extension phase, with a normalization of bowel function at 24 weeks in the total population (mean BFI 26.7). Median pain score was 4.0 in patients who had received Oxn PR or Oxy PR in the RCT phase; this level of pain control was sustained during the extension phase. AEs during the RCT phase were comparable in the two arms; no treatment-related serious AEs (SAEs) were reported. In the extension phase, 13 of the 36 SAEs reported were considered causally related to study medication. No unexpected AEs were recorded.
Conclusion
OXN PR provided comparable pain relief as Oxy PR but with improved bowel function. Long-term analgesic efficacy with maintained bowel function was observed up to 7 months. AEs observed were consistent with the established safety profile of OXN PR. 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: Combination Pharmacotherapy For The Treatment Of Neuropathic Pain In Adults: Update 2016

Poster Number PW0306

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Aim of Investigation
Pharmacotherapy is an important modality for the treatment of neuropathic pain. Combining two or more different drugs may improve analgesic efficacy and, in some situations, reduce overall side effects. This review is an update of a Cochrane review first published in 2012 and evaluates the efficacy, tolerability and safety of various drug combinations for the treatment of neuropathic pain.

Results
At the time of writing, we identified and added 6 new studies to the 21 that were included in the original review. Upon pooling these 6 new studies with the original 21: five (837 participants) evaluated the combination of an opioid with gabapentin or pregabalin; three (116 participants) evaluated an opioid with a tricyclic antidepressant (TCAs); two (125 participants) evaluated the combination of TCAs with gabapentin or pregabalin; one (290 participants) of duloxetine and pregabalin; one (15 participants) of duloxetine and methadone; one (15 participants) of nabilone and gabapentin; one (120 participants) of gabapentin and alpha-lipoic acid, three (90 participants) of fluphenazine with a tricyclic antidepressant; three (90 participants) of an N-methyl-D-aspartate (NMDA) blocker with an agent from a different drug class; five (604 participants) of various topical medications; one (313 participants) of tramadol with acetaminophen; and another one (44 participants) of a cholecystokinin blocker (L-365,260) with morphine. The vast majority of combinations evaluated drugs, each of which share some element of central nervous system (CNS) depression (e.g. sedation). This overlapping was often reflected in similar or higher dropout rates for the combination and may thus substantially limit the utility of such drug combinations. Most of the included studies demonstrated superior efficacy of two-drug combinations over the other trial comparator(s).

Conclusion
The number of available studies for any one specific combination, as well as other study factors (e.g.
limited trial size and duration), preclude the recommendation of any one specific drug combination for neuropathic pain. We strongly recommend for future neuropathic pain studies of two-drug combinations include comparisons with placebo and both single-agent components. Given the apparent adverse impact of combining agents with similar adverse effect profiles, the development of non-sedating neuropathic pain agents could lead to the identification of more favorable analgesic drug combinations in which side effects are not compounded.
Title: Insular Cortex Stimulation As A Novel Target For The Relief Of Refractory Pain

Poster Number PW0307

Authors
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Aim of Investigation
To develop and assess an animal model of insular stimulation in rodents, allowing the parametric study of the mechanisms of pain relief by insular stimulation as a novel target for the relief of refractory pain.

Results
CCI induced a decrease on nociceptive threshold on both evaluated paws of rats for both Sham and ICS groups, when compared the Baseline with Pre-stimulation measurements. After a 15-minute session of ICS a significant increase of the nociceptive threshold of rats was seen when compared to Sham. The increase of the nociceptive threshold was observed specifically at the right hind paw, contralateral to the stimulated hemisphere, demonstrating that ICS induces antinociception on rats with peripheral neuropathy. No changes on nociceptive threshold were observed for the left hind paw when compared pre- and post-stimulation measurements.

Conclusion
Electrical stimulation of the posterior insular cortex induces antinociceptive effect in rodents.
Title: Ultrasound Guided Suprascapular Nerve Pulse Radiofrequency Lesioning For Treatment Of Frozen Shoulder

Poster Number PW0308

Authors
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Aim of Investigation
To evaluate the efficacy of pulsed radiofrequency of suprascapular nerve for the treatment of frozen shoulder. Frozen shoulder or adhesive capsulitis is troublesome disease of shoulder joint characterized by pain and decreased range of motion. It is managed by use of NSAIDS, intraarticular steroids, therapeutic exercises and more recently suprascapular nerve block. Suprascapular nerve block can be performed blindly, fluoroscopic guided and by ultrasound guidance. In the present study we are describing use of ultrasound guidance for suprascapular nerve block in patients of adhesive capsulitis not responding to intraarticular steroids.

Results
Mean VAS score for pain was 8.85±.87, 3.40±1.09, 4.35±0.87 and 5.05±0.94 at baseline, 1 week, 4 week and 12 week respectively. There is significant decline in VAS score at 1 week (p<0.1), 4 week (p<0.1) and 12 week (p<0.1).

Conclusion
Ultrasound guided suprascapular pulse radiofrequency lesioning is viable treatment option for relieving pain in patients of frozen shoulder.
Title: Burst Stimulation For Treatment Of Lumbar Radicular Pain In Previously Non Operated Chronic Back Pain: A Case Report

Poster Number PW0309

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Aim of Investigation
The present case shows the outcome of burst stimulation compared to tonic spinal cord stimulation in a previously non operated patient with chronic lumbar radicular pain. Burst stimulation has shown to be beneficial and often superior to tonic spinal cord stimulation in patients with recurrent lumbar radicular pain who have undergone previous spine surgery. To our knowledge there is no data known if burst stimulation provides significant more pain relief for lumbar radicular pain in previously non operated patients if compared to tonic stimulation.

Results
During trial period VAS pain scores were equally reduced by more than 50% using tonic or burst mode. Following permanent SCS device implantation reduction of pain scores were 20-30% with burst mode and 50% with tonic stimulation.

Conclusion
Burst stimulation was effective but not superior to tonic spinal cord stimulation for treating lumbar radicular pain in a previously non operated patient. Further studies are desirable to evaluate the beneficial effect of burst stimulation in previously non operated chronic radicular lumbar pain.
Title: The Availability And Safety Of Diskectomy With Dekompressor And Disclysis With Collagenase In The Treatment Of Massive Cervical Disc Herniation

Poster Number PW0310

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Aim of Investigation
To explore the availability and safety of diskectomy with dekompressor and Disclysis with collagenase in the treatment of massive cervical disc herniation.

Results
The effects in all patients were evaluated according to the Macnab method. Of the 6 patients who received both interdisclysis and exterdiscolysis 4 patients gained 'excellent' effect and 2 gained 'good' effect. Of the other 10 patients who underwent only exterdisclysis 2 patients gained 'excellent' effect (see MRI and CT pre- and post- treatment), 6 gained 'good' and 2 gained 'poor' effect. There were no any complications happened in all patients.

Conclusion
Diskectomy with Dekompressor and Disclysis with collagenase is effective and safe in the treatment of massive cervical disc herniation.
Title: Peripheral Neurostimulation In The Treatment Of Neuropathic Pain

Poster Number PW0311

Authors
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Aim of Investigation
This observational retrospective study is aimed to evaluate the efficacy of peripheral nerve and nerve field stimulation (PNS and PNFS) in the treatment of patients with neuropathic pain (NP) syndromes.

Results
In follow-up good results have been obtained in the majority of cases with positive trial. Absolute recovery (90%-100% pain relief) was observed in 9 patients (21.9%), good recovery (pain relief more than 50%) – in 21 patients (51.2%). In 11 cases (26.8%) results were considered as volatile (pain relief have become less than 50% in follow up). In these 11 cases, patients had very high scores of personal anxiety, and pain catastrophizing. No serious or unanticipated adverse events have occurred. During the study, only one type of complications have occurred in six patients – lead migration. In all those patients, stimulation efficacy had been completely restored after electrode position compensation.

Conclusion
In the right selected patients suffering from chronic neuropathic pain, PNS and PNFS have demonstrated high effectiveness. Further investigations are necessary for exacter definition of neurostimulation efficacy predictors.
Date: 09/28/2016 09:30:00 AM

**Title:** Enhancing Cognitive Pain Inhibition By Anodal Transcranial Direct Current Stimulation Of The Left Dorsolateral Prefrontal Cortex Through Improvement Of Working Memory And Inhibition Of Spinal Nociceptive Transmission.

**Poster Number** PW0312

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**Aim of Investigation**
Cognition can profoundly alter pain perception by modulating nociceptive processes. For instance, pain perception can be increased or decreased depending on the allocation of attention to nociceptive signals. Disengagement of attention from pain as well as engaging cognitive processes to perform a concurrent task are necessary for cognitive pain inhibition. In this case, working memory (WM) selects the most relevant information and directs attention towards performing the cognitive task while attenuating nociceptive signals. According to neuroimaging studies, this occurs through activation of the dorsolateral prefrontal cortex (DLPFC), which is at the center of a cerebral network supporting WM. WM performance can be improved by anodal transcranial direct current stimulation (tDCS) of the left DLPFC. The aim of the present study was to examine whether anodal tDCS of the left DLPFC may enhance pain inhibition through improving WM function and whether this effect involves descending inhibition of spinal nociceptive transmission.

**Results**
When pain was evoked alone or in combination with the zero-back task, perception was not significantly affected by either sham or anodal tDCS compared with the pre-tDCS baseline (all p's > 0.05). However, when pain was evoked in combination with the two-back task, it was not significantly affected by sham tDCS (p = 0.7), but it was decreased by anodal tDCS (p = 0.03) compared with the pre-tDCS baseline. To test whether this effect involved WM and descending inhibition, reaction times and NFR amplitude were compared for the same conditions. Reaction times and NFR amplitude for the two-back task were both
significantly decreased by anodal tDCS (p = 0.04 and p < 0.001, respectively). Sham tDCS had no significant effect on reaction times for the two-back task (p = 0.29) while NFR amplitude was decreased (p < 0.05). However, the decrease of NFR amplitude was greater for anodal compared with sham tDCS (p < 0.01).

**Conclusion**
The present results suggest that enhanced hypoalgesia by anodal tDCS of the left DLPFC during the two-back task occurs through improvement of WM and activation of descending inhibitory pathways. Whether improvement of WM and activation of descending inhibitory pathways rely on a common or separate mechanism remains to be clarified. This project was funded by the Natural Science and Engineering Research council (NSERC) of Canada. Nabi Rustamov was supported by a grant from the Fondation Chiropratique de Recherche du Québec.
Title: The Simplified Epiduralysis After Laminectomy/Fusion (Seal) Procedure For Post-Surgical Radicular Low Back Pain

Poster Number PW0313

Authors
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Aim of Investigation
Chronic radicular low back pain (LBP) following lumbar spine surgery is common (prevalence estimates range from 10-40% of patients) and can lead to surgical reinterventions or other procedures. Epidural lysis of adhesions has been proposed as a treatment for refractory post-operative back pain, and typically utilizes specialized catheters and extended procedures. Here we reviewed the outcomes of patients receiving a Simplified Epiduralysis After Laminectomy/fusion (SEAL) procedure at a large city hospital.

Results
35 patients were identified, 5 patients were eliminated due to malignancy, multiple SEAL procedures, or lost to follow-up. 85% of patients reported improvement of pain symptoms at 1 week with 65% reporting pain relief greater than 50%. At subsequent follow-up, 74% of patients reported improvement with 39% reporting pain relief greater than 50%. 10% of patients reported feeling pain free or nearly pain free at follow-up.

Conclusion
In this case-series, the SEAL procedure resulted in short term benefit in 74% of post-surgical radicular LBP. This procedure may be a useful treatment modality for patients with persistent pain symptoms after lumbar spine surgery as an effective treatment option. Further study should be done to determine more specific outcomes (disability index, function) and a prospective trial is planned.
Title: Injury Caused By Pulsed Radiofrequency (Prf) In Chronic Pain Shoulder

Poster Number PW0314

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Aim of Investigation
1. Evaluate the clinical efficacy of PRF treatment of the suprascapular nerve in chronic shoulder pain in the short and medium term.  2. Know the degree of patient satisfaction, assessing developments pain, range of motion and quality of sleep.

Results
Statistical analysis of the data was carried out using SPSS 10.0. The results show a significant improvement (p <0.005) in all the variables studied (pain intensity at rest and in motion, and quality of sleep) Descriptive analysis for all variables, proportions and association between qualitative variables (Fisher exact test). Analysis for pain intensity with the Wilcoxon test and bivariate to assess the association between pain relief with a history of previous surgery diagnosis shoulder pain and neuropathic features analysis. a lower level of statistical significance of 5%, with confidence intervals of 95%.

Conclusion
The injury pulsed radiofrequency (PRF) is a symptomatic treatment, minimally invasive, that reduces pain, improves joint mobility and quality of sleep. It is well tolerated by patients who show a high level of satisfaction.
Title: Determine The Role Of Chemical Genicular Neurotomy In Chronic (Oa) Knee Pain

Poster Number PW0315

Authors
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Aim of Investigation
Chronic (OA) pain of the knee is often not effectively managed with current non-pharmacological or pharmacological treatments. Different medical therapies used to control pain and improve the quality of life include analgesics, NSAIDs, steroid intra-articular injections, Inj. hyaluronic acid, pain killer ointments etc. Although total knee replacement is generally effective for patients with advanced disease, individuals with co-morbidities may not be eligible candidates. Neurolytic blockade is a therapeutic option when actual source of pain cannot be treated. The objective is to relieve the pain by blocking the nerves that transmit nociception from its source. The primary indication is complete relief of pain when the target is anesthetized temporarily with control local anesthetic. Long lasting relief can then be achieved using chemical or physical agents. We used phenol in a concentration of 6.7%. It is locally neurotoxic in a dose dependant manner. This is a dehydrating agent causing non selective destruction of neuronal tissues followed by necrosis, non segmental demyelination, wallerian degeneration and complete conduction block occurring within 10 mins of application.

Results
Out of 23 patients in Group A who were followed after 2 weeks, 21 reported marked improvement in pain. Their regular pain medications were stopped and they were advised to take acetaminophen only if needed. After 8 months of monthly followup, 80% (21/23) continued to have significant pain relief. The remaining 2, who did not respond to the first injection, were given a repeat injection of phenol after 2 weeks. They also responded with good pain relief thereafter. In the control group (Group B), 5 dropped out and 20 patients were followed for 8 months. On the first follow-up they continued to complain of significant pain and restriction of motion. At the end of study, Group B needed repeated intra-articular steroid injections and multiple pain medications.
Conclusion
The group of patients receiving phenol for chemical neurotomy of genicular nerves reported significant improvement in their chronic knee pain and remained symptom free even after 8 months as compared to control group. In developing countries, where resources for knee replacement for end stage osteoarthritis are not fully available or where patients are unwilling to undergo surgery, chemical neurotomy is an inexpensive and safe alternate for pain relief. It can significantly improve the quality of life for the ageing population as it is an effective, out-patient minimally invasive procedure for chronic knee pain. It can also be repeated when nerves regenerate.
Title: Efficacy Of Pulsed Radiofrequency As Treatment For Chronic Headache

Poster Number PW0316

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Aim of Investigation
Chronic headache give rise to significant health, economic and social costs. Despite the undoubted benefits of medication, many patients continue to experience significant distress and social disruption. Pulsed radiofrequency (PRF) progresses to manage a wide spectrum of chronic pain modalities of non-neural tissue. In this study, we examined the efficacy of application PRF for chronic headache.

Results
Both groups had a significant decrease of headache frequency (p= .0001) and severity (p= .0001) in the first month compared with the initial baseline results. There were progressive increased in the both severity and frequency of headache in the third month and sixth month in ARF group to the level of no significant differences from the initial baseline results. In other side, there still decreased in the frequency and severity of headache in URF group in the third and sixth month to a significant differences from the initial baseline results (p= .0001 for both).

Conclusion
The results of this clinical study suggest that : 1- PRF is a safe, well-tolerated intervention in patients with chronic headache. No discontinuations due to adverse events occurred, nor were any treatment-related serious adverse events reported. 2- Single session effective. 3- Cost tolerance 4- No case resistance
Aim of Investigation
Tendons are the load-bearing attachments of muscles into bones that allow a muscle contraction to translate into mechanical movement of the skeleton. About 40% of all sports-related injuries involve tendons e.g. Patellar tendon (jumping sports) Achilles tendon (runners), rotator cuff injuries (throwers) etc. However, sedentary people are also at risk of developing tendon injuries Tendon injuries frequently progress to chronic tendinopathies due to suboptimal healing, pain and dysfunction. Although tendinopathies constitute a heterogeneous group of conditions, they are often treated by similar combinations of local and systemic symptomatic interventions. The vast number of causes, pathophysiological mechanisms, and histological changes that characterizes tendinopathies may explain that the standard treatment fails in some patients. Platelet rich plasma (PRP), an autologous sample of blood with a platelet concentration above baseline values, is known to augment soft tissue healing and provide significant improvement in both pain and functional scores. PRP contains a host of soluble mediators including growth factors and has been suggested as a second-line treatment for refractory tendinopathy, with the goal of expediting tendon healing or remodeling. The purpose of this observational pilot study was to prospectively investigate the clinical efficacy of treatment with PRP injection in patients with chronic painful tendinopathy.

Results
49 tendons were treated with average age of patients being 44.2 years (range 18-65). 44.9% were female and 55.1% were male. Patients had symptoms for an average of 4.4 months prior to treatment. Conditions treated included lateral epicondylitis (7), medial epicondylitis (8), Achilles tendinosis (11), rotator cuff (9) bicipital tendinosis (3), plantar fasciitis (9) and other tendinopathies (2). All patients had 3 PRP injections at weekly interval. Clinically significant improvement in terms of more than 30% reduction in pain score was seen in all the patients enrolled for the study. There was a significant
decrease in NRS Score in 16.3% patients at 4 wks., 51% at 8 wks., in 75.5% at 12 weeks (p=0.002), & in 89.8% patients (p<0.0005) at 16 wks follow up. QOL Score improved by 14.3% in 4 wks., 57.1% in 8 wks., 73.4% in 12 wks. and by 93.9% in 16 wks period. & Patient Satisfaction Score (SF 36) improved by 12.2% in 4 wks., 61.2% in 8 wks. (p=0.041), 71.4% in 12 wks and 91.8% in 16 wks (p<0.0005) follow up. There was no serious adverse event or allergic reaction that was noted. There was a slight increase in pain lasting for a maximum of two days in 12.24% patients.

**Conclusion**

The result of this study supports the potential application of PRP injection for treatment of chronic partial tendon tears, plantar fasciitis, chronically painful tendons that have failed to improve despite appropriate conservative treatments. Certainly, the benefits of PRP seem to outweigh the potential risks. Nonetheless, there is a need for more randomized clinical trials on PRP treatment of tendinopathy.
Title: Selection Of An Approach For Cervical Epidural Steroid Injection

Poster Number PW0318

Authors
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Aim of Investigation
Cervical epidural steroid injection (CESI) is probably one of the most common pain procedure, referred to and performed by pain specialists. It can be delivered through either transforaminal (TF) or interlaminar (IL) approach. The advocates for TF approach argue that it could be more efficacious than IL approach because of more direct spread of the injectate to the target pathology. Pattern of consult requests may vary significantly among referral sources. Specialty such as physical medicine and neurosurgery tend to request specific approach and target level. Transforaminal approach appears to be still preferred among them, however, rare but serious complications have been reported including injury or injection to the vertebral artery. Decision to offer CESI and choice of approach should be based on not only clinical impressions but assessment of technical feasibility on each patient’s unique anatomy. The aim of this investigation was to estimate candidacy and technical feasibility of transforaminal approach of CESI among the consults referred to a pain clinic.

Results
Of 100 consults, 61 came from specialty including physical medicine and neurosurgery. Eighty five percent of consults from specialty requested/suggested TF approach for a specific level, whereas none of the consults from primary care specified approach. Seventy seven percent of those requesting TF ESI were deemed potential candidates, compared to 45% of those from primary care. Only 23% of candidates for TF ESI were considered technically feasible, however, 83% of those actually received IL ESI instead. Seventy nine percent of candidates for IL ESI were considered technically feasible and 89% of those received it.

Conclusion
In a pain clinic at a VA medical center, majority of consults for CESI from specialty clinics requested transforaminal approach and were deemed potential candidates from clinical impressions, whereas it was technically feasible for only 23% of those patients based on MRI assessment. In contrast, referrals
from primary care were non-specific and more than half of those considered less than ideal indication. These results highlighted the gap between popularity of transforaminal approach for CESI among referring providers and actual candidacy for the procedure, and raised a question of its clinical usefulness.
Aim of Investigation
A salutary improvement in precision has been put into effect through the diffusion of ultrasonographic (US) devices in the practice of regional anesthesia for surgery and nerve block anesthesia as a measure to control chronic pain. Even if US-guiding is employed, hemorrhagic complications in the region around a target vertebra would pose a problem of surgical concern unless visualization of a puncture needle tip suffices. We explored the coursing of vasculatures for avoiding complications of nerve block using spinal column and spinal nerve specimens from cadavers donated for the dissection practice of students. This report presents the findings we thus have gained regarding the region ranging from middle thoracic to lumbar vertebral levels.

Results
As for the arterial system of the paravertebral region, somatic arteries (intercostal and lumbar arteries) branching off from the thoracoabdominal aorta were noted to be coursing in an upward convex pattern over the laterocentral surface of the vertebral body toward the spinal cord, then rolled around at the lateral aspect of the periphery of a spinal ganglion, entered along the nerve root into the subarachnoidal space, where they coursed together with the nerve root over a long distance. In the lumbosacral region, the arterial system ascended cephalad, possibly functioning in part as spinal cord feeding arteries. The venous system was found to be distributed primarily over the dorsal aspect from the ventral aspect of the spinal nerve root, then rolled around at the ganglion to penetrate the dura mater and anastomose with the internal and external vertebral venous plexus or reach the spinal cord.

Conclusion
In the practice of celiac nerve block or sympathetic ganglion block via a puncture point in the lateral
aspect of the vertebral body, the operator should avoid repeated mechanical abrasions on the mid-lateral surface of the vertebral body taking hemorrhagic or ischemic complications into consideration. The same caution seems also mandatory in the practice of upper-level paravertebral nerve block.
Title: Programmed Intermittent Administration Via Epidural Analgesia Improved Pain Scores After Total Knee Replacement And Total Hip Replacement.

Poster Number PW0320

Authors

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Aim of Investigation
This prospective, randomized, double-blinded study is to compare pain relief, side effects, and ability to ambulate during patient-controlled epidural analgesia with continuous versus intermittent administration mode after major joint surgery. The continuous lumbar epidural analgesia with patient-controlled analgesia (PCA) is widely used for pain control. Whereas, this method was not satisfied in pain-control after Total knee replacement (TKR) and Total hip replacement (THR) patients. One reason of difficulty of their pain control is considered that: The pain interception area may limited because of their anatomical problems, such as spinal canal stenosis or deformity of the spine, thus it has been clear that necessity to improve setting in the current epidural analgesic method. Intermittent administration of epidural local anesthetics has been recognized more effective than continuous infusion in post-operative analgesics in many surgical procedures, such as obstetric analgesia for labor. In This study, we investigated the intermittent dosage method may be superior to the continuous dosage method with expanse of the local anesthetics in the extradural space.

Results
Twenty-eight patients received IB regimen and 31 patients received CI regimen. There were significant difference in pain score between IB group and CI group: with VAS-rest (Mean±SD, IB vs. CI: 14.7±16.9 vs. 28.4±24.6 at 2 POD, p<0.01) with VAS-movement (33.8±19.6 vs. 53.9 ±19.6 at 2 POD, p<0.01). The pain blockade area was significantly large in IB group: p<0.01 during 1 to 2 POD (Mean±SD, 7.1±1.5 vs. 4.6±1.8 at 1 POD, 5.9±1.5 vs. 4.3±1.7 at 2 POD with spinal neural segment). The incidence of side effects were not different in two groups (number of patients, nausea: 3 vs. 4, vomit: 0 vs. 1).Hypotension, motor disability and unable to ambulate did not occur in both groups. One patient of IB group fell down inside the hospital two days after catheter withdrawal. The effective PCA counts were not different in two groups (17.3±13.8 vs. 18.6±11.2 at 2 POD, p=0.29)
Conclusion
The IB group, compared with the CI group, pain intensity was significantly lower, and pain blockade area was significantly large. We conclude that expanse of the drug of the epidural space was large, so that the IB group exhibited superior pain control after surgery.
Aim of Investigation
Trauma-induced peripheral nerve injury often results in not only functional disability, but also neuropathic pain. Although several types of artificial substitutes have been developed for peripheral nerve repair, these materials are sometimes insufficient for bridging long nerve defects in the clinical situation. Here, we developed a novel treatment, which is oriented collagen tubes (OCT) combined with basic fibroblast growth factor (bFGF) for the repair of 15-mm sciatic nerve defects in rats.

Results
In rats treated with either OCT/bFGF or OCT/PBS, the walking function parameter of paw print area returned to normal levels 4 weeks after treatment and the regeneration of myelinated fibers was detected after 8 weeks. However, more regenerated myelinated fibers were observed in the OCT/bFGF group compared with the OCT/PBS group at 4 weeks. In addition, the paw print area, max contact area, and swing speed in the OCT/bFGF group were significantly improved compared to the OCT/PBS and PBS groups at 8 weeks (p<0.05).

Conclusion
In this study, the treatment of a large sciatic nerve rat defect model with OCT promoted the formation of myelinated fibers and significantly improved walking function. As cell orientation structure was previously reported to affect Schwann cell survival and directionality, the present findings suggest that OCT might accelerate nerve repair by promoting Schwann cell proliferation. In addition, the combination of bFGF and OCT was superior to OCT alone for nerve regeneration and functional recovery. Thus, because bFGF has a role in regulating Schwann cell proliferation and axonal regrowth, bFGF appears to accelerate nerve regeneration when administered in combination with OCT. In conclusion, OCT and the
OCT/bFGF composite promoted nerve repair in a large nerve defect rat model and are therefore promising materials for the treatment of large peripheral nerve defects in the clinical setting.
**Title:** Caudal Epidural And Ozone Nucleolysis For Management Of Pain And Disability In Prolapsed Lumbar Intervertebral Disc- A Prospective Cohort Study

**Poster Number** PW0322

**Authors**
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**Aim of Investigation**
There are complaints of pain immediately after the ozone nucleolysis as its pain relief activity starts gradually to take its lasting effect. The study was to observe if caudal epidural may help to alleviate immediate pain of patient and also to observe overall improvement in pain relief through the procedure.

**Results**
A total of thirty four patients were included in the study (twenty males, fourteen females) with mean age of 37.6±7.1 and body weight 60.8±7.6. Twenty two patients had L 4-5 and 12 patients had L5-S1 intervertebral disc herniation. The mean pain score before intervention was 8.8±0.5, immediate after intervention at recovery room 1.6±0.72, after one week it was 1.7±0.4, at month 1.5±0.5, at three month 1.1±0.3, at six month 1.0±0.4 (p<0.001 within subjects, reached by ANOVA). Oswestry Disability Index (ODI) showed significant improvement in the followed up period compared to pre-intervention level. The mean ODI before intervention was 64.1±6.7, at one week 12.8±1.1, at one month 11.5±1.2, at three month 10.3±.7 and at six month 10.2±0.6 which was statistically significant compared to pre-intervention value (p<0.001 within subjects, reached by ANOVA).

**Conclusion**
Caudal epidural and ozone nucleolysis provides excellent pain relief immediate after intervention and also in chronic low back pain caused by prolapsed lumbar intervertebral disc.
Title: The Effect Of Microvascular Decompression In Patients With Trigeminal Neuralgia Of Longer Duration Than Its Definition

Poster Number PW0323

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Aim of Investigation
Trigeminal neuralgia is described as 'unilateral brief electric shock-like pain' and the duration of the pain was defined as 'from a fraction of a second to 2 minutes' (ICHD-III β). However we sometimes encounter patients who have longer duration of unilateral neuralgia than its definition, but not dysesthesia or paresthesia, and other feature of his neuralgia completely fit to the definition of trigeminal neuralgia. We reviewed our experience of microvascular decompression (MVD) in patients with trigeminal neuralgia of longer duration than its definition.

Results
Among 226 trigeminal neuralgia patients who received MVD in our department from 1980 to 2015, four patients met the survey condition. They described their neuralgia it self, but not the inter-ictal dysesthesia or paresthesia, continued 5 to 20 minutes. There were apparent vascular compression to the affected trigeminal nerve and all of the patients experienced complete relief of their trigeminal neuralgia after MVD.

Conclusion
In our 226 experience of MVD for trigeminal neuralgia, we found four patients whose duration of neuralgia itself is longer than its definition. The incidence of these patients seems to be small, but we found complete relief of TN with MVD in these patients. We believe that these patients also could be diagnosed as trigeminal neuralgia.
Title: Effectiveness Of Percutaneous Radiofrequency Thermo-Coagulation Of Primary Hyperhydrosis. Anterior Or Posterior Approach?

Poster Number PW0324

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Aim of Investigation
Primary hyperhydrosis (PH) is secondary to hyper-functioning central sudomotor output. It has a predominant emotional component. There is a tonically active sympathetic innervation of downstream vasomotor effectors and a more labile sudomotor connatives. Sympathetic denervation is the current standard-of-care treatment of PH. Case report A 25-year-old female presented with complaints of childhood-onset severe primary upper limb hyperhydrosis. Examination revealed cold and clammy extremities and axillary sweating. No familial link and/or specific factor (aggravating/relieving) could be isolated. History of thyrotoxicosis, carcinoid syndrome, phaocromocytoma, and autonomic dysfunction was negative. General physical and specific neurological examination returned insignificant. With no respite from sustained conservative management, bilateral image-guided stellate ganglion block with percutaneous radiofrequency thermo-coagulation (RFT) was planned.

Results
In our case study, the posterior approach of RFT at T2 & T3 provided long lasting relief of hyperhydrosis compared with anterior approach at C7. Quality of life was excellent at discharge and better at the time of follow up at 8-months post intervention.

Conclusion
The treatment of palmar hyperhydrosis with RF application provided better and long standing relief with applied via the 'posterior' approach T2-T3 thoracic ganglion after treatment with preformed C7 sympathectomy with an anterior approach had failed.
Title: The Clinical Efficacy And Disc Volume Change Of Percutaneous Epiduroscopic Laser Disc Decompression (PELDD) Compared To Percutaneous Epidural Neuroplasty (PEN)

Poster Number PW0325

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Aim of Investigation
At the present time, percutaneous epiduroscopic laser disc decompression (PELDD) has been widely introduced and used for herniated lumbar disc or lumbar spinal stenosis. However, very few articles have been reported about only clinical outcomes compared with using laser decompression or not. Therefore, for the herniated lumbar disc patients, the authors evaluated the clinical efficacy of PELDD compared to percutaneous epidural neuroplasty (PEN) as well as the relationship with the change of disc volume and clinical outcome from pre- to post-PELDD through the pre- and post-operative MRI.

Results
The mean age was 58.0 (range, from 18 to 84) and 44.8 (range, from 19 to 72) years in PEN and PELDD groups, respectively (p< 0.001). There was no significant difference in gender (p = 0.07), duration of symptoms (p = 0.37), and the distributions of level (p = 0.09) between two groups. Between two groups, preoperative VAS, SF-12 had no significant differences except preoperative ODI. Preoperative ODI, 46.0±17.2 in PELDD group were higher than 19.3±7.0 in PEN group (p = 0.004). In the PEN group, the differences between preoperative and postoperative 1,3,6 months VAS, ODI and SF-12 were significant, respectively (p < 0.001). Macnab criteria became 1.93 at 1month postoperatively, 1.65 at 3months postoperatively, and 1.65 at 6months postoperatively (p <0.003). In the PELDD group, the differences between preoperative and postoperative 1,3,6months VAS, ODI and SF-12 were significant, respectively (p < 0.001). Macnab criteria became 2.50 at 1month postoperatively, 2.71 at 3months postoperatively, and 2.78 at 6months postoperatively (p < 0.003). Furthermore, change of VAS, ODI, SF-12, Macnab criteria of PELDD group were better than those of PEN group. The mean disc volume was 150.84 ± 107.36 mm³ preoperatively and 120.56 ± 113.03 mm³ at 6 months postoperatively (p= 0.034). Furthermore, the change of disc volume after PELDD correlated with the difference of ODI between preoperative and postoperative 3months (p=0.006), 6months (p=0.004) values.
Conclusion
To our knowledge, this is the first comparative study to investigate the outcomes of patients undergoing PEN and PELDD in herniated lumbar disc. All clinical outcomes became better in each group. Especially, the PELDD group was superior to PEN group regarding degree of improvement in clinical outcomes. Improvement of pre and postoperative ODI correlated with the change of disc volume after PELDD. Therefore, PELDD could produce significantly greater clinical improvements compared with PEN.
**Title:** Effects Of Prolonged Pulsed Radio Frequency Current On Cytotoxicity, Microvesicle Shedding, And Mrna Expression For Proopiomelanocortin (Pomc) In Human Monocytic Cells

**Poster Number** PW0326

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**Aim of Investigation**
Pulsed radiofrequency (RF) current is an alternative modality to continuous RF applied for thermal coagulation of peripheral nerves in pain intervention. The maximum temperature of probe elevates up to 70 – 90°C during ablation using continuous RF current. By contrast, temperature of pulsed RF probe is limited to be below 43°C. Mechanisms of action of pulsed RF modality thus remain to be established. Because a certain part of parenchymal glial cells is suggested to be recruited from circulating monocytes, and that immune cell-derived endorphin has been implicated in the reduction of pain, we have previously examined whether RF applications influence cytotoxicity and mRNA expression for proopiomelanocortin (POMC) in a human monocytic cell line (THP-1). We have reported that continuous but not pulsed RF current for 90 s increased the mRNA expression for POMC and caused necrotic cell death (PT173, 13th World Congress on Pain, Montréal, 2010). In this report, we further examined the effects of prolonged pulsed RF on the shedding of microvesicles that are known to carry mRNA as cargos as well as on other outcome measures evaluated in our previous report.

**Results**
Continuous RF current for 90 s caused significant necrotic cell death, while pulsed RF for up to 540 s failed to provoke apoptotic as well as necrotic cell death. The mRNA level for POMC was increased by continuous RF for 90 s. Pulsed RF current for up to 180 s failed to influence the mRNA level for POMC. However, increase in the mRNA expression for POMC was observed after application of pulsed RF current for 540 s. Both RF modality failed to increase the number of microvesicle shed from parental THP-1 cells.
Conclusion
Prolonged application of pulsed RF increased the mRNA expression for POMC in THP-1 cells without provoking significant cytotoxicity. Pulsed RF did not affect the number of microvesicle that may carry mRNA to remote location. However, the level of mRNA for POMC in microvesicles remains to be clarified in the present study. Such phenomenon may explain how pulsed RF application works in pain intervention.
Title: Post-Market Registry Of Implantable Spinal Cord Neurostimulators: Patient Baseline Characteristics And 1 Year Efficacy Results (French SCS Registry)

Poster Number PW0327

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Aim of Investigation
In agreement with the French authority called Haute Autorité de Santé (HAS), a real-world, prospective, open label, registry has been conducted in France to evaluate the long term efficacy of implantable spinal cord stimulation (SCS) systems. The study population and efficacy results at one year are presented here.

Results
Of 401 patients enrolled, 271 were primo-implanted (SCS naïve patient) and 130 were enrolled at time of device replacement. Slightly more men (57%) than women (43%) were implanted. The average age was 52 years. The most common indication for SCS implant was intractable neuropathic chronic pain (98%), of which, 77% presented with chronic radicular pain. Pain was most frequently located in the lower limbs (LL) and low back combined (64%). LL alone was the second most common location (22%). The pain was mostly extended (i.e., covering several dermatomes, 70%), unilateral (26%) and bilateral (4%). For primo-implanted patients, average pain duration prior to first SCS implant was 5 years and pain was most frequently managed with drug treatments (i.e. analgesics, anti-epileptic drugs, NSAIDs, antidepressants, 99%), transcutaneous stimulation (74%), and/or rehabilitation (54%). At 1 year follow-up, average pain intensity was reduced by 51% for LL, 41% for back and 60% for upper limbs (UL) from baseline corresponding to responder rates of 62% for LL, 41% for back and 73% for UL. In addition an important decrease of treatment use is observed between baseline and 1 year. Satisfaction (evaluated over 4 criteria with a binary variable) was high for patients with 1 year follow-up (n=261): pain relief (88%), daily life activity improvement (81%), treatment satisfaction (90%) and willingness to start again the treatment (93%).

Conclusion
The French SCS Registry is the first prospective study under real-world conditions, performed on a large
scale in France in chronic pain patients implanted with SCS. Analyses of patient characteristics show SCS implants are performed according to the French Authority (HAS) recommendations (i.e. in chronic pain of neuropathic origin after failure of other more conservative therapeutic alternatives). At 1 year, a high percentage of patients are satisfied and the average predominant pain intensity was reduced for most patients. Acknowledgments French SCS Registry group Béatrice Petzold
Title: Through What Mechanism Does Demopressin Modulate Pain?

