The longitudinal effect of habitual physical activity change on pain tolerance in a population-based cohort – The Tromsø Study 6 & 7

Årnes, AP¹, Fjeld, MK², Johansen, A¹, Morseth, B^{3,4}, Nielsen, CS^{2,5}, Strand, BH², Stubhaug, A^{5,6}, Wilsgaard, T⁴, Steingrímsdóttir, ÓA²

- 1. Department of Pain, University Hospital of North Norway, Tromsø, Norway
- 2. Division of Mental and Physical Health, The Norwegian Institute of Public Health, Oslo, Norway
- 3. School of Sport Sciences, UiT The Arctic University of Norway, Tromsø, Norway
- 4. Department of Community Medicine, UiT The Arctic University of Norway, Tromsø, Norway
- 5. Department of Pain Management and Research, Oslo University Hospital, Oslo, Norway
- 6. Institute of Clinical Medicine, University of Oslo

Aims:

Quantifying longitudinal changes in pain tolerance threshold with a change in level of habitual physical activity (PA) in a population-based sample.

Method:

This study uses data from the sixth and seventh surveys of the prospective population-based Tromsø Study (2007-08 and 2015-16) conducted in the municipality of Tromsø, Northern Norway, since 1974. Information on PA was obtained by questionnaire, and experimental pain tolerance through the cold-pressor test (CPT), a test measuring how long the participant is able to hold the dominant hand in circulating cold water (3°C, maximum test-time 106 seconds). Participants reported total amount of leisure-time PA by selecting one out of four mutually exclusive categories. We plan to use analysis of covariance to assess the relationship between a positive, negative, or null change in PA, and CPT pain tolerance. Models will be adjusted for sex, age, and body-mass index, as well as self-reported education level, chronic pain, smoking, alcohol consumption and health status. Sex-PA interactions will be explored.

Results:

Participation rates in Tromsø 6 & 7 were 66% and 65%, respectively. Altogether, 8,906 participants attended both occasions, with 7,991 participants returning information regarding habitual PA. Of these, 5,957 participated in CPT in both Tromsø 6 and 7 and were therefore included in the present study. Participants were on average aged 55 years in Tromsø 6 and 63 years in Tromsø 7, with 50% being females. Preliminary data show mean CPT tolerance at 91 seconds for Tromsø 6 (sd 27), and 68 seconds for Tromsø 7 (sd 44). Analyses of PA and CPT tolerance are still pending.

Conclusion:

This article aims to be an informative contribution to the discussion of the temporal relationship between changes in habitual PA and pain tolerance, and subsequently how PA and pain tolerance are related.

Single-Base Resolution Analysis of DNA Methylation in Fibromyalgia Women Compared with Their Healthy Sisters

Gerra, MC, Pedersen, IS, Carnevali, D, González-Villar, A, Triñanes, Y, Pidal-Miranda, M, Arendt-Nielsen, L, Carrillo-de-la-Peña, MT

Aalborg University

Aims:

Fibromyalgia (FM) is a pathological condition characterized by chronic widespread pain and comorbid symptoms, including sleep problems, inflammation, depression and other psychiatric traits. The multifactorial nature of the disease makes complex the diagnosis, the identification of effective therapies and to unravel the causative underlying mechanisms. Epigenetic biomarkers could clarify the relationship between experienced stress and FM development through the modulation of genome function; in particular, the present pilot study aims to investigate DNA methylation in targeted genome regions of eight FM women compared to their healthy sisters.

Methods:

Methylation status was tested in the DNA extracted from leukocytes by bisulfite sequencing of 240.134 kbp (Agilent SureSelectXT Target Enrichment for Illumina Multiplexed Sequencing), including CpGs promoters of genes previously found associated with FM or related symptoms. Chronic pain, sleep problems and depression were respectively explored utilizing FIQ (Fibromyalgia Impact Questionnaire), WPI (Widespread Index), SSS (Symptom Severity Scale), VAS (Visual Analogue Scale), PSQI (Pittsburgh Sleep Quality Index) and BDI (Beck Depression Inventory).

Results:

No significantly differentially methylated regions comparing FM patients and their sisters were found; few differentially methylated cytosines were identified with p-value<0.05, but none of them survived the correction for multiple comparisons.