Poster Number PW0328

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Aim of Investigation
Neuropathic pain is a major public health problem due to its persistence and prevalence in the population. A number of biological studies have shown the cannabinoid system is involved in modulation of acute nociceptive stimulation and in chronic pain processes via the cannabinoid 1 receptor (CB1). Consequently, drugs which can bind to the CB1 receptor are potential therapeutics for pain modulation. Hemopressin, a haemoglobin-derived peptide, was previously identified as a putative antagonist with antinociceptive properties, and as the first peptide ligand of the CB1 receptor. Studies following on from the identification of hemopressin resulted in inconsistent and variable data regarding the mechanism of action through which hemopressin acts. Therefore we have focused on determining the direct interaction of hemopressin with its receptor, starting with the CB1 receptor.

Results
All agonists stimulated concentration-dependent CB1 responses with the presence of AM251 antagonising the agonist-induced responses. Agonists in the presence of hemopressin caused no alteration in CB1 receptor activity and there was no significant CB1 receptor inhibition (or activation) in comparison to AM251.

Conclusion
Results from our whole cell studies show that hemopressin does not directly antagonise CB1 receptor signalling, nor cause any activation or modulation of the ligand responses. Documented effects of hemopressin may possibly act through different types of receptors that couple with CB1 receptors. Further elucidation in the binding partner of hemopressin will be through microarray analysis of hemopressin on the transcriptional fingerprint of another cell line.
Title: Blocking Spinal P2X7Rs Attenuates Morphine Withdrawal

Poster Number PW0330

Authors
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Aim of Investigation
Opioids, such as morphine, are among the most powerful and widely prescribed analgesics for managing pain. However, their repeated use can lead to opioid physical dependence, which manifests as a withdrawal syndrome upon discontinuing opioid use. Opioid withdrawal is associated with a host of intensely unpleasant and aversive symptoms (such as irritability, tachycardia, muscle aches and allodynia), causing individuals to become motivated to continue using opioids as a means to avoid unpleasant episodes of withdrawal. Converging evidence suggests that opioid withdrawal is critically mediated by cellular and molecular changes in the spinal dorsal horn (SDH), which is a primary site of action for opioid analgesia. Furthermore, the adverse effects associated with opioid use have become increasingly linked to the activity of microglia, which are immune cells in the central nervous system. Here, we investigated the role spinal microglial P2X7Rs in morphine withdrawal.

Results
We found that morphine treated animals displayed a robust spectrum of withdrawal behaviours characterized by autonomic and somatic hyperactivity. An acute intrathecal injection of A-74003 into morphine dependent animals 1-hour prior to naloxone significantly attenuated the physical signs of morphine withdrawal, while continuous delivery of A-74003 into the intrathecal space for the first 72 hours of morphine treatment did not attenuate withdrawal signs. Protein analysis of spinal cord homogenates from morphine-withdrawn and control animals revealed a marked increase in spinal P2X7R protein following morphine treatment. Using flow cytometry, we identified that morphine-induced P2X7R upregulation exclusively within the spinal CD11b+ (microglial) population.

Conclusion
Here, we report a novel role for spinal P2X7R receptors in the expression of morphine withdrawal. Our findings suggest that the involvement of P2X7Rs is specific to microglia within the spinal cord, and
provide a novel mechanistic framework for the understanding of morphine withdrawal. By studying the adverse effects associated with repeated opioid use, such as withdrawal, we aim to improve opioids for the management of chronic pain.
Title: Does An Increase In Total Daily Dose Of Outpatient Ketamine Infusions Improve Outcomes In Chronic Neuropathic Pain Patients? A Pilot Study

Poster Number PW0331

Authors
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Aim of Investigation
Ketamine infusions have been shown to provide significant relief in patients with chronic neuropathic pain. At our institution, patients have demonstrated improvement in mood and ambulation after treatment with four-hour outpatient ketamine infusions at subanesthetic doses. In this study, we compared four and five-hour infusions in the same patient to determine if a longer duration of infusion or a higher daily ketamine dose improved quality of life (QOL) outcomes.

Results
Ten patients underwent four and five-hour ketamine infusions. There was no significant difference in QOL outcome measurements between the infusion sessions. The mean pain score did not show statistical significance when duration of infusion was increased.

Conclusion
Although patients infused with subanesthetic doses of ketamine over five hours reported improvement in level of pain, activity, mood, work, relationships and sleep, these results were not statistically significant. We will further evaluate the impact of dose and duration of ketamine infusions with a larger patient population.
Title: Intraoperative Lignocaine Versus Esmolol Infusion For Postoperative Analgesia In Laparoscopic Cholecystectomy: A Randomized Clinical Trial

Poster Number PW0332

Authors
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Aim of Investigation
Acute pain after laparoscopic cholecystectomy (LC) is complex and requires a multimodal analgesic approach. In recent years, systemic lignocaine as co-analgesic has gained renewed interest in abdominal surgery. Similarly, esmolol, a β1 receptor antagonist has been found to have an opioid sparing effect in the perioperative period. Therefore, the aim of this study was to compare the effectiveness of intraoperative lignocaine and esmolol infusion on postoperative pain and opioid requirements after laparoscopic cholecystectomy.

Results
Two patients in each group were excluded from the analysis. The mean morphine consumption in PACU in the lignocaine and esmolol group was 0.86 ± 0.74 mg and 0.75 ± 0.78 mg respectively (p=0.50). There was no significant difference in tramadol consumption in the ward between the two groups (esmolol group, 16.28 ± 23.71 mg versus 18.60 ± 24.5 mg in lignocaine group, p=0.65). The median pain score at various time intervals were comparable between the two groups.

Conclusion
There was no difference in postoperative opioid requirement and VAS for pain score in the first 24 h of surgery between the lignocaine and esmolol group. (This study was registered at ClinicalTrials.gov. Identifier number: NCT02327923)
Title: Assessing The Analgesic Efficacy Of The Asic Blockers, Diminazene Aceturate And Apetx2, In A Rat Model Of Inflammatory Pain

Poster Number PW0333

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Aim of Investigation
Tissue acidosis is associated with inflammation and pain such that the drop in the pH of the external cellular environment causes activation of acid sensing ion channels (ASICs), the primary acid sensors in human nociceptive neurons. Recent work by others showed that the ASIC3 inhibitor, APETx2, produced pain relief in rodent pain models. Diarylamindines such as diminazene aceturate (used as a veterinary anti-infective agent) also inhibit the activity of various ASIC subtypes (ASIC1a, 1b, 2a and 3) but their analgesic potential is unknown. Hence, the objective of this study was to assess the anti-hyperalgesic efficacy of single bolus doses of diminazene aceturate relative to that of APETx2 in a widely accepted rat model of inflammatory pain.

Results
Examination of the extent and duration of anti-hyperalgesia (ΔPPT AUC values) evoked by single i.pl. bolus doses of diminazene aceturate and APETx2 relative to morphine in individual FCA-rats, showed that the responses could be classified as responders/high responders (R/HR) or non-responders/low responders (NR/LR). Ipsilateral R/HR ΔPPT AUC values for i.pl. bolus doses of diminazene aceturate at 5.8–581.9 nmol and morphine at 700.8 nmol were significantly higher (P<0.05) than the corresponding vehicle ΔPPT AUC values. There was no significant difference (P>0.05) between the ΔPPT AUC values produced by vehicle or diminazene aceturate at 1.9 nmol. Similarly, ipsilateral R/HR ΔPPT AUC values evoked by i.pl. bolus doses of APETx2 at 0.1–11 pmol, and morphine at 700.8 nmol were significantly higher (P<0.05) than the ΔPPT AUC values produced by vehicle. There was no significant difference (P>0.05) between the ΔPPT AUC values evoked by vehicle and APETx2 at 0.033 and 3.3 pmol. For the
NR/LRs, there was no significant difference (P>0.05) between the ΔPPT AUC values evoked by single i.pl. bolus doses of vehicle and the test compounds (morphine, diminazene aceturate and APETx2).

**Conclusion**

Our data show that single i.pl. bolus doses of the ASIC blockers, diminazene aceturate and APETx2, produced potent relief of mechanical hyperalgesia in some but not all FCA-rats, a widely used rat model of peripheral inflammatory pain. There was also a trend for higher doses of these ASIC blockers to produce a pro-hyperalgesic effect, possibly via effects on peripheral immune cells, which warrants further investigation.
Title: The Role Of Vesicular Gaba Transporter (Vgat) In Hypnotic And Analgesic Actions Of General Anesthetics

Poster Number PW0334

Authors
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Aim of Investigation
GABA and glycine are principal inhibitory neurotransmitters in the central nervous system and are loaded into synaptic vesicles via the vesicular GABA transporter (VGAT). Thus, VGAT is as essential molecule in recycling of inhibitory neurotransmitters. To elucidate the significance of VGAT in pain neurotransmission, we have previously reported that heterozygous VGAT knockout (VGAT+/-) mice showed enhanced sensitivity to thermal stimulation and chemical inflammation (Mol Pharmacol 2012). However, the role of VGAT in anesthetic actions remains unknown. Therefore, we investigated the influence of down-regulation of VGAT on hypnotic and analgesic actions of general anesthetics in mice.

Results
LORR produced by sevoflurane was similar between both genotypes (ED50, 1.20% [1.16-1.23] for WT mice, n = 8; 1.17% [1.12-1.21] for VGAT+/-, n=7). LTWR produced by sevoflurane was also similar between both genotypes (ED50, 1.97% [1.94-2.00] for WT mice, n = 10; 2.03% [2.00-2.06] for VGAT+/-, n = 7). In addition, there was no significant difference in the duration of LORR produced by sevoflurane between these genotypes (ED50, 2.69% [2.65-2.74] for WT mice, n = 7; 2.68% [2.65-2.74] for VGAT+/-, n = 8). No genotype difference was found for propofol-induced LORR (ED50, 5.11 g/mg [4.43-5.76] for WT mice; 5.05 g/mg [4.24-5.81] for VGAT+/-).

Conclusion
Complete VGAT knockout leads to embryonic lethality, which prevent us analyzing the influence of complete inactivation of VGAT in anesthetic actions, showing VGAT is a key molecule in inhibitory neurotransmission. We therefore investigated how down-regulation of VGAT might affect anesthetic actions. Using mice with reduced expression of VGAT, we found that partial reduction of VGAT did not affect hypnotic and analgesic actions of general anesthetics, sevoflurane and propofol. These results
suggest that these anesthetics can enhance inhibitory neurotransmission and, as a result, produce hypnotic and analgesic actions via postsynaptic actions in spite of reduced expression of VGAT.
Title: Medical Cannabis Associated With Decreased Opiate Medication Use In Retrospective Cross-Sectional Survey Of Medical Cannabis Patients

Poster Number PW0335

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Aim of Investigation
Medical cannabis is now legal in approximately half of the states in the US and in other countries. While randomized control trials support efficacy of cannabis or synthetic cannabinoids in some conditions – such as chronic pain – fewer studies examine the effectiveness of cannabis in real-life settings. However, since cannabis is typically not prescribed and dispensed by physicians or other licensed healthcare providers, these drugs might be efficacious in highly controlled settings but not effective in settings where patients are given less guidance regarding their use. Our aim was to examine what conditions cannabis was used for, how patients viewed the success of this treatment, and whether using medical cannabis for chronic pain and other conditions changed individual patterns of medication use (including opiates).

Results
To examine whether our pilot results (n=185 chronic pain patients) held up in this larger sample, we first examined those study participants with chronic pain (n=304). Consistent with previous results, among study participants with chronic pain, medical cannabis use was associated with a 65% decrease in opioid use (n=189), 0.48 fewer medication classes used, decreased side effects of medications (-3.73 points on a scale from 1-10), and 47% improved quality of life. Among the 304 participants with chronic pain, 158 also used cannabis for anxiety, 127 for acute pain, and 98 for severe and persistent muscle spasms. 80 used medical cannabis for chronic pain alone. Thus, we stratified by co-morbidity to see how these modulated participant outcomes. Compared to study participants with chronic pain alone, those with co-morbidities had no significant differences in opiate use, quality of life changes, or medication side effects. However, participants with spasms had a significantly larger drop in number of medication classes used than those with chronic pain alone (-0.48, 95% CI [-0.9, -0.06], p=0.022), and than all those with chronic pain but without spasms (-0.63, 95% CI [-0.95, -0.31], p<0.0005).
**Conclusion**

In our study population of medical cannabis patients, these results suggest that chronic pain patients with comorbidities of anxiety, acute pain, and spasms are essentially substituting medical cannabis for opioids and other medications, and finding the benefit and side effect profile of cannabis to be greater than these other classes of medications (especially among those with spasms). This study is limited by selection bias since we only surveyed those who patronized a medical cannabis dispensary. Further, by only sampling at a single time point, we were unable to fully gauge how medical cannabis affected study participants. However, our findings suggest that people use cannabis to treat multiple conditions at once. While we hypothesized that co-morbidities may modulate cannabis’s effectiveness as medicine for chronic pain treatment, we found no evidence to support this, though this may be a limitation of our sample size. More research is needed to validate these findings.
**Title:** Pharmacokinetic Simulations Of Steady State Profiles Of Buprenorphine Following Three-Day Or Seven-Day Application Of Transdermal Patches In Japanese Subjects

**Poster Number** PW0336

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**Aim of Investigation**
Buprenorphine Transdermal System (BTDS) patches are available in varying dosages for 7-day or twice-weekly application. Following a single-dose pharmacokinetic study in healthy Japanese and Caucasian subjects (reported by Fukase et al at this meeting), a series of pharmacokinetic (PK) simulations were performed to project the likely patterns of systemic exposure to buprenorphine following regular 3-day, 3-day and 4-day, and 7-day transdermal application.

**Results**
As expected, the two extreme scenarios of every 3-day and every 7-day application of BTDS of increasing strengths were associated with very different accumulation patterns. During the more frequent 3-day administration, a much quicker accumulation of plasma concentrations over time was observed compared with 7-day administration. This highlights the opportunity to achieve high systemic exposure to buprenorphine in a relatively short period through the use of 3-day patches. Also, as anticipated, the two scenarios of 3-day followed by 4-day delivery, or 4-day followed by 3-day delivery of 40 mg BTDS were demonstrated to provide higher plasma concentrations than the corresponding 7-day application of 40 mg BTDS. These outcomes reflect the greater efficiency of transdermal delivery of buprenorphine during the first few days of wear, compared with days 5, 6 and 7.

**Conclusion**
Three-day application of BTDS, or 3-day followed by 4-day application of BTDS resulted in higher plasma concentrations of buprenorphine compared with a 7-day dosing regimen. Patients requiring higher doses and higher systemic exposure to buprenorphine may benefit from a more frequent dosing regimen than is possible with the current 7-day patch. This study was funded by Mundipharma K.K.
Aim of Investigation
We implemented exercise therapy for outpatients with chronic pain who are resistant to conventional treatment collaborated with the Center for Pain Management, Osaka University. This longitudinal study evaluates the long-term effects of exercise therapy for nine months on outpatients with chronic debilitating pain.

Results
The results of post-hoc paired t-tests showed improvements in the PDAS, HADS-D, PCS, and EQ-5D after completing the exercise program (P<0.05). The PDAS, PCS, and EQ-5D remained significantly improved until the end of the study period (nine months of follow-up) compared with pre-intervention levels in 10 patients (paired t-test, P<0.05).

Conclusion
Exercise therapy for 60 min/week for three months conferred significant and positive short- and long-term benefits upon outpatients with chronic pain and significantly improved the PDAS, PCS, and EQ-5D for nine months thereafter.
Title: The Effect Of Mindfulness-Based Stress Reduction On Wound Healing

Poster Number PW0338

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Aim of Investigation
Research has demonstrated that wound healing can be affected by psychological factors. This study aimed to examine the effect of Mindfulness-Based Stress Reduction (MBSR) on the speed of wound healing. Further, the local production of pro-inflammatory cytokines and growth factors was studied as a potential underlying mechanism.

Results
A significant increase in mindfulness was found in the MBSR group. MBSR led to accelerated wound healing in terms of a greater decrease in wound size at day 3 after blister induction in men and between day 7 and 10 in women. A greater decrease in TEWL reflecting faster wound healing was observed in men only at day 3 and 4 post wound induction. In addition, MBSR decreased levels of IL-1β, IL-8, and PIGF in the wound fluid 22 hours after wound induction.

Conclusion
The current outcomes provide preliminary evidence for the accelerating effects of MBSR on early stages of wound healing primarily in men. Additionally, the decrease in IL-1β, IL-8, and PIGF levels 22 hours after wounding in the MBSR group suggests that changes in pro-inflammatory cytokine and growth factor production may underlie the effects of MBSR. The current outcomes suggest that MBSR may be of clinical relevance for the speed of wound healing.
Date: 09/28/2016 03:15:00 PM

Title: Evaluation Of Community General Practitioner And Physiotherapy Pain Self-Management

Poster Number PW0339

Authors
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Aim of Investigation
This pilot study examined how effective General Practitioners (GP) and/or Physiotherapists (PT) were in managing individuals with chronic pain using pain self-management strategies. The results were intended to allow us to determine effect sizes for developing a larger RCT on the topic.

Results
Data collection is almost complete, and the results to date indicate small overall effect sizes, but marked variance between cases. However, satisfaction ratings by both patients and providers were positive. The final data will be collected by April 2016.

Conclusion
The results to date indicate that individual health care providers, whether family doctors or physical therapists, can successfully implement a pain-self-management intervention for patients with a range of chronic pain conditions. The effect sizes are generally small, but the satisfaction ratings for both providers and patients are encouraging. Nevertheless, we have encountered a number of barriers to the study which should inform further studies involving individual health care providers in their attempts to teach pain self-management skills to their chronic pain patients. The barriers encountered include: perceived lack of appropriate patients, time restraints, limited literacy of patients, and clinician perception that asking patients to fill in outcome measures will somehow discourage their returning for treatment. We have addressed these barriers with changes to the method of data collection and preparation of providers. We also plan to explore the clinician's and patients’ perceptions regarding use of outcome measures with semi-structured interviews once all the data are collected. The next step in our program is to implement a study comparing instruction in pain self-management with usual care by physiotherapists and general medical practitioners in primary care settings.
Date: 09/28/2016 09:30:00 AM

**Title:** Brain Training To Improve Cognitive Functioning For Patients With Chronic Pain

**Poster Number** PW0340

**Authors**
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**Aim of Investigation**
Chronic pain is known to affect cognitive abilities, including attention and concentration, speed of information processing, and executive functions such as working memory, mental set-shifting and regulation of emotions. However, there is little research on remediation of such skills in chronic pain populations. Our study aimed to assess how subjective cognitive concerns reported by patients with chronic pain map onto objective neurocognitive test performance, and to pilot a computerised cognitive training protocol to determine whether such cognitive difficulties can be remediated with repeated practice of the impaired skill.

**Results**
Baseline data replicated our previous findings in which patients reported particular difficulty with working memory, the ability to mentally manipulate information. We additionally showed that greater self-reported working memory problems were consistently associated with poorer performance across all formal tests of attention and executive function ($r = 0.5$ to $0.72$, $p < .05$), independent of age, education and estimated IQ. Poorer performances on tests of attention and executive function at baseline were associated with higher pain intensity and interference, anxiety and catastrophising. Preliminary post-intervention data in both the training and control groups showed improvements in self-reported cognitive functioning, and mild improvements on formal neurocognitive tests. Patients subjectively found the training intervention to be mentally stimulating, particularly for those not currently working; beneficial in terms of providing a distraction from the pain; and that it increased their awareness of, and confidence in, their cognitive abilities.
Conclusion

We report that patients' self-reported cognitive concerns reflect objectively measured deficits. Our results suggest that it is possible to improve cognitive functioning in these patients, and computerised cognitive training may be one viable method of achieving this. Further research should examine predictors of program success, including features of the training program itself as well as personal characteristics of patients who are most likely to benefit from such programs. Disclosures: The authors have no personal financial interest in any commercial brain-training company.
Date: 09/28/2016 03:15:00 PM

**Title:** The Effect Of Hand Dominance On Implicit Motor Imagery Performance – A Systematic Review And Meta-Analysis

**Poster Number** PW0341

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**Aim of Investigation**
A growing body of evidence suggests that people in pain have impaired implicit motor imagery performance for bodily images. When shown pictures of the painful body part, they are less accurate or slower at identifying whether the picture is of left or right orientation. Recent work has identified that there may be a spatial component to this impairment: people with pain on the left side of the body are significantly less accurate at recognising images of left body parts than images of right body parts, regardless of whether the image is of the painful body part. It is unclear whether this spatial effect may also be a function of handedness and resultant cerebral dominance. This has relevant implications for chronic pain treatment paradigms such as Graded Motor Imagery. Thus, this systematic review and meta-analysis aims to synthesize available data for the effect of handedness on left/right hand recognition.

**Results**
Of 4,480 citations, 7 studies (9 datasets) were included, evaluating 237 left-handed and 1229 right-handed subjects; of these, 5 datasets could be pooled. We were unable to contact one author for required data and one used a judgement task that was too disparate to allow pooling. Risk of bias was high due to small sample sizes, lack of blinding and poor reporting of recruitment sources. For overall RT (five datasets), pooled results found that right-handers were 117.96ms (95% CI: 8.75, 227.18) faster than left-handers at recognising the laterality of hands (p = 0.03). Right-handed individuals were also significantly faster at recognising images of right hands compared with left-handed individuals (MD: 92.45ms, 95% CI: 8.06, 176.83, p = 0.03). For images of left hands there was no significant difference between left- and right-handed groups (MD: 105.45ms, 95% CI: -23.19, 234.10, p = 0.11). For overall
error rate (2 datasets), right-handed individuals were more accurate (MD 1.42%, 95% CI: 0.11, 2.73, p = 0.03) at recognising hand laterality.

**Conclusion**
We found limited evidence that right-handed individuals are faster and more accurate than left-handed individuals. That right-handers were faster for images of right hands, but left-handers were not faster for images of left hands, may reflect that left-handers had less hand dominance (i.e., ambidextrous). Future research recruiting larger samples of naïve left- and right-handed individuals is required.
Title: Restoring Movement Representation Through Neurorehabilitation With A Virtual Reality System Alleviate Phantom Limb Pain

Poster Number PW0342

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Aim of Investigation
Restoring voluntary movement representation of a phantom limb possibly alleviates phantom limb pain (PLP). We quantitatively measured movement representations of a phantom upper limb using a bimanual circle-line coordination task (BCT) with the intact hand. We investigated whether neurorehabilitation with a virtual reality system restores voluntary movement representations as measured by BCT and alleviates PLP.

Results
VR neurorehabilitation restored voluntary movement representations in the BCT and alleviated PLP (p<0.05). A reduction in PLP intensity and phantom-limb movement representations were linearly linked (p<0.05).

Conclusion
Restoring the movement representation of a phantom limb with the VR neurorehabilitation system was directly linked to improvement of PLP.
Title: Effects Of Low-Intensity Muscle Contraction And Sensory Input During The Early Stages Of Arthritis On Joint Swelling And Pain

Authors
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Aim of Investigation
This study examined the effects of low-intensity muscle contraction and sensory input by neuromuscular electrical stimulation during early stages of arthritis on swelling and pain.

Results
There were no significant differences in joint swelling among the AR, IM, MC, and SE groups. In the MC and SE groups, the PPT recovered by 3 weeks after injection. By contrast, the PPT in the AR and IM group remained significantly low until 4 weeks after injection, compared to that of the Sham group. The PWR in the MC group showed significant recovery from 2 weeks after injection compared to that of the AR, IM, and SE groups; a significantly increase in the PWR in these groups was noted until 4 weeks after the injection, compared to the Sham group. The number of CD68-positive cells per sq.mm in the AR, IM, MC, and SE was increased significantly compared to that in the Sham group; in the MC group; however, a significant decrease was noted compared to the AR, IM, and SE groups.

Conclusion
The results in the MC group indicated that low-intensity muscle contraction during the early stages of arthritis reduced inflammation histologically, which may alleviate peripheral and central sensitization. Thus, early improvement of secondary hyperalgesia was observed in the MC group. By contrast, relieving the effect of sensory input without muscle contraction on inflammation was inadequate compared to that of low-intensity muscle contraction. Therefore, secondary hyperalgesia in the SE group was sustained.
Title: The Mindful Brain In Pain: The Impact Of Disability, Mindfulness, Emotion Regulation And Action Control On Depression

Poster Number PW0344

Authors
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Aim of Investigation
It is well-known that mindfulness-based interventions involve non-judgemental attention to present-moment experience and promote increased tolerance of negative affective states such as pain or depression. Furthermore, a disposition towards state orientation is associated with higher vulnerability to emotional disturbances. However, the precise neurocognitive and affective/motivational mechanisms underlying mindful mood regulation are poorly understood. The aim of the present study was to investigate pain-related disability, mindfulness, emotion-regulation and action control in a student sample with subclinical levels of pain and depression. We tested the predictive role of pain intensity, disability, mindfulness, action control and emotion-regulation for depressed symptomatology.

Results
Depressive symptomatology was positively correlated with disability and suppression. The FFMQ-subscale acting with awareness and the action control scales were negatively correlated with depression. The final regression model, including action control, mindfulness and disability predicted a total of 40.1% of the variance of depression. In line with other research, mindfulness, pain-related disability and state orientation were significant predictors of depression.

Conclusion
The current results give an indication that trait-mindfulness and action orientation might be protective dispositions against the development of clinical depression in the context of pain-related disability and persistent pain. Our approach could help to typify patients on the basis of psychological parameters
included here. This could facilitate a more accurate future assignment of patients to individualized therapies based on their profile and maximize the chances of therapeutic success.
Title: Effects Of (Dis)Confirmed Pain Expectations On Pain Perception

Poster Number PW0345

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Aim of Investigation
In everyday life and in clinical settings people often have expectations about future pain outcomes. Such pain-specific expectations have a well-documented influence on the subjective experience of pain and responses to pain, and are generally considered a major predictor of pain treatment outcomes. Pain-specific expectations do not however occur in a social vacuum. Moreover, information provided by others about anticipated pain outcomes is often in conflict or disagreement with one's own expectations. Yet the possible impact of incongruence between one’s own pain expectations and information communicated by others has not yet been systematically investigated. Such incongruence may create a situation high in cognitive conflict. The proposed study provides a first experimental attempt to explore the impact of confirmation and disconfirmation of pain-specific expectations by communication messages on pain perception.

Results
Our preliminary results, based on a total sample of 101 participants, demonstrated that pain ratings depended on the interactive effect of type of feedback and expectation (dis)confirmation, $F(1, 97) = 6.98, p = .01, \eta^2_p = .07$. Unsurprisingly, participants who were confirmed in their high pain expectations reported the highest pain ratings. Interestingly, positive feedback counteracted high pain expectations, resulting in lower pain ratings. On the other hand, giving disconfirming feedback to participants expecting low pain only shifted their pain experience a little upwards, though non-significantly so.

Conclusion
These first findings underline the importance of taking into account expectations and their (dis)confirmation in pain communication. Further analyses will determine the effect of subjective certainty of expectations, perceived cognitive conflict (aversiveness), and personality traits on the findings in this healthy group of volunteers. Our findings call for further research to understand better...
the relationship between pain-specific expectations and responses to pain within a social communication context, and to ultimately improve communication in pain treatment programs.
Title: Influence Of The Appearance Of The Therapeutic Equipment On The Placebo Effect Of The Transcutaneous Electrical Nerve Stimulation Using An Ischemic Pain Model In Healthy Participants. A Randomized Placebo-Controlled Experimental Study

Poster Number PW0346

Authors
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Aim of Investigation
Current conceptualization for the placebo phenomenon includes the psychosocial context surrounding the patient. For example, recent evidence has confirmed the positive effect of the interaction patient-clinician and patients' expectations on the placebo analgesia. However, other aspects of the therapeutic encounter, such as the appearance of the therapeutic equipment and its impact on the placebo effect in experimental pain has not been fully explored. Therefore, the objective of this study was to evaluate the effect of the appearance of the therapeutic equipment in the placebo effect of the transcutaneous electrical nerve stimulation using an experimentally-induced ischemic pain.

Results
The test of multivariate analysis of variance (MANOVA) with repeated measures showed significant differences among groups (p=0.007). Pain tolerance was statistically different (p = 0.003). Compared to control group, pain tolerance was delayed 22 % and 20.5% for the portable placebo TENS and cabinet placebo TENS respectively. Pain threshold did not show differences among groups (p=0.76). Changes in pain intensity (PI-NRS) were significant different between the control group and portable placebo TENS group (p = 0.05). No other comparisons for PI-NRS were significant. Effect size (ES) calculated for PI-NRS changes between control and portable placebo TENS group was large (d= 1.09). Moderate ES were calculated for the differences between control and cabinet placebo TENS (d= 0.52), and between portable placebo TENS and cabinet placebo TENS group (d= 0.57).

Conclusion
The results of this study show that pain is a context dependent variable being influenced by the appearance of the therapeutic equipment and therapists’ positive verbal suggestions. These factors should be considered when implementing interventions in physical therapy for a better response to
treatments. An enhanced placebo effect was obtained during the portable placebo TENS intervention for the participants of this study. Therefore, it is possible that in young people experiencing clinical pain, its application may be associated with a better treatment responsiveness. However, these results need to be confirmed in a clinical setting.
Aim of Investigation
Response expectancies, i.e., the anticipation of an involuntary response like pain, are considered to be the core mechanism of placebo effects, and are as such important predictors of analgesic treatment outcomes. These response expectancies are commonly considered to be formed by instructions (verbal suggestion), prior experiences (conditioning), and observation of others (social learning). Possibly also mental imagery, or simulation, of a response can induce comparable expectancy effects on pain, given previously demonstrated effects on expectations, pain, and brain activation. However, this has not yet been studied systematically. In two experimental studies, we assessed whether response imagery of pain reduction can induce expectations of pain relief and thereby reduce actual pain.

Results
Results of both studies showed that participants experienced significantly less pain after response imagery than after control imagery or no intervention (\( \eta_p = .05 \) and \( \eta_p = .19 \), respectively). These effects of imagery on pain were significantly mediated by pain expectancies. Moreover, results of Study 2 showed that adding a verbal suggestion further reduced pain marginally significantly (\( \eta_p = .04 \)). These effects of the additional verbal suggestion on pain were also mediated by pain expectancies.

Conclusion
In line with research on placebo effects, the current results indicate that response imagery, like verbal suggestion, conditioning, and social learning, can induce expectations of pain reduction and thereby reduce actually experienced pain. These results extend both previous research on placebo effects and previous research on mental imagery. Our findings emphasize the importance of expectations in the experience of pain and suggest the possibility of modulating these expectations by a brief imagery intervention.
Title: The Effect On Return-To-Work Of Boosted Follow-Up After Occupational Rehabilitation. A Randomized Controlled Study.

Poster Number PW0348

Authors
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Aim of Investigation
Musculoskeletal disease is worldwide a leading cause of both temporary and permanent work disability. Pain is the cardinal symptom. The costs for the individual and society are high, and government efforts to curb pain related sick leave are extensive. Research has shown that programs that integrate medical and occupational rehabilitation have a better outcome on return to work than more one-dimensional programs. The effect of many multidisciplinary occupational rehabilitation programs have unfortunately been modest and at high cost. In practice, programs are often dismissed as too costly compared to the size of the effect. The main objective of this study is to investigate if a low cost regime of boosted follow up, prescribed directly after administering a multidisciplinary, occupational rehabilitation program, effects return-to-work after 1 year.

Results
There were 213 participants; 80% females. Mean age was 42 years. Main causes for registered sick leave were psychiatric disorders (38%) and musculoskeletal disorders (30%). Regardless of cause of sick leave, 76% of participants reported chronic pain (> 6 months) of at least moderate intensity. There was major overlap in symptoms, and 41% of participants experienced a combination of substantial pain, fatigue and mental distress. 56% of participants had been out of work for more than 1 year or never been in paid work at all. The 6 month intervention on average consisted of 5.1 individual contacts and 0.8
collaborative contacts per participant. Average time spent per telephone contact, including preparation and administrative work, was estimated to be 70 minutes per contact. The RTW coordinator roughly spent one day of extra work per participant over the course of the 6 month intervention. Initially the control group returned to work at a quicker pace, but by 6 months they were surpassed by the intervention group. At 12 months the intervention group worked on average 1 day more per 4-week period, compared with the control group. The odds for the intervention group being in work ≥1 day per week increased by 151% during the 12 month period (Odds ratio (OR) 2.51, 95% confidence interval (CI) 1.67 - 3.77). The equivalent odds increase for the control group was 29% (OR 1.29, 95% CI 0.87 - 1.91). The odds of being in work ≥1 day per week 12 months after the rehabilitation program was 95% higher for the intervention group (OR 1.95, 95% CI 1.11 - 3.42) compared with the control group.

Conclusion
Participants receiving a low cost regime of boosted follow-up had a higher chance of being in paid work ≥1 day per week after one year, when compared with the control group. The cost of the intervention was low compared to the gain in terms of increased work participation one year after completing occupational rehabilitation.
Title: Analysis Of Follow-Up Data In Outpatient Pain Management Program For Refractory Chronic Pain

Poster Number PW0349

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Aim of Investigation
We have carried out the outpatient pain management program which has been established in Western countries for the patients with refractory chronic pain, combined lectures with exercise based on the cognitive-behavioral therapy. In the previous study, we reported that the measurements in relation to pain and physical function showed significant improvements after a 9-week intervention at the meeting IASP 2014. On the other hand, it is difficult to keep running such pain management program profitably under Japan's health insurance system and hence we could not know the long-term outcomes of the patients after this program. In this study, we investigated the effect of our pain management program for the patients with refractory chronic pain at 6 months after a program.

Results
VAS, PDAS, HADS Anxiety and Depression, PCS, EQ-5D, PSEQ, GLFS-25, seated forward bends, time of 10-meter zig-zag walk, standing and sitting ability speed test, self-care ability test and 6-minute walking distance showed significant improvements (p<0.002) with medium-level efficacy or higher (r≥0.3) at the end of the program. Moreover we found significant improvements of the above parameters were also observed at 6 months after the program (p<0.002), although there were a few participants who deteriorated.

Conclusion
In spite of just a 9-week intervention, we confirmed that the efficacies of our pain management program were kept for at least 6 months after a program. However we must consider periodic follow-up programs if the patients repeatedly deteriorate after an intervention.
Aim of Investigation
In our daily life, we generate actions based on the sensory information from the external world. The interaction of sensory and motor systems is essential to healthy survival in humans. Growing evidence suggests that this interaction is subserved by the motor-related neural network, including the basal ganglia, cerebellum, premotor area, and supplementary motor area (SMA). Moreover, these motor-relative regions are frequently activated during painful stimulation, and preliminary evidence further suggests a benefit of pain reduction after rhythmic music entrainment. Given that discrimination of pain is critical to healthy survival, it is important to understand mechanisms related to the discrimination of non-painful stimulation and the influence of the motor system before exploring those underlying pain discrimination. However, interplays between these neural substrates underpinning sensorimotor interaction remain elusive. The current research recruit healthy adults to investigate the neural basis related to the discrimination of vibrotactile stimulation and the influence of motor system.

Results
The difficulty ratings between TD and SD were not significantly different. Compare with SD, TD was associated with increased activity in the cerebellum and SMA. After RAS training, 2 of the 3 subjects displayed a reduction in TD threshold, while the TD threshold for the rest one subject remained unchanged. Compared with pre-RAS data, post-RAS brain activity showed an increase in the cerebellum and SMA.
Conclusion
These results suggest different neural substrates for TD and SD, and motor training benefits TD. We will increase subject number to improve the statistical power of the study. Findings obtained from the study provide as the basis to understand the decision process for pain and the potential benefits of entraining rehabilitation course in chronic pain conditions in the future.
Title: Does Group Composition Matter In Cbt For Chronic Pain?

Poster Number PW0351

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Aim of Investigation
Cognitive Behavioural Therapy (CBT) programmes for chronic pain are delivered in groups for efficiencies of cost, time and resources. Whether the composition of a group (size, gender mix, age range) is associated with outcomes for individuals in that group is not known. The aim of this study was to determine whether the size of the group, the age of its members and the mix of age and gender were related to outcomes for individuals.

Results
Group size was associated with improved outcomes for pain intensity (p <0.05) and self-reported disability (p <0.01) with large groups faring better. The variance explained by group size was low, however, ranging from 1.9% to 5.0%, depending on the outcome assessed. The median age of group members was associated with improved outcomes of the 6 minute walk test (p <0.01) - individuals in groups where the median age was between 42 and 50 years performed better than those in other groups. The mix (ie homogeneity/heterogeneity) of members' age or gender of the group did not have an effect on outcomes.

Conclusion
These results provide preliminary evidence that group composition influences individual pain and disability outcomes of a group CBT program. We propose that groups of 9–16 members are more effective than smaller groups and that having a median age in the 40s is ideal, but that the mix of age and gender are not important.
**Title:** The Relationship Between Changes In Sense Of Injustice And Treatment Outcome In Patients With Chronic Pain Participating In A Cognitive-Behavioral Pain Management Program.

**Poster Number** PW0352

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**Aim of Investigation**
Sense of injustice relates to perceived unfairness or undeserved outcomes. The main aim of this investigation was to examine the relationship between changes in the construct of sense of injustice and treatment outcome of patients with chronic pain participating in a 3-week multidisciplinary cognitive-behavioral pain management program. The overarching aim of this investigation was to provide a better understanding of the mechanisms that underlie treatment success and provide further support for a cognitive-behavioral model of chronic pain.

**Results**
The main finding of this investigation was that changes in the process variable of sense of injustice from pre-to post-treatment significantly mediated changes in the outcome variables of disability and distress from post-treatment to 1-month follow-up.

**Conclusion**
This finding demonstrates that cognitive factors, in this case sense of injustice, are important mediators of treatment outcomes in patients completing a cognitive-behavioral pain management program. This finding increases support for a cognitive-behavioral model of chronic pain and emphasizes the importance of using interventions to reduce sense of injustice in chronic pain patients.
Aim of Investigation
The behavioral therapy is an alternative treatment of temporomandibular disorders (TMD) and has been frequently used since studies showed the relationship between psychological factors and chronic pain. Systematic reviews recently confirmed scientifically the evidences of behavioral therapy efficiency on the management of orofacial pain. The aim of this study is to verify the results of psychoeducation as a behavioral therapy in patients from 'Occlusion, TMD, and Orofacial Pain Center' in the School of Dentistry at University of Sao Paulo (CODD).

Results
The GL quality score from 85% of the patients was good or great; they considered the most important guidance was to not keep teeth in touch when awake and maintain a mandibular rest position. Considering pain, there was a reduction of at least 20% of pain for 54% of the patients.

Conclusion
The guidance lecture as a psychoeducational behavioral therapy is effective and a relevant supporting treatment to TMD and Orofacial pain patients in treatment at CODD.
Title: Effectiveness Of Low Level Laser Therapy In Post-Stroke Shoulder Pain

Poster Number PW0354

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Aim of Investigation
This hospital based Quasi- experimental study was carried out to study effectiveness of Low Level Laser Therapy (LLLT) in management of post-stroke shoulder pain and improvement of arm function in hemiplegic patients, in Yangon General Hospital, Myanmar, from August 2014 to September 2015. The objectives were to assess the improvement in shoulder pain, range of motion and muscle power of affected shoulder, and improvement of shoulder function in patients with post stroke shoulder pain after giving LLLT for 4 weeks.

Results
Out of 54 patients, 55.6% were male and 44.4 % were female. Mean age was 61.2 year (+10.318) and 60-69 years is the most commonly affected age group. 79.6% was ischemic stroke and 20.4% was affected by hemorrhagic stroke. Mean VAS improved from 4.11 at the base line to 1.31 at follow up week 6. Mean values of VAS from the pre-treatment to end of 2nd week treatment, from the pre-treatment to the end of the treatment week 4 and from the pre-treatment to the end of the follow up week 6, were significantly and statistically different respectively (p< 0.001, paired t test ). Range of motion of the shoulder (abduction, flexion, extension, internal and external rotation) and muscle power of the affected arm before and after the treatment have been analyzed and significant improvements were found (p< 0.001). Mean values of DASH score from pre-treatment to end of 2nd week, 4th week of treatment and follow up (2 weeks after end of treatment) were also statistically improved (p< 0.001).

Conclusion
Pain intensity of the hemiplegic shoulder was significantly reduced in this study. Reduction in intensity of pain had positive influence on the possibility to achieve wider range of mobility and improvement in arm function. The results of the study showed Low Level Laser Therapy can be used as one of the effective treatment options for the patients with post-stroke shoulder pain.
Title: Increasing Self-Efficacy And Reducing Fear-Avoidance Of Movement Beliefs In Chronic Low Back Pain Patients Through Proame

Poster Number PW0355

Authors
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Aim of Investigation
Misconceptions and dysfunctional beliefs influence on disability in chronic low back pain patients and strategies for change them are desirable. The aim of this investigation was to analyze the effects of an educational and exposure to movement’s Program (PROAME) in modifying Self-efficacy and Fear-avoidance beliefs and disability in chronic low back pain patients.

Results
Patients in Groups A and B improved self-efficacy and decreased fear of pain and avoidance of movement and catastrophic thoughts (p<0.001). The Group C patients were stable in all these variables.

Conclusion
The educational part of the PROAME was able to improve dysfunctional beliefs and disability independently of the exposure to movement. It is fundamental to emphasize the educational sessions were carefully designed to change patient’s dysfunctional beliefs, through group and individual sessions, and written educational material was given to the patients. However, only those exposed to the movement’s sessions changed the pain intensity and the low back pain diagnostics tests. These results will be present in other opportunity.
Title: In Vivo Investigation Of The Role Of Acid-Sensing Ion Channel 1 In Pain Using Mambalgin Peptide Inhibitors

Poster Number PW0356

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Aim of Investigation
We are taking advantage of mambalgin peptide toxins derived from snake venom, which specifically block different subtypes of ASIC1-containing channels, to evaluate the role of these channels in pain perception in inflammatory and neuropathic pain models.

Results
Intravenous injection of mambalgin-1 evoked an anti-hyperalgesic effect in carrageenan-induced inflammatory pain by decreasing the von Frey score in response to noxious mechanical stimuli and by increasing the paw withdrawal latency in response to noxious heat. This effect required peripheral ASIC1b-containing channels and also involved to some extent ASIC1a channels, as shown by combining the use of ASIC1b-knockdown and ASIC1a-knockout animals. Intravenous injection of mambalgin-1 in the model of neuropathic pain transiently reversed mechanical hyperalgesia as well as heat hyperalgesia that are both present two weeks after surgical ligature of the sciatic nerve. The effect was still present in mice pretreated with naloxone and in ASIC1a-knockout animals, supporting an opioid- and ASIC1a-independent mechanism of action. Intrathecal injection of mambalgin-1 also evoked a strong analgesia similar to the one induced by morphine, but the effect was ASIC1a-dependent (it was completely lost in ASIC1a-knockout mice) and partially naloxone-sensitive.

Conclusion
These data further support the role of peripheral and central ASIC1-containing channels in pain. Peripheral ASIC1b-containing channels contribute to inflammatory and probably neuropathic pain, and central ASIC1a-containing channels contribute to neuropathic pain, in addition to the previously described effect in inflammatory pain. The effect of mambalgin-1 also unveils a differential participation
of ASIC1a-containing channels expressed in the central nervous system in different pain conditions, i.e., acute and inflammatory pain vs neuropathic pain, which may reflect pathophysiological changes in the expression of ASIC channel subtypes in particular neurons of the spinal cord and/or the brain. Finally, this work strengthens the therapeutic potential of mambalgin peptides that are active in a broader range of experimental pain models (inflammatory and neuropathic), and through i.v. systemic delivery, in addition to the previously described analgesic effects through s.c. and i.t. injections.
Title: Can Drug Exposure In The Mouse The Formalin Paw Test Be Used To Predict The Dose Of Novel Pain Treatments? Compounds With Efficacy In The Treatment Of Neuropathic Pain Inhibit Nociceptive Behaviors In The Mouse Formalin Paw Test At Concentrations Required

Poster Number PW0357

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Aim of Investigation
To determine the effects of compounds, which efficacy in patients with neuropathic pain, in the mouse formalin paw test (FPT). Furthermore, determine if the concentration required for efficacy in the mouse FPT was similar to the exposure used to achieve clinical efficacy.

Results
All of the compounds displayed dose-dependent inhibition of formalin-induced nociceptive behaviors in phase 2 (20-35min post formalin injection) of the assay. The calculated EC50 values and associated 95% confidence intervals were 24.7 (19.3-30), 0.15 (0.08-0.2), 0.28 (0.02-0.5), 27.43 (8.3-46.6) and 21.3 (10.6-32) µM for CNV1014802, duloxetine, EMA401, gabapentin and pregabalin, respectively. From the available data we determined the unboundCss, average for gabapentin, pregabalin, CNV1014802 & EMA401 was 20.2-33.3, 19.8-65.3, 0.1-0.2, 0.003 µM. For duloxetine, the unbound Css,min was determined to be 0.005 µM.

Conclusion
We demonstrated that the calculated EC50 (µM) value for the phase 2 of the formalin correlated well with the concentrations used to achieve clinical efficacy. It should be noted that no correction for species differences in potency against the target was made, as these data were not available.
Aim of Investigation
The ability to accurately assess acute pain in mice is critical for both the success of translational pain models and for providing optimal welfare to the most widely utilized species in research. Ethograms and grimace scores can be subjective and influenced by the presence of an observer. Nest quality and time to nest incorporation are subjective or binary, making it challenging to discern between gradations of pain alleviation. There is an urgent need for a rapid, objective, titratable, cageside pain assessment for use in mice. Glo Germ (GG) is a non-toxic inert material that glows under black light. Normal grooming transfers GG from the top of the head to the paws, face, body, nest and cage environment. Additionally, mice readily gather nesting material; therefore we developed a method to quantify nest consolidation anywhere in the home cage. Here we describe two novel cageside methods to quickly and objectively identify unalleviated post-operative pain in mice.

Results
Nest Consolidation Test: At baseline, mice consolidated an average of 3.8 nestlet pieces by 1 hour, this score remained consistent through 24 hours. After anesthesia, regardless of whether buprenorphine was provided, an average of 2.3 pieces were consolidated in the first hour, 3 pieces by 5 hours, and 4 pieces by 24 hours. After surgery no pieces were consolidated through 5 hours and an average of 1.2 pieces were consolidated by 24 hours. Mice provided a dose of buprenorphine before surgery consolidated an average of 2 pieces by 5 hours, but no additional pieces by 24 hours. Glo Germ Transfer Test: At baseline mice transferred GG to all parts of their body, nests and cage environment within 1 hour. By 24 hours, either no or trace GG was remaining. In the first hour after anesthesia, particularly in those that received buprenorphine, mice were delayed in transferring GG to their face, flank and cage environment. However at 5 and 24 hours, all GG scores were equivalent to time-matched baseline scores. Approximately half of post-surgical mice transferred GG to nestlet material (but no body
locations) by 5 hours, including all buprenorphine treated mice. By 24 hours, all post-surgical mice had transferred GG to nestlet pieces and 75% had transfer to their paws, as well.

**Conclusion**
While anesthesia and buprenorphine delayed return to normal grooming and nesting behavior for approximately an hour, surgery produced a 23+ hour delay, demonstrating pain specific changes. A single dose of buprenorphine partially rescued these behaviors in the first 5 hours after surgery. However, by 24 hours these mice did not differ from saline controls, indicating additional analgesia was needed. This pilot study provided proof of concept that the Nest Consolidation Test and Glo Germ Transfer Test are effective cageside methods for assessing unalleviated post-laparotomy pain.
Title: Age-Dependent Variations In Response To Cutaneous Inflammation

Poster Number PW0359

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Aim of Investigation
Intraplantar injection of complete Freund's adjuvant (CFA) in adult rats induces a local inflammatory response and accompanying decrease in thermal and mechanical nociceptive thresholds. However it has previously been shown that responses to inflammmogens are different at both a cellular and behavioural level in the postnatal period. The aim of this study was to characterise these differences and begin to elucidate their functional impact.

Results
Intraplantar injection of CFA at postnatal day 1 (P1) does not cause a significant decrease in PWT vs saline, despite the presence of significant inflammation for up to 7 days (2-way ANOVA with Bonferroni post-hoc test; n = 15; P > 0.05). Examination of skin samples show that 24hrs after CFA administration in adults there are significantly higher numbers of macrophages that only express the mannose receptor compared to those expressing only ED1 (P<0.0001) or those that express both ED1 and mannose (P<0.0001). In the neonate cells which express both ED1 and mannose significantly outnumber those that express just ED1 (P<0.0001) or mannose (P<0.0001). Comparisons between ages show that total numbers of infiltrating monocytes are significantly (P<0.001) higher in neonates compared to adults, that there are greater numbers of ED1 positive and ED1 and mannose co-expressing cells in the skin of neonates than adults (P<0.05 and P<0.0001 respectively) but significantly fewer (P<0.0001) mannose only cells in the younger age-group. No differences in neutrophil numbers were seen.

Conclusion
Intraplantar injection of CFA at P1 does not induce a decrease in mechanical withdrawal threshold despite the presence of significant inflammation in contrast to adult rats. This is the result of altered infiltration of monocytes into the site of inflammation. These findings suggest that inflammatory
nociception and inflammation itself are significantly different in early life and that this has a significant functional effect. How adult like immune responses mature and why inflammation promotes one phenotype of macrophage over another in early life requires further investigation.
**Title:** Mechanical Pressure Stimulation Of The Hindlimb Muscles Induces Sympathetically-Regulated Heart Rate Responses In Anesthetized Rats

**Poster Number** PW0360

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**Aim of Investigation**
Stimulation of mechanoreceptors in skeletal muscles by contraction and stretch elicits autonomic regulation and cardiovascular responses. There are also pressure-sensitive mechanoreceptors in skeletal muscles and some studies reported that mechanical pressure stimulation applied to the hindlimb induces cardiovascular responses. However, the details of the neural mechanisms for the pressure-induced cardiovascular responses are not elucidated. The present study was aimed to examine the contribution of cardiac autonomic nerves to heart rate (HR) responses to mechanical pressure stimulation of the hindlimb muscles.

**Results**
The mechanical pressure stimulation of the hindlimb increased HR (40% of trials; ranged from +3.6 to +9.5 bpm), decreased (55% of trials; ranged from -4.7 to -55.6 bpm) or did not change (5% of trials). The HR responses were negatively correlated with pre-stimulus level of HR ($r=-0.65$, $p=0.001$). Compared with these HR responses obtained in the autonomic nerve intact condition, HR responses to muscle stimulation were significantly smaller in the sympathetic nerve blocked condition ($p<0.0001$), but not significantly different in the vagal nerve blocked condition ($p=0.17$). In the subsequent experiment with recordings of cardiac sympathetic efferent nerve activity, we found that the frequency of sympathetic nerve activity increased or decreased in response to the pressure stimulation and HR changed concurrently. These changes of sympathetic nerve activity and HR were positively correlated ($r=0.88$, $p<0.0001$). Further, the sympathetic nerve activity changes were negatively correlated with its tonus level before the stimulation ($r=-0.52$, $p=0.031$).

**Conclusion**
The present study results suggest that cardiac sympathetic efferent nerve activity regulates HR...
responses to mechanical pressure stimulation of the hindlimb muscles and the direction of HR responses is determined by tonus level of the cardiac sympathetic nerve.
Title: Signaling Events Underlying The Analgesic Effect Of Propofol In An Inflammatory Pain Model

Post Number PW0361

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Aim of Investigation
Propofol (2, 6-diisopropylphenol), an intravenous anaesthetic, has been showed to alleviate post-operative pain clinically. Spinal N-methyl-D-aspartic acid (NMDA, GluN) receptors that are subtypes of excitatory glutamate receptors contributing to central sensitisation in pain state may be involved in propofol-induced analgesia. SH-SY5Y is a subline of neuroblastoma which has been widely used to investigate the function of neuron such as activation of GluN receptors. Extracellular regulated protein kinases 1/2 (Erk1/2), P38 mitogen-activated protein kinases (P38), c-Jun N-terminal kinases (JNK) are three important members in Mitogen-activated protein kinases (MAPKs) family activated by GluN receptors, which play important roles in the induction and maintenance of pain hypersensitivity. This study aims to explore whether NMDA receptors and its downstream signalling pathway are involved in propofol-induced analgesia.

Results
Either 30 min or 2h after intravenous infusion of 0.6 or 1 mg/kg/min of propofol for 1h reduced nociceptive responses caused by injection of formalin from 20-40 min (P<0.01). Both doses of propofol reduced phosphorylated NR2B in the ipsilateral (p<0.01) dorsal horn and had no effect on contralateral side (P>0.01). Expression of phosphorylated Erk1/2, rather than P38 and JNK, decreased in the ipsilateral dorsal horn in both higher and lower dose of propofol pre-treated groups (P<0.01). Pre-treatment of 3 μM or 10 μM propofol for 1 hour before the stimulation of NMDA and Glycine in SH-SY5Y cells reduced the influx of calcium into cells (P<0.01).

Conclusion
As low as 0.6 mg/kg/min of propofol appears to offer analgesic effect on formalin-induced inflammatory pain and this effect was found to last for at least 2h. The underlying analgesic mechanisms of propofol
could be attributed to the inhibition of GluN2B activation in spinal dorsal horn. Erk1/2 was also found to be involved in the downstream signaling pathway of GluN2B receptor in formalin pain model.
Title: Evaluation Of The Antinociceptive Activity Of The Root, Bark And Leaf Extracts Of Croton Megalocarpus

Poster Number PW0362

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Aim of Investigation
Medicinal plants, which form the backbone of traditional medicine, have in the last few decades been the subject of very intense pharmacological studies. This has been brought about by the acknowledgement of the value of medicinal plants as potential sources of new compounds of therapeutic value and as sources of lead compounds in drug development. Almost one fourth of pharmaceutical drugs are derived from botanicals. Besides, there also exists a very large market of minimally processed medicinal plant parts especially in Europe and America, which are usually dispensed as over-the-counter medication. In developing countries, it is estimated that about 80% of the population rely on traditional medicine for their primary health care according to WHO. The use of plant parts for therapeutic purposes has been widely practiced in Africa. Croton megalocarpus is a tree of the euphorbiaceous family found widely distributed in East Africa. The tree is found growing in cleared parts of natural forests, forest margins or as a canopy tree. It is native in Burundi, Democratic Republic of Congo, Kenya, Malawi, Mozambique, Rwanda, Tanzania and Uganda. In northern Kenya the bark is used as medicine for fever and the roots for treatment of malaria, fever, chest pains, pneumonia and abdominal pains. Croton megalocarpus organic extracts have very mild antibacterial activity. Both the aqueous and organic extracts of the roots and leaves were found to have high inhibitory activity on cyclooxygenase activity. A phytochemical analysis of the extracts of Croton megalocarpus showed the presence of alkaloids, glycosides, terpenoids, flavonoids, flavones reducing sugars and saponins in the extracts. However, animal studies have not been done to evaluate this claimed antinociceptive activity. The aim of this study was to investigate the antinociceptive activity of Croton megalocarpus using the formalin test in mice.

Results
In early phase of formalin test, one of the positive controls, morphine exhibited very significant antinociceptive effects (p < 0.001) compared to the negative control. Aspirin exhibited significant
antinociceptive effects (p < 0.05) compared to the vehicle. The 50mg/kg dose extract did not exhibit significant antinociceptive effect compared to the vehicle. However, the extract 100 mg / kg and 200 mg/ kg doses exhibited significant antinociceptive effects compared to the vehicle. In late phase of the formalin test, the positive controls of Morphine and Aspirin exhibited highly significant antinociceptive (p < 0.001) effects compared to the negative control (vehicle). The 50 mg / kg dose of the extract exhibited significant (p < 0.05) compared to the vehicle with the 100 mg / kg and 200 mg / kg doses exhibiting highly significant (p < 0.01) antinociceptive effects compared to the vehicle.

**Conclusion**
The formalin test, which represents a model of prolonged pain, is very useful in studies of pain mechanism and in the evaluation of analgesic drugs. The early phase, classified as neurogenic pain, is an acute response observed immediately after the administration of formalin as a result of direct action of injected formalin on nociceptors. The late phase, classified as inflammatory pain, is a tonic response resulting from the inflammatory processes generated by the release of inflammatory mediators such as histamine, serotonin, prostaglandins, bradykinin and activation of the dorsal horns of the spinal cord. Centrally acting drugs (e.g., opioids) inhibit both phases while peripherally acting drugs (e.g., NSAIDs) inhibit only the late phase. Aspirin has been found to inhibit both phases of pain in mice. Conclusion: Results from this study suggest that the extract exhibits both phasic and tonic antinociceptive effects in the Swiss albino mice compared to the negative controls.
Title: Modulation Of Nociception By Social Bonds In Monogamous Animal, Prairie Voles.

Poster Number PW0363

Authors
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Aim of Investigation
Social stressors cause several harmful consequences including effects on behavior, emotion, autonomic functions, and central nervous system processes. Conversely, the presence of social bonds positively impacts general health and buffers against environmental stressors. Nociception is also modulated by social environmental factors and stressful events, and 'stress-induced hyperalgesia' are actually common clinical symptoms in chronic pain disorders. However, the mechanisms underlying the social environment-nociception link have not been well elucidated. Prairie voles (Microtus ochrogaster) are socially monogamous rodents and have served as a good animal model for investigating the neurobiological mechanism for social bonding. The present study used prairie voles to test whether social bonds altered anxiety-like and pain-related behaviors. Specifically, we compared anxiety-like behavior in open field test and pain-related behavior in plantar test and in formalin test between paired and partner-loss male voles.

Results
In bonds (+) group, paired males showed significantly decreased anxiety-like behaviors in the open field test and high threshold of thermal stimulus in the plantar test compared to partner-loss males, and a positive correlation was found between open field test and planter test data. Furthermore, partner-loss males in bonds (+) showed significantly elevated pain behaviors in the formalin test as compared to paired ones. Interestingly, no such differences in anxiety-like and pain-related behaviors were observed in bonds (-) group.

Conclusion
The present results suggest that social bonds modulate nociception as well as emotion, depending on
relationship characteristics of social bonds. Thus, the prairie vole provides a useful model for understanding how the social environment contributes to changes in pain behavior and nociceptive processing in humans.
Title: Modulation Of Nociception By Social Bonds In Monogamous Prairie Voles: Fos Expression In The Spinal Cord And The Brain “Pain Matrix” Under Conditions Of Inflammatory Pain.

Poster Number PW0364

Authors
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Aim of Investigation
Pain sensitivity is significantly modulated by a variety of psychosocial factors. For instance, viewing pictures of the romantic partner reduced pain rating relative to viewing pictures of strangers. Although, there has been recently growing interest in questions concerning the influence of social factors on the experience of pain and associated pain behavior, the neural mechanisms are still not well understood. We established the socially monogamous rodent, prairie vole, as an animal model with which to examine neurobiological mechanisms underlying social modulation of pain. In our model, significant differences between paired and partner-loss males were found in thermal threshold and pain-related behavior as well as in anxiety-like behavior depending on pair bond formation. Using this model, we explored the neural mechanisms underlying social modulation of pain processing by comparison of expression of Fos protein in the spinal cord and the brain pain matrix under conditions of inflammatory pain.

Results
Partner-loss males showed increased of Fos immunoreactivity in the spinal dorsal horn and decreased in the medial prefrontal cortex and nucleus accumbens as compared to paired ones, while no significant differences were found in the anterior cingulate cortex and the insula cortex.

Conclusion
The nucleus accumbens and medial prefrontal cortex, which are component of the mesolimbic dopamine reward system and are known to be important for pair bond formation, also play a key role in
pain modulation. Several lines of evidence suggest that exposure to chronic stress attenuate analgesic action of mesolimbic dopamine system, and conversely, a feeling safety by partner presence activate the action. Consistent with these findings, the present study suggests that mesolimbic dopamine system is involved in neural processes underlying the pain modulation by social bonds in prairie voles. To further explore the neural pathway for social pain modulation, we are proceeding to analyze Fos expression in other components of pain matrix and will report the results on the day.
Date: 09/28/2016 03:15:00 PM

Title: A New Preclinical Pain Model Of Oral Ulcer By Orthodontic Wire Appliance

Poster Number PW0365

Authors
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Aim of Investigation
Orthodontic appliances frequently cause oral mucosal lesions, resulting severe pain induction. However, little study has reported about the mechanisms underlying oral ulceration and subsequent pain induction in the orthodontic appliances. In the present study, we developed a new preclinical rat model for oral ulcer pain following an orthodontic wire appliance and evaluated ulceration in the oral mucosa and pain-related behaviors.

Results
The severe oral ulceration was induced in the model rats on day 1. The wire-induced oral ulcer was cured completely until day 5 after the procedure. In control group, there was no mucosal lesion. Compared with control group, spontaneous pain was induced in the model on day 1. The mechanical allodynia was induced on days 1-3. Antibacterial pretreatment did not affect the inductions of spontaneous pain and mechanical allodynia. Indomethacin pretreatment largely suppressed the spontaneous pain, but not the mechanical allodynia.

Conclusion
These results suggest that spontaneous pain is mainly mediated by injury-associated COX-dependent inflammation and mechanical allodynia is independent on infectious inflammation in the model. The new pre-clinical animal model for orthodontic wire-induced oral ulcer pain can be utilized in evaluations of new drug treatments for oral ulcer pain in dental practices.
Title: A New Rat Model To Study Neuropathic Pain’s Influence On Cancer Development

Poster Number PW0366

Authors
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Aim of Investigation
Pain is a common syndrome and has a substantial impact on health and quality of life. Cancer pain incidence in all stages of cancer patients is rather high, and a large proportion of these patients are suffering moderate-to-severe pain. However, the relationship and potential mechanism between pain and cancer is still unclear. Appropriate animal models which can probe into the influence of pain to cancer development are lacked. This study is aimed to create a novel animal model which provides a new approach to reveal the relationship between pain and tumor.

Results
When giving 10^7 cells per rat subcutaneously, the trial group rats' success rate of tumor bearing was much higher than the sham group and control group(11/11, 6/10, 5/9, sham VS trial p<0.05; control VS trial p<0.05); While giving 10^8 cells per rat subcutaneously, the trial group rats' weight loss much more than control group, as well as the sham group (on day 6, p<0.05; day 8, p<0.01; day 10, p<0.05. After 11 days' observation, rats bearing with tumor experienced subcutaneous tumor resection. Tumors from the trial group weighed much more heavier than the control group, also the sham group (p<0.001 and p<0.05, respectively), and the volumes of the tumors in the trial group presented much larger comparing with other groups (p<0.01 and p<0.05, respectively).

Conclusion
Pain may be a potential impetus to cancer incidence and development, as our data indicated that rats with neuropathic pain (chronic constriction injury of the sciatic nerve, CCI) had an increased risk of cancer development. What's worse, according to the rats' weight loss statistics, under the influence of pain, the life quality of rats might become lower and the prognosis was much worse.
Title: Back-Translation Of Experimental Pain Models And Analysis Of Correlation Between Experimental Pain With Pathological Pain In Rat

Poster Number PW0367

Authors

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Aim of Investigation
In the field of pain research, experimental pain models have been growing in importance, which may be valuable tools to bridge the translational gap between preclinical research and clinical trials. Among them, ultraviolet B (UVB)-induced pain model and intradermal capsaicin-induced pain model are well characterized in human. Recently, the correlation between drug efficacy in human experimental and clinical pain settings have been analyzed to the selection of suitable pain models which can correctly predict drug efficacy in particular clinical settings, but there are few reports about correlation between experimental and pathological pain in animals. In the present study, we back-translated both UVB and capsaicin model into rats and examined the effects of morphine and standard analgesics employed in the clinical management of neuropathic (pregabalin) and inflammatory (ibuprofen) pain to compare with those in pathological pain models.

Results
Both UVB-irradiation to the hind paw and intraplantar injection of capsaicin produced significant dose-dependent reductions in mechanical paw withdrawal thresholds as reported in human. Slight erythema, mild edema, increase in blood flow and up-regulation of inflammatory factors were also observed in the UVB-irradiated site in rats. In capsaicin-treated rats, flare-related changes such as blood flow and skin temperature were observed and peaked in 30 minutes after injection. Ibuprofen and morphine significantly reduced mechanical hypersensitivity but pregabalin were less effective in the UVB-irradiated rats. On the other hands, pregabalin and morphine showed efficacy on capsaicin-induced mechanical hypersensitivity but ibuprofen did not. We compared efficacy of these analgesics between experimental pain (UVB and capsaicin model) and pathological pain (pSNL, STZ, CEC, MIA, CFA model). Whereas the responses to analgesics in UVB model was relatively similar to MIA and CFA model, those in capsaicin model was similar to pSNL, and STZ model.
Conclusion
In the present study, we back-translated UVB and capsaicin models into rats and characterized the mechanical hypersensitivity pharmacologically. Rat UVB model and capsaicin model showed similar pathophysiological and pharmacological properties to these in the corresponding human pain models, suggesting that these models may be good translational models to bridge the gap between animal studies and clinical observations. We also tested the effects of analgesics in pathological pain models and comprehensively analyzed the correlation between the efficacy in rat experimental and pathological pain. Future studies using other analgesics in both experimental and pathological pain models may contribute to mechanism-based classification of pain and thereby to a better understanding of the underlying symptoms as well as clinical studies.
Title: Immobilization-Induced Muscle Pain Is Associated With The Upregulation Of Nerve Growth Factor And Increased Peripheral Nerve Density In Rat Skeletal Muscle

Poster Number PW0368

Authors
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Aim of Investigation
Recently, studies have reported that cast immobilization of joints induces mechanical hyperalgesia associated with the upregulation of nerve growth factor (NGF) in the skin. However, it is unclear whether immobilization-induced pain also occurs in other organs, and if so, mechanisms associated with this pain are not yet known. Therefore, the purpose of this study was to clarify whether immobilization-induced hyperalgesia occurs in the muscle, and to investigate whether there is a relationship between mechanical hyperalgesia and upregulation of NGF. For this, 2 experiments were performed using an experimental animal model. This study was approved by the Ethics Review Committee for Animal Experimentation of Nagasaki University (approval no. 1305201061).

Results
Experiment 1: The withdrawal threshold of IM group rats was significantly decreased 2 weeks after immobilization, and this decrease was maintained until the end of testing at 4 weeks post-immobilization. Furthermore, NGF expression and C fiber density were significantly increased in the IM group compared to those in the CON group at 2 and 4 weeks post-immobilization. Experiment 2: Pre-injection, withdrawal thresholds of the gastrocnemius muscle in the K252a and vehicle groups were significantly lower than those of the CON group. The withdrawal threshold was significantly elevated in the K252a group 10 minutes post-injection, and this change was maintained until 60 minutes after injection. However, withdrawal thresholds in the K252a group did not reach the level of those in the CON group.

Conclusion
It was confirmed that immobilization-induced hyperalgesia occurs in the skeletal muscle. The increase in the withdrawal threshold of the gastrocnemius muscle following NGF receptor inhibitor injection
showed that upregulated NGF expression may be associated with the mechanism by which this hyperalgesia is induced. However, it is possible that other factors may have contributed to immobilization-induced hyperalgesia because mechanical pain sensitivity did not return to control levels by NGF receptor inhibitor injection. The increase in C fiber density found in immobilized rats may be one of the other factors involved.
**Title:** Effect Of Implanted Adipose Tissue-Derived Mesenchymal Stem Cells Obtained From Infrapatellar Fat Pad (If-Ascs) On Cartilage Damage And Pain Associated With Osteochondral Defect In A Rat Model

**Poster Number** PW0369

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**Aim of Investigation**
The present study aimed to investigate the potential of using implanted scaffold free cartilage construct of adipose tissue-derived mesenchymal stem cells (ASCs) obtained from infrapatellar fat pad (IF-ASCs) to restore the hyaline cartilage regeneration as well as to provide pain relief in a rat model of osteochondral defect.

**Results**
During the first two weeks, there was a significant difference in pain associated with osteochondral defect observed between the control defect group and sham-operated group. This pain can spontaneously resolve within three weeks post-induction as indicated by a complete reversal of the percentage of weight bearing distribution back to baseline. In addition, no significant improvement in pain was observed in animals that implanted with IF-ASCs at any time point. However, immunohistochemistry results revealed a positive staining for type II collagen and aggrecan in the implanted site, suggesting the hyaline cartilage regeneration.

**Conclusion**
Our results demonstrated that pain associated with osteochondral defect can be resolved regardless of implantation of IF-ASCs. Despite of this, implantation of IF-ASCs for four weeks could restore the hyaline cartilage regeneration in a rat model of osteochondral defect.
Title: Possible Contribution Of The C-Type Lectin Receptor, Mincle, To Induction Of Neuropathic Pain After Peripheral Nerve Injury In Mice

Poster Number PW0370

Authors

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Aim of Investigation
Recent investigations have revealed that numerous immune-related molecules are involved in neuropathic pain after peripheral nerve injury (PNI). While a lot of cytokines and chemokines have been reported to contribute to neuropathic pain, little is known about pattern recognition receptors (PRRs) which play an important role to sense pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs). The ability of PRRs to be activated by DAMPs is particularly interesting because cells express PRRs could be activated in injured tissue and then could trigger reactions that lead to neuropathic pain. Toll-like receptors (TLRs) are known as a well-studied family of PRRs and have a significant role in innate immunity. Interestingly, the latest studies revealed that TLRs also contribute to neuropathic pain condition. While evidence about roles of TLRs in neuropathic pain is accumulating, another type of PRRs consists C-type lectin receptors (CLRs) has not yet been investigated. One of the CLRs, Mincle (macrophage inducible C-type lectin) is known to recognize DAMPs and to induce inflammatory responses. We hypothesized that Mincle would have an important role in induction of neuropathic pain after PNI. In this study, we analyzed pain behavior of Mincle knockout (KO) mice which were subjected to neuropathic pain model to test our hypothesis.

Results
First we asked whether Mincle KO mice would show any change in mechanical threshold after PNI. After PNI treatment, we found that mechanical threshold was reduced in WT mice but not in Mincle KO mice obtained from an ipsilateral hind paw of each mouse. Although Mincle KO mice did not show tactile allodynia, we observed massive proliferation of microglia in the spinal dorsal horn of both WT mice and in Mincle KO mice and could not detect significant difference in number of microglia between them. Next, we asked when and where Mincle mRNA was expressed. We found rapid and remarkable
induction of Mincle mRNA in injured spinal nerves. Moderate expression of Mincle mRNA was also observed in DRGs although we could not detect any induction in the spinal dorsal horn. We observed infiltrating cells in injured spinal nerve and populations of these cells were identified as neutrophils by Flow cytometry and Mincle KO mice did not differ from WT mice in neutrophil infiltration.

**Conclusion**
Our observation that PNI treatment failed to induce mechanical allodynia in Mincle KO mice suggest that Mincle is essential for development of tactile allodynia after PNI. Since Mincle mRNA expression was largely restricted in injured spinal nerves, and since a lot of infiltrating neutrophils which were known as a population possessing Mincle expression were found in the same area, molecule(s) released from neutrophils such as cytokines and/or chemokines might be important to induce ensuing events leading to neuropathic pain. Increase in number of microglia in the dorsal horn of Mincle KO mouse suggest that molecule(s) induced by Mincle activation after PNI possibly contribute to phenotypic change but not to proliferation of microglia.
Constitutive Control Of Pain Sensitivity In Physiological And Pathological Condition By Interleukin-27 In Mice

Poster Number PW0371

Authors
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Aim of Investigation
Interleukin (IL)-27 is a member of the IL-12 cytokine family and has been shown to have an immunosuppressive and anti-inflammatory role. The immunosuppressive effect of IL-27 is thought to depend on inhibition of the development of Th 17 cells (a newly identified inflammatory T-helper population) and on induction of IL-10 production. On the other hand, one of recent developments in pain research is the finding that cytokines, including IL-1β, IL-6, TNFα, IL-17 and IL-10, have an important role in pain regulation. For example, IL-17 induces pain behavior, while IL-10 has an anti-nociceptive effect. Because of its potent ability to negatively regulate IL-17 (which is pro-nociceptive) and to promote the production of IL-10 (anti-nociceptive), we hypothesized that IL-27 could have a major impact in the control of pain and tested pain behavior of mice which carry a null mutation in IL-27 or IL-27 receptor gene(s). IL-27 is a heterodimeric cytokine consisting of IL-27p28 and Epstein-Barr virus induced gene 3 (EBI3), while the IL-27 receptor consists of a specific receptor WSX-1, together with gp130, which can also be coupled with other cytokine receptors, such as the IL-6 receptor.

Results
These mice appeared healthy and had no obvious abnormality by visual inspection. We also observed that WSX-1/-, EBI3/- and p28/- mice were indistinguishable from wild type mice in the open-field test, indicating that null mutation of these genes would not affect locomotor activity or anxiety level. Interestingly, we found that they exhibited enhanced responses in most assessments of pain behavior tested, including the hotplate, von Frey and formalin tests. Furthermore intraperitoneal injection of rIL-27 normalized the altered phenotypes in pain behavior in EBI3/- and p28/- but not WSX-1/- mice. Although these mutant mice showed much lower mechanical threshold than that of wild type mice
without any treatment, we observed further reduction in threshold when these mice were subjected to chronic inflammatory and neuropathic pain models.

**Conclusion**

Results of rIL-27 administration suggested 1) that the action of rIL-27 depended on the specific receptor, WSX-1, 2) that enhanced pain behavior observed in mutant mice was not a result of developmental abnormality, and 3) that IL-27 might contribute to regulate physiological sensitivity of pain sensation even in normal condition without inflammation. The effects of IL-27 restoration were observed from one hour after injection. This time course would not be long enough to induce T cell differentiation. Furthermore, molecular size of rIL-27 would be too large to penetrate the blood brain barrier. Thus, IL-27 might act on peripheral tissues directly. Finally, the fact that further hypersensitivity was induced by treatment of chronic pain models in these mutant mice suggest that mechanisms underlying hypersensitivity observed in these mutant mice without any treatment did not share those of known chronic pain models. This novel mechanism to control pain sensitivity might shed new light on certain types of pain disorders.
Title: Effects Of Suvorexant On Secondary Sleep Disturbance Induced By Chronic Neuropathic Pain

Poster Number PW0372

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Aim of Investigation
It is said that chronic neuropathic pain leads to sleep disturbance, which has a negative impact on treatments for pain. Since chronic pain and sleeping are so relevant that their improvements are considered to be important. It is reported that secondary sleep disturbance induced by chronic pain could associate with the hyperactivity of brain stem reticular system. Suvorexant, a dual orexin receptor antagonist, inhibits the projections of orexin neurons from hypothalamus to brain stem, and controls the activity of brain stem inhibitory. Because of this pharmacological action, suvorexant could make the sleep condition much better than traditional sleeping agents. In this study, we analyzed the sleep conditions at neuropathic pain like state, and evaluated the effects of suvorexant on the secondary sleep disturbance induced by chronic neuropathic pain.