Conclusion:

This is the first study profiling DNA methylation patterns at single-base resolution in targeted regions of FM patients and their sisters. The similar trend in DNA methylation does not support that FM is associated to epigenetic changes and invites to carefully consider previous epigenetic findings. Nevertheless, given the small sample size, further genome-wide researches correlating genetics with potential stressful life events might reveal new perspectives in FM pathogenesis.

Spatial integration of electrical stimulation on the sole of the foot

Henrich, MC; Frahm, KS; Andersen, OK

Aalborg University, Denmark

Aim: To investigate the effects of lateral inhibition and/or spatial summation during electrical stimulation on the sole of the foot. Secondly, to investigate whether these effects depend on the stimulation site on the sole of the foot.

Methods: 14 healthy subjects participated in this study. Five stimulation electrodes were evenly distributed on the sole of the foot following a transversal line. Single and double stimulations (all combinations of two electrodes, applied simultaneously) were delivered seven times in randomized order. The stimulation intensity was defined as 1.5 times the intensity needed to elicit a reflex in Tibialis Anterior (assessed by EMG). Subjects rated the intensity using a Numerical Rating Scale and identified which electrode/s was/were activated.

Results: On average, single stimulation had significantly lower ratings than double stimulation, regardless the distance between stimuli (ANOVA p<0.05 for all cases). During double stimulation there were no significant differences in NRS relative to the location of the stimulus (medial or lateral). Additionally, the reported NRS for double stimulation was not significantly related to the distance between stimuli. Subjects could discriminate the single stimulations as being single stimulus in 87% of the single stimulus presentations, while they could only discriminate 44 % of the double stimulations correctly. For single stimulations, 90% of medial region stimuli were correctly discriminated and decreased to 60% on lateral region.

Conclusion: This study indicates that spatial summation is present when applying simultaneous double stimulation, regardless the distance between activated electrodes and the location on the sole of the foot. This also means that no evidence of lateral inhibition was found. Moreover, a differential modulation of the spatial integration of the stimuli was not found through the width of the sole of the foot. Regarding localization of stimuli, for single stimulation accuracy rates were higher when stimulating towards medial region.

Persistent Pain in a Sami and Non-Sami Population. A SAMINOR study

Damsgård, E, Thrane, G, Fleten, N, Bagge, J, Sørli, T, Anke, A, Broderstad, AR

UiT/The Arctic University of Norway

Aims:

International studies show that the prevalence of persistent pain is higher in indigenous populations compared to the main populations. In Norway, the Sami people are recognized as indigenous; however, persistent pain has not been investigated in a Sami and non-Sami population. The aim is to investigate the prevalence of persistent pain and pain characteristics in a Sami and non-Sami population.

Methods:

SAMINOR 2, part 2, is a population based cross sectional survey on health and living conditions in Norwegian areas with Sami and non-Sami populations. All inhabitants aged 40-79 years and registered in the National Registry as residents in one of the ten municipalities, were invited. Of the 12,455 people invited, 6004 attended the present study and 5546 were included in the analysis. Men and women were analyzed separately.

Results:

A total of 2426 (43.2 %) participants reported persistent pain the last 3 months. In women, we found a lower proportion of Sami participants with persistent pain (44.1%) compared to non-Sami participants (51.1%). There was no difference between Sami (38.7%) and non-Sami men (38.2%). Sami women of 60-79 years were less likely to report pain compared to non-Sami women in the corresponding age group (OR 0.65, p = 0.022). Other covariates, including marital status, level of education, gross income and psychological distress (HSCL-5), did not influence the relationship between ethnicity and pain. Regarding pain location and severity, we found no differences between Sami and non- Sami participants. In the Sami population more women than men reported "moderate" and "severe" pain (p = 0.036).

Conclusion:

In this study, Sami women were less likely to report persistent pain compared to non-Sami women, while there was no difference in men. This result is in contrast to studies from other indigenous areas showing an increased prevalence of pain in minority populations.

Patient-clinician brain concordance supports therapeutic alliance, facial mirroring, and placebo analgesia during pain treatment: A fMRI hyperscanning study

Ellingsen, DM^{1,2}, Isenburg, K², Jung, C^{2,3}, Lee, J², Gerber, J², Mawla, I⁴, Sclocco, R^{2,5}, Edwards, RR⁶, Kelley, J⁷, Kirsch, I⁸, Kaptchuk, T⁸, Napadow, V^{2,5,6}

- 1. Department of Psychology, University of Oslo, Oslo, Norway
- 2. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA
- 3. KM Fundamental Research Division, Korea Institute of Oriental Medicine, Daejeon, Korea (the Republic of)
- 4. Neuroscience Graduate Program, University of Michigan Medical School, Ann Arbor MI, USA
- 5. Department of Radiology, Logan University, Chesterfield, MO USA
- 6. Department of Anesthesiology, Brigham and Women's Hospital, Boston, MA, USA
- 7. Endicott College, Beverly, MA, USA
- 8. Program in Placebo Studies & Therapeutic Encounter (PiPS), Harvard Medical School, Boston, MA, USA

Aims: The patient-clinician relationship can powerfully shape pain, but the brain mechanisms are unknown. We simultaneously recorded functional MRI in patient-clinician dyads, who interacted via on-line video, while clinicians treated patients' pain. We hypothesized that placebo analgesia and non-verbal communication would be supported concordant activation of ventrolateral Prefrontal Cortex (vIPFC), anterior Insula (aINS), and Temporoparietal Junction (TPJ), which are implicated in social mirroring, empathy, and theory-of-mind.

Method: We enrolled patients with chronic pain (fibromyalgia) and clinicians (acupuncturists). Each patient was matched with a clinician (n=37 dyads). During block-design fMRI, patients received 12 moderately painful cuff pressures to the left leg while the clinician used a button box to control (real/sham, double-blind) electro-acupuncture stimulation (EA) to reduce cuff pain. Participants rated self-pain (patients) or vicarious pain of the patient (clinicians) after each stimulus block.

Results: While cuff pressure was identical for all stimulus blocks, patients' pain was significantly decreased during both real (mean \pm SD: 28.2 \pm 13.4) and sham (28.0 \pm 15.1) EA treatment compared to overt no-treatment (35.3 \pm 15.9, 'real EA'-'no-treat': t=2.89,p=0.01; 'sham EA'-'no-treat': t=2.70,p=0.01). Correspondingly, clinicians rated vicarious pain as decreased with treatment (real and sham combined) (20.9 \pm 12.0), relative to no treatment (34.3 \pm 14.5, t=4.88,p<0.0001). Furthermore, patients' placebo analgesia (i.e. no-treat – treat) correlated with clinicians' perceived efficacy (no-treat – treat) (r=0.37,p=0.02).

A conjunction analysis of patients' (evoked pain+treatment) and clinicians' (observing pain+treating) brain response demonstrated consistent activation of vIPFC, aINS, and TPJ. Furthermore, stronger patient/clinician concordance in right TPJ was associated with higher mirroring in facial expressions (r=0.44,p=0.03) and stronger patient-rated placebo analgesia (Treat – No-treat; r=-0.45,p=0.005). Finally, higher facial mirroring was associated with higher therapeutic alliance (CARE questionnaire at intake) and stronger placebo analgesia (r=-0.48,p=0.01).

Conclusion: Consistent with literature highlighting the TPJ as central in social mirroring and theory-of-mind, brain-to-brain coupling of TPJ activity between interacting patients and clinicians may underpin therapeutic alliance and psychosocially facilitated analgesia.

Development of neuro-sensitivity after oxaliplatin administration

Ezzatpanah, S, Haugen, F

National Institute of Occupational health (STAMI), Department of Work Psychology and Physiology, Oslo, Norway

Aims:

In the clinic, oxaliplatin is used in the treatment of advanced colorectal cancer and more broadly of digestive cancers, but has severe side effects including mechanical hypersensitivity, cold-triggered paresthesia and dysesthesia, muscle fasciculations, and cramps. The aim of this study is to find the effect of oxaliplatin on thermo- and mechano-sensory thresholds and find the mechanisms underlying the development of thermal hyperalgesia and mechanical allodynia.