Results
In the PSNL mice, wakefulness time was significantly longer, and non-REM and REM sleep times were significantly shorter than sham-operated mice. We also examined the effect of suvorexant on sleep conditions of mice under chronic neuropathic pain like state. In the PSNL mice treated with suvorexant, wakefulness time was shortened 53.4% (p <0.01) as compared with the PSNL group. This effect was accompanied by increase of both REM and non-REM sleep times (+108.0%, p <0.01 and +39.7%, p <0.05). However, episode duration of wakefulness was found no difference among the three groups of sham, PSNL and PSNL-suvorexant at both light and dark phases.

Conclusion
Suvorexant recovered the reduced amount of sleep under chronic neuropathic pain like state. However, suvorexant didn't interfere the ability to sustain wakefulness. Our results suggest that suvorexant can improve secondary sleep disturbance induced by chronic neuropathic pain and work as an analgesic medicine simultaneously in near future.
Title: Axonal Transport Disruption Along Intact Axons Causes Neuropathic Pain Behaviours And Signs Of Central Sensitisation In The Absence Of Ongoing A- And C- Fibre Activity

Poster Number PW0374

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Aim of Investigation
In many patients, signs of neuropathic pain can occur in the absence of overt nerve injury. Studies suggest that peripheral nerves may be inflamed in these patients and that symptoms are generated from otherwise uninjured axons (1). We have previously shown that nerve inflammation (neuritis) disrupts axonal transport, and have hypothesised that transported ion channels accumulate at the site of disruption, which causes a 'hot spot' of excitability (2). Consistent with the current understanding of neuropathic pain, aberrant firing from this site may drive spinal mechanisms that lead to painful symptoms. The role of axonal transport disruption in these mechanisms can be examined by applying low doses of the antimitotic agent vinblastine to the rat sciatic nerve, which disrupts axonal transport in the absence of inflammation or axonal degeneration. In this model, animals develop mechanical allodynia and C-fibre axons become mechanically sensitive (2,3). The aim of this study is to assess the extent of pain behaviours associated with vinblastine-induced axonal transport disruption. It will also determine the levels of ongoing activity from A- and C-fibre axons and whether there are signs of central sensitisation. Comparisons are made to the neuritis model.

Results
Both neuritis and vinblastine induced the development of mechanical allodynia that peaked on 4-5 days, with signs of recovery on day 8. Cold allodynia also peaked at days 4-5 following vinblastine treatment but was not observed in neuritis animals. In contrast, heat hyperalgesia was observed in neuritis animals but not following vinblastine treatment. There were no signs of mechanical hyperalgesia. Burrowing behaviour was decreased on days 4-5 in both groups compared to shams. In neuritis animals, 25% of C-fibre neurons developed ongoing activity 4-5 days post-surgery. In contrast, levels of C-fibre ongoing activity following vinblastine treatment were low (<10%) and comparable to untreated animals (p=0.29). A-fibre ongoing activity was also low in all groups (<10%). C-fos expression was increased by > 90% in ipsilateral dorsal horn neurons in vinblastine and neuritis groups following A-fibre sciatic nerve
stimulation (3v, 50 ms, 5 Hz for 5 min) compared to untreated animals. Following C-fibre stimulation (30v, 500 ms, 5 Hz for 5 min), c-fos expression was increased ipsilaterally in the dorsal horn of neuritis animals only.

**Conclusion**
Vinblastine-induced axonal transport disruption leads to signs of neuropathic pain. Differences in the pattern of behavioural changes compared to neuritis may be in part due to the absence of inflammation. The lack of significant ongoing activity following vinblastine treatment contrasts from neuritis as well as our current understanding of neuropathic pain mechanisms. However, the upregulation of c-fos in this model suggests that axonal transport disruption may induce spinal changes via an alternative mechanism. In summary, ongoing activity from the periphery may not be critical for the development of neuropathic pain. These findings may also be important in understanding pain associated with chemotherapy induced neuropathy.

2. Dilley et al 2013, J Pain 14:1437-1449
Title: Assessment Of Effects Of Swimming In The Treatment Of A Neuropathic Pain Model And Your Implications In Peripheral Functionality.

Poster Number PW0375

Authors
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Aim of Investigation
Neuropathic pain is a type of pain sensation that occurs in one or more parts of the body, it is associate with diseases which affect the central nervous system. Nonpharmacological treatment modalities increasingly are being investigated in animal models of chronic pain, like a swimming. Therefore we tested the effects of swimming in the model of neuropathic pain, it can cause in the rates of mechanical nociception and peripheral functionality.

Results
After surgery, decreased paw withdrawal threshold in SNI and Shan groups. These groups showed a significant increase in paw withdrawal threshold after the completion of swimming everyday, showing an analgesic effect induced by exercise. However there was no significant improvement in functional tibial index after physical exercise. The blood lactate had significant difference comparing before and after swimming.

Conclusion
In summary, swimming was effective in reducing the hyperalgesia in a model of neuropathic pain. In the gait analysis, animals not showed significant positive response after swimming.
Title: High Fat Diet Exacerbates Pain-Like Behaviors And Periarticular Bone Loss In Mice With Cfa-Induced Knee Arthritis

Poster Number PW0376

Authors

Aim of Investigation
To determine whether high fat diet (HFD) exacerbates pain-related behaviors, functional disability, knee joint edema, and periarticular bone loss, in a mouse model of CFA-induced unilateral knee joint arthritis

Results
HFD-fed mice injected with CFA showed greater spontaneous pain-like behaviors of the affected extremity as well as a decrease in the weight-bearing index compared to SD-fed mice injected with CFA. Knee edema was not significantly different between diets. HFD significantly exacerbated arthritis-induced bone loss at the distal femoral metaphysis but had no effect on femoral diaphyseal cortical bone.

Conclusion
HFD exacerbates pain-like behaviors and significantly increases the magnitude of periarticular trabecular bone loss in a murine model of unilateral arthritis.
**Title:** Aldehyde Dehydrogenase-2 Mutation (E487K) Contributes To Chronic-Pain Sensation In Mice

**Poster Number** PW0377

**Authors**
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**Aim of Investigation**
Aldehyde-dehydrogenase 2 (ALDH2) is a mitochondrial enzyme which metabolizes reactive aldehydes. Aldehydes accumulation has been related to increased pain. Our group showed that activation of ALDH2, using a small molecule called Alda-1, displays antinoceptive effect in inflammatory pain models. However, the role of ALDH2 in neuropathic pain control is unknown. We aimed to examine how ALDH2 may modulate the neuropathic pain in wild type, WT, and genetically modified mice having the common inactivating ALDH2 mutation present in Asians, ALDH2*1/*2, and also, to determine whether Alda-1 could reduce pain.

**Results**
CCI decreased the pain threshold in WT mice when compared to baseline, which was exacerbated in ALDH2*1/*2 (1.53±0.1g vs 0.68±0.06g vs 0.27±0.06g, respectively), at day 7. No differences were detected in WT vs ALDH2*1/*2 pain thresholds, at day 14. Alda-1 (10 mg/Kg) increased the pain threshold compared to vehicle-treated WT mice at 1h, 0.59±0.07g vs 1.52±0.07g, at day 7 and 0.66±0.07g vs 1.49±0.03g, at day 14 day. CCI induces an increase in 4-HNE levels in spinal cord and sciatic nerve (4 and 2 fold, respectively). Alda-1 significantly decreased these adducts levels.

**Conclusion**
In summary, Alda-1 induced analgesia by decreasing the aldehydic load. Here, we propose a novel mitochondrial target for neuropathic pain control. Therefore, Alda-1 may be a novel therapeutic drug class to reduce neuropathic pain.
Title: Discovery Of Novel T-Type Calcium Channel Blockers (Nip-301 And Nip-302): Involvement Of State-And Use-Dependent Blockade In Analgesic Effects

Poster Number PW0378

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Aim of Investigation
T-type calcium channel (TCC) blockers in dorsal root ganglia (DRG) regulate the action potential firing properties of sensory neurons that result in pain signals. In chronic pathological conditions, high-frequency firing can lead to the accumulation of inactivated TCCs. It has been previously reported that state-dependent TCC blockers (TCCBs) have analgesic effects in rodent models of pain. These compounds have also been reported to exhibit a use-dependent profile, in that they inhibit inactivated TCCs during high-frequency firing. We hypothesized that we could achieve a greater therapeutic effect on neuropathic pain through the application of not only use-dependent TCC inhibition, but also state-dependent TCC inhibition. We focused on the use-dependent blockade of TCC to counter neuropathic pain. Our lead compound for studying state-dependency, P11520031, was not appropriate for evaluating the use-dependent blockade of TCC. We discovered NIP-301 and NIP-302 through optimization of this lead. In the present study, we investigated 1) state-dependency, 2) use-dependency, and 3) the analgesic effects of TCCBs in rodent models of inflammatory and neuropathic pain.

Results
At 30% channel inactivation (holding potential: HP = −75 mV), the IC50 value for NIP-301 (central transitional type) was 81 nM. NIP-301 did not affect the closed state (HP= −110 mV). The IC50 values toward hCav3.2, mCav3.2 and rCav3.2 were almost the same. On the other hand, in the use-dependent blockade of hCav3.2, the IC50 value for NIP-301 was 780 nM. NIP-301 decreased the duration of paw-
licking in phase II (10-35 min) in both the mouse and rat formalin models. In the mouse models of neuropathic pain (CCI and PSNL), the anti-allodynic effects of NIP-301 were equivalent to those of pregabalin at 10 mg/kg. Moreover, in Rota-rod tests, NIP-301 did not cause significant effects at doses up to 3 times higher than the effective dose in models of neuropathic pain. NIP-301 showed limited efficacy in rat models of neuropathic pain, although the plasma concentration was thought be high enough to observe an analgesic effect. The results with NIP-302 were not different from those with NIP-301, except with respect to central transitional pharmacokinetics.

**Conclusion**

We discovered novel TCCBs, NIP-301 and NIP-302, which produce both the state- and use-dependent blockade of Cav3.2, where the use-dependent blockades were about 10-fold weaker than the state-dependent blockades. Both compounds showed analgesic effects toward inflammatory pain and mouse neuropathic pain. However, our hypothesis can not easily explain the results regarding rat neuropathic pain. We plan to investigate TCCs under pathological conditions to better understand this inconsistency between the state- and use-dependency of TCC blockade and the analgesic effects on neuropathic pain.
Title: Anxiolytic Effects Of The Novel A2δ Ligand Mirogabalin (Ds-5565) In Sluka Model, An Experimental Animal Model Of Fibromyalgia

Poster Number PW0379

Authors
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Aim of Investigation
Mirogabalin (DS-5565) is a novel ligand of the α2δ subunit of voltage-gated calcium channels. Mirogabalin possesses unique binding characteristics to α2δ subunits, and potent and long-lasting analgesic effects in fibromyalgia models and neuropathic pain models. Phase III clinical trials of mirogabalin in patients with fibromyalgia, diabetic peripheral neuropathic pain and postherpetic neuralgia are ongoing. Fibromyalgia is often associated with anxiety and depressive symptoms. In the present study, we investigated the anxiolytic effects of mirogabalin in intramuscular acidic saline injection model (Sluka model) in rats, an experimental animal model for fibromyalgia.

Results
Sluka model rats showed mechanical hyperalgesia demonstrated by decreased pain thresholds to von Frey filaments. In the open filed test, Sluka model rats significantly preferred the wall-area to the central-area compared with normal rats. In the elevated plus maze test, Sluka model rats exhibited significant decreases in the number of entries and time spent in the open-arm, and significant increases in time spent in the closed-arm. Taken together, Sluka model rats showed anxiety-related behaviors. A single oral administration of mirogabalin (3 and 10 mg/kg) significantly alleviated and normalized above anxiety-related behaviors in both tests.

Conclusion
Sluka model rats showed anxiety-related behaviors in open field test and elevated plus maze test. Mirogabalin alleviated the anxiety-related behaviors in Sluka model rats. Mirogabalin may provide effective anxiety relief for patients with fibromyalgia, as well as pain relief.
Title: Analgesic Effects Of The Novel A2Δ Ligand Mirogabalin (Ds-5565) In Spinal Cord Injury Model Rats

Poster Number PW0380

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Aim of Investigation
Mirogabalin (DS-5565) is a novel ligand of the α2δ subunit of voltage-gated calcium channels. Mirogabalin possesses unique binding characteristics to α2δ subunits, and potent and long-lasting analgesic effects in fibromyalgia models and neuropathic pain models. Phase III clinical trials of mirogabalin in patients with fibromyalgia, diabetic peripheral neuropathic pain and postherpetic neuralgia are ongoing. In the present study, we investigated the analgesic effects of mirogabalin in spinal cord injury (SCI) model rats, an experimental animal model for central neuropathic pain.

Results
In SCI model rats, mechanical allodynia was demonstrated by decreased 50% paw withdrawal thresholds. A single oral administration of mirogabalin (2.5, 5 and 10 mg/kg) significantly increased the 50% paw withdrawal thresholds. The effects of mirogabalin were still significant at 6 or 8 hours after administration, and the AUC0-8h and AUC0-24h were significantly higher than those of the control group.

Conclusion
Mirogabalin showed potent and long-lasting analgesic effects in SCI rats. The effective doses were similar to those in peripheral neuropathic pain models and fibromyalgia models. Mirogabalin may provide effective pain relief for patients with central neuropathic pain.
Title: Attenuation Of Learned, Persistent Pain By Preferred Olfactory Or Taste Stimulus In Mice

Poster Number PW0381

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Aim of Investigation
Aim of investigation: In animals and humans, neuropathic pain from damage to neuronal components results in a successive state of pain. Under these conditions, the organism learns stress and aversive pain by continuous reinforcement because of pain distress. In previous studies, we demonstrated that enduring pain involves a conditioned nociceptive response (CR), learned pain. These results are compatible with the universally accepted definition of learning: 'Learning is an enduring change in the mechanisms of behavior involving specific stimuli and/or responses that result from prior experience with similar stimuli and responses.' We noted that both nociceptive and olfactory perceptions were involved in this essential function for the maintenance of life, and nociceptive and olfactory neural circuitries in the brain are closely related. Recently, we found that exposure to olfactory stimuli attenuated learned pain in mice. The relationship between odor intensity and odor preference is delicate. The main aims of the present study were to investigate in mice the relationships first between the intensity of an olfactory stimulus and inhibition of the CR and second between memory and inhibition of the CR with preferred odors.

Results
Results: The intensity of the preferred odor and the attenuation of the CR were correlated. The preferred odor administered in the training phase inhibited the unconditioned response (UCR), impairing development of the CR. The preferred odor applied in the test phase also reduced the CR. A low dose of scopolamine that had no effect on the UCR inhibited development of the UCR to the CR. Mice pretreated with scopolamine and then exposed to a preferred odor did not develop either an UCR or a CR. The results of the effect on the CR of a preferred substance given orally will also be presented.
Conclusion
Conclusions: The attenuation of the CR was correlated with the intensity of the olfactory stimulus. The preferred odor may suppress the activities of the neural pathways involved in the cognitive memory of the CS and hence the CR to pain. Alternatively, the preferred odor may elevate the threshold of pain perception.
Title: How To Best Measure Effects On Weight Bearing And Gait In Rodents With Inflammatory Joint Pain

Poster Number PW0382

Authors
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Aim of Investigation
Chronic pain remains a leading cause of disability, and joint pain with pain at walking as a major complaint affects a large portion of the aging population. Rats are commonly used in pharmacological research and we have previously shown that a readout that in many ways mirrors movement-related pain; gait and weight bearing analysis with the PawPrint setup, can be used as a tool to measure effects in a rat model of monoarthritis induced by Freund's complete adjuvant (FCA). One of the aims of this study was to extend the rat gait studies by using the commercially available CatWalk setup, and to compare the results from the gait analysis with measurements of mechanical hypersensitivity. Studies with mice are frequent as genetic modifications are common in mice and cost has an impact on research. Thus, in addition to the rat studies we have investigated three different ways of assessing gait in monoarthritic mice: CatWalk (Noldus), Advanced Dynamic Weight Bearing (DWB; Bioseb), and TreadScan (CleverSys).

Results
The CatWalk analysis showed irregular step sequences and reduced floor contact time, longer steps, slower swing speed and less weight bearing of the injected paw of monoarthritic rats. Naproxen partly reversed all these changes. Mechanical sensitivity increased in rats with monoarthritis, and naproxen completely reversed the hypersensitivity to the same level as of naïve rats. In mice with monoarthritis the CatWalk analysis showed changes similar to those observed in rats. A clear reduction of weight bearing of the injected paw in monoarthritic mice was found using the DWB device. However, using the TreadScan system no differences in irregularity of step sequence, print areas or weight bearing were observed between monoarthritis and control mice. Accordingly, pharmacological effects could be measured using the CatWalk and the DWB, but not with the TreadScan.
Conclusion
Our results support the use of gait analysis to assess movement-related pain-like behaviour and anti-nociceptive efficacy of drugs, a readout which resembles a major complaint in patients with joint pain. The difference in efficacy of naproxen between the gait analysis and measurement of mechanical sensitivity in rats shows an advantage towards the gait, which more resembles what is found in the clinic where patients with OA don't get full pain relief by naproxen. Mice with monoarthritis show similar results to those found in rats when using the CatWalk, and a reduction of weight bearing was found with DWB, but in contrast, when forced locomotion was assessed by the TreadScan it was not possible to detect changes in gait or weight bearing in monoarthritic compared to saline injected mice.
Title: Effects Of Strontium Ranelate On Pain Behavior In Experimental Model Of Osteoarthritis - A Pilot Study

Poster Number PW0383

Authors
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Aim of Investigation
Strontium Ranelate (SR) is a medicine usually prescribed to treat osteoporosis, which has been claimed as a compound with evidenced effects on the decrement of the risk of fractures and with some increasing suggestions to reduce progression of osteoarthritis (OA). This study aimed to investigate the effects of SR as either a prophylactic or as a treatment drug, using an OA model in rat, assessing their pain behavior.

Results
Articular incapacitation assessed with weight-bearing test as well as a rotary drum test (rotarod) have not showed a statistical significance (with p value >0.05) when comparing the groups treated with 25 mg/kg/day or 50 mg/kg/day of SR and the group which received oral saline solution. No statistical differences between the group that received SR prophylactically and the group with oral saline administration have been found as well.

Conclusion
SR have not provided analgesia in either treated rats or prophylactic users with the administrated doses. New studies are claimed to be performed further, with higher doses and using other pain assessment methods.
Title: Pkcδ-Targeted Intervention Relieves Chronic Pain In Sickle Cell Disease

Poster Number PW0384

Authors

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Aim of Investigation
As a marker of disease severity and mortality predictor, pain is one of the most dreadful symptoms in sickle cell disease (SCD) and is refractory to currently available analgesics. Patients with SCD start experiencing pain as early as three months old and continue throughout their lives. Although many aspects of this inherited disease are well understood, little progress has been made in understanding and treating pain in SCD. Taking advantage of a humanized targeted knock-in mouse model of SCD, this study aimed to investigate a key cellular mechanism, namely the neuronal protein kinase Cδ (PKCδ), for chronic pain in SCD.

Results
We found the presence of ongoing spontaneous pain as well as evoked hyperalgesia in TOW mice with SCD. Prominent activation of PKCδ was observed in the superficial laminae of the spinal cord dorsal horn in TOW mice. Functional inhibition (by selective peptide inhibitor, δV1-1, i.t.) or neuronal specific silencing (by RVG/siRNA, i.t.) of PKCδ significantly attenuated ongoing spontaneous pain, mechanical allodynia, and heat hyperalgesia in TOW mice. Furthermore, employing hematopoietic stem cell transplantation approach, we were able to generate a sickle cell anemia model in PKCδ-null mice, allowing us to specifically target neuronal PKCδ in SCD. Neither evoked pain nor ongoing spontaneous pain was developed in the mice lacking PKCδ, despite the full establishment of disease phenotypes.

Conclusion
This study is the first to identify the presence of ongoing spontaneous pain in transgenic mice with sickle cell anemia. These findings demonstrated a critical regulatory role of spinal PKCδ in the development of chronic pain in SCD, which may ultimately offer new pharmacological intervention targets.
Title: Morus Alba L. Stem Extract Attenuates Pain And Articular Cartilage Damage In The Anterior Cruciate Ligament Transection (ACLT) - Induced Rat Osteoarthritis Model

Poster Number PW0385

Authors
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Aim of Investigation
This study was designed to investigate the analgesic effect of M. alba stem extract as well as its cartilage protection activity in anterior cruciate ligament transection (ACLT)-induced rat OA model.

Results
Oral administration of M. alba stem extract (56 and 560 mg/kg) significantly (p < 0.05) attenuated joint pain. A significant improvement in the Mankin score was also observed in rats treated with 560 mg/kg M. alba stem extract, which was in agreement with its pain-relieving effect. Moreover, at the same dose, M. alba stem extract significantly ameliorated lipid peroxidation in liver homogenates obtained from OA-induced rats.

Conclusion
The results showed that M. alba stem extract exhibited analgesic effect as well as cartilage protecting ability in ACLT-induced rat OA model, supporting its potential use as an alternative therapy for treating OA.
Title: Contribution Of Glia To Spinal Wdr Neurons Long Term Potentiation After L5 Spinal Nerve Transection

Poster Number PW0386

Authors
H. Manaheji, L. Rezaee, S. Oryan, Z. Bahari

Aim of Investigation
Glial cells, including astrocytes and microglia, have been recently revealed in neuropathic pain. The aim of this study was to investigate the contribution of glia to spinal WDR neurons long term potentiation (LTP) after L5 spinal nerve transection.

Results
The results showed that after SNL, mechanical allodynia was created. Electrophysiological studies showed the LTP induction and expression of glia markers GFAB and Iba1 increased significantly. Administration of Propentofylline not only decreased mechanical allodynia but also inhibit spinal LTP induction.

Conclusion
It seems that activity of spinal LTP contribute to enhanced sensory responses after injury. The glial cells may modulate nociceptive transmission under pathological conditions. Therefore inhibition of glia cells could open a new way to alleviate neuropathic pain.
Title: Ifnα-Induced Hyperalgesia: A Role For The Endocannabinoid System

Poster Number PW0387

Authors
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Aim of Investigation
Interferon alpha (IFNα) is a pro-inflammatory cytokine used in the treatment various cancers and infections. However, this treatment regime is associated with depression in up to 60% of patients and increased reporting of pain. Recent studies from our laboratory have demonstrated that these side effects can be mimicked pre-clinically in mice repeatedly administered IFNα. The endocannabinoid system plays an important role in modulating emotional and nociceptive processing, however it is unknown if endocannabinoid tone is altered in response to chronic IFNα administration and if so, whether this underlies the associated depressive and/or nociceptive behaviour. The present study sought to investigate if repeated IFNα administration to mice alters anandamide (AEA) or 2-arachidoylglycerol (2-AG) levels in the descending pain pathway or periphery, in the presence and absence of formalin-evoked inflammatory pain. Furthermore, this study examined if global or local enhancement of endocannabinoid tone following inhibition of the enzymes responsible for the metabolism of AEA and 2-AG modulates formalin-evoked nociceptive responding in IFNα- and saline-treated animals.

Results
IFNα-treated mice exhibited enhanced late phase formalin-evoked nociceptive behaviour compared with saline-treated counterparts, an effect associated with enhanced 2-AG levels in the PAG and enhanced 2-AG and AEA levels in the RVM. 2-AG levels in the paw tissue were reduced in IFNα-treated animals, an effect not altered by formalin administration, while formalin administration tended to increase AEA levels in the paw tissue of saline-treated animals, an effect not observed in IFNα-treated animals. Systemic administration of MJN110, but not PF-3845, attenuated formalin-evoked nociceptive behaviour of both saline- and IFNα-treated mice. In comparison, intraplantar administration of either MJN110 or PF-3845 significantly reduced late phase formalin-evoked nociceptive behaviour in IFNα-, but not saline-treated, mice.
Conclusion
Repeated systemic administration of IFNα enhances nociceptive responding in the formalin test, an effect associated with altered endocannabinoid tone in the paw and in the descending pain pathway. Although global enhancement of 2-AG elicits anti-nociceptive effects in saline- and IFNα-treated animals, enhancing either AEA or 2-AG levels at the site of injury attenuated IFNα-induced hyperalgesia only. Taken together, these data highlight an important role for the peripheral endocannabinoid system in modulating hyperalgesia associated with chronic IFNα administration.
Title: Investigating The Mechanisms Of Hyperalgesic Priming In The Rat

Poster Number PW0388

Authors
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Aim of Investigation
Hyperalgesic priming models the transition from acute to chronic pain. Subcutaneous inflammogens applied 72hrs apart induce a long-term hyperalgesia to mechanical stimulation that outlasts the resolution of the systemic swelling. The aim of this study was to investigate the role of peripheral immune cell activation and central spinal processing in the mechanisms underlying hyperalgesic priming.

Results
Carrageenan evoked mechanical hyperalgesia (indexed by lowered PWTs) resolved within 3-5 days. Subsequent PGE<sub>2</sub> injection lowered PWTs (by >40%) in carrageenan and saline pre-treated rats. PGE<sub>2</sub> mediated responses were short-lived (1h) in saline-treated rats (unprimed), but in carrageenan-treated rats PGE<sub>2</sub> mediated responses were still present for at least 7 days (primed). 17-(R)-HDoHE treatment significantly reduced the mechanical hyperalgesia generated by hyperalgesic priming (p<0.05). Significantly more macrophages were present in skin sections in PGE<sub>2</sub> treated rats, but there were no differences between primed and unprimed rats. Numbers of activated IBA1 positive microglia in the ipsilateral dorsal horn 7 days post PGE<sub>2</sub> injection were decreased in primed rats, compared to unprimed rats. Injection of PGE<sub>2</sub> increased mechanically-evoked firing of WDR neurones to a comparable extent regardless of whether rats had previously received carrageenan or saline.

Conclusion
Behavioural hyperalgesic priming was not associated with alterations in PGE<sub>2</sub>-evoked responses of WDR spinal neurones in anesthetised rats, which may suggest a predominant change in primary afferent fibre function although effects of anaesthesia cannot be discounted. Differences in spinal immune cell morphology following PGE<sub>2</sub> injection were not as anticipated, with significantly less microglia present in the primed rats, compared to the unprimed rats. PGE<sub>2</sub>
increased numbers of macrophages within skin samples; but there was no significant difference in numbers between primed and unprimed rats 7 days after PGE$_2$ injection, indicating that hyperalgesic priming is not the result of carrageenan mediated alterations in subsequent immune cell responses to further inflammation. Administration of 17-(R)-HDoHE partially blocked hyperalgesia in primed rats, compared to vehicle controls. Our studies suggest that priming is made up of several processes that contribute to the induction of long-term hyperalgesia.
Title: Multimodal Imaging Of Brain Function By fMRI And Mass Spectrometry Imaging Reveal Metabolic Processing Of Lipids In An Animal Model Of Chronic Overlapping Pain

Poster Number PW0389

Authors
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Aim of Investigation
Chronic overlapping pain conditions (COPCs) comprise a group of idiopathic pain conditions that often overlap in presentation, occur more frequently in women, are commonly comorbid with stress and/or depression and pose a pain management challenge for the physician and patient. In order to identify novel pharmacological targets to develop better treatment options, we have combined genetic, molecular, imaging, and behavioral approaches in order to gain a more comprehensive understanding of the neurobiology underlying comorbid pain conditions. To this end, we have developed, in rats, a preclinical model of temporomandibular disorder (TMD) patients with comorbid irritable bowel syndrome (IBS). In this model, masseter muscle inflammation followed by stress induces chronic visceral hypersensitivity. Here we report a pilot study using multiple brain imaging techniques to identify metabolic changes in the brain during development of stress-induced visceral hypersensitivity.

Results
In this pilot study, naïve rats were compared to stressed rats at baseline and 6 days following the end of the stress (comparable times in naïve rats). Stressed rats showed significant visceral hypersensitivity relative to baseline and naïve rats. Eight days post stress fMRI revealed an increase in colorectal distention-evoked activity in the stressed rats, but not naïve rats in the infralimbic cortex in the medial prefrontal cortex (MPFC). Brains from 1 rat in each group were harvested for MSI. Examination of brain sections containing the MPFC by MSI showed dramatic differences in lipid distribution: Phosphatidylinositol (PI) 32:1 (acyl carbons:unsaturations) [m/z 809.5] changed as a result of stress, but the control lipid phosphatidylcholine (PC) 32:0 [m/z 734.5] expression did not differ. Alterations of PI levels in the brain implies involvement of potent lipid metabolic pathways.
Conclusion
Chronic overlapping pain conditions constitute a significant pain management dilemma. Using standard techniques to evaluate visceral pain combined with multiple imaging methodologies, we can identify tens or hundreds of small molecules that change expression in areas of the brain that are thought to contribute to the perception of visceral hypersensitivity following stress. Identification of such molecules presents novel targets for drug discovery and new therapeutic approaches to alleviate these difficult to treat chronic pain conditions.
Title: Relative Changing Between The Expression Of Gabaars Δsubunit Mrna In Sg Neurons And Pain Behavior.

Poster Number PW0390

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Aim of Investigation
Gamma-aminobutyric acid (GABA)-ergic inhibitory transmission operates through both phasic and tonic current in CNS. Decreased phasic GABAergic inhibitory transmission in the spinal cord is thought to be responsible for the development of neuropathic pain. However, the role of GABAergic tonic current in substantia gelatinosa (SG) neurons in neuropathic pain remains to be fully elucidated. In our previous study, we revealed GABAergic tonic current was reduced in chronic constriction injury (CCI) mice with electrophysiological study. CCI mice are well known as the model of neuropathic pain mice and show mechanical allodynia and thermal hypersensitivity. In this study, we investigated the expression of GABAA receptor δ subunit which contributes to tonic current in SG with real time PCR. We also assessed the effect of δ subunit preferring agonist 4,5,6,7-tetrahydroisoxazolo [5,4-c]pyridine-3-ol (THIP) on the threshold of thermal and mechanical stimulation with behavior experiments.

Results
In our experiments, CCI mice also showed both mechanical allodynia and thermal hypersensitivity. The expression of δ subunit mRNA was reduced in the right dorsal horn SG of CCI mice compare to Naive mice correlating with the period CCI mice showed mechanical allodynia and thermal hypersensitivity. Intrathecal administration of THIP improved significantly both mechanical (2.6±0.9 g vs 5.6±1.6 g) thermal (4.6±0.8 s vs. 6.6±1.1 s : pre vs. post) thresholds (p<0.05, paired t-test) of right hindpaw without significant change of left hindpaw of CCI mice. On the other hand, NS did not effect on both mechanical (3.1±0.5 g vs. 3.7±1.0 g) and thermal (4.2±0.9 s vs. 4.3±1.2 s) thresholds of right hindpaw of CCI mice.

Conclusion
The expression of δ subunit mRNA was reduced in SG of CCI mice. THIP improved both mechanical and
thermal hypersensitivity of CCI mice. These results might be suggested that δ subunit GABAA receptor mediated tonic current contributes to the mechanism of neuropathic pain of CCI mice. From now on we'll research the transitional change of mRNA with real-time PCR, and reveal the correlation between the thresholds and the expression of δ subunit in SG of CCI mice.
**Title:** Nerve Injury Triggers A Differential Response To Appetitive Motivated Behaviour Which Correlates With Accumbal Expression Of Mcp-1

**Poster Number** PW0391

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**Aim of Investigation**
Chronic constriction injury (CCI) evokes alldynia in all rats, but evokes disturbances in complex behaviours in only a sub-group. Nerve injury has been shown to reduce time in an aversive environment and reduce motivation for food rewards in rodents. Nerve injury in rats increases the expression of TNF in the nucleus accumbens (NAcc) a region critical for motivated behaviours, leading to a reduction in conditioned place-preference. Here we examined the effect of CCI and sham injury on the motivation to seek a food in an aversive environment in rats. Expression of TNF and the pro-inflammatory chemokine MCP-1 were also assessed in the NAcc.

**Results**
Sham injured rats displayed no change in mechanical threshold, whereas CCI rats displayed significant mechanical alldynia in the ipsilateral paw (p<0.05). Both CCI (-33.0±4.9%) and sham (-30.0±8.2%) rats spent less time in the light-side after injury. Following sham injury, no rats displayed a reduction in muesli consumption >1 standard deviation (SD) from mean, and 1 rat increased consumption >1 SD. Following CCI there was greater variability in muesli consumption, with ~40% of rats showing a change in muesli consumption. Of these, muesli consumption was reduced >1 SD in four rats, whilst consumption was increased >1 SD in three rats. Rats that increased consumption after CCI or sham, showed a reduction in risk-assessment behaviour and increased the number of times they stole muesli. Rats that decreased consumption after CCI showed more risk-aversive behaviours (increased risk-assessment and increased latency to eat) and/or reduced the number of times they stole muesli. Expression of MCP-1 in the ipsilateral NAcc negatively correlated with muesli consumption (R=0.32, P<0.05).

**Conclusion**
A reduction in time spent in the light by both CCI and sham rats may indicate a global increase in
sensitivity to an aversive stimulus after injury. CCI does however lead to a differential response in appetitive motivated behaviour not seen in shams. The emergence of sub-groups with reduced and elevated consumption after CCI can be explained by the characteristic behaviours of each group. The differential response in feeding behaviour also appears to be related to changes in supra-spinal inflammatory mediators, with elevated accumbal MCP-1 in rats who decrease their muesli consumption after nerve injury. Individual differences in affective behaviour after nerve injury maybe related to an individuals behavioural traits and their inflammatory response.
**Title:** Pharmacological Profile Of A Novel Nonhuman Primate Model Of Knee Osteoarthritis

**Poster Number** PW0392

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**Aim of Investigation**
Osteoarthritis (OA) is characterized by diminished functioning and pain. While a consequence of aging, OA may also result from acute injury or excessive stress to joints. As there are currently no treatments that attenuate or reverse the disease process, management of pain remains the primary focus of OA treatment. While numerous potential analgesics have been proposed based on preclinical rodent OA models, few, if any, of these have shown clinical efficacy. A potential limitation of rodents is their phylogenetic distance from humans. The current study pharmacologically characterized a new cynomolgus macaque model of knee OA following a unilateral medial meniscectomy (MMx).

**Results**
Microscopic examination of the ipsilateral knee joint showed marked articular cartilage erosion and clusters of chondrocytes ('cloning') throughout remaining cartilage matrix, consistent with clinical osteoarthritis histopathology. Robust pain-related behaviors were observed following MMx including significantly decreased ipsilateral knee pressure threshold, or pressure hyperalgesia, and decreased ipsilateral weight bearing, suggestive of resting pain. A single dose of the nonsteroidal anti-inflammatory drug diclofenac (p.o.), the serotonin-norepinephrine reuptake inhibitor duloxetine (p.o.) and opioid morphine (i.m.) increased both knee pressure threshold and ipsilateral weight bearing. Once daily dosing of diclofenac further increased both pressure threshold and weight bearing. By contrast, after either a single dose or repeated dosing, the neurokinin-1 (NK1) receptor antagonist aprepitant did not affect either pressure threshold or weight bearing. Also, a single dose of the anticonvulsant pregabalin did not affect either pressure threshold or weight bearing.

**Conclusion**
Clinical analgesics attenuated both unilateral pressure hyperalgesia and resting pain in the current
macaque model of knee OA pain. However, drugs that have previously demonstrated efficacy in rodent models of arthritis, such as NK1 receptor antagonists, did now show efficacy in the current model. The findings suggest that the macaque model could be used to further preselect compounds for clinical testing for OA pain, thereby increasing successful translation of preclinical findings to useful treatments.
**Title:** The Association Between Pressure Pain Sensitivity And Autonomic Function As Assessed By Tilt Table Test

**Poster Number** PW0393

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**Aim of Investigation**

Background: Persistent stress autonomic nervous system (ANS) dysfunction are associated with increased risk of ischemic heart disease (IHD) morbidity and mortality. ANS dysfunction is also associated with generally increased pain sensitivity. A tilt table test (TTT) leads to a controllable increase in ANS, as assessed by the changes in systolic blood pressure (SBP) and heart rate (HR). Pressure pain sensitivity (PPS) can be measured by algometry and hence assumed to be modulated by TTT. Aims: In patients with IHD, measuring PPS on the chest bone, to evaluate the association between resting PPS and the PPS response to TTT on the one side, and the SBP and HR response to TTT on the other side.