Method:

After 1-4 weeks acclimatization at thermoneutral temperature (27°C); the mice intraperitoneally injected with either oxaliplatin (6 mg/kg) or vehicle (5% glucose). Thermal gradient and tail flick tests, and electronic Von Frey test were used for studying the thermal hypersensitivity and mechanical allodynia, respectively. Tissues (like dorsal root ganglion) and blood samples were collected for further investigations. Behavioral tests were done 4 days after the injections.

Results:

The results obtained from the gradient test revealed that thermal preference in oxaliplatin-injected mice changed compared to the vehicle-injected mice. They showed cold avoidance (P < 0.05) and vehicle-injected mice occupied a wider range of temperatures. In addition, tail withdrawal latency in tail flick test decreased in oxaliplatin-injected mice compared to vehicle group. Paw withdrawal latency was also attenuated in oxaliplatin-injected mice as compared to control group (P < 0.05).

Conclusion:

Oxaliplatin changed the function of somatosensory system and induced thermal hypersensitivity and mechanical allodynia in mice. The results of this study suggest that thermal and mechanical sensitivity in mice may be assessed using tail-flick, gradient test and electrical von Frey tests. Tissue experiments and blood analysis are needed to shed light on the mechanisms underlying the development of thermal hypersensitivity and mechanical allodynia in mice treated with oxaliplatin. Increasing the knowledge about the mechanisms underlying the development of oxaliplatin-induced thermal hyperalgesia and mechanical allodynia help the experimental researches to develop better strategies to prevent thermal hypersensitivity and mechanical allodynia in its clinical use.

The association between different levels of leisure time physical activity and chronic pain – The Tromsø Study 7

Fjeld MK^1 , Årnes AP^2 , Engdahl B^1 , Strand $BH^{1,3,4}$, Stubhaug $A^{5,6}$, Nielsen $CS^{1,6}$, Steingrímsdóttir $\acute{O}A^1$

- 1. Division of Mental and Physical Health, The Norwegian Institute of Public Health, Oslo, Norway
- 2. Department of Pain, University Hospital of North Norway, Tromsø. Norway
- 3. Institute of Health and Society, University of Oslo, Oslo, Norway
- 4. Norwegian National Advisory Unit on Ageing and Health, Tønsberg, Norway
- 5. Department of Pain Management and Research, Oslo University Hospital, Oslo, Norway
- 6. Institute of Clinical Medicine, University of Oslo

Aims:

To describe the association between different levels of leisure time physical activity and chronic pain.

Method:

The subjects are all participants from the seventh wave of the population based Tromsø study (2015-2016). Data on pain characteristics were obtained through a novel hierarchical digital body map, the Graphical Index of Pain (GRIP). The instrument consists of 10 first tier regions (head, neck left arm, right arm, back, left leg, right leg, chest, abdomen, genitals) followed by 167 (men) 168 (women) second tier regions (not analysed). Chronic pain was defined as pain expeirenced within the last 4 weeks in at least one of 10 of the first tier loci with an instensity ≥3 VAS and duration of ≥3 months. PA was assessed with Saltin-Grimby physical activity level scale with four levels (sedentary, low, moderate or vigorous). To test the association between PA (predictor) and chronic pain (outcome), complete case logistic regression analysis was applied, adjusting for age, BMI, smoking status, alcohol consumption and education level with sedentary as reference group.

Results:

A total of 10 009 women and 11 074 men participated in the T7 (attendance rate 65%); 20 844 subjects (61.5%) reported on GRIP (52.5% women, 47.5% men). The prevalence of chronic pain decreased with levels of physical activity in both men and women. In all physical activity levels, the prevalence was highest for chronic back pain among men, and for chronic back and neck pain among women. Genital chronic pain had the lowest prevalence of chronic pain in all activity levels in both sexes. Odds ratio for chronic pain in moderate and vigorous levels of physical activity was 0.88 and 0.71, respectively.

Conclusion:

The association between leisure time PA and chronic pain is inversely related.

Acknowledgement: Mats K. Fjeld is supported by a grant from the Norwegian Fund for Post-Graduate Training in Physiotherapy.