**Results**

Baseline study: Resting PPS correlated to the PPS response to TTT \( r = -0.37, p < 0.0001 \), but not to the HR and SBP response to TTT. This means that when resting PPS is elevated, the PPS response to TTT is reduced. During TTT, the changes in PPS, SBP and HR were positively and strongly correlated \( r = 0.44, \) and \( r = 0.49 \), respectively \( (p < 0.0001) \) \( (N = 361) \). This means that the change in PPS during TTT changes in parallel with the changes in SBP and HR. Intervention study: The changes in resting PPS correlated strongly to the changes in PPS response to TTT \( r = -0.52, p < 0.0001 \), as well as to the changes in SBP response to TTT. This means that when resting pressure pain sensitivity was reduced by
the intervention, then the change in PPS and SBP in response to TTT were increased, as possible signs of ANS dysfunction restoration.

Conclusion
The findings suggest that 1) pressure pain sensitivity at the chest bone at rest and in response to a tilt table test reflects autonomic nervous system function as assessed by the SBP response to a tilt table test, 2) that increased pressure pain sensitivity of the chest bone is associated with autonomic nervous system dysfunction, and 3) that 3 months of non-pharmacological intervention can reduce resting PPS, increase the PPS response to a tilt table test, and thus restore autonomic nervous system dysfunction as assessed by the SBP response to TTT. Reference: 1) Bergmann N, Ballegaard S, Bech P, Hjalmarsen A, Krogh J, Gyntelberg F, et al. The effect of daily self-measurement of pressure pain sensitivity followed by acupressure on depression and quality of life versus treatment as usual in ischemic heart disease: a randomized clinical trial. PLOS ONE 2014;9(5):e97553.
Title: Anatomical Spread Of Persistent Pain Is Related To Psychological Variables

Poster Number PW0394

Authors
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Aim of Investigation
We aimed to determine whether the area in which persistent pain is experienced relates to psychological variables.

Results
Pain catastrophising and anxiety predicted anatomical spread of pain intensity defined by the sum of pain ratings across all areas (\(\beta = .24, p < .01\), \(\beta = .18, p < .01\), respectively). Only anxiety predicted the total number of painful areas (\(\beta = .15, p = .03\)). Fear of pain was not significantly related to spread of pain.

Conclusion
Psychological variables are known for their role in the disability and distress aspects of persistent pain, however, their role in the sensory aspects is less clear. This research suggests a link between psychological variables and the anatomical spread of persistent pain, which furthers research showing that the spread of acute (experimental and clinical) pain relates to psychological variables. Notably, the effect appeared greater for the spread of pain intensity. That anxiety was the strongest predictor is also notable given the suggested overlap in the underlying mechanisms of generalised anxiety and generalised pain disorders.
Title: Motion-Sickness Susceptibility And Development Of Chronic Pain Are Related: Two Problems Of Sensory-Motor Incongruence?

Poster Number PW0395

Authors
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Aim of Investigation
We aimed to determine whether people with chronic pain had a greater pre-chronic pain motion sickness susceptibility relative to pain-free and rheumatoid arthritis controls.

Results
372 people completed the survey including 269 people with chronic pain (Low back pain n = 107; Fibromyalgia Syndrome n = 54; Neck pain n = 43; Whiplash associated disorder n = 34; Migraine n = 31), 78 pain-free controls, and 25 Rheumatoid Arthritis controls. ANOVA revealed a significant effect of group (e.g. chronic pain, arthritis, pain free controls; F(2) = 1, p <.05). Bonferroni corrected post hoc comparisons revealed that chronic pain participants had a greater pre-existing motion sickness susceptibility compared to healthy controls (p < .05). Participants suffering from rheumatoid arthritis did not differ from healthy controls in terms of motion sickness susceptibility. Participants with whiplash associated disorder and fibromyalgia demonstrated the largest pre-existing motion sickness susceptibility, when compared to healthy controls (Mean [SD] = 6.3 [6.8], 8.9 [7.6] and 11.5 [7.9] respectively).

Conclusion
People with chronic pain appear to have greater pre-chronic pain motion sickness susceptibility compared to pain-free controls; however, susceptibility varies between chronic pain conditions. The findings support theories suggesting a potential overlap between mechanisms responsible for motion sickness, and those responsible for some chronic pain conditions.
Title: Is Corticomotor Excitability Altered In People With Chronic Pain? A Systematic Review And Meta-Analysis

Poster Number PW0396

Authors
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Aim of Investigation
The current study aimed to systematically review papers examining corticomotor and intracortical excitability in people with chronic pain compared to healthy controls. Additionally, the study aimed to provide a meta-analysis of corticomotor excitability outcome measures, which included the cortical silent period and assessments of intracortical inhibition and facilitation.

Results
Forty-three studies were included, encompassing a pooled total of 1009 people with chronic pain and 658 control participants. The meta-analyses indicated that in chronic pain populations, both the duration of the cortical silent period and extent of short-interval intracortical inhibition were reduced and short-interval intracortical facilitation was enhanced (all $P<0.05$). The subgroup analysis revealed that only the neuropathic pain group exhibited significant effect sizes for these outcome measures ($P<0.05$). In the migraine group, there was a trend towards increased resting motor threshold ($P=0.054$), reduced short-interval intracortical inhibition ($P=0.06$) and increased long-interval intracortical inhibition ($P=0.06$). Effect sizes for the remaining outcome measures were not significant (all $P>0.08$).

Conclusion
There is evidence of motor cortex disinhibition in chronic pain populations, suggestive of a disruption in cortical gamma-aminobutyric acid (GABA)-mediated inhibition. Motor cortex disinhibition was more pronounced in people with neuropathic pain than those experiencing migraine and musculoskeletal pain, suggestive of differential changes within the nociceptive system depending on the underlying pathology. These findings provide new insights into the relationship between chronic pain and motor cortex excitability, which may have meaningful implications for the future treatment of chronic pain conditions.
Title: Anterior Nucleus Of Paraventricular Thalamus Mediates Chronic Mechanical Hyperalgesia

Poster Number PW0397

Authors
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Aim of Investigation
Nociceptive brain matrix is an obscure labyrinth while solving it would help patients suffering from chronic pain. Functional MRI brain images identified that medial thalamus activity increases in both chronic pain patients and studied animals. However, how these brain loci contribute to the physiological and pathological change in chronic pain development is unclear. Anterior nucleus of paraventricular thalamus (PVA) is a locus situated in medial thalamus and possibly involved in nociception brain circuitry. This study aims to clarify the role of PVA in mechanical hyperalgesia and how PVA neurons response to nociceptive stimuli in different pain models.

Results
ERK phosphorylation, a nociceptive marker, increased in PVA in both models. In vivo electrophysiological recording in anesthetized mice further illustrates the increase of PVA neuronal activity in response to noxious stimulus on sciatic nerve. Firing pattern switches after nociceptive induction and increase of the major scaffolding protein at postsynaptic density, PSD95, suggesting a neuronal plasticity change in PVA. Inhibition of PVA neuronal activity targeting to ERK activity or applying a chemogenetic tool, AAV-hM4D (Gi), alleviates the development of mechanical hyperalgesia in these pain models. In PVA, translation machinery is also involved in this ERK-dependent modulation of chronic mechanical hyperalgesia. Furthermore, an increase of PVA neuronal activity activating Channelrhodopsin-2(H134R) or PKC-ERK pathway specifically is enough to induce mechanical hyperalgesia in naïve mice.

Conclusion
Taken together, PVA, the locus per se, plays an important role for the development of mechanical hyperalgesia during central sensitisation, and ERK functions as a key molecule in mediating this phenomenon via influencing translation modulation.
Title: Optogenetic Inhibition Of Rostral Anterior Cingulate Cortex Neurons Attenuates Pain-Related Affective Response In Inflammatory Pain Rat Model

Poster Number PW0398

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Aim of Investigation
Pain consists of sensory-discriminative and affective-motivational dimensions. Mechanisms of the affective dimension of pain have been less investigated compared with those of the sensory dimension of pain. The affective component of pain may be assessed with conditioned place avoidance (CPA) to a pain-paired compartment. Lesion of the rostral anterior cingulated cortex (rACC) decreased the development of place-avoidance behavior in a formalin-CPA model. We hypothesized that inhibition of neuronal activities of the rACC attenuates pain-related affective response.

Results
The results showed that 1) rats with hind paw inflammation spent less time in pain-paired compartment during the post-conditioning test than during the preconditioning test, demonstrating place aversion to this compartment, 2) yellow light stimulation inhibited rACC neuron's spikes that were more frequent in CFA-injected rats than in naive rats, 3) yellow light stimulation during pain-paired conditioning increased the amount of time rats spent in the pain-paired compartment during the post-conditioning test, and 4) the light stimulation did not produce a reward effect in naive rats, nor interrupted rat's learning and memory during water maze performance.

Conclusion
Our data indicate that higher frequency of rACC neuronal spikes during pain-paired conditioning is correlated with pain-related avoidance response, and inhibition of such activities attenuates pain-related affective response. Inhibition of rACC neuronal activities may be targeted for control of affective dimension of pain. Supported by NIH R21 AT008467.
Title: Functional Differences Between Left And Right Cerebral Hemisphere Control Of Bladder Pain

Poster Number PW0399

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Aim of Investigation
Supraspinal control of visceral pain is poorly understood. Due to its involvement in processing both nociceptive and affective stimuli, two hallmarks of visceral pain, the central nucleus of the amygdala (CeA) has been highlighted as a potential therapeutic target for those suffering from chronic visceral pain conditions. In line with established neuroanatomy, it is hypothesized that the left and right cerebral hemispheres, and therefore left and right CeA, are equally involved in processing sensory information from midline visceral organs such as the bladder. Interestingly however, the homonymous left and right CeA exhibit unequal activation during different somatic pain states. In these studies, we aimed to determine whether such lateralization existed in the context of visceral bladder pain.

Results
We found that optogenetic activation of the right CeA with ChR2 was sufficient to increase pain-like responses to bladder distention. Activation of the left CeA however, did not alter bladder-distention evoked pain-like changes. In contrast, optogenetic inhibition of the left CeA with halorhodopsin, but not the right CeA, actually increased bladder pain-like changes. Optogenetic lateralization was further investigated by modulating known neuropeptides in the left and right CeA. Pharmacological administration of pituitary adenylate cyclase-activating peptide (PACAP) in the right CeA, but not the left CeA, increased pain-like responses to bladder distention.

Conclusion
Overall, these data suggest complementary anti- and pro-nociceptive roles of the left and right CeA that may rely on the differential release of distinct neuropeptides and distinct physiologic responses of the left and right CeA during visceral pain modulation.
Aim of Investigation
In primates, habituation of pain is a natural analgesic process, but the underlying neural mechanisms remain largely unknown. Previous long-term habituation studies have revealed heterotopic habituation to pain (i.e., habituation developed at non-stimulated sites), but whether the same phenomenon exists in short-term pain habituation is unclear. We hypothesize a different process during short-term habituation and explore its underlying neural correlates in the current study.

Results
Compared with the NP session, P session showed a significant increase in pain threshold. However, this habituation phenomenon only occurred in the LMF, not in the rest two sites. By comparing brain activity between P and NP sessions and correlating BOLD signals with behavioral data, we found that the rostral anterior cingulate cortex underlay the short-term pain habituation.

Conclusion
Two novel findings are disclosed in the current study. First, there is no heterotopic habituation to short-term painful repetitive stimuli. Second, short-term pain habituation involves distinct neural mechanisms from long-term pain habituation.
Title: Continuous, High Temporal-Resolution Recording Of Extracellular Glutamate In The Cingulate Cortex Following A Painful Insult In Conscious, Freely Moving Rats

Poster Number PW0401

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Aim of Investigation
Glutamate is the primary excitatory neurotransmitter in the brain and is presumed to play a critical role in pain processing. Microdialysis studies have shown that extracellular glutamate in the periaqueductal gray (PAG) and the ventral posterolateral thalamus (VPL) are elevated following a noxious insult with intraplantar formalin. Imaging studies have also identified multiple brain regions (ex. somatosensory cortex, cingulate cortex, periaqueductal gray, thalamus) activated by formalin injection. Recent development of enzyme-based amperometric biosensors has allowed continuous, second-by-second measurement of extracellular glutamate. The goal of the present study was to utilize glutamate biosensor technology to evaluate extracellular glutamate levels in the cingulate cortex of conscious rats after an intraplantar formalin injection.

Results
Intraplantar administration of formalin produced a robust increase in extracellular glutamate concentrations in the cingulate cortex in association with visible behaviors (biting, scratching and licking of the affected hindpaw). Gabapentin pretreatment, at a non-impairing dose that inhibited formalin-induced behavior, attenuated the elevated levels of glutamate in the cingulate cortex. Pretreatment with local intraplantar lidocaine also attenuated formalin-induced behaviors and normalized levels of glutamate in the cingulate cortex.

Conclusion
Our studies demonstrate that implantable glutamate biosensors can be utilized to record continuous real-time changes in extracellular glutamate concentrations in the cingulate cortex of conscious rats following a painful insult. These findings are supported by the prevention of the neurochemical changes produced by a painful formalin insult by systemic administration of gabapentin, and by the local
blockade of the nociceptive signal by intraplantar lidocaine. The cingulate cortex is thought to have an important role in pain processing; however, there is a paucity of data regarding the real-time neurochemistry associated with painful signaling. These studies provide insight by quantifying neuronal activity as indicated by the extracellular levels of glutamate in the cingulate cortex of freely moving rats while experiencing pain.
Title: Comparison Between Peripherally And Centrally Induced Pain Modulation In High And Low Hypnotizable Persons

Poster Number PW0402

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Aim of Investigation
The aim of the study was to compare the efficacy of explicit suggestions of analgesia with the efficacy of the Diffuse Noxious Inhibitory Control (DNIC) in healthy participants with high (highs) and low (lows) hypnotizability scores receiving nociceptive stimulation. Suggestions were expected to be more efficacious in highs than in lows, whereas no earlier study investigated the hypnotizability-related differences in DNIC.

Results
Pain intensity decreased significantly in both highs and lows during DNIC and Analgesia (F(2,2)=18.386, p<.0001); decomposition of the significant group x condition interaction (F(2,19)=4.530, p<.017) revealed that pain was significantly more reduced in highs than in lows in Analgesia ( t(1,20)=17.12, p<.006) whereas no group difference was found in DNIC. Autonomic variables are under analysis.

Conclusion
The highs' response to the explicit suggestions of analgesia are in line with earlier reports and are known to depend on central non opioid mechanisms involving several parts of the pain matrix. The lows' response to suggestions, in contrast, should be attributed to placebo-like mechanisms induced by suggestions (distraction, motivation). The similar efficacy of DNIC in highs and lows indicates that the two groups can rely on similar bottom-up activation of descending mechanisms for pain reduction.
Title: Mu Opioid Receptor Function In The Anterior Cingulate Cortex

Poster Number PW0403

Authors
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Aim of Investigation
Morphine isolated from the opium poppy has long been used as an effective pain killer. Its ability to induce analgesia relies mainly on the presence of the mu opioid G protein-coupled receptor (MOR) in pain pathways. Interestingly, MOR is expressed in the anterior cingulate cortex (ACC), a subdivision of the medial prefrontal cortex involved in higher order pain information processing, such as the emotional and affective aspect of pain experience. Patients experiencing pain show a decrease in MOR availability in the ACC. Recent studies in rodents suggest that pain relief is dependent on the release of endogenous opioids in the ACC. Our investigation aims to determine the function and localization of MOR in the ACC as it is currently unknown which neuronal cell types express MOR in this brain region.

Results
We found that roughly 60% of layer 2/3 pyramidal cells in the ACC are sensitive to DAMGO as they respond with a reversible decrease in cellular excitability. We confirm that the cells we are recording are in fact pyramidal shaped with a prominent apical dendrite. Our data show that pyramidal cells in the ACC are able to modulate their information processing properties to reflect changes in ambient opioids.

Conclusion
We demonstrate that selective activation of MOR results in changes in firing activity of a significant fraction of layer 2/3 pyramidal cells in the ACC. We will determine whether this effect is mediated through postsynaptic and/or presynaptic inhibitory mechanisms. In future experiments, we will also investigate changes in MOR availability in the ACC in neuropathic pain conditions.
Title: Evidence For Spatial Contrast/Summative Coding In Determining Perception Of Itch Vs. Pain Induced By Cutaneous Application Capsaicin But Not By Application Of Histamine

Poster Number PW0404

Authors
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Aim of Investigation
It has recently been shown that cutaneous application of a few capsaicin-coated inert cowhage spicules (non-histamine evoked itch) predominantly evokes itch instead of pain. As capsaicin application by spicules is characterized by high spatial contrast this has prompted the notion that spatial contrast is a determining factor in how pruriceptive/nociceptive stimuli are processed and hence perceived. The primary aim of this study was to assess comparatively if the perception of capsaicin and histamine evoked pain and itch was shifted for experimental conditions varying from low spatial contrast application to very high spatial contrast application. A secondary aim was to investigate the somatosensory changes induced in a skin area following capsaicin and histamine administration using thermal quantitative sensory testing.

Results
Mean peak magnitude of itch was significantly higher for the high spatial contrast condition of capsaicin application (27.3 ± 6.09) compared with the low spatial contrast condition (18.6 ± 5.97, P<0.05). Furthermore, an insignificant trend towards a decreased mean peak magnitude of pain induced by capsaicin was observed for high (26.3 ± 5.34) vs. low spatial contrast application (34.4 ± 8.01, P = 0.09). The itch-to-pain ratio showed a dominant sensation of itch at high spatial contrast of capsaicin and a dominant sensation of pain at the low spatial contrast of capsaicin. Oppositely, histamine primarily induced itch (37.3 ± 6.19) and to a much lesser extent pain (10.3 ± 3.20) and was unaffected by the spatial contrast of administration (P>0.05). Finally, warmth detection threshold (WDT) for histamine was significantly increased (35.3 ± 0.27 °C) compared with WDT at baseline (34.7 ± 0.27 °C), P<0.05, and heat pain threshold (HPT) for histamine and capsaicin were significantly decreased (40.5 ± 0.7 °C and 38.3 ± 0.74 °C, respectively) compared with HPT at baseline (43.4 ± 0.65 °C).
Conclusion
This preliminary study indicates a notable difference in the somatosensation evoked by topical capsaicin with different spatial contrast intensities and spatial extent. The itch-to-pain ratio perceived in response to capsaicin (traditionally perceived as an algogen) is shifted towards pain as spatial contrast decrease. Oppositely, the itch-to-pain ratio for histamine appears to be independent of the spatial application characteristics. Hence, our results indicate that itch induced by capsaicin but not by histamine is processed according to spatial contrast coding but our design does not preclude indirect effects related to the different administration patterns and particularly spatial summation effects.
**Title:** In Vivo Calcium Imaging Of Dorsal Root Ganglion Neurons

**Poster Number** PW0405

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**Aim of Investigation**
Dorsal root ganglion neurons are the primary sensory neurons for nociception. In order to understand how DRG neurons represent the noxious stimuli, it is important to record the activities of a population of DRG neurons simultaneously in vivo. Here, we report in vivo calcium imaging of a subpopulation of DRG neurons on anesthetized wildtype mice expressing genetically-encoded calcium sensor, GCaMP6s.

**Results**
Subcutaneous injection of virus AAV9 carrying GCaMP6s into newborn P5 mice could result in relatively specific expression of GCaMP6s in DRG neurons. Immunostaining results indicated that the expression of GCaMP6s driven by CAG promoter was quite random. The GCaMP6s-positive DRG neurons were equally distributed in CGRP-positive peptidergic neurons, IB4-positive non-peptidergic neurons and NF200-positive myelinated neurons. Four to six weeks after injection of virus, laminectomy was performed on anesthetized mice to expose L4 or L5 DRG. Then DRG neurons were imaged by a home-made video-rate two-photon microscope. The activities of a sub-population of DRG neurons were recorded while noxious thermal and mechanical stimuli were applied on the hind paws.

**Conclusion**
In vivo calcium imaging of DRG neurons opens a new avenue to study the function of DRG neurons in physiological and pathological pain. Also, our study showed a new method to introduce genes into DRG neurons non-selectively in a simply and cheap way.
Title: Positive Correlation Between Itch- And Pain-Evoked Dysesthesiae – An Observational Study Implying Similar Mechanisms

Poster Number PW0406

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Aim of Investigation
Dysesthesiae are bothering sensory symptoms frequently accompanying chronic and acute itch and pain conditions. The mechanisms responsible for development of alloknesis and hyperknesis have been proposed to share, at least to some degree, similar sensitization mechanisms as those underlying allodynia and hyperalgesia, respectively. This could be reflected in intra-individual consistency between the propensity to develop itch- and pain-induced dysesthetic areas. The aim of this preliminary study was to investigate the development of itch- and pain-related dysesthesiae in response to histamine and capsaicin, and to assess whether there was a relationship between the extent of these dysesthetic states. Furthermore, the study investigated skin prick lancet application as a method of inducing capsaicin provoked pain, itch, and neurogenic inflammation.

Results
Six subjects were considered non-responders as they failed to achieve a peak VAS score of 10 out of 100 for itch following histamine, or pain following capsaicin. In addition, VAS data recorded from 3 subjects was ineligible due to technical failures. As such, 24 subjects were included in data analyses pertaining to VAS data, whereas 27 subjects were included in analyses not involving data obtained by VAS. Intradermal histamine was found to induce itch of moderate intensity (VAS peak itch intensity = 38.3 ± 3.6) accompanied by pain (14.7 ± 2.3) of lower intensity (paired-samples t-test, P < 0.001), while capsaicin evoked more pain (33.8 ± 3.6) than itch (18.8 ± 4.0) (P < 0.001). The AUC of the first half of the stimulus-response curve for itch established by von Frey stimulation was larger following histamine than at baseline (P = 0.043) and following capsaicin application (P = 0.014), indicating that the subjects became sensitized to itch-inducing stimuli, and that the applied method is of sufficient sensitivity to detect this change. Histamine elicited areas of alloknesis (60.4 cm ± 3.2) and hyperknesis (49.2 cm ± 3.8)
as well as allodynia (49.0 cm ± 3.7) and hyperalgesia (49.7 cm ± 2.9). Similarly, capsaicin evoked areas of alloknesis (57.3 cm ± 4.0) and hyperknesis (49.9 cm ± 3.4) as well as allodynia (52.4 cm ± 4.2) and hyperalgesia (51.1 cm ± 3.4). Following histamine, the area of alloknesis was larger than those of hyperknesis and allodynia (RM-ANOVA, P < 0.013), however there were no differences in dyesthetic areas between histamine or capsaicin. The areas of itch-related dysesthesiae following histamine showed a correlation with the areas of pain-related dysesthesiae following capsaicin (Pearson’s product-moment coefficient: alloknesis/allodynia r = 0.654, P < 0.001; hyperknesis/hyperalgesia r = 0.405, P = 0.036).

**Conclusion**
Capsaicin applied by skin prick test lancets induces pain of an intensity similar to that of itch evoked by histamine (paired-samples t-test: P>0.2). The relationships between the extent of alloknesis and allodynia, and hyperknesis and hyperalgesia supports the notion that to some degree similar mechanisms may underlie the development of these dyesthetic states, and central sensitization may be one such mechanism.
Title: The Complex Therapy For Patients Suffered From Diffuse Pruritus

Poster Number PW0407

Authors
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Aim of Investigation
The aim was to test the antipruritus therapy created on the base of molecular and NMDA-blocking pre-screening criteria of psychotropics.

Results
Our preliminary clinical investigation revealed all patients suffered from diffuse pruritus and neuropathic pain needed in mental state correction; average pruritus level was 29.75±12.3. 17 patients were received antidepressant trittico (trazodone) in its standard doses (50-100 mg per day); after 6-10 weeks therapy we observed normalization of mental status for all patients; 2/3 of them remarked pain and itch level reduction up to 70%. Earlier we formulated 2 criteria for selection among psychotropics to determine drugs having antipruritus potency: V-like molecular structure and voltage- and magnesium-dependent open NMDA-channel blocking mechanism. According to our prescreening electrophysiological and molecular modeling procedures trittico doesn't satisfy criteria but neuroleptic chlorprothixene does. 12 patients not getting pruritus relief under monotherapy prolonged trittico in complex with chlorprothixene in standard doses (15mg per day). The tolerance of the therapy was satisfactory. After a month of the complex therapy all patients reported: diffuse pruritus episodes vanished fully; their sleep, indicators of anxiety and depression levels settled down.

Conclusion
The clinical investigations have confirmed our criteria for pre-screening among psychotropics the medicines having antipruritus and analgesic potencies. The complex antipruritus therapy is used at the State Pavlov Medical University clinics.
**Title:** Challenging The Labeled Line Theory: Itch And Pain Can Be Coded By A Single Afferent Population

**Poster Number** PW0408

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**Aim of Investigation**
Itch, or pruritus, can be described as an unpleasant sensation that leads to scratching behavior or the desire to scratch. Due to high prevalence in numerous diseases and widespread occurrence as a side effect of many medications, itch has become a prevailing research topic in recent years. Despite significant structural and behavioral overlap of pruriception and nociception, the underlying neurophysiological basis of itch sensation and its relation to pain is still unclear. More specifically, the enigma of how the somatosensory system differentiates itch and pain sensations and triggers distinct fight or flight behaviors remains to be solved. There have been several theories proposed for this discrimination process and one of the most popular ones is the 'labeled line' or 'specificity' theory. According to this theory, dedicated components of the somatosensory system, from the periphery to the brain, are specifically specialized for detection, transmission and perception of each sensory modality.

**Results**
Selective expression and trafficking of hM3D-mCherry and ChR2-eYFP to the surface and terminals of MrgprA3 neurons were confirmed in fluorescence microscopy. Functionality of the actuators was validated using calcium imaging and electrophysiology on dissociated DRG neurons in vitro. Using the cheek model of itch (Shimada and LaMotte, 2008), we observed that CNO injection evokes stereotypical itch behavior rather than pain responses. Surprisingly, optical activation of these neurons through ChR2 predominantly induces pain avoidance behaviors rather than scratching.
Conclusion
Our results dispute the 'labeled line theory' and show that in vivo a single population of C-fibers is capable to convey itch sensation in certain stimulation conditions and pain sensation in others. This calls for other models to explain how itch and pain are distinctly coded in the central nervous system.
Title: Hide Your Pain: The Effects Of Intentional Pain On Pain Expression And Appraisal

Poster Number PW0409

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Aim of Investigation
Social context has been shown to modulate several pain-relevant outcomes such as reported pain intensity, perceived threat of pain, pain expression and the learning of pain-related fear and might therefore be a valuable target for intervention. The present experiment investigated the effects of social threat (i.e. intentional pain) on reported pain and facial pain expression. In addition, we evaluated the effects of social threat on empathy and aggression. A single study (Peeters & Vlaeyen, 2011) has shown that social threat can lead to an inhibition of painful facial expressions but a simultaneous increase in reported pain intensity. This finding has important clinical implications, as it would indicate that social threat worsens pain experiences but at the same time prevents the communication of pain to others. Moreover, the experience of social threat might also have interpersonal consequences for the individual. For instance, social exclusion can lead to aggression and diminished empathy towards others (Twenge, Baumeister, Tice, & Stucke, 2001). We hypothesized that social threat will lead to (1) reduced expression of painful facial expression, (2) increased self-report of pain and (3) increased aggression towards the confederate.

Results
The confederate was rated as less friendly, trustworthy and altruistic in the threat group compared to the control group indicating a successful manipulation of social threat. Pain intensity, unpleasantness and threat ratings tend to be higher in the threat group compared to the control group, indicating that participants experienced the pain as worse in the threat group. Moreover, participants indicated that they would administer more painful stimuli back to the confederate in the threat group compared to control group, indicating that aggression was higher in the threat group. Analyses of facial expression is currently ongoing and will be presented at the meeting.
Conclusion
Social threat was successfully manipulated in the lab. Moreover, social threat was associated with increased pain reports and aggression towards the confederate. The current study provides support for the importance of social context in pain research and specifically demonstrates that a threatening social context can worsen the experience of pain and lead to interpersonal aggression. These results are clinically relevant because they warrant further attention to evaluate the social context in which acute and chronic pain occurs, especially when this context is perceived as threatening (e.g. social exclusion, perceptions of injustice, perceptions of hostility). Acknowledgements: This research was funded by the Research Foundation Flanders (FWO Vlaanderen), Belgium, granted to K.K. (grant ID = 1111015N).
Title: Experimental Pain And Digital Neuromirror

Poster Number PW0410

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Aim of Investigation
This study's main objective is the analysis of changes in intensity threshold and pain tolerance upon use of the Digital Neuromirror.

Results
The intersubject results show statistically significant differences for time threshold (p = 0.00071170), threshold intensity (p =0.001211682801) and time tolerance (p =0.00980661351). The intrasubject results reveal a significant change in the pain experience produced by motor and sensorial illusions by digital mirror effect and relief upon inmersion when subject is embedded in a chromatic and accoustic peripersonal space.

Conclusion
Digital mirror effect and multisensorial stimulation in peripersonal space favor the emergence of phenomena which modify the painful experience. This results can be used in the clinical field, particulary in ghost and complex regional pains.
Title: Trpa1-Mediated Pain In Human Subjects

Poster Number PW0411

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Aim of Investigation
TRP channels play a key role in sensing environmental and endogenous stimuli. TRPA1 is expressed in primary afferent neurons and senses a multiplicity of exogenous and endogenous chemicals. Agonists can be separated in non-electrophilic and electrophilic agents. Previously established human pain models targeting TRPA1 rely on the electrophilic agonists cinnamon aldehyde and mustard oil. The aim was to establish a reliable human pain model which allows to validate the TRPA1 contribution using a respective antagonist.

Results
Human subjects reported a concentration-dependent carvacrol-induced pain. To validate TRPA1 as the target for carvacrol in humans, TRPA1 antagonist A-967079 was co-injected. The reported pain intensity was substantially lower in the presence of A-967079. As reference for painful stimulation and fractional receptor inhibition, TRPV1 antagonist BCTC was tested against capsaicin in human subjects.

Conclusion
TRPA1 activation could be validated by pharmacological channel inhibition in human subjects. In cellular models this A-967079 acts against all modes of activation, indicating that it might be used to identify the TRPA1-activating component of a substance.
Title: Sweet Is Pleasure After Pain: Investigating The Effect Of Pain Offset On Sweet And Bitter Tastes On Brain Activity

Poster Number PW0412

Authors
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Aim of Investigation
It has been suggested that pain offset relief produces a positive hedonic state. Pain relief is rewarding and activates brain reward/motivation circuits. Furthermore, animal studies have suggested that the activation of the opioid system during pain relief increases the pleasantness of sweetness and decreases the aversive reaction to bitterness. The present study examines if pain offset can produce changes in the processing of taste stimuli of different affective valence (positive and negative) enhancing their intensity and hedonic value.

Results
Sweet taste stimuli produced a significant increase in alpha activity over the left frontal and bilateral medial cortical areas as compared with the bitter taste stimuli (p=0.02). Compared to the control condition, pain offset produced a significant increase of theta activity for sweet taste over the posterior areas in both hemispheres (left hemisphere, p<0.001; right hemisphere, p<0.001), whereas a significant decrease of theta activity for bitter taste over the posterior areas in right hemisphere was observed (p=0.002). Furthermore, a significant decrease of delta activity over the posterior areas for bitter stimuli (p=0.03) was also found. A significant positive correlation between sweet pleasantness and theta activity over the posterior areas was observed (r=.60, p=0.05), whereas a significant positive correlation between bitter pleasantness and delta activity over the anterior areas was observed (r=.67, p=0.02).

Conclusion
The present findings showed that pain offset was able to modulate brain activity related to sweet and bitter tastes in opposite directions. Pain offset produced an increase or decrease of brain activity in relation to the valence (positive vs. negative) of the stimulus, suggesting that pain relief can affect the
enjoyment of immediate sensory experience, in particular enhancing the processing of sweet taste stimuli.
Title: Experimental Tonic Hand Pain Modulates The Corticospinal Plasticity Induced By A Subsequent Hand Deafferentation: Implications For Phantom Limb Pain

Poster Number PW0413

Authors
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Aim of Investigation
Sensorimotor reorganization is believed to play an important role in the development and maintenance of phantom limb pain, but pain itself might modulate sensorimotor plasticity induced by deafferentation. Clinical and basic research support this idea, as pain prior to amputation increases the risk of developing post-amputation pain. The aim of this study was to examine the influence of experimental tonic cutaneous hand pain on the plasticity induced by temporary ischemic hand deafferentation.

Results
The pattern of changes was similar in both muscles (Muscle: p=0.861) and motor evoked potentials (MEPs) were larger in the Post-inflation phase (Time: p=0.002). The increase in MEPs amplitude in the post-inflation phase was greater for the Pain than the No Pain condition (Time x Condition: p=0.006). Post-hoc analyses revealed a significant difference between the two conditions during the Post-inflation phase (p=0.030) but no difference during the Pre-inflation phase (p=0.601). In other words, the increase in MEPs amplitude induced by cuff inflation was greater when pain was present prior to cuff inflation. Importantly, the presence of hand pain did not affect corticospinal excitability of forearm muscles (as no difference between conditions was observed in the Pre-inflation phase), but it enhanced the plasticity induced by subsequent ischaemic deafferentation of the hand.

Conclusion
These results indicate that pain can modulate the plasticity induced by another event (e.g. deafferentation/deefferentation), which could contribute to explain the sensorimotor reorganization often reported in chronic pain populations.
Title: The Association Between Thermal Pain Thresholds And Pain Catastrophizing In Healthy Individuals

Poster Number PW0414

Authors
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Aim of Investigation
Low back pain (LBP) is a significant public health problem, and the most common risk factor for the development of LBP is a previous episode of LBP. The prolonged standing paradigm, where participants stand for a period of 2 hours while performing simulated light work tasks, provides a unique way to examine potential risk factors for the initial development of LBP. During the 2 hours of standing, approximately half of back-healthy individuals without a history of LBP report symptoms that are similar to symptoms reported by people with clinical LBP. We hypothesize that people who develop pain during the prolonged standing paradigm (PDs: pain developers) have baseline differences in sensory processing compared to people who do not develop pain during standing (NPDs: non-pain developers).

Results
Six participants were classified as NPDs and nine as PDs. There were no differences between groups in age, height, BMI, sex distribution, prior exposure to standing, thermal thresholds or any of the PCS sub-scores or total score. As expected, the PCS total score and sub-scores were highly correlated (rs = 0.59-0.93, ps< 0.05). Interestingly, despite a lack of group differences, we found significant relationships between the PCS sub-score of magnification and both the cold (r = 0.77, p < 0.01) and heat pain thresholds (r = -0.55, p = 0.03). Higher magnification scores were associated with higher temperatures for the cold pain threshold and lower temperatures for the heat pain threshold.

Conclusion
These preliminary results do not support our hypothesis that PDs would report higher PCS scores than NPDs. However, the element of magnification ('I become afraid that the pain will get worse') of the PCS was positively related to higher thermal pain sensitivity, as indexed by the cold and heat pain thresholds. The large relationship between magnification and each thermal pain threshold is surprising given that participants are healthy and have no prior exposure to persistent pain. The next step is to complete the planned recruitment of 75 individuals for the current study to examine if there is a
difference in the relationship between PCS scores and thermal pain threshold measures between PDs and NPDs. We also plan to expand the testing to other induced pain paradigms in order to see if PCS scores can predict pain development status.
Title: The Influence Of Experimenter Characteristics On Placebo Hypoalgesia

Poster Number PW0415

Authors
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Aim of Investigation
Placebo interventions such as manipulations of an individual's expectation (placebo instruction) or the actual manipulation of a treatment experience (placebo conditioning) were found to reduce the perception of pain. A series of crucial factors have been identified, which affect the occurrence and magnitude of the resulting placebo effects. Especially the psychosocial context, which comprises for instance the interaction of patient and healthcare professional, the appearance, status and level of experience of a caregiver or the patient's gender, is supposed to have a strong influence on the placebo effect. However, so far only few studies systematically manipulated and investigated these phenomena. In the present study, we focused on the influence of the professional role of the experimenter on placebo hypalgesia. Therefore, two groups of participants (men vs. women) were investigated by an experimenter, who pretended to be either a physician or a psychologist. Based on previous findings, we expected placebo effects to be stronger in male participants, and further assumed that placebo effects might be more pronounced when instructed by a physician.

Results
In the conditioning phase, pain ratings and SCRs revealed a successful discrimination between high (control) and low (placebo) heat pain stimuli. Furthermore, female participants showed a greater difference between placebo and control trials than male participants. Interestingly, PSY experimenters led to higher differences between placebo and control trials than MED experimenters, especially in female participants. During the test phase, participants rated the identical pain stimuli significantly lower in placebo compared to control trials. However, pain intensity ratings showed no significant placebo effect in male participants when treated by a PSY experimenter. Female participants showed significantly stronger placebo effects than male participants for pain unpleasantness ratings. In general, pain ratings were lower for MED compared to PSY experimenter. SCR during the test phase failed to
show a significant difference between placebo and control trials, however pain ratings and SCRs were significantly correlated.

**Conclusion**
The present results replicate previous findings, showing a significant modulation of pain even by a mere psychological placebo manipulation. Pain ratings of the conditioning and the test phase demonstrate a general pain modulating effect by the MED experimenter, which might be suggestive for a 'white coat hypoalgesia'. Against our assumption, women were more likely to show a placebo effect. The findings demonstrate the impact of the professional role on placebo hypoalgesia and pain in general and suggest the consideration of social context variables when harnessing placebo effects. Acknowledgments and Disclosures All experiments were approved by the ethics committee of the medical faculty of the University of Würzburg. All authors declare no conflict of interest. This study was supported by the Research Group 'Emotion and Behavior', FOR 605, Wi2714/3-2, and the Collaborative Research Centre SFB-TRR 58 'Fear, Anxiety, Anxiety Disorders', project B05, sponsored by the German Research Society (DFG). Reference Reicherts, P., Gerdes, A. B., Pauli, P., & Wieser, M. J. (2016). Psychological Placebo and Nocebo Effects on Pain Rely on Expectation and Previous Experience. The journal of pain : official journal of the American Pain Society
Aim of Investigation
The aim was to evaluate possible sex-related differences in integrated jaw-neck motor strategy during jaw opening-closing following induced masseter muscle pain.

Results
There were no significant sex-related differences in jaw and head movement amplitudes. Head movement amplitudes were significantly greater in the pain trial, but jaw movement amplitudes and cycle times did not differ between the trials. The achievement of the individual target position did not differ between men and women in any of the trials.

Conclusion
For both men and women, the proportional involvement of the neck motor system increased during jaw movements in induced pain. These results indicate that there are no sex-related differences in the strategy of the integrated jaw-neck motor system, when performing a specific precision jaw-opening task during acute masseter muscle pain.
Title: Demonstrating A Link Between Opioid-Induced Hyperalgesia And Withdrawal-Associated Injury Site Pain: A Case Report

Poster Number PW0417

Authors
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Aim of Investigation
When daily opioid use is stopped, some people experience a temporary return of pain at healed injury sites, a phenomenon that we have termed withdrawal-associated injury site pain (WISP). This case study outlines one individual's pain experience with opioid use and withdrawal that may shed light on the relationship between WISP and opioid-induced hyperalgesia (OIH).

Results
A 34 year-old white woman (henceforth referred to pseudonymously as 'Alice') recruited in 2014 from a primary care clinic providing methadone treatment reported experiencing several twisting injuries of her right knee playing sports as a teenager. The pain (rated 4/10) associated with these injuries resolved in 2-3 days. She reported no knee pain, though an occasional click, for the subsequent 15 years and was medication and drug free. Then Alice began snorting oxycodone recreationally and developed an opioid use disorder (OUD). In 2012, she stopped oxycodone (morphine equivalent daily dose 225mg) and experienced moderate generalized withdrawal symptoms. In addition, Alice reported experiencing severe right knee pain (i.e., WISP 10/10 for 30 days, then 4/10 for 15 days). Subsequently, she reported being pain free for seven months while drug abstinent. Alice then had oxycodone relapse and found to her surprise that her right knee pain returned. She perceived escalation of injury site pain as her dose of opioid escalated and attributed the etiology of the pain to oxycodone use. In addition, each subsequent attempt at opioid withdrawal produced even more WISP, towards which she developed fear and
aversion. She cited WISP as a barrier to detoxification. Despite two hundred attempts, in two years she managed to get through the full six weeks of symptoms of WISP just three times and every time her right knee pain resolved. General withdrawal symptoms were a contributor to relapse, but were less intense (4/10) and shorter than WISP (30 days). Alice reported that naproxen, gabapentin, and phenobarbital all diminished WISP somewhat. She eventually tried detoxification with prescribed methadone (i.e., 30mg, then tapered by 5mg per day), which she felt assisted with easing WISP. At the time of the interview, she was initiating methadone maintenance treatment for the management of her OUD, as well as to avoid going into withdrawal and experiencing WISP.

**Conclusion**
This case study illustrates that opioid use can activate old injury site pain, increasing with dose escalation and repeated withdrawal events. This trajectory would be consistent with the development of OIH, which has been shown to be both opioid dose and withdrawal episode dependent. In addition, there can be a concurrent increase in perceived intensity and aversive quality of WISP that acts as a barrier to detoxification.
Title: Salience And Intensity Coding Of Nociceptive And Non-Nociceptive Stimuli In The Human Insula: Evidence From Intracerebral Recordings

Poster Number PW0418

Authors
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Aim of Investigation
We recently showed that both nociceptive stimuli and non-nociceptive vibrotactile, auditory and visual stimuli elicit consistent local field potentials (LFPs) in the posterior and anterior insula, with matching spatial distributions. (Liberati et al. 2016, PLoS Biol). Hence, insular LFPs reflect activity unrelated to nociception, and cannot be considered as a signature for the perception of pain. We hypothesized that LFPs elicited in the insula by nociceptive and non-nociceptive stimuli could reflect multimodal activities related to the re-orientation of attention towards salient stimuli. To this end, we assessed whether the magnitude of insular LFPs elicited by thermonociceptive, vibrotactile, and auditory stimuli could be modulated by stimulus salience, independently of the intensity of perception.

Results
For all three subjects, and for all three modalities, participants rated the 'high' intensity stimuli as more intense than the 'low' intensity stimuli. In contrast, intensity ratings were not affected by stimulus repetition: similar ratings were provided for each of the three stimuli belonging to a given triplet. A linear mixed model (LMM) analysis performed on the average peak-to-peak amplitude of the LFPs elicited by each triplet using 'modality' (nociceptive, vibrotactile, auditory), 'stimulus intensity' (high, low), and 'stimulus repetition' (S1, S2, S3) as fixed factors, and 'subject' as a contextual variable, showed a main effect of 'stimulus repetition' (F=31.91, p<.001): the LFPs elicited by the first stimulus of the triplets (S1) were significantly greater in amplitude than the amplitudes of the LFPs elicited by the second (S2) and third (S3) stimuli (p<.001). Furthermore, there was a main effect of stimulus 'intensity' (F=11.47, p<.001): the LFPs elicited by high intensity stimuli were larger than the LFPs elicited by low intensity stimuli (p<.001). Finally, there was a main effect of 'modality' (F=28.01; p<.001): nociceptive LFPs were, on average, smaller than auditory LFPs and larger than vibrotactile LFPs.
Conclusion
In all participants, and for all three types of sensory stimuli (nociceptive, vibrotactile, auditory), stimulus repetition at a short and constant 1-s ISI had no effect on the intensity of perception. In contrast, the reduction of stimulus salience induced by stimulus repetition was associated with a significant decrease of LFP amplitude. Although obtained from a limited number of subjects, these results suggest that the LFPs elicited in the human insula by transient nociceptive and non-nociceptive stimuli reflect multimodal activity involved in detecting, orienting attention towards, and/or reacting to the occurrence of salient sensory events, regardless of the sensory modality through which these events are conveyed, and independently of perceived intensity.
Title: Long-Term Changes In Pain Sensitivity Induced By Electrical High-Frequency Stimulation Of The Skin, Fascia And Muscle In Humans

Poster Number PW0419

Authors
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Aim of Investigation
Long-term potentiation and depression of pain sensation (pain-LTP and pain-LTD) have been recognized as an important mechanism of pain plasticity. Pain-LTP has been extensively studied in skin, but little is known about LTP in deep tissue. Thus, we have investigated whether pain-LTP can also be elicited from deep soft tissue following high-frequency electrical stimulation (HFS) of the thoracolumbar fascia and the multifidus muscle, i.e. deep soft tissue of the lower back and compared the results with stimulations of the skin.

Results
Fascial HFS increased fascia pain ratings 2.17 times compared to the unconditioned control site (P<0.001). But it had no significant effect on pain sensitivity of the muscle. Muscular HFS had no significant effect on muscle pain, but decreased the pain sensitivity of the overlying fascia by 20% (P<0.05; n=16). The pain threshold of the fascia (3.02 ± 1.92 mA) was 6.4-fold higher than its electrical detection threshold (0.47 ± 0.12 mA; P<0.05) which was only marginally lower than the detection threshold of the muscle (0.71 ± 0.25 mA; P=0.81). The pain threshold of the muscle (8.54 ± 5.57 mA) was 12-fold higher than its detection threshold (P<0.001) meaning almost 3-fold higher than the fascia pain threshold (P<0.001). Detection threshold changed increased after HFS in both tissues. HFS of the skin led to a total increase of pain to 143% after 20 minutes followed by a decrease to 79% after 38 minutes, an increase to a total of 140% after 64 minutes and a decrease to the minimum of 50% at the end of the observation period (n=4). Fascia-HFS resulted in a net facilitation that changed over time similar to skin-HFS. The HFS led to a total increase of pain to 214% after 28 minutes followed by a decrease to 76% after 34 minutes, an increase to a total of 254% after 52 minutes and a decrease to the minimum of 75% at the end of the observation period (n=4).
Conclusion
High frequency electrical stimulation of the skin and fascia induced signs of LTP at the site of stimulation, whereas sensitivity of the overlying fascia decreased after HFS of the muscle. Moreover, high frequency electrical stimulation of this muscle did not induce signs of long term potentiation at the site of stimulation. This study suggests a potential contribution of fascia nociceptors to the development of pain plasticity in the low-back area. Due to elicited muscle contractions after muscle stimulation, conclusions are limited. But, the stimulation with bipolar concentric needle electrodes seems to be an adequate approach to target fascia or other thin tissue layers. Funded by the Federal Ministry of Education and Research (Grant # 01EC1010B).
Title: Venlafaxine And Oxycodone Have Different Effects On Spinal And Supra-Spinal Activity In Man: A Somatosensory Evoked Potential Study

Poster Number PW0420

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Aim of Investigation
Opioids and antidepressants that inhibit serotonin and norepinephrine reuptake (SNRI) are recognized as analgesics to treat severe and moderate pain, but for both of them the mechanisms in humans remain unclear. This study aimed to explore how oxycodone (opioid) and venlafaxine (SNRI) modulate spinal and supraspinal sensory processing.

Results
In the venlafaxine arm, the spinal P11 and the late cortical N60-80 latencies were reduced (P<0.01), whereas the early cortical P25 amplitude was decreased (P=0.01). Oxycodone increased the sub-cortical P14 (P=0.03), early cortical N30 (P=0.04) amplitudes and the late cortical N60-80 latency (P<0.05). The brainstem and primary somatosensory cortex source strengths were increased in oxycodone arm, whereas the primary somatosensory cortex strength was decreased in venlafaxine arm (P<0.05).

Conclusion
Opioids and SNRI drugs exert different central effects. This study contributes to the much needed human models of the mechanisms of drugs with effects on the central nervous system.
Title: Within Days Changes In Sensory Profiles Assessed By Cuff Algometry In Healthy Male Subjects

Poster Number: PW0421

Authors
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Aim of Investigation
Sensory pain profiles have been widely used to study pain mechanisms in patients with chronic pain. Cuff algometry is newly developed assessment tool, which can quantify pressure detection (PDT) and tolerance thresholds (PTT), temporal summation of pain (TSP) and conditioning pain modulation (CPM), which have been shown as important pain mechanisms for chronic pain patients. The aim of this study was to evaluate the intra-day variability of cuff algometry.

Results
No significant difference comparing morning and afternoon session was found for PDT (P>0.20), PTT (P>0.15) or temporal summation (P>0.35). CPM was significantly lower in the afternoon session compared with the morning session (P<0.02). Within day reliability from the different measures were: PDT: ICC=0.55, PTT: ICC=0.71, TSP: ICC=0.70 CPM: ICC=0.58.

Conclusion
The study indicates that PDT, PTT and TSP have moderate to good reliability and that these parameters are unaffected during the day. CPM showed moderate reliability and was affected during the day.
Title: Hyperalgesia Persists After Pain Resolution In Healthy Adults Following An Acute Experimentally Induced Episode Of Low Back Pain.

Post Number PW0422

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Aim of Investigation
Background: Individuals with acute low back pain (LBP) have greater pressure pain sensitivity over the lumbar spine than persons without pain, and the pain sensitivity diminishes to 'normal' levels as the acute episode resolves. For obvious practical reasons, the pre-injury levels of pain sensitivity in persons with acute LBP are unknown. Thus we do not know whether an individual's pressure pain sensitivity returns to his or her pre-injury level or lingers below their pre-injury level but within a 'normal' pain-free distribution. Aim of Investigation: To investigate longitudinal changes in lumbar pressure pain sensitivity, movement-evoked pain and LBP intensity before, during, and after an acute episode of experimentally induced LBP.

Results
Results: 48 subjects who underwent DOMS met the definition of an acute episode of LBP, and were compared to 11 control subjects. Significant between visit, within group, and group by visit effects were observed for LBP intensity and local pressure pain sensitivity, while only within group effects were observed for movement-evoked pain (p<0.01). No outcome measure differed between groups at baseline. All outcome measures remained stable in the control group across time. LBP intensity significantly increased above baseline and control values (peak pain) and remained elevated at 48 hours and 72 hours. At 96 hours, LBP intensity did not differ from control subjects or baseline. Lumbar pressure pain sensitivity significantly increased above baseline and controls values at 48 and 72 hours. At 96 hours pressure pain sensitivity did not differ from controls, but remained above baseline. Movement-evoked pain was elevated above baseline but not controls at 48 and 72 hours. No differences were noted at 96 hours.

Conclusion
Conclusions: Following the resolution of an acute episode of experimentally induced LBP, pressure pain
hyperalgesia diminishes and is within a 'normal' pain free distribution, but remains above pre-injury levels. How long it remains elevated was not determined as no measurements were taken after 96 hours. Our findings of prolonged hyperalgesia are similar to other observations of lingering effects on muscular strength and coordination following an acute experimentally induced episode of LBP. The clinical significance of residual motor and sensory changes follow acute pain needs further investigation.
Title: Facilitated Pain Sensitivity And Cortical Event Related Potentials After Night Shift Work

Poster Number PW0423

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Aim of Investigation
Sleep restriction is associated with increased pain sensitivity. Shift workers commonly report reduced sleep. The aim of the present study was to determine whether night shift work (NSW) affects pain sensitivity and pain modulation, measured subjectively and by cortical event related potentials (ERPs).

Results
Total sleep time (TST by actigraphy) was 59 min shorter and subjective sleepiness (Karolinska sleepiness scale) was higher in the NSW condition (p < 0.001). A hyperalgesic effect of NSW was found on heat pain (28% increase, p = 0.001) and electrical pain (11% increase, p < 0.001), but not on cold pain (5% increase, p = 0.14) and mechanical pain (2% increase, p = 0.57). The ERP magnitude was facilitated in the NSW condition across a majority of the electrodes. In the time domain, a 11-15% increase in N2 amplitude was seen on the contralateral and central electrodes (F3/4c, Cz, C3/4c and P3/4c, p < 0.001). In the time-frequency domain, the increase in magnitude was stronger (19-46%, p < 0.001). Electrical pain was rated 20% more painful in the nocebo condition (p < 0.001), whereas the nocebo condition led to reduced ERP magnitude from several electrodes by 5-7% in the time domain (p < 0.01) and by 12-14% in the time-frequency domain (p < 0.024). The nocebo effect was not facilitated by NSW (p = 0.60). The inhibitory CPM-effect was 25% stronger after NSW (p < 0.001).

Conclusion
Night work facilitates heat pain and electrical pinprick pain, as well as the magnitude of electrically induced ERPs. The increased pain following NSW could not be explained by increased negative expectation or by reduced pain inhibition.
Title: Vicarious Facilitation: Is It Specific To Pain?

Poster Number PW0424

Authors
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Aim of Investigation
Pain communication is a transaction between a person in pain and an observer. This triggers a response from the observer in response to pain observation. It has been shown that this response may involve facilitated spinal and supraspinal processing of nociceptive information. Different mechanisms suggested for this facilitation which different viewpoints toward the specificity of this effect. We aimed to investigate to investigate the effect observation of pain and other type of negative expressions on the vicarious facilitation of responses to pain.

Results
Both pain ratings and reflexes were transformed to z-scores to be able to compare them together and remove inter-individual variability in ratings and reflex intensity. The RIII reflex magnitude was the integral of the rectified EMG signal between 90 and 180ms post-stimulation. Results showed that observation of pain increased both pain rating and RIII reflex as compared to the observation of neutral and happy expressions. Pain observation also resulted in greater reflexes as compared to fear and disgust but not angry expressions.

Conclusion
Findings of the current study were in line with earlier studies which showed vicarious facilitation of responses to pain. They also may suggest a relationship between the arousal level of the expression and facilitated reaction in the observer. This is in accordance hypothesized role of emotional expression observation in the improvement and the facilitation of the social interaction.
Title: A Disconnect Between Pain Unpleasantness And Intensity In Less Resilient Individuals

Poster Number PW0425

Authors
K. Hemington, J. Cheng, R. Bosma, A. Rogachov, A. Kim, K. Davis

Aim of Investigation
Resilience is a positive psychological factor capturing an individual's ability to cope with stress. Resilience predicts chronic pain outcomes independent of negative psychological factors (Ramirez-Maestre et al., 2012, Ruiz-Párraga et al., 2012, Smith et al., 2008), possibly by mediating the impact of emotional distress on chronic pain acceptance (Ruiz-Párraga et al., 2014). However, positive psychological factors like resilience are largely excluded from psychological models of pain sensitivity, in part because the fundamental relationships between resilience, emotional/affective aspects of acute pain, and negative psychological traits in healthy individuals are unknown. Thus, the aim of this study was to examine the relationship between resilience, psychological vulnerability factors, and pain unpleasantness which reflects an emotion/affective dimension often enhanced in chronic pain (Apkarian et al., 2004). We hypothesized that resilience 1) is negatively correlated with psychological vulnerability factors, and 2) exhibits a negative relationship with pain unpleasantness when controlling for pain intensity, which cannot be explained by psychological vulnerability factors.

Results
Resilience ranged from 107-172 (mean= 147+/−14(SD)) with no significant sex differences (p=0.28). RS scores were positively correlated with PVAC scores (r=0.32, p=0.041), and showed a trend towards a negative correlation with PCS scores (r=−0.24, p=0.07) but were not significantly correlated with BDI or STAI scores. RS scores were also negatively correlated with relative pain unpleasantness (r=−0.34, p=0.03). In the final linear regression model, RS negatively predicted 12% and STAI positively predicted 10% of the total variance in relative unpleasantness respectively (PCS, BDI and PVAC were not significant predictors).
Conclusion
We found that resilience contributes to the pain experience in healthy individuals. Specifically, we found that low relative pain unpleasantness in healthy individuals was predicted independently by resilience and low anxiety. Conversely, there was a disconnect between pain intensity and unpleasantness in less resilient, more anxious individuals. Further studies of unpleasantness and resilience are needed to understand how resilience can act as a protective factor in chronic pain.
**Title:** Individual Differences In Strategy For Adaptation Of Movement During Pain: “Taking Action” To Reduce Pain

**Poster Number** PW0426

**Authors**
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**Aim of Investigation**
Movement variability is increased during acute pain in complex tasks, but is reduced in simple tasks when the induced pain has little direct relationship to movement. We investigated whether participants purposefully search for and find a less painful solution during exposure to acute elbow pain and whether this search was associated with an initial increase in movement variability.

**Results**
On average, wrist/forearm position changed during the painful trials and was perceived as less painful, but did not correspond to greater use of the movement option that induced less intense electrical stimulation (less painful range of angles in the flexion-extension direction). Participants used one of three different movement strategies during Pain 5-1 and Pain 5-0. These involved either (i) no change in overall angle (but greater use of the less painful region), or a (ii) small or (iii) large change of wrist/forearm position to move to a different region of flexion-extension, but not the region associated with less painful stimulation. Participants who used the option that induced less intense stimulation did not experience a greater reduction in pain.

**Conclusion**
In summary, participants searched for, and found, a less painful movement strategy during pain, but it was not necessarily the solution with complete or near complete pain reduction. It appears that reduction of pain was linked to 'taking action to relieve the pain' and did not depend on a true reduction in intensity of the stimulus.
Title: Anatomy Of Human Ganglion Impar For Radiofrequency Thermocoagulation Under Cadaver Research.

Poster Number PW0427

Authors

Tokyo Medical University, Dep. of Anesthesiology, Tokyo, Japan, Tokyo medical University, Dep. of Anesthesiology, Tokyo, Japan, Tokyo medical university, Dep. of Anesthesiology, Tokyo, -- SELECT --

Aim of Investigation
Background: When ganglion impar block is performed with radiofrequency thermocoagulation (RFT), the active tip of the needle should be correctly inserted into the ganglion impar. Despite several clinical reports on ganglion impar block with RFT, the anatomical position of this ganglion for RFT has not been determined. In this presentation, we report the anatomical features that is necessary for accurate ganglion impar block combined with RFT delivery.

Results
Because sympathetic nerves around the sacral region are extremely thin and difficult to identify, this method was useful. In 20 subjects the ganglion impar were located caudal to the sacrococcygeal joint. The most common ganglion site was a region 0-10 mm caudal to the sacrococcygeal joint. In one subject, the ganglion was cranial to the joint. It showed the tendencies that distance between right and left sacral sympathetic nerves on the joint of females were longer than these of males.

Conclusion
We revealed the ganglion impar to be more wide range than previously reported and clarified the positional relation between the sacrococcygeal joint region and the impar. Because this region is often the target for ganglion impar block, measurement on the axial midline was useful for block under X-ray fluoroscopic, computed tomographic, and ultrasonic echo guidance. These results may lead to establishment of accurate ganglion impar block with RFT. Our results are consistent with positions in several clinical reports on ganglion impar block. However, further clinical studies are needed.
**Title:** Is Resting Blood Pressure Associated With Temporal Summation Of Pain And NFR?

**Poster Number** PW0428

**Authors**
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**Aim of Investigation**
Cardiovascular responses are associated with pain perception. For example, resting blood pressure (BP) is associated with the effectiveness of endogenous pain modulation tasks (e.g., conditioned pain modulation, emotional modulation of pain). To our knowledge, no study has investigated the relationship between resting BP and temporal summation of pain (TS-Pain) and temporal summation of a nociception flexion reflex (TS-NFR), both of which are markers of central sensitization.

**Results**
Significant positive correlations were noted between systolic/diastolic BP, age, and BMI (ps<.05); thus, age and BMI were entered as control variables in the models. Age, BMI and Train number (due to sensitization effects across trains) were controlled for in all models. Outliers greater than 2.5 SD or lower than -2.5 SD were winsorized. A positive relationship was seen between train number and pain ratings (ps<.05), but not NFR (ps>.05), indicating pain ratings increased across trains. Stimulus trains were associated with increases in pain ratings and NFR (ps<.05), indicating significant temporal summation of both outcomes. Higher systolic and diastolic BP was associated with increased TS-NFR (ps<.05). Moreover, higher systolic BP was associated with increased TS-Pain (ps<.05) and there was a trend for the same relationship with diastolic BP (p=.10).

**Conclusion**
Hyperexcitability of dorsal horn neurons (as measured by TS-NFR) may be amplified by increased BP which may also be reflected in the conscious pain experiences (as measured by TS-Pain).
**Title:** Inflammation And Neuropathic Pain: The Role Of Alpha[Sub]1/[Sub]-Adrenergic Receptors.

**Poster Number** PW0429

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**Aim of Investigation**
The skin may play an important role in the initiation and the maintenance of neuropathic pain. Our previous studies indicated that alpha[Sub]1-adrenergic receptors (AR1) may mediate these processes. In animal models and patients with neuropathic pain, the expression of AR1 has been found to increase in the epidermis and dermal nerve bundles of the affected limb. In addition, the levels of inflammatory mediators (IM), such as TNFα and IL-6, were also found to be elevated. Cross-talk between IM and AR1 has also been shown in some studies, which indicates a possible positive-feedback mechanism in maintaining chronic pain. Keratinocytes constitute almost 95% of the epidermis of the skin, provide a barrier to the external environment, and initiate both sensory transduction and inflammatory reactions to injury. Therefore, the purpose of this study was to elucidate the interaction between IM and AR1, using a keratinocyte cell line (HaCaT) as an *in vitro* model.

**Results**
TNFα treatments of HaCaT cells resulted in the production of IL-1β, IL-6, IL-8, and βNGF, in a dose-dependent manner. Interestingly, there was also a similar increase in the gene expression of AR1[Sub]B, a sub-species of AR1.

**Conclusion**
The results show the capability of TNFα in releasing inflammatory mediators from keratinocytes. This inflammatory state induced the expression of AR1[Sub]B, which may indicate the potential interaction between IM and AR1 in keratinocytes. Further experiments to determine if further stimulation of AR1[Sub]B through its agonist (phenylephrine) can enhance the production of those IM will provide a better understanding of the role of AR1[Sub]B in mediating persistent inflammatory conditions that exist in neuropathic pain patients.
Title: Inhibition Of Action Potential Conduction In The Frog Sciatic Nerve By Various Plant-Derived Chemicals Involved In Antinociception

Poster Number PW0430

Authors

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Aim of Investigation
An inhibition of action potentials conducting on nerve fibers contributes to at least a part of antinociception produced by analgesics. We have previously reported the inhibitory effects of a variety of drugs involved in antinociception on voltage-gated Na<sup>+</sup>-channel blocker tetrodotoxin-sensitive compound action potential (CAP) recorded from the frog sciatic nerve. Among the drugs, there are opioids such as morphine and tramadol, local anesthetics, α<sub>2</sub>-adrenoceptor agonist dexmedetomidine and anticonvulsants. Plant-derived chemicals also produce antinociception while inhibiting nerve conduction. Although many of plant-derived chemicals have an ability to activate transient receptor potential (TRP) channels, we have previously shown that capsaicin, menthol and allyl isothiocyanate inhibit frog sciatic nerve CAPs without TRP activation. CAP inhibition is also seen for analogs of capsaicin or menthol and for traditional Japanese medicines including daikenchuto used to alleviate pain. The aim of the present study was to know whether there is a relationship between CAP inhibitions produced by various plant-derived chemicals and their chemical structures. It was also addressed whether the CAP inhibitions are mediated by TRP activation.

Results
Citral attenuated CAP peak amplitudes with the IC<sub>50</sub> value of 0.48 mM; this action was resistant to a non-selective TRP antagonist ruthenium red. Camphor (TRPV1 and TRPV3 agonist) at 5 mM reduced CAP amplitudes by 33% and (+)-borneol (TRPV3 agonist) inhibited CAPs with the IC<sub>50</sub> value of 2.0 mM; these actions were insensitive to ruthenium red. Lavender-oil compounds, linalyl acetate and (±)-linalool, reduced CAP amplitudes with the IC<sub>50</sub> value of 2.0 mM; these actions were insensitive to ruthenium red. Lavender-oil compounds, linalyl acetate and (±)-linalool, reduced CAP amplitudes with the IC<sub>50</sub> value of 2.0 mM; these actions were insensitive to ruthenium red. Lavender-oil compounds, linalyl acetate and (±)-linalool, reduced CAP amplitudes with the IC<sub>50</sub> value of 2.0 mM; these actions were insensitive to ruthenium red.
1.5, 1.8, 1.1, 0.51, 0.65 and 2.0 mM, respectively. On the other hand, myrcene and \textit{p}-cymene at 5 mM reduced CAP amplitudes by 7 and 20%, respectively. Taking into consideration previously-reported data, an efficacy sequence of plant-derived chemicals for the CAP inhibitions was phenols (thymol, carvacrol and eugenol) ≥ aldehydes (citral and citronellal) ≥ esters (bornyl acetate, linalyl acetate and geranyl acetate) > alcohols ((±)-linalool, (-)-linalool, (+)-borneol, (-)-borneol, α-terpineol, geraniol, citronellol and menthol) > ketones (carbone, menthone and plegone) > oxides (rose oxide and cineole) >> hydrocarbons (\textit{p}-cymene, myrcene and limonene), except for a ketone camphor that was less effective than oxides.

**Conclusion**

There was a relationship between the extents of CAP inhibitions by plant-derived chemicals and their chemical structures. Such an inhibition was not mediated by TRP activation. This result may serve to develop new analgesics based on plant-derived chemicals.
Title: Characterization Of Molecular Changes In Ascending Pain Pathways In The Animal Model Of Osteoarthritis

Poster Number PW0431

Authors
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Aim of Investigation
Pain associated with osteoarthritis (OA) is one of the most common chronic pain disorder in elderly population that is caused by functional impairment of OA affected joints. Currently used pharmacotherapy involves symptomatic treatment based mostly on nonsteroidal anti-inflammatory drugs that do not always provide adequate pain relief. This may be due to concomitance of central sensitization and development of pain with neuropathic features in OA patients. Our objective was to examine neuropathic pain component contribution to OA knee pain in a model widely used for investigating the pathogenesis of joint pain. We performed detailed molecular characteristics of the OA pain ascending pathways in order to evaluate the possibility of neuropathic pain pathogenesis in osteoarthritis.

Results
Presented results refer to mechanisms of sensitization produced by perpetual input from the periphery to central nervous system in OA. We observed biphasic development of primary hypersensitivity (PAM test) with inflammatory phase ending around day 4 after MIA injection and phase connected to gradual loss of cartilage starting 10 day later. Ongoing development of allodynia (von Frey’s test) after MIA administration, indicated presence of neuropathic component in OA pain. Our results showed that, amongst DRGs innervating knee joint, development of central sensitization is most likely due to peripheral input of stimuli through DRGs L3 (upregulation of BK1, CB2, CGRP, NGF, IL1β) and L5 (upregulation of NPY, IL1β, CGRP). In SC, development of secondary hypersensitivity correlated with increased expression of TAC1 (involved in inflammatory response), BDNF (contributing to increased sensitivity to nociceptive stimuli) and NPY.
Conclusion
Our studies provided data on abnormal activation of pain transmission markers in DRG neurons during development of OA, that lead to manifestation of neuropathic pain features. Obtained results may contribute to readdressing treatment OA pain options lead to development of treatment targeting peripheral factors of central sensitization. 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. Natalia Malek is a holder of a KNOW scholarship (Ministry of Science and Higher Education, Poland).
Title: Orofacial Cutaneous Mechanical Hypersensitivity Following Infraorbital Nerve Injury Is Attenuated By Peripheral Oxytocin In Rats.

Poster Number PW0432

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Aim of Investigation
Oxytocin (OXT) is one of the neuropeptides synthesized and secreted from neurons in the paraventricular nucleus and supraoptic nucleus of the hypothalamus. OXT has been reported to play a significant role in pain modulation. However, the underlying mechanisms regarding the anti-nociceptive effect on orofacial neuropathic pain are not fully understood. We examined the peripheral effect of OXT in mechanical hypersensitivity in whisker pad skin induced by partial ligation of the infraorbital nerve in rats.

Results
The reduced MHWTs were significantly recovered at 2 and 5 h after the OXT administration compared with that of the vehicle (PBS) (2 h: OXT group, 35.4 ± 4.2 g; PBS group, 10.8 ± 3.9 g; p < 0.01, 5 h: OXT group, 35.6 ± 10.9 g; PBS group, 14.8 ± 5.2 g; p < 0.05). The effect did not sustain until 8 h after administration and ultimately returned to the pre-administration level 24 h after the OXT administration. In patch-clamp recording, the resting membrane potential of OXT–treated TG neurons was significantly decreased (OXT group, -63.4 ± 1.1 mV; PBS group, -56.2 ± 2.2 mV; p < 0.01). Threshold currents in OXT–treated TG neurons for spike generation were also significantly greater than that of PBS (OXT group, -163.3 ± 27.6 pA; PBS group, -89.2 ± 12.4 pA; p < 0.05). The percentage of OXT receptor immunoreactive (IR) neurons was 12.1 ± 3.5%, while that of vasopressin 1A receptor IR neurons was 43.4 ± 3.3% in the TG neurons innervating the whisker pad skin 6 days after the nerve ligation.

Conclusion
Present findings suggest that OXT is at least partially effective in the suppression of TG neuronal hyperexcitability following infraorbital nerve injury. OXT signaling may be a therapeutic target for treating orofacial neuropathic pain.
Title: Remote Control Of Nociceptors

Poster Number PW0433

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Aim of Investigation
Sensory neurons in general and nociceptors in particular, are heterogeneous. Recent advances have been made in stratifying sub-populations by molecular profiling, however information pertaining to their functional role in nociceptive processing is lacking. Chemogenetics is providing neuroscience with a method to remotely control the activity of neurons in vivo. In comparison to optogenetics, chemogenetics is suitable for long-term experiments and does not require the use of sometimes invasive light sources. We aim to use chemogenetic tools to reversibly silence discreet nociceptor populations. By targeting our strategy to specific populations, we will study the contribution of these sub-populations of neurons to a variety of neuropathic pain states.

Results
Whole-cell patch clamping of dissociated mouse DRG show IVM induces a dose-dependent Cl-conductance of up to 42.9±7.3nS (20nM IVM) in GluCl+ neurons that is not seen in GluCl- neurons (IVM induced conductance: GluCl+ = 42.9±7.3nS vs GluCl- = 1.73±0.2nS, p=0.004) . Current clamp recordings and Ca2+ imaging experiments illustrate that this conductance is sufficient to block spontaneous and evoked action potential firing. In patch clamp recordings, 94.1% of cells (16/17) tested could not fire an action potential after injection of depolarising current >10-fold the pre-IVM rheobase level. Additionally, by Ca2+ imaging only 7.6±3.5% of neurons that respond to KCl stimulation, respond following IVM-silencing (p=0.002 vs vehicle treatment). Using AAV delivery systems, we have established proof of concept for translating in vitro findings into the in vivo setting.

Conclusion
Current work is focussed upon generating new transgenic models where our system can be specifically targeted to discreet nociceptor populations by using an intersectional genetics approach. Models in which nociceptors can be externally manipulated should provide an excellent tool to delineate the
pathways leading to neuropathic pain. A more detailed knowledge as to the specific role of nociceptor subgroups may lead to the development of improved therapeutics with enhanced specificity.
Title: Comparison Of Structure, Neuronal Marker, Ion Channel Expression And Function Of Three Neuronal Cell Lines With Primary Drg Neurons In Culture And The Effect Of Serum Starvation/Differentiation

Poster Number PW0434

Authors
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Aim of Investigation
Primary neuronal cultures from dorsal root ganglia (DRG) serve as a useful tool in studies of mechanisms regulating pain signal transduction and in the development of pain therapeutics. However, a high number of experimental animals is required to produce those cultures. The aim of this work was to validate in-vitro systems that can serve as an alternative to DRG neuronal cultures. Hence, we investigated if neuroblastoma and immortalized DRG cell lines display structural and functional similarities to DRG neuronal cultures.

Results
B35, but not N2a or F11, cells displayed marked changes in morphology upon serum starvation and differentiation. Compared to cells in complete media, both serum starvation and differentiation resulted in a lower number of cells and lower mitochondrial metabolic activity in B35 and F11 cells. The opposite was observed for N2a cells. Tuj1, PGP9.5, NF200 and peripherin expression and IB4 signal were present in the three cell lines and in all three conditions, but at different levels. Undifferentiated N2a and F11 had the highest Tuj-1 expression. Undifferentiated N2a cells had the highest PGP9.5, NF200 and peripherin expression and IB4 signal. Compared to serum starvation, differentiating media was more effective increasing the expression of some of the markers. As expected, mRNA for the listed nociception-associated genes were found in the DRG neuronal culture. In the cell lines cultured in complete media, Scn8a and Scn9a, Cacna2d2, Cacna1b, P2xr3, Trpv1, TrkA, and MrgprD gene expression were detectable. Scn7a was only expressed in B35 cells and Scn10a was not detected in any of the three cell lines. Scn9a and MrgprD mRNA levels were similar in the three cell lines. Scn8a, Cacna1b, P2Xr3 and Trpv1 mRNA levels were higher in F11 and N2a cells while Cacna2d2 and TrkA mRNA levels were the highest in F11 cells. Calca1 gene expression was detected only in B35 and F11 cells, with no significant
differences between the two cell lines. Serum starvation had a more pronounced effect inducing the expression of some genes compared to differentiation media. Assessment of calcium flux in the cells in response to KCl application was used as a measure of cell functionality. While 90% of DRG neurons had a positive calcium signal, 66% of the F11 and 37% of the N2a cells, but no B35 cells, showed a response to KCl. The amplitude of response was not different between the F11 and N2a cell lines and was approximately 20% of the amplitude in DRG neurons.

**Conclusion**

In conclusion, of the three cell lines, the mouse neuroblastoma cell line N2a and the DRG/neuroblastoma hybrid cell line (F11) showed higher resemblance to DRG primary neuronal culture in the expression of sensory neuronal markers as well as ion channels and receptors. Functionally, F11 cells were the closest to DRG neurons. Hence, our data show the strongest support for the use of F11 cells as an auxiliary system to DRG neuronal cultures to study cellular pain mechanisms when applicable.
Title: Peripheral Inflammatory Hyperalgesia Depends On P2X7 Receptors Activation And Interleukin-1Beta Release From Rat Satellite Glial Cells In Drg

Poster Number PW0435

Authors
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Aim of Investigation
P2X7 receptors (P2X7R) expressed on immune cells and microglia have been shown to play an essential role in pain. However, the contribution of P2X7R on satellite glial cells (SGC) in dorsal root ganglia (DRG) is unknown. P2X7 receptors activation is essential to maturation and release of interleukin-1beta (IL-1β).

Inflammation in peripheral tissue leads to IL-1β upregulation in SGC. Therefore, the aim in this work was to investigate if peripheral inflammatory hyperalgesia depends on the activation of P2X7R and IL-1β release in DRG.

Results
The immunofluorescence of DRG cells demonstrated that P2X7R and IL-1β are co-stained in GS-immunoreactive cells, confirming their expression only by SGC. The treatment with ODN antisense in DRG against P2X7R demonstrated a significant antihyperalgesic effect (F=188.8; P<0.001; n=6/group) when compared to CFA-treated group. Also, P2X7R antisense significantly reduced CFA-induced upregulation of P2X7R relative expression (F=58.14; P<0.001; n=5/group). These results demonstrate that P2X7R activation participate in the development of peripheral inflammatory hyperalgesia. Assessing IL-1β release in LPS-stimulated SGC culture, P2X7R activation induced the release of IL-1β in the culture medium that was prevented by P2X7R blockage with A740003 (F=16.60; P<0.001; n=5/group). In addition, relative expression of IL-1β was upregulated almost 5-fold in CFA-treated groups. Thus, these results confirmed that the IL-1β released in DRG during peripheral tissue inflammation depends on P2X7R activation on SGC.

Conclusion
We demonstrated that P2X7R activation lead to IL-1β releasing from SGC in DRG during inflammation of peripheral tissue. As a result, IL-1β can directly enhance neuronal excitability by biding on interleukin-1
receptor 1 expressed on nociceptors and indirectly by activated pro-nociceptive mediators such as cyclooxygenases enzymes. Therefore, our work has provided evidences that P2X7R activation and IL-1β releasing in DRG during inflammatory stimuli contribute to hyperalgesia.
Title: Peripheral Neuroimmune Mechanisms In Non-Neuropathic Persistent Pain: A Systematic Review And Meta-Analysis

Poster Number PW0436

Authors
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Aim of Investigation
We conducted a systematic review of the literature to determine if non-neuropathic persistent pain is associated with peripheral neuroimmune mechanisms. In this preliminary report we report a subset of findings concerning the evidence that the conditions fibromyalgia, complex regional pain syndrome (CRPS), and vulvodynia are associated with local pathological changes in epithelial nerves.

Results
Fifteen studies were included in the systematic review. Of these, five studies were included in a meta-analysis of epidermal nerve density in FM, and two studies were included in a meta-analysis of epithelial nerve density in vulvodynia. FM was associated with a significantly decreased epidermal nerve fiber density (standardized mean difference (SMD) -0.75 [-1.02, -0.49], pooled n=150 cases and n=199 controls). Generally, the quality of studies was mixed; a number of risks of bias were identified, including the almost ubiquitous lack of clear blinding during the assessment of histological samples. Vulvodynia was not associated with a significant difference in epithelial nerve fiber density (SMD 3.64 [-0.07, 7.36] pooled n=19 cases and n=15 controls). These studies were judged as being at a high risk of bias, in particular on case representativeness and the definitions of controls. Data that could not be pooled in a meta-analysis suggest that fibromyalgia is associated with morphological nerve changes such as Schwann cell ballooning and a smaller diameter of small unmyelinated nerve fibers (2 studies; n=45 cases and n=29 controls), that vulvodynia is associated with an up-regulation of vanilloid type 1 receptors in peripheral nerve fibers (1 study, n=10 vulvodynia and n=8 controls), and that CRPS is also associated with a decrease in epidermal nerve fiber density (1 study, n=2 cases and n=5 'and additional control human finger skin'). All studies were rated as being at risk of bias on at least one criterion.
Conclusion
A small number of studies with a moderately high risk of bias provide evidence that fibromyalgia is associated with decreased epidermal nerve fiber density, though the evidence for similar changes in vulvodynia is inconclusive. There is limited evidence for a variety of other peripheral nerve changes. However, our findings suggest that there is a need for larger and more rigorous studies of these parameters across all three chronic pain conditions.
Title: Collagens Modulate Ngf-Induced Sensitization And Cgrp Expression Of Nociceptors – A Screening Approach On Primary Sensory Neurons

Poster Number PW0437

Authors
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Aim of Investigation
Many painful processes such as wounding, tumor development, and disc degeneration are accompanied by changes in the extracellular matrix (ECM). The impact of ECM proteins on e.g. neurite outgrowth of sensory neurons has been studied extensively. However, their influence on pain sensitization signaling remains to be studied in detail. We aimed to identify ECM proteins which alter sensitization signaling by monitoring baseline states and ligand-initiated phosphorylation kinetics of sensitization signaling components such as PKA and Erk1/2 in primary nociceptive neurons.

Results
Our screen analyzed for potential changes of 17 ECM proteins on nociceptor sensitization signaling. We tested for alterations in basal and ligand-induced (NGF-, GDNF-, 5-HT, and OSM) Erk1/2 or PKA phosphorylation levels at eight time points resulting in 398 tested conditions. We identified various members of the collagen family to specifically modulate NGF-induced amplitude of Erk1/2 but not of PKA kinetics. In contrast, none of the other tested ECM proteins altered basal Erk1/2 and/or PKA phosphorylation or 5-HT, OSM or GDNF induced Erk/PKA kinetics. Subgroup analysis in combination with ODE-MM excluded differential subgroup compositions to explain the observed Erk1/2 activation differences. In fact, immunocytochemistry revealed altered receptor and Erk1/2 expression in NGF-treated neurons on collagen coatings. Corroborating our signaling analysis results, we found that collagens elevate CGRP expression in sensory neurons.

Conclusion
By this first screen using a High-Content Screening microscopy approach on 950,000 primary sensory neurons for factors modulating sensitization signaling we identified collagens to increase specifically NGF-induced Erk1/2 pain sensitization signaling. Since collagens are especially upregulated or altered in
wounds, tumors and disc degeneration, our results suggest this specific group of extracellular matrix proteins to augment nociceptor sensitivity in these highly painful conditions. The observed effect on CGRP expression and thus most likely on CGRP secretion implies a positive feedback mechanism to surrounding cells.
Title: Using Microfluidic Cultures To Investigate Molecular Mechanisms Of Pain-Associated Hypersensitivity In Nociceptive Axons

Poster Number PW0438

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Aim of Investigation
Chronic pain is an unmet clinical challenge with significant impact on patients' quality of life. The lack of adequate novel efficacious analgesics is attributed to our limited understanding of the underlying mechanisms of chronic pain. Direct investigation of the nerve terminals and nociceptive axons, where the pain responses are initiated, has been difficult due to technical limitations. Moreover, our current knowledge of the molecular changes that take place in damaged or sensitized primary afferents is often based on extrapolation from observations made on the dorsal root ganglion (DRG) cell soma. Using a novel microfluidic based cell culture system, the aim of this project is to develop an in vitro model that recapitulates the maladaptation of the peripheral nerves following injury or inflammation and to understand the axonal mechanisms of peripheral hypersensitivity.

Results
DRG neurons from adult mice can be optimally maintained in microfluidic cultures for up to six days. Fluidically isolated axons were sensitized with treatment with inflammatory mediators for two minutes or two hours resulting in a significant increase in the calcium signal detected at the soma in response to axonal stimulation with 15mM potassium chloride (KCl). Axonal inflammatory sensitisation results in increase of the number of axons responding to KCl stimulation, as well as enhancement in the magnitude of the axonal responses to KCl. Interestingly, application of inflammatory mediators to the axonal compartment results in local increase in the axoplasmic calcium concentrations and potentially generation of action potentials. Hyperpolarization-activated cyclic nucleotide-gated (HCN) channels have recently been shown to be involved in the peripheral mechanisms of inflammatory and neuropathic pain hypersensitivity. Blockade of axonal HCN channels, with Zatebradine (a non-selective HCN blocker) reversed the inflammation-induced axonal sensitisation.
Conclusion
Our knowledge of changes in axonal function remain limited however, these cultures provide a platform via which to examine such changes in molecular detail. We show that fluidically isolated nociceptive axons are readily sensitized after localized inflammatory treatment, demonstrating increased responsiveness and reduction in activation threshold of primary afferents. We also found that HCN channels play an important role in inflammation-induced sensitisation of axons. This in vitro system enables the study of electrophysiological properties of isolated naïve and sensitized DRG axons as a model of pain-associated hypersensitivity.
Title: The Mechanism Of Sensitization Of Sensory Neurons By Macrophages Activated By Vgf-Derived Neuropeptide.

Poster Number PW0439

Authors
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Aim of Investigation
Immune cells have been shown to play a role not only in inflammatory pain, but also in neuropathic pain. Here we introduce VGF, a novel key player in neuro-immune crosstalk, and discuss the roles of immune cells, namely macrophages and microglia, in the development and maintenance of hypersensitivity in neuropathic pain. VGF (non-acronymic) is a neuropeptide precursor, upregulated in a number of neuropathic pain models. Our aim is to focus on the role of one of the VGF-derived peptides TLQP-21 and its receptor gC1qR in activation of macrophages, and subsequent sensitization mechanism of sensory neurons.

Results
In order to investigate the mechanism of hyper-sensitization of sensory neurons by the activated macrophages, we studied the effect of conditioned medium from TLQP-21 peptide-treated macrophages on the excitability of rat DRG neurons. The conditioned medium did not elicit membrane depolarization of DRG neurons by itself. However, the DRG neurons became more sensitized following the incubation with the conditioned medium, as a smaller stimulus which normally does not cause membrane excitation can now promote the excitation of the cells measured by intracellular calcium imaging. Gene expression analysis revealed upregulation of several cytokines and pro-inflammatory genes in macrophages by TLQP-21 treatment. We identified one of these cytokines which actually induced hypersensitivity of primary DRG neurons.

Conclusion
Upon nerve damage, VGF is generated and released from sensory neurons. One of the VGF derived peptides, TLQP-21, stimulate macrophages via its receptor gC1qR. The activated macrophages release certain cytokines which in turn sensitise sensory neurons. Our results demonstrated a two-way
interaction between sensory neurons and macrophages, and these interactions may contribute to onset of pain.
Title: Roles Of Extracellular Signal-Regulated Protein Kinase 2 (Erk2) In The Peripheral Nervous System For The Mechanism Of Pain Transmission

Poster Number PW0440

Authors

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Aim of Investigation
Accumulating evidence indicates that extracellular signal-regulated protein kinases play important roles in pain transmission mechanism. We previously reported that abrogation of ERK2, one of ERK isoform, in the central nervous system (CNS) caused aberrant sensitization to the inflammatory pain and alleviated alldynia in a mouse neuropathic pain model, indicating that ERK2 in the CNS plays important roles in pain transmission mechanism. On the other hand, the roles of ERK2 in the peripheral nervous system (PNS) for pain transmission mechanism is still largely unknown. The aim of this study is to elucidate the roles of ERK2 in the PNS for pain transmission mechanism, employing mice deficient for Erk2 especially in the dorsal root ganglion (DRG).

Results
In the PSNL model, Erk2CKO(PNS) mice exhibited normal mechanical alldynia and thermal alldynia comparable to control mice. Nociceptive response of Erk2CKO(PNS) mice following a formalin injection was significantly reduced in the second phase compared to control mice, indicating the aberrant sensitization in the formalin model of inflammatory pain.

Conclusion
These results suggest that ERK2 in the PNS plays an important role in the sensitization of inflammatory pain but not in the induction of neuropathic pain.
Aim of Investigation
Individual inflammatory mediators are known to have a profound effect on the excitability of primary sensory neurons and the secretory profile of non-neuronal cells. This process is known to be critical in the transition from acute pain to chronic pain states. However, in vivo, these mediators are not secreted in isolation but rather as a complex mixture of both pro- and anti-inflammatory molecules. Here we tested the hypothesis that additive or synergistic interactions exist between two pain-relevant mediators, nerve growth factor (NGF) and tumour necrosis factor (TNFα), and as such contribute to pain-relevant signalling in neuronal and/or non-neuronal cell types.

Results
Our results suggested a possible interaction of NGF and TNFα in several cell types. The HTRF assay showed that both NGF and TNFα activated phospho-p38 in PC-12 cells via non-redundant pathways, with possible synergistic actions seen in the co-treatment group. In a purified population of primary sensory neurons, a possible negative impact of TNFα on NGF-dependent neurite outgrowth was observed. Furthermore, qPCR revealed that TNFα may downregulate several NGF-induced genes, including NTRK1, SCN10a/11a and CALCA, whereas delayed administration of TNFα to NGF-treated cells initiated a possible additive effect. Finally in BMDM, qPCR revealed that TNFα and NGF interactions may also exist to drive expression of pain-relevant genes such as IL-10 and TNFα itself.

Conclusion
We observed evidence for a possible interaction between NGF and TNFα signalling. Further experiments are required to clarify this observation. Future work will continue to focus on the interaction of these two inflammatory mediators at both a signalling level and also at a more integrative level in a series of in vivo experiments. These preliminary data suggest that NGF and TNFα signalling interactions can occur in multiple cell types that may significantly contribute to the development of chronic pain.
states. This work has the potential to further our understanding of the basic signalling pathways associated with inflammatory mediators and chronic pain, a process crucial for the development of novel, effective, drug targets.
Title: Loss Of Mu Opioid Receptor Signaling In Nociceptors Abrogates Morphine Tolerance Without Disrupting Analgesic Efficacy

Poster Number PW0442

Authors
E. Sypek, G. Corder, V. Tawfik, D. Wang, S. Low, C. Sotoudeh, B. Barres, C. Bohlen, G. Scherrer

Aim of Investigation
Opioids remain the gold standard to treat severe pain, however efficacy decreases with use and this analgesic tolerance increases risk of transition to addiction, respiratory depression and a paradoxical pain state referred to as opioid-induced hyperalgesia (OIH). Whether the mechanisms underlying opioid analgesia are distinct and dissociable from those promoting deleterious side effects is currently unclear. We aim to identify the cell type and receptor responsible for the analgesic effects of morphine, to allow selective targeting of desirable outcomes.

Results
We confirm selective loss of MOR in dorsal root ganglion, with intact expression in spinal neurons. Knockout of MOR in nociceptors was sufficient to eliminate tolerance and OIH, as well as maladaptive opioid-induced long-term potentiation (LTP) between nociceptors and dorsal horn neurons. Importantly, MOR cKO mice display intact analgesia following systemic morphine, suggesting that MOR in nociceptors is dispensable for analgesia. Finally, we demonstrate that administration of a peripherally-restricted MOR antagonist prevents morphine tolerance and OIH without diminishing analgesia.

Conclusion
We conclude that MOR expressed on nociceptors initiates maladaptive processes that promote the development of tolerance and OIH. Collectively, our data support the development of strategies interfering with MOR function in peripheral nociceptors and their combination with opioid analgesics to stabilize morphine's antinociceptive efficacy during chronic treatment. This work was supported by the DoD National Defense Science & Engineering Graduate (NDSEG) Fellowship (E.S.), National Institutes of Health (NIH) Grant DA031777 (G.S.), the Rita Allen Foundation and American Pain Society Award in Pain (G.S.), NIH Postdoctoral Fellowship (G.C., T32DA035165-01), Foundation for Anesthesia Education and
Research (FAER) Mentored Research Training Grant (V.T.), NIH Postdoctoral Fellowship (D.W. T32GM089626), NIH R37 Grant (B.B., DA15043), and Damon Runyon Cancer Research Foundation Postdoctoral Fellowship (C.B.).
Title: Trpa1-Carrying C-Fibers Contribute To Cool And Noxious Cold Sensing In The Mouse

Poster Number: PW0443

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Aim of Investigation:
Previous research identified TRPM8 and TRPA1 as transducers of cold and noxious cold. TRPM8-deficient mice present overt deficits in the detection of environmental cool and TRPA1-deficient mice show clear deficits in assays quantifying noxious cold detection. However, mice lacking both TRPM8 and TRPA1 were described as indifferent from TRPM8-/- in cold avoidance based on results from a 2-temperature choice assay and by measurement of c-fos expression [Knowlton et al., 2010]. Nonetheless, our fMRI measurements in TRPA1-deficient mice evidence a contribution of TRPA1 to cold sensing at 15°C [Vetter et al., 2012]. The present study was designed to provide insight into the exact contribution of TRPA1 and TRPM8 to primary afferent cold detection.

Results:
We previously described that CC-fibers are very scarce in TRPM8-/- and that they suffer both static and dynamic encoding deficits [Toro et al., 2015]. In addition, TRPM8-/- largely lack the menthol-sensitive CMC-type nociceptors, but retain menthol-insensitive CMCH-type nociceptors in normal frequency [Zimmermann et al., 2011]. Due to the paucity and poor cold coding in TRPM8-/- we did not attempt to quantify CC-fibers. In contrast, an unbiased sampling of 36 mechanosensitive fibers in TRPM8/A1-/- revealed only 4 cold-sensitive fibers (2 CMCH, 2 CMC) that were repeatedly responsive to cold stimulation and 2 which responded only once to a cold stimulus. They fired 6.7±2.4 spikes per 60 s cold ramp. This is similar to the average response recorded from cold-sensitive nociceptors of TRPM8-/- (8.0±4.9 spikes per 60 s, n=16, in a sample of 54 fibers) and represents only about 20% of the response produced by TRPM8-expressing nociceptors probed positive for menthol sensitivity and recorded from skins of C57BL6J mice (34.6±4.1 spikes per 60 s cold ramp, n=16). The large lack of cold-sensitive nociceptors among the primary afferents of TRPM8/A1-/- in comparison to TRPM8-/-, 11% in comparison to 30%, corresponded to a much lower preferred temperature and a larger lack of cold...
avoidance of TRPM8/A1-deficient mice (n=20) in comparison to TRPM8/- (n=19) and C57BL6J (n=20) observed in our gradient assay. In that sense C57BL/6J mice required 13 min to spend 80% or more time in the warmer semicircle (i.e. above 17.5°C), TRPM8/- 21 min and TRPM8/A1/- at least 38 min. In addition, in the first 15 min of exposure, TRPM8/A1/- spent more time in the fields <15°C (representing 42% of the ring surface) than the other strains: 36% in contrast to 25% (TRPM8/-) and 19% (C57BL/6J). TRPA1-deficient mice however, showed no lack of cold avoidance and behaved like C57BL/6J mice in the gradient paradigm.

Conclusion
Both TRPM8 and TRPA1 are required for the detection of environmental cool and noxious cold and seem to represent complementary or synergistic cold transducers. TRPA1's contribution to cold sensing is less ostensible: lack of TRPA1 alone does not overtly affect thermal selection behavior, potentially because it affects CMCH-type fibers which fire at much lower rates than TRPM8-expressing CMCs. TRPA1's distinctive contribution to cold sensing becomes more apparent in the absence of TRPM8: TRPM8/A1-deficient mice have larger cold avoidance deficits that TRPM8/-
. Nevertheless, TRPM8/A1/- still judge warmer areas as preferable during late observation periods which may account for cold transduction by potassium channels supported by cooling-induced excitability increase. The circular thermal gradient device will be available for purchase through Ugo Basile Srl, Gemonio, Varese, Italy.
http://www.ugobasile.com/
Title: 5-HT3A Receptor Contributes To Mirror-Image Pain Induced By Co-Injection Of 5-HT And Acid Through Activation Of Satellite Glial Cells

Poster Number PW0444

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Aim of Investigation
Chronic pain has profound effects on personal life quality and the society. Understanding the mechanism of chronic pain is important for development of the new analgesic treatments. Serotonin (5-HT), acid, and prostaglandin E2 (PGE2) are well-known inflammatory mediators resulting in pain and hyperalgesia. Mirror-image pain (MIP) that occurs in associated with some clinic pain syndromes such as complex regional pain syndrome, rheumatoid arthritis, and chronic migraine, is characterized by increased pain sensitivity in non-injured or –inflamed sites. Several lines of evidence suggest that satellite glial cells (SGC) are important for developing mirror-image pain. We previously found that single administration of 5-HT or acid in mice hind paw induced unilateral and transient hyperalgesia, but co-injection of 5-HT and acid induced MIP. The results indicated that proton and serotonin receptors could be essential for development of MIP. However, it remains unclear which 5-HT or proton-sensing receptors mediate MIP. The objective of this research proposal is to explore involvement of 5-HT or proton-sensing receptors in MIP.

Results
The results showed that pretreatment of 5-HT3A antagonist, but not other antagonists of 5-HT receptor, inhibited contralateral hyperalgesia induced by co-injection of 5-HT and acid. Both immunohistochemistry and immunoblotting showed that satellite glia in DRG were activated after co-injection of 5-HT and acid and were inactivated by 5-HT3A antagonist pretreatment.

Conclusion
5-HT3A participates in mirror-image pain induced by co-injection of acid and 5-HT through regulation of glial cell activation.
Title: Analgesic Effects Of Menthol Through Inhibition Of Trpv1 Activation

Poster Number PW0445

Authors

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Aim of Investigation
Transient receptor potential vanilloid type 1 (TRPV1) is a nonselective cation channel that can be activated by noxious heat, low pH and vanilloid compounds such as capsaicin. Since TRPV1 acts as an integrator of painful stimuli, TRPV1 antagonists can be used for promising therapeutics as novel types of analgesics. TRPV1 antagonists such as capsazepine, BCTC and CTPC were reported to have an inhibitory effect on TRPM8, a cold receptor. In addition, ethanol has opposite effects on TRPV1 and TRPM8: it inhibits TRPM8 whereas potentiating the activity of TRPV1. These reports suggest that the effect of chemicals on TRPV1 and TRPM8 channels are intricately related each other. Menthol is used not only for analgesic balms but also for an additive for foods or oral hygiene products as a food preservative or oral analgesic with cooling sensation. In spite of its wide use, mechanisms of analgesic effect are not well understood. Although menthol, the most famous TRPM8 agonist, has been studied as an analgesic ingredient, its effect on TRPV1 has not been reported.

Results
In this study, we examined the effects of menthol on human TRPV1 (hTRPV1) using patch-clamp techniques with HEK293T cells expressing hTRPV1. The hTRPV1 currents induced by capsaicin were inhibited by menthol in a dose-dependent manner, with a half-maximal inhibitory concentration (IC50) of 1.17 mM. In addition, an in vivo sensory irritation test showed that menthol conferred an analgesic effect on the sensory irritation produced by VBE (vanillyl butyl ether), a TRPV1 agonist. Furthermore, we found that Y511, S512 and T550 of hTRPV1, which are binding sites of capsaicin, were little involved in the inhibitory effects by menthol. These data suggest that menthol interacts with sites different from those of capsaicin. This study shows that an analgesic effect of high-dose of menthol might be through its inhibition of hTRPV1 activity. We also examined effects of capsaicin on hTRPM8 using patch-clamp techniques with HEK293T cells expressing hTRPM8. The hTRPM8 currents induced by menthol were inhibited by capsaicin in a dose-dependent manner, with
IC<sub>50</sub> of 39.88 µM. Moreover, we found that Y745, which is a binding site of menthol, was slightly involved in the inhibitory effects by capsaicin.

**Conclusion**

Our findings suggest that capsaicin/VBE and menthol interact with both TRPV1 and TRPM8, respectively. The anti-nociceptive effects of menthol could be partially explained by this phenomenon.
Title: Differential Effects Of Paclitaxel And Platinum Derivatives On Primary Cultured Schwann Cells Are Involved In The Pathogenesis Of Peripheral Neuropathy

Poster Number PW0446

Authors
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Aim of Investigation
Chemotherapeutic agents such as taxanes and platinum derivatives frequently induce chemotherapy-induced peripheral neuropathy. Unfortunately, chemotherapy-induced peripheral neuropathy can become chronic, persisting for months or years even after the termination of chemotherapy, and is commonly refractory to current treatment strategies. It has been considered that the direct impairment of peripheral sensory neurons should be a major mechanism for the pathogenesis of persistent chemotherapy-induced peripheral neuropathy. However, these notions may not be sufficient to explain the mechanisms involving the developmental stage of chemotherapy-induced peripheral neuropathy. To address this issue, we focused on major supportive roles of Schwann cells in the maintenance of peripheral nerve systems, and evaluated the effects of anti-cancer agents on primary cultured rat Schwann cells.

Results
Treatment on primary cultured Schwann cells with either cisplatin (1 μM) or oxaliplatin (3 μM) induced cell toxicity accompanied with mitochondrial dysfunction even after the washout of each drug. By contrast, the treatment with paclitaxel (0.01 μM) to Schwann cells reverted to the immature state accompanied with its bipolar process retraction. After the washout of paclitaxel, immature Schwann cells differentiated into the mature state. The same treatment with each drug did not show any effect on primary cultured dorsal root ganglia neurons, whereas cell numbers and its dendritic trees decreased after the treatment with paclitaxel, cisplatin or oxaliplatin at higher concentration.
Conclusion
The present findings can explain different mechanisms of chemotherapy-induced peripheral neuropathy depending on classes of anti-cancer agents. Furthermore, we propose here that such diverse effects of anti-cancer agents on Schwann cells prior to induction of neurotoxicity are likely responsible for the disruption of reciprocal communication between myelin-forming mature Schwann cells and neural axons, and may closely related to the early step of the development of chemotherapy-induced peripheral neuropathy.
Date: 09/28/2016 03:15:00 PM

**Title:** In Vivo Patch−Clamp Analysis Of Knee Osteoarthritis Pain By Activation Of Trpv1

**Poster Number** PW0447

**Authors**

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**Aim of Investigation**
Osteoarthritis (OA) of knee is a common disease in the elderly, but the cellular mechanism of chronic pain in this disease has been unclear. Recently many reports have suggested that transient receptor potential vanilloid 1 (TRPV1) is involved in various kinds of persistent pain, including knee OA pain. In this study to clarify the mechanisms underlying knee OA pain, we analyzed the nociceptive signals from the knee joint by recording spontaneous excitatory postsynaptic currents (sEPSCs) in spinal dorsal horn neurons by in vivo patch-clamp technique.

**Results**
The average frequency and amplitude of sEPSCs in OA model rats were $18.3 \pm 2.5$ Hz and $18.0 \pm 2.5$ pA ($n = 53$), respectively. In comparison, those in normal rats model were $7.9 \pm 1.0$ Hz and $18.5 \pm 3.2$ pA ($n = 25$), respectively. The average frequency of sEPSC in OA model rats was significantly larger than that of normal rats ($P < 0.05$). Moreover, we analyzed sEPSCs at each spinal segment in normal and OA rats. At L3, L4 level the average frequency of sEPSCs in OA rats are significantly larger than normal rats. The significantly difference was found between L3 and L5 about the average frequency of sEPSCs in OA rats. Next, after the injection of a TRPV1 agonist, capsaicin into right knee of normal rats, sEPSC increase. But this effect was weak and had ended instantly. The capsaicin-induced increases of sEPSC frequency and amplitude in normal rats averaged $113.0 \pm 11.8\%$ and $104.9 \pm 4.3\%$ ($n = 10$), respectively. While in OA model rats sEPSC largely increased immediately after capsaicin injection and it had lasted for a long time. The capsaicin-induced increases of sEPSC frequency and amplitude averaged $247.5 \pm 44.2\%$ and $141.1 \pm 11.0\%$ ($n = 20$), respectively in OA model rats. These values were significantly larger than those in normal.
Conclusion
These results suggest that TRPV1 is an important contributor to OA pain enhancement. And TRPV1 could be the target of pain relief in the patients suffering from the persistent knee OA pain.
Title: Characterising Peripheral And Central Sensory Nerve Fibre Changes Associated With Paclitaxel-Induced Peripheral Neuropathy

Poster Number PW0448

Authors
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Aim of Investigation
Chemotherapy-induced peripheral neuropathy (CIPN) and associated neuropathic pain can severely affect the quality of life of cancer patients during and after treatment with drugs, such as Paclitaxel (an anti-tubulin chemotherapeutic). Current understanding of the mechanisms underpinning CIPN is limited and there are no effective treatment strategies. Here, we used a mouse model of Paclitaxel-induced peripheral neuropathy to examine neuropathic pain behaviour and characterise changes in sensory nerve fibres in the peripheral and central nervous system.

Results
Paclitaxel treatment induced mechanical allodynia in mice, peaking on day 13 and 16 post-1st injection. On day 13, we detected an increase in ATF-3 expression in DRG sensory neurons of Paclitaxel-treated mice compared to saline controls. The increased ATF-3 was found to be co-localised in NF200+ myelinated sensory neurons, but not in IB4+ and CGRP+ C-fibre neurons. However, proportions of NF200+, IB4+ and CGRP+ neurons remained unchanged. In the spinal cord, expression of IB4 and CGRP nerve terminals in lamina 1 and 2 region of the dorsal horn was reduced in Paclitaxel treated mice, compared to saline controls.

Conclusion
We observed damage to myelinated sensory neurons and a reduction in C-fibre nerve terminals in spinal cord lamina 1 and 2 at a peak stage of mechanical allodynia following Paclitaxel treatment. This may contribute to Paclitaxel-induced neuropathic pain.
Date: 09/28/2016 03:15:00 PM

Title: The Phospho-Rii Assay - A Novel Method To Screen Opioid Receptor Ligands In Sensory Neurons

Poster Number PW0449

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Aim of Investigation
The study of opioids and other inhibitory GPCRs on nociceptive neurons is hampered by the need to either express reporter proteins or to indirectly measure their effects on e.g. ion channel properties. Both procedures do not allow a broader screening on primary nociceptors. Recently, we found the cAMP-dependent protein kinase A (PKA) regulatory subunit RIIβ to be enriched in nociceptors. We also showed that phospho-RII immunoreactivity (pRII) represents an endogenous readout to quantify inflammatory mediator induced stimulatory GPCR signaling (Isensee et al., J Cell Sci, 2014). We now analyzed if this assay could be extended to study the balance of stimulatory and inhibitory GPCR signaling in sensory neurons at the single cell level.

Results
Fentanyl and also MOR- and KOR-specific agonists did not affect basal pRll levels, but dose-dependently inhibited the pRll response of 5-HT or PGI2, whereas DOR-specific agonists were not effective. The competitive OR-antagonist naltrexone reversed the inhibition by opioids. The effect of opioids on Fsk-induced pRll immunoreactivity was transient indicating rapid deactivation of opioid receptors. Single cell analysis identified that opioids were selectively acting on RIIβ-positive neurons.

Conclusion
We demonstrate that the pRll assay represents a novel approach to analyze the effect of analgesic substances such as opioids on sensory neurons on the single cell level. This allows to screen inhibitory patterns of opioid receptor isoform-specific agonists or combinations thereof after stimulation with relevant inflammatory mediators.
Date: 09/28/2016 09:30:00 AM

Title: Reduction Of The Action Potential Plateau By ω-Conotoxin In The Nociceptive Dorsal Root Ganglion Neurons Of Adult Rats

Poster Number PW0450

Authors
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Aim of Investigation
ω-Conotoxin, a constituent of the cone snail venom, inhibits N-type calcium channels and has a highly potent analgesic effect on chronic pain. It is thought that ω-conotoxin inhibits excitatory synaptic transmission from primary afferents to dorsal horn neurons in the spinal cord. Interestingly, ω-conotoxin selectively reduces the sensitivity of chronic pain but has little effect on acute pain and tactile sensation. To investigate the mechanism of this selective effect, dorsal root ganglion (DRG) neurons were classified into nociceptive and tactile types, and the effect of ω-conotoxin on their action potential shapes was examined.

Results
C-type HTM DRG neurons were characterized by a long action potential with a noticeable inflection on the falling phase (action potential plateau), whereas C-type LTM and Aδ-type LTM neurons were characterized by short action potentials. ω-Conotoxin MVIIA (1 µM) reduced the action potential plateau of C-type HTM neurons but had little effect on the action potential shape of C-type LTM and Aδ-type LTM neurons.

Conclusion
ω-Conotoxin MVIIA selectively reduced the action potential plateau of nociceptive neurons, suggesting that calcium influx during the action potential plateau causes the release of transmitters associated with chronic pain.
Title: Which Is The Best Evoked Potential Technique For Assessing The Nociceptive System? Preliminary Results Of A Neurophysiological Study In Healthy Humans

Poster Number PW0451

Authors
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Aim of Investigation
Laser evoked potentials (LEPs) and contact heat evoked potentials (CHEPs) are widely agreed method for investigating nociceptive system. Concentric electrodes (CE) have also recently been introduced to measure pain-related evoked potentials (PREPs) and, thereby, to assess nociceptive system in patients. Although some Authors have reported that low intensity CE stimulation, evoking pinprick sensation, selectively activates nociceptive fibres, the CE reliability in the assessment of nociceptive system is still unclear. In this study we aimed at verifying whether low and high intensity CE stimulation selectively activates nociceptive fibres. To do so we recorded LEPs, CHEPs and PREPs before and after capsaicin-induced skin denervation.

Results
While LEPs and CHEPs were suppressed after topical application of capsaicin, low and high intensity PREPs did not differ before and after capsaicin-induced skin denervation. The skin biopsy documented the skin denervation induced by the capsaicin plaster.

Conclusion
Our data indicate that both low and high intensity CE stimulation elicit PREPs after skin denervation, thus probably suggesting that the CE stimulation coactive non-nociceptive fibres.
Title: Cancer Chemotherapeutics In Early Life Alter Spinal Nociceptive Processing In The Adult

Poster Number PW0452

Authors
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Aim of Investigation
Cancer chemotherapy in early life is associated with increased pain, anxiety and depression in adulthood. We hypothesised that exposure to chemotherapeutics during postnatal development alter the maturation of spinal nociceptive pathways. Our aim was to determine the nature and extent of these changes.

Results
Treatment with cisplatin in the second postnatal week resulted in a significant reduction in both mechanical (P<0.001) and thermal (P<0.001) thresholds when compared to vehicle treated littermate controls. Cisplatin treatment did not result in any significant decrease in neuronal number in the dorsal horn (DH) but significant (P<0.0001) decreases in GFAP immunoreactivity were observed throughout this structure. There was a significant (P<0.05) increase in IBA1 staining in lamina V indicating activation of microglia within this deep structure. Patterns of peptidergic sensory neuron termination within superficial laminae were unaltered by cisplatin treatment but non-peptidergic innervation was significantly (P<0.001) increased. The NGF receptor TrkA immunoreactivity was significantly (P<0.0001) increased by cisplatin as were the numbers of peptidergic interneurons present in the DH (P<0.0001) and the myelinated fibre density in deep DH (P<0.0001).

Conclusion
Cancer chemotherapeutic treatment in early life significantly alters the structure and function of spinal nociceptive networks in later life. This changes explain the altered sensory and pain perceptual changes experienced by cancer survivors and indicate alterations in other central nervous system structures.
Title: The Stress Regulator Fkbp51 Drives Chronic Pain By Modulating Spinal Glucocorticoid Signaling

Poster Number PW0453

Authors
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Aim of Investigation
Our ability to treat chronic pain is currently limited and we need a better understanding of the neurobiology of pain states for more effective treatments. Here, we propose the protein FK506 binding protein 51 (FKBP51) as a new target for the treatment of chronic pain. FKBP51 is up-regulated after activation of the glucocorticoid receptor (GR) and modulates the stress response by antagonizing GR. Moreover, polymorphisms in FKBP51 are consistently associated with stress-related mood disorders. Our previous study has shown that the expression of FKBP51 in the dorsal horn increases after injury. Furthermore, polymorphisms in FKBP51 in humans influence the severity of pain symptoms experienced after trauma suggesting that FKBP51 could play a role in the development of chronic pain states. The aim of this project was to characterise the expression of FKBP51 in the rodent spinal cord and to investigate its role on pain processing.

Results
Immunohistochemistry analysis showed that FKBP51 was expressed exclusively in neurons in mouse dorsal horn and that FKBP51 colocalized with GR. Global deletion of FKBP51 did not affect acute nociception nor cutaneous mechanical and thermal thresholds. However, FKBP51 KO mice, as well as mice that received anti-FKBP51 siRNA intrathecally, showed reduced hypersensitivity in a number of chronic pain models. Crucially, the intrathecal injection of the specific FKBP51 inhibitor, SAFit2, reduced the severity of established pain states. Furthermore, motor functions were improved after SNI both in KO and in mice that received SAFit2 compared with WT and vehicle treated mice, respectively. Finally, KO mice had lower corticosterone levels than WT mice, in naïve and in persistent pain states, and injection of the GR antagonist mifepristone confirmed that glucocorticoid signalling was impaired in FKBP51 KO mice.
Conclusion
In conclusion, our study showed that FKBP51 regulates chronic pain by modulating glucocorticoid signalling and is a suitable target for the treatment of long-term pain states, opening the way for the development of new therapeutic strategies.
Title: Novel Peptides From Cerebellin-1 And Cerebellin-2 Induce Mechanical Hypersensitivity

Poster Number PW0454

Authors
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Aim of Investigation
Neuropeptides play important roles in peripheral and central pain signaling including formation, transmission and modulation of nociception. Limited work has been focused on unconditional characterization of neuropeptides in mouse spinal cord using mass spectrometry (MS). We have previously demonstrated that the atypical peptide desCER [des-Ser1]-cerebellin, originating from the precursor protein cerebellin 1 (CBLN1), is predominantly expressed in the dorsal horn of the spinal cord of naïve mice, and that intrathecal injection of desCER induces mechanical hypersensitivity in a dose-dependent manner. The current study was designed to further investigate the relative expression of other peptides derived from the cerebellin protein family (CBLN1-4) in naïve mouse spinal cord and to examine if they also have nociceptive properties in naïve mice.

Results
Using MS we identified and relatively quantified ten novel peptides originating from cerebellin precursor proteins CBLN1 (3 peptides), CBLN2 (3 peptides) and CBLN4 (4 peptides). Nine out of ten peptides displayed statistically significantly (p<0.05) higher expression levels (200-600%) in the dorsal horn compared to the ventral horn. Intrathecal injection of 2 of the 3 CBLN1 and 1 of the 3 CBLN2 derived peptides evoked mechanical hypersensitivity in mice during the first 6 hours post-injection compared to saline injected mice (p<0.01, n=8/group). Withdrawal thresholds returned to baseline 24 hours after peptide injection. None of the four CBLN4 derived peptides induced mechanical hypersensitivity.

Conclusion
This study demonstrated that high performance MS is an effective tool for detecting novel neuropeptides in CNS tissues. Here we provide support for our previous findings and demonstrate that atypical peptides originating from not only the CBLN1 but also CBLN2 and CBLN4 precursor proteins are predominantly expressed in the mouse dorsal horn compared to the ventral horn. Importantly, we found that not all CBLN derived peptides induce pain-like behavior upon intrathecal injection, but that
this property is restricted to CBLN1 and CBLN2 derived peptides. Thus, our study has defined CBLN1 and CBLN2 derived peptides as novel pain-associated peptides present in the spinal dorsal horn. Ongoing experiments are aimed at investigating the mechanisms by which CBLN1 and CBLN2 derived peptides modulate nociceptive signal transmission as this may represent novel pathways in pain transmission.
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Title: Interleukin-18 Produced By Spinal Microglia Is Involved In Herpetic Alldynia In Mice

Poster Number PW0455

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Aim of Investigation
Patients with herpes zoster suffer from severe pain such as alldynia. However, the underlying mechanisms are still unclear. Recent studies have shown that spinal interleukin-18 (IL-18) contributes to neuropathic pain. In this study, we examined whether spinal IL-18 was involved in herpetic alldynia.

Results
An inoculation of HSV-1 elicited dynamic alldynia in the plantar region of the hind paw, an affected dermatome; it became apparent in some mice on day 3 after the inoculation, was obvious in all inoculated mice on day 7. The dynamic alldynia was inhibited by intrathecal anti-IL-18 neutralizing antibody. Immunoreactivities to IL-18 and the receptor in the dorsal spinal cord were increased by HSV-1 inoculation. In addition, the expressions of IL-18 and the receptor were detected in microglia and T cells, respectively, in spinal cord of mice infected with HSV-1, but not naïve mice. Neutralization of IL-18 decreased the number of T cells in the dorsal spinal cord. T cell recruitment inhibitor also suppressed HSV-1-induced dynamic alldynia.

Conclusion
These results suggest that IL-18 released from microglia plays an important role to infiltration of T cells contributed to herpetic alldynia.
Title: Spinal Astrocyte Activation Triggered By Pacap-Pac1 Receptor Signaling Pathway Contributes To Both Induction And Maintenance Of Long-Lasting Mechanical Allodynia

Poster Number PW0456

Authors
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Aim of Investigation
Pituitary adenylate cyclase activating polypeptide (PACAP) is a pleiotropic neuropeptide, which functions as a neurotransmitter, neuromodulator or hypothalamic hormone. There are three distinct G protein-coupled PACAP receptors, PACAP-specific receptor, PAC1 and PACAP/vasoactive intestinal polypeptide (VIP)-common receptor, VPAC1 and VAPC2. PACAP is present in spinal dorsal horn and dorsal root ganglia, and PAC1 receptor also exists in spinal dorsal horn, suggesting that PACAP-PAC1 receptor signaling could play an important role in the modulation of spinal nociceptive transmission. However, the functional significance of PAC1 receptor and its downstream signaling mechanism still remain to be clarified. We have previously reported that a single intrathecal (i.t.) injection of PACAP or PAC1 receptor selective agonist, maxadilan, in mice induced dose-dependent spontaneous aversive behaviors, such as licking, biting and scratching directed toward the caudal part of body for more than 1 hour, and suggested that activation of spinal PAC1 receptor induces the prolonged aversive responses through the interaction between neurons and astrocytes. To further address the nature of the PAC1 receptor-mediated nociceptive responses, we examined whether the single i.t. administration of PACAP or maxadilan would affect evoked-nociceptive behaviors by measuring hindpaw mechanical and thermal thresholds in mice.

Results
A single i.t. administration of PACAP or maxadilan, but not that of VIP, induced long-lasting hindpaw mechanical allodynia in mice, which started at day 1 and was maintained at day 84 without affecting thermal nociceptive threshold. Induction of this long-lasting mechanical allodynia was almost completely inhibited by the i.t. pretreatment of max.d.4, a PAC1 specific antagonist. Intriguingly, we found that single i.t. injection of PACAP or maxadilan induced rapid and persistent upregulation of an astrocyte marker, glial fibrillary acidic protein expression (GFAP), which started at 30 min after the injection and was also maintained at day 84. Thus, we then examined whether spinal astrocytic
activation contributes to development and/or maintenance of the PAC1 receptor-induced mechanical allodynia. I.t. co-administration of L-α-amino adipate (AA), an astroglial inhibitor, with PACAP/maxadilan almost completely prevented the induction of mechanical allodynia. Moreover, i.t. injection of L-α-AA at day 84 transiently reversed the mechanical allodynia. Immunoblot analysis further suggested that L-α-AA decreased the elevated expression of GFAP to control level. In addition, the development of PACAP/maxadilan-induced mechanical allodynia was inhibited by i.t. co-administration with PD98059, a MAP kinase/extracellular signal-regulated kinase (ERK) kinase inhibitor or SP600125, a c-Jun N-terminal kinase (JNK) inhibitor.

**Conclusion**
These finding suggest that spinal PACAP-PAC1 receptor system activates ERK and JNK signaling pathway to induce mechanical allodynia, and that spinal astroglial activation contributes to both induction and maintenance of the PAC1 receptor-triggered long-term mechanical allodynia.
Title: Expression Of Anti-Inflammatory Cytokine Interleukin 4 And Its Receptor In Dorsal Horn Of Neuropathic Pain Model Rats

Poster Number PW0457

Authors
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Aim of Investigation
The aim of this study was to investigate the expression and role of the anti-inflammatory cytokine IL4 in the spinal cord of neuropathic pain model rats.

Results
In the spinal cord of SNI rats, we could not detect expression of IL4 mRNA both in dorsal root ganglia and spinal cord. In contrast RT-PCR revealed that peripheral nerve injury increased the expression of IL4-R mRNA in spinal cord. The increase of the IL4-R mRNA began from 12 hours, peaked at 48 hours and continued for at least 14 days after nerve injury. ISH showed that nerve injury increased the IL4-R mRNA positive cells in the dorsal horn ipsilateral to the injury. In the double labeling analysis of ISH with immunohistochemistry, we detected IL4-R mRNA positive signals exclusively in the Iba1 immunolabeled microglia in the dorsal horn of SNI rats. Intrathecal administration of IL4 suppressed mechanical hypersensitivity of hind paw of SNI model rats.

Conclusion
These results suggest that activated microglia in spinal cord has endogenous regulatory systems that reduce inflammatory responses. Utilizing these anti-nociceptive mechanisms may provide novel therapeutic strategy for neuropathic pain.
Title: Activated Microglia Produce Arachidonic Acid In The Dorsal Horn After Spared Nerve Injury.

Poster Number PW0458

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Aim of Investigation
To reveal the mechanism of neuropathic pain, several genotic or proteomic approach have been made. However there are only few studies revealing from a lipidomic point of view. Imaging mass spectrometry (IMS) is an established method that allows visualization of a wide range of metabolites with high sensitivity and spatial resolution. IMS can be used to visualize the distribution of phospholipids in injured CNS tissues such as spinal cord injury. Here we aimed to identify spatiotemporal alteration of phosphatidylcholine (PC) in the dorsal horn after spared nerve injury (SNI) by utilizing IMS.

Results
The SNI mice (n=6) developed a marked hypersensitivity to innocuous mechanical von Frey filament stimulation. In mice receiving SNI, arachidonic acid (AA) containing PC; PC (diacyl-16:0/20:4) showed apparent increase in the ipsilateral dorsal horn compared with contralateral side 7 days after SNI. Immunochemistry analysis showed increased intensity of Iba-1 positive cells in the ipsilateral dorsal horn from 3 days after SNI, while the intensity of GFAP showed no specific changes in the spinal cord throughout the period of investigation. In comparison with the distribution pattern of PC (diacyl-16:0/20:4) and glia cells in the dorsal horn 7 days after SNI, PC change resembled the changes of microglia. Minocycline injection attenuated both hypersensitivity and this PC (diacyl-16:0/20:4) elevation in the ipsilateral dorsal horn after SNI.

Conclusion
Using IMS, we visualized the AA containing PC (diacyl-16:0/20:4) and observed that the PC was increased in the ipsilateral superficial dorsal horn 7 days after SNI. The alteration was related to the microglial activities and the suppression of microglia by minocycline administration suppressed the
regulation. The PC (diacyl-16:0/20:4) located in the cell membrane of microglia are considered to be the precursor of AA and PG via AA metabolism which lead to the development and maintenance of neuropathic pain.
Title: Involvement Of Spinal Cyr61 In Pac1 Receptor-Mediated Long-Term Mechanical Allodynia In Mice.

Poster Number PW0459

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Aim of Investigation
Pituitary adenylate cyclase activating polypeptide (PACAP) is a pleiotropic neuropeptide, which functions as a neurotransmitter, neuromodulator or hypothalamic hormone. There are three distinct G protein-coupled receptors, PAC1, VPAC1 and VAPC2. Recently, we found that intrathecal injection of PACAP or maxadilan, a selective PAC1 receptor agonist, in mice induces long-term mechanical allodynia which persisted at least 84 days, suggesting the major roles of PAC1 receptor in the induction of mechanical allodynia. To clarify the mechanisms of PAC1 receptor-mediated long-lasting allodynia, a genome-wide microarray analysis was carried out to find genes showing significant increase in expression in the spinal cord after intrathecal injection of maxadilan. As a result, the expression of Cyr61 (Cysteine-rich protein 61), a multifunctional matricellular protein secreted by various types of cells, was significantly increased after maxadilan treatment. At present, the involvement of Cyr61 to allodynia has not been reported. Therefore, in this study, we examined the role of Cyr61 in PAC1 receptor-mediated long-term allodynia.

Results
Intrathecal PACAP and Maxadilan markedly increased the Cyr61 mRNA expression in the spinal cord. Maxadilan-induced upregulation of Cyr61 mRNA was significantly inhibited by the max.d.4, a specific antagonist of PAC1 receptor. Intrathecal injection of recombinant Cyr61 protein (rCyr61,50 ng) induced mechanical allodynia in mice which was lasted at least for 3 days. In C6 glioma and NG108-15 cells, the stimulation of rCyr61 dose-dependently increased the expression of MCP-1 (CCL2) mRNA, a chemokine reported to be involved in alldonic responses. Intrathecal injection of rCyr61 also increased the expression of MCP-1 mRNA in the spinal dorsal horn.

Conclusion
In this study, we found for the first time that intrathecal Cyr61 induces mechanical allodynia in mice. Our present results suggest that the production of MCP-1 by Cyr61 in astrocyte and/or neuron is involved in part in the PAC1 receptor-triggered long-term mechanical allodynia.
Title: A Brainstem-Spinal Cord Disynaptic Inhibitory Circuit For Pain Control By Gaba And Endogenous Opioids

Poster Number PW0460

Authors
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Aim of Investigation
The spinal cord dorsal horn integrates information both from sensory neurons and the brain to shape pain experience. Specifically, a population of brainstem neurons in the rostral ventromedial medulla (RVM) projects directly to the dorsal horn to facilitate or inhibit nociception as a function of emotional and internal states. This process is known as the descending control of pain. Previous studies have shown that endogenous opioids are integral to the brain's ability to modulate pain thresholds via descending neural pathways. Identification of neurons expressing endogenous opioid peptides revealed that enkephalins are present within these circuits with marked abundance in the spinal cord. The analgesic properties of exogenous enkephalins are well established; however, the precise identity of the cells that produce enkephalins within the dorsal horn, the circuits that control their release and the neurons on which they act to modulate pain are unknown. The aim of this investigation is to characterize the function of endogenous enkephalins in the spinal cord as well as the mechanisms and neuronal circuit controlling their release.

Results
Using viral tracing and electrophysiology we identify a disynaptic brainstem-spinal cord circuit in which enkephalins modulate neural activity and control pain. We demonstrate that spinal enkephalinergic interneurons gate primary afferent inputs through temporally-coordinated presynaptic inhibition by enkephalins and GABA. Furthermore, activity of spinal enkephalinergic neurons is inhibited by a population of GABAergic neurons in the rostral ventromedial medulla.

Conclusion
Our results identify the key components of a circuit and the molecular steps by which activity in the
brain can cause pain facilitation at the level of the spinal cord by controlling spinal endogenous opioid levels.
Aim of Investigation
Peripheral nerve injury induces proliferation of microglia in the spinal cord, which can contribute to neuropathic pain conditions. However, candidate molecules for proliferation of spinal microglia after injury in rats remain unclear. We focused on the colony-stimulating factors (CSFs) and interleukin-34 (IL-34) that are involved in the proliferation of the mononuclear phagocyte lineage.

Results
We examined the expression of mRNAs for macrophage-CSF (M-CSF), granulocyte macrophage-CSF (GM-CSF), granulocyte-CSF (G-CSF) and IL-34 in the dorsal root ganglion (DRG) and spinal cord after SNI in rats. RT-PCR and ISHH revealed that M-CSF and IL-34, but not GM- or G-CSF, mRNAs were constitutively expressed in the DRG, and M-CSF robustly increased in injured-DRG neurons. M-CSF receptor mRNA was expressed in naive rats and increased in spinal microglia following SNI. Intrathecal injection of M-CSF receptor inhibitor partially but significantly reversed the proliferation of spinal microglia and mechanical allodynia induced by SNI. Furthermore, intrathecal injection of recombinant M-CSF induced microglial proliferation and mechanical allodynia.

Conclusion
We demonstrate that M-CSF is a candidate molecule derived from primary afferents that induces proliferation of microglia in the spinal cord and leads to neuropathic pain after peripheral nerve injury in rats.
Aim of Investigation
Transient receptor potentials (TRPs), non-selective cation channels, are expressed in a dorsal root ganglion (DRG) neuron that transmits nociceptive information to the spinal dorsal horn from the periphery. TRPs expressed in the peripheral terminal of the DRG neuron receive nociceptive stimuli given to the periphery while TRPs in its central terminal play a role in modulating nociceptive transmission. The central terminal TRPs located in the spinal dorsal horn lamina II (substantia gelatinosa, SG), which plays a pivotal role in regulating nociceptive transmission, are activated by various plant-derived chemicals including capsaicin, allyl isothiocyanate and menthol in <i>in vitro</i> spinal cord slice preparations. We have previously suggested that the peripheral and central terminal TRPs may be different in properties from each other. Although stereoisomers are known to modulate ion channels in a manner different from each other, it remains to be addressed whether this is so for TRPs. In order to know more about the central terminal TRPs, we examined the effects of stereoisomers on glutamatergic spontaneous excitatory transmission in SG neurons.

Results
All of the drugs increased sEPSC frequency in a reversible and concentration-dependent manner. EC<sub>50</sub> values for the activities of carvacrol, thymol, (-)-carvone, (+)-carvone, 1,8-cineole and 1,4-cineole were 0.69, 0.18, 0.70, 0.72, 3.2 and 0.42 mM, respectively. The (-)-carvone and 1,4-cineole but not (+)-carvone, 1,8-cineole, carvacrol and thymol effects were inhibited by a TRPV1 antagonist capsazepine. On the other hand, the (+)-carvone 1,8-cineole, carvacrol and thymol but not (-)-carvone and 1,4-cineole effects were inhibited by a TRPA1 antagonist HC-030031. The thymol, 1,8-cineole and 1,4-cineole activities were not affected by a TRPM8 antagonist BCTC.
Conclusion
These results indicate that (1) both carvacrol and thymol activate TRPA1, albeit the latter is more effective by about 4-fold than the former, (2) (-)-carvone and (+)-carvone activate TRPV1 and TRPA1, respectively, with almost the same efficacy, and (3) 1,8-cineole and 1,4-cineole activate TRPA1 and TRPV1, respectively; the efficacy of the former activation is about 10-fold less than the latter one. All of the activations result in an increase in spontaneous L-glutamate release onto SG neurons. The difference in TRP activation between the stereoisomers may serve to know the properties of the central terminal TRPs involved in the modulation of nociceptive transmission in the SG.
Title: Annexin A2 In Primary Afferents Contributes To Neuropathic Pain Associated With Tissue Type Plasminogen Activator

Poster Number PW0463

Authors
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Aim of Investigation
Annexin A2 (ANX2) is known as the binding protein of tissue type plasminogen activator (tPA) and exert the proteolytic activity of tPA. The recent findings reported that ANX2 is involved in plastic changes such as learning and neuronal activities. Here we examined the expression of ANX2 in the dorsal root gangliae (DRG) and dorsal horn of spinal cord following peripheral nerve injury.

Results
Peripheral nerve injury increased ANX2 mRNA level in DRG. With in situ hybridization, ANX2 mRNA was detected in most of DRG neurons. Immunohistochemistry revealed that the ANX2 protein level was very low in large size neurons. In contrast, high levels of ANX2 immunoreactivities were detected on the membrane of the small size neuronal cell somata and seemly on the terminal in laminae I-II of the spinal cord. Experimental inhibition of ANX2 and tPA interaction by intrathecal administration of homocysteine significantly prevented and reversed SNI-induced mechanical allodynia. Thus, alterations of ANX2 may be involved in tPA-dependent plasticity after peripheral nerve injury and have an important role in neuropathic pain.

Conclusion
These results suggest that the alterations of ANX2 may be involved in tPA-dependent plasticity after peripheral nerve injury and have an important role in neuropathic pain.
Title: Expression Of The Pge2 Synthases And Receptors In Spinal Cord Following Peripheral Nerve Injury

Poster Number PW0464

Authors
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Aim of Investigation
Prostaglandins (PGs) are lipid mediators derived from arachidonic acid by the cyclooxygenase (COX) pathway. In particularly, it is known that PGE2 has potent inflammatory effects in peripheral and central nerve systems and is involved in inflammation, fever and pain. PGE2 is synthesized by three types of prostaglandin E synthases (mPGES-1, mPGES-2 and cPGES) and it activates EP receptors (EP1-4). Whereas the function of PGE2 in spinal cord after peripheral nerve injury is well studied, the detailed distribution of these synthases and receptors in spinal cord remains obscure.

Results
RT-PCR revealed that nerve injury significantly increased the expression of mPGES-1 mRNAs in the ipsilateral spinal cord from 1d and peaked at 2d after SNI. Peripheral nerve injury did not affect on the expression of mPGES-2 and cPGES mRNAs. ISHH revealed that endothelial cells expressed the high levels of mPGES-1 mRNAs in the ipsilateral spinal cord at 1d after SNI. The results of double labeling of ISHH with immunohistochemistry showed co-localization of mPGES-1 in COX-2 immunoreactive vascular endothelial cells. In contrast to the mPGES-1, spinal neurons expressed mPGES-2 and cPGES mRNAs in naive and SNI model rats. RT-PCR analysis showed that SNI significantly increased EP3 and EP4 mRNAs in spinal cord, but did not EP1 and EP2. ISHH revealed that spinal neurons expressed all of PGE2 receptors in dorsal horn. Next, we investigated whether the TNF-alpha is involved in the induction of mPGES-1. Intrathecal injection of TNF-alpha induced mPGES-1 mRNA in blood vessels of spinal cord. In addition intrathecal injection of neutral antibody of TNF-alpha partially inhibited nerve injury-induced mPGES-1 in blood vessels.

Conclusion
These results indicated that the PGE2 was synthesized in endothelial cells by COX-2/mPGES-1 pathway and was regulated by TNF-alpha after peripheral nerve injury.
Title: Neuronal Aromatase Expression In Spinal Cord And Trigeminal Nucleus Caudalis Suggests Local Estrogen Synthesis Contributes To Pain Processing

Poster Number PW0465

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Aim of Investigation
In both acute and chronic pain conditions, women tend to be more sensitive than men. Although estrogens, such as estradiol, may underlie this sex difference, whether estrogen is pro- or anti-nociceptive is unclear. Estrogen's effects presumably depend on the pain model used, how hormone levels are manipulated, and where the hormone acts. For example, the superficial dorsal horn contains a large number of estrogen receptor α (ERα)-positive neurons and several groups report that estrogen in the spinal cord is pro-nociceptive. Moreover, these authors propose that the spinal cord itself locally synthesizes this estrogen. To address a potential cellular source of local estrogen, here we examined the expression of aromatase, the enzyme that catalyzes the conversion of testosterone to estradiol. Our studies focused on primary afferent neurons and on their central targets in the spinal cord and brainstem as well as in the nucleus of the solitary tract, the target of nodose ganglion-derived visceral afferents.

Results
Aromatase is expressed by neurons in laminae I and V of the Sp5c and spinal cord and in the NTS, but is not detectable in the TG or DRG. On average, we observed 50 cells per section in the Sp5c, 7 in spinal cord dorsal horn, and 10 in the NTS. Males and females showed similar numbers of aromatase-expressing cells in all areas examined. In addition, approximately 80% of aromatase neurons overlap with Pax2, but not with sst2A or with retrogradely labeled spino-parabrachial projection neurons. These findings indicate that the aromatase-expressing cells comprise a distinct subset of GABAergic interneurons. Lastly, in contrast to previous reports, we found no change in aromatase expression in DRG or spinal cord 7 days after peripheral nerve injury.

Conclusion
We have identified a unique subpopulation of inhibitory interneurons that produce aromatase, a key
enzyme for estrogen synthesis. Given that many neurons in lamina II of the dorsal horn express ERα, the aromatase-expressing cells in laminae I and V are ideally positioned to generate estrogen that engages local receptors. The lack of sexual dimorphism in spinal and brainstem aromatase expression and absence of injury-induced changes suggests that factors other than the quantity of cells regulate estrogen-related sex differences in pain. Nonetheless, the aromatase neurons may be critical to our understanding of this phenomenon. In fact, the heavy concentration of aromatase-expressing cells in spinal trigeminal nucleus pars caudalis could be especially relevant to pain disorders that affect the face and head, such as temporomandibular joint disorder and migraine, which have a marked female prevalence. Consequently, our characterization of these cells opens the door to further explorations of their circuitry and signaling mechanisms to uncover how they may influence pain.
**Title**: The Involvement Of Medullary Dorsal Horn 5-HT3A Receptors In Enhanced Synaptic Transmission And Plasticity Underlying The Maintenance Of Neuropathic Pain

**Poster Number** PW0466

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**Aim of Investigation**
Our recent studies have demonstrated a critical role of 5-HT-dependent descending facilitation from rostral ventromedial medulla (RVM) and the involvement of medullary dorsal horn 5-HT3A receptors (5-HT3ARs) in the maintenance of neuropathic pain. However, it is not clear how 5-HT/5-HT3AR system modulates synaptic nociceptive transmission and mediates long-lasting synaptic plasticity in the spinal or trigeminal dorsal horn during the maintenance of neuropathic pain conditions. In this study, we investigated the trigeminal mechanisms of 5-HT-dependent descending facilitation underlying orofacial pain after nerve injury.

**Results**
Bath application of exogenous 5-HT (10 μM) significantly increased both the frequency and amplitude of spontaneous excitatory postsynaptic currents (sEPSCs) in SG neurons of the Vc slices from mice with CCI-ION 14d but not in naïve mice. Depletion of 5-HT in the RVM significantly attenuated CCI-induced increase of both the frequency and amplitude of sEPSCs in mice at 14 d after CCI-ION but not in naïve mice. Although Western Blot analysis demonstrated a long-lasting upregulation of 5-HT3AR expression in the ipsilateral Vc tissue at 3-14d after CCI, the CCI-induced increase of the frequency but not the amplitude of sEPSCs was partially blocked by the 5-HT3AR antagonist Y25130 (5 μM). Next, we examined changes of evoked monosynaptic excitatory postsynaptic currents (eEPSCs) in SG neurons induced by electrically stimulating Aδ or C fibers (0.1 ms, 150-500 μA) at its attached trigeminal dorsal root or its entrance zone. Bath application of exogenous 5-HT (10 μM) significantly decreased the amplitude of eEPSCs in SG neurons of Vc slices from naïve mice but showed less inhibition in injured mice at 14d after CCI. In addition, a lower dose of 5-HT (0.1 μM) had no effects on the amplitude of eEPSCs in naïve mice but slightly increased the amplitude of eEPSCs in CCI 14d mice. Furthermore,
repetitive application with presynaptic stimulation paired with postsynaptic depolarization induced long-term potentiation (LTP) of the synaptic response lasting for at least 1 hour. Pretreatment with Y25130 (5 μM) in Vc slices partially blocked the induction of LTP in mice at 14d after CCI.

**Conclusion**
Together with our previous studies, these findings indicate that disinhibition or facilitatory action of 5-HT and upregulation of dorsal horn 5-HT3AR expression occur in the Vc under neuropathic pain conditions. Hyperactivity of presynaptic 5-HT3ARs on central terminals of primary afferents in the Vc after CCI-ION may be implicated in central mechanisms underlying 5-HT-dependent descending facilitation by maintaining enhanced excitatory presynaptic input and dorsal horn hyperexcitability during persistent neuropathic pain.
**Title:** Patch-Clamp Analysis Of Reactive Oxygen Species Actions On Excitatory Synaptic Transmission In Spinal Substantia Gelatinosa Neurons

**Poster Number** PW0467

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**Aim of Investigation**
Central neuropathic pain (CNP) in the spinal cord, such as chronic pain after spinal cord injury (SCI), is an incurable ailment. However, little is known about the spinal cord mechanisms underlying CNP. Recently, reactive oxygen species (ROS) have been recognized to play an important role in CNP of the spinal cord. However, it is unclear how ROS affect synaptic transmission in the dorsal horn of the spinal cord. To clarify how ROS impact on synaptic transmission, we investigated the effects of ROS on synaptic transmission in rat spinal cord substantia gelatinosa (SG) neurons using whole-cell patch-clamp recordings.

**Results**
Administration of tert-butyl hydroperoxide (t-BOOH), an ROS donor, into the spinal cord markedly increased the frequency and amplitude of spontaneous excitatory postsynaptic currents (sEPSCs) in SG neurons. This t-BOOH induced enhancement was not suppressed by the Na+ channel blocker tetrodotoxin. However, in the presence of a non-N-methyl-D-aspartate glutamate receptor antagonist, 6-cyano-7-nitroquinoxaline-2, 3-dione, t-BOOH did not generate any sEPSCs. Furthermore, in the presence of a transient receptor potential ankyrin 1 (TRPA1) channel antagonist (HC-030031) or a transient receptor potential vanilloid 1 (TRPV1) channel antagonist (capsazepine or AMG9810), the t-BOOH-induced increase in the frequency of sEPSCs was inhibited.

**Conclusion**
ROS enhance the spontaneous release of glutamate from presynaptic terminals onto SG neurons through TRPA1 and TRPV1 channel activation. Excessive activation of these ion channels by ROS may induce central sensitization in the spinal cord and result in chronic pain such as that following SCI.
Title: Electrophysiological Analysis Of Local Anesthetic Actions On Nociceptive Synaptic Transmission In The Adult Rat Spinal Cord.

Poster Number PW0468

Authors
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Aim of Investigation
Although single S(-) enantiomers of local anesthetics have less toxic effect on the cardiovascular and central nervous systems, their analgesic action on nociceptive transmission is not fully understood. In this study, we examined the effects of the S(-) enantiomer, levobupivacaine and R(+) bupivacaine on excitatory synaptic responses in spinal dorsal horn neurons evoked by mechanical stimulation, and on action potentials (APs) in dorsal root ganglion (DRG) neurons generated by dorsal root stimulation.

Results
Under voltage-clamp conditions, all spinal dorsal horn neurons tested exhibited spontaneous excitatory postsynaptic currents (EPSCs). Levobupivacaine reversibly suppressed the frequency and amplitude of pinch-evoked EPSCs. However, the same concentration of levobupivacaine had little effect on touch-evoked EPSCs. On the contrary, R(+) bupivacaine equally suppressed the frequency and amplitude of pinch- and touch-evoked EPSCs. All of these local anesthetics did not change the frequency and amplitude of miniature (spontaneous) EPSCs. In DRG neurons, the amplitude of APs were reversibly blocked by the local anesthetics. The half-maximum inhibitory concentrations (IC50s) of R(+) bupivacaine for Aβ, Aδ and C DRG neurons were almost equal. However, the IC50s of levobupivacaine was lower for Aδ and C DRG neurons than that for Aβ neurons. In addition, R(+) bupivacaine was almost equally inhibited TTX-resistant and TTX-sensitive Na+ currents. On the contrary, levobupivacaine suppressed TTX-resistant but not TTX-sensitive Na+ currents.

Conclusion
The present results suggest that pure S(-) enantiomers especially levobupivacaine are capable of effectively inhibiting noxious responses in the spinal dorsal horn mediated by Aδ and C afferent fibers.
Title: Nociceptin/Orphanin Fq-Induced Allodynia Via C-Jun N-Terminal Kinase And Monocyte Chemoattractant Protein-1 In The Spinal Cord

Poster Number PW0469

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Aim of Investigation
Intrathecal administration of nociceptin/orphanin FQ (N/OFQ), an endogenous ligand for the orphan opioid receptor-like receptor, at fmol range induces touch-evoked allodynia. N/OFQ has been implicated in multiple signaling pathways, such as the inhibition of cyclic AMP production and mitogen-activated protein kinase (MAPK), although the signaling pathways of N/OFQ-induced allodynia remain unclear. Here, we developed a novel ex vivo MAPK assay using intact slices of mouse spinal cord, to elucidate the molecular mechanisms of allodynia evoked by intrathecal administration of N/OFQ.

Results
N/OFQ markedly increased the phosphorylation of c-Jun N-terminal kinase (JNK) in the superficial dorsal horn of spinal cord. The maximum effect of N/OFQ was observed with exposure at 10 nM for 10–15 min. The N/OFQ-stimulated JNK phosphorylation was significantly inhibited by pertussis toxin, the phospholipase C inhibitor U73122, and the inositol trisphosphate (IP3) receptor antagonist Xestospongion C. Intrathecal administration of the JNK inhibitor SP600125 inhibited the N/OFQ-evoked allodynia. The N/OFQ-induced increase in JNK phosphorylation was observed in astrocytes that expressed glial fibrillary acidic protein. N/OFQ also induced MCP-1 release via the JNK pathway, and the N/OFQ-induced JNK phosphorylation was observed in the MCP-1 immunoreactive astrocytes. Intrathecal administration of the MCP-1 receptor antagonist RS504393 inhibited the N/OFQ-evoked allodynia.

Conclusion
These results suggest that N/OFQ induces allodynia through the activation of JNK via the phospholipase C-IP3 pathway in spinal dorsal horn, followed by the release of MCP-1 from astrocytes.
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Title: Central Vegf Participates In The Development Of Trigeminal Neuropathic Pain In Rats

Poster Number PW0470

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Aim of Investigation
Growth factors including the vascular endothelial growth factor (VEGF) family have been suggested as useful treatments for prevention of neurodegeneration. VEGF is a potent regulator of vascular function through modulation of endothelial cell functions and vascular permeability. However, participation of central VEGF in the development of trigeminal neuropathic pain remains unclear. Therefore, this study investigated the role of the VEGF in the development of trigeminal neuropathic pain.

Results
Inferior alveolar nerve injury by mal-positioned dental implant produced prolonged mechanical allodynia compared to the sham group. Intracisternal infusion of VEGF antibody (250, 500 ng/24 hr/7 days) significantly inhibited mechanical allodynia produced by mal-positioned dental implants. Intracisternal injection of VEGF Receptor 1 (100 μg) or 2 inhibitor (20 μg) produced inhibition of mechanical allodynia. Inferior alveolar nerve injury up-regulated HIF-1α and VEGF expression in the medullary dorsal horn. Double immunoﬂuorescence data showed that the VEGF and its receptor signals co-localizations in the medullary dorsal horn. In addition, inferior alveolar nerve injury increased extravasated NaF level which was blocked by intracisternal infusion of VEGF antibody.

Conclusion
These results suggest that central VEGF pathway play a critical role in the development of trigeminal neuropathic pain and blocking of VEGF pathway is a new potential therapeutic target for neuropathic pain control including the orofacial area. (Supported by 2008-0062282, 2012M-3A9B6055414)
Aim of Investigation
The locus coeruleus (LC) is located in the dorsal pons and sends noradrenergic projections throughout the neuroaxis which are implicated in the control of many homeostatic functions such as arousal, cardiorespiratory control. In addition, the LC is also a major source of noradrenergic projections to the spinal superficial dorsal horn which play a significant role in pain modulation. In this study, we examined how descending noradrenergic system inhibits spinal nociceptive transmission.

Results
LC neurons in vivo fired spontaneously and cutaneous noxious stimuli applied to the contralateral hind limb biphasically increased and then decreased the frequency of action potential discharge. Voltage-clamp recordings from LC neurons showed that paw pinch evoked a small slow inward current without eliciting fast excitatory postsynaptic currents. Optogenetic stimulation of LC neurons expressing ChR2, increased their firing frequency. While spontaneous and noxious stimuli-evoked firings of LC neurons were completely suppressed by deeper anesthesia by supplemental administration of isoflurane it was still possible to optogenetically activate the neurons. When noradrenaline was superfused to the surface of the spinal cord, it induced an outward (hyperpolarizing) current and increased the frequency of inhibitory postsynaptic currents in spinal superficial dorsal horn neurons. Optogenetic activation of the LC neurons expressing ChR2 elicited a barrage of inhibitory postsynaptic currents in spinal superficial dorsal horn neurons. GABAergic neurons in the spinal cord were excited by noradrenaline mediated by alpha-1 adrenoceptors.
Conclusion
The LC responds to noxious stimulation and the activation of the neurons inhibits spinal nociceptive information at least in part through an augmentation of inhibitory synaptic transmission.
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**Title:** Somatosensory Phenotype Of 1187 Patients With Lesion Of The Nervous System In Relation To Paradoxical Heat Sensations

**Poster Number** PW0472

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**Aim of Investigation**
Paradoxical Heat Sensations (PHS) are the paradoxical perceptions of warmth during skin cooling and occur rarely in healthy subjects but frequently in patients suffering lesion or disease of the somatosensory system (Maier et al., 2010). A mechanistic suggestion includes loss of Aδ-fibres, which causes disinhibition of C-fibre neurons (Craig and Bushnell, 1995), but loss of C-fibres has also been linked to PHS (Hansen et al., 1996). Aim of the analysis was to identify Quantitative Sensory Testing (QST, Rolke et al., 2006) parameters and Neuropathic Pain Symptom Inventory (NPSI, Bouhassira et al., 2004) items that correlate with the presence of PHS in patients with painful or painless lesion or disease of the nervous system of several etiologies. Our focus was set on the following hypothesis: PHS frequency is increased when there is (a) increased Cold Detection Threshold (CDT) and increased Thermal Sensory Limen (TSL), representing loss of Aδ-fibres, (b) increased Warm Detection Threshold (WDT), representing loss of C-fibres, (c) decreased Cold Pain Threshold (CPT) or Heat Pain Threshold (HPT), (d) burning pain quality and not electric shock like pain.

**Results**
There were no differences found in frequency of PHS between patients with and without pain. For central pain and painful unilateral peripheral neuropathy, patients with PHS presented with significantly increased CDT, WDT and TSL (p < 0.05) in comparison to patients without PHS, confirming hypotheses
Though the pattern was similar for painless neuropathies, significance was found only for WDT (p < 0.05), which may be due to the much smaller patient group sizes. There was no significant decrease in CPT, HPT or increased burning pain quality in any of the patient groups, so neither hypothesis (c) nor (d) could be substantiated. QST profiles for patients suffering from polyneuropathy showed virtually no differences in any QST parameter between patients with and without PHS.

**Conclusion**

Our findings show that PHS are associated with small fiber loss. This is not specific for thinly-myelinated Aδ-fibres (CDT), but also includes unmyelinated C-fibres (WDT). Thus, PHS are a marker for damaged small fibres, but not for pain nor its burning quality. Acknowledgements The EUROPAIN project is a public-private partnership and has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n°115007, resources for which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and European Federation of Pharmaceutical Industries and Associations (EFPIA) companies' in kind contribution. The NEUROPAIN project is an investigator-initiated European multicentre study with Prof. Dr. Ralf Baron as principle investigator and 10 co-investigator sites, supported by an independent investigator initiated research grant from Pfizer Ltd. The funding source had no role in study design, data collection and analysis, or writing of the manuscript.