The association between shift intensity and headache in nurses

Maria Katsifaraki, Kristian Bernhard Nilsen, Jan Olav Christensen, Morten Wærsted, Stein Knardahl, Bjørn Bjorvatn, Mikko Härmä, Dagfinn Matre

National Institute of Occupational Health

Aims:

Night work has been associated with short sleep duration and with various pain complaints, including headache. This field study investigated the effect of shift intensity on headache incidence, and whether this was mediated through sleep duration. Shift intensity was conceptualized as i) consecutive night shifts or ii) short rest breaks between shifts/quick returns (< 11 hours between shifts).

Method:

A Norwegian sample of 679 nurses (18-63 years old) working rotating shifts responded to a diary about sleep, shift type and headache (1-5 Lickert scale) for 28 days. It was hypothesized that headache after the third shift would be more intense than after the second shift, and that this difference would be larger for night shifts vs. morning shifts. Furthermore, it was hypothesized that headache would be more intense after two shifts with short rest breaks between shifts vs. after two shifts with longer than 11 hours rest breaks. The analyses (Generalised Structural Equation Modeling) were adjusted for use of sleep medication, age, psychological, social, physical work factors and baseline pain and baseline insomnia.

Results:

After the second consecutive shift, approximately 16% of the nurses experienced headache irrespective of shift type. After the third night shift, headache was experienced by 13%, vs. by 18% after the third morning shift (p = 0.22). After a short rest break between shifts, headache was experienced by approximately 22%, vs. by 16% with longer than 11 hours rest breaks between shifts (p = 0.37).

Conclusions:

According to the current sample of nurses, working three consecutive nights or having < 11 hours rest break between shifts do not seem to be associated with increased headache risk.

Device survival and explant patterns in 449 patients treated with spinal cord stimulation

Kirketeig T, Wåhlstedt A, Leljevahl E, Gordh T, Söderdahl F, Karlsten R

Pain Center, Uppsala University Hospital / Dept. Surgical Sciences, Uppsala University

Aims:

Multiple trials have established the efficacy and safety of spinal cord stimulation. However, long term data on clinical effectiveness is scarce. Aims were: (1) To describe the patient cohort treated with spinal cord stimulation (SCS) and implanted hardware and (2) to analyze device survival and cause for explantation of both Implantable Pulse Generators (IPGs) and leads.

Method:

RAY is a database of 534 prospectively consenting patients treated with invasive neurostimulation for pain 2010-2017 at Uppsala University Hospital, Sweden. Core data collected include: (1) Patient demographics and indications, (2) baseline outcomes, (3) type of implant and delivered waveform and (4) surgical and adverse events. This analysis is limited to (1) patients treated with SCS, (2) events related to first (de novo) IPGs and leads. Device survival will be reported using Kaplan-Meyer analysis and Cox regression models.

Results:

449 of 534 patients were treated with SCS. Core patient demographics were: 249 (55.8%) female and 200 (44.5%) male patients; mean age at implantation: 52 years (SD 12); mean pain duration: 9,2 years (SD 7.8). The main indication was chronic back and leg pain (N=256, 57.0%). Approximately one fourth of all IPGs were explanted during the study period. The most common reason for IPG explantation was insufficient analgesic effect. The cumulative probability for being explanted for insufficient analgesic effect was 14% two years and 31% five years after implantation. In the multivariate Cox regression analysis, increasing age was associated with higher risk of explantation due to loss of analgesic effect (HR 1,025; p = 0,022), as well as 10 KHz stimulation (HR 4,279, p = 0,039).

Conclusion:

The need for unexpected revision surgery and explantation due to insufficient analgesic effect has been reported to be common and our findings support this. Efforts to create larger multinational registries for further investigations are warranted.

Associations between genetic variants and experimental pain sensitivity

Lie, MU, Winsvold, B, Gjerstad, J, Matre, D, Pedersen, LM, Heuch, I, Zwart, JA, Nilsen, KB

- 1. Faculty of medicine, University of Oslo
- 2. Research and communication unit for musculoskeletal health, Oslo University Hospital

Aims:

There is large variation in experimental pain sensitivity, and genetic variation is hypothesized to be an important factor explaining some of this variation. Therefore, the aim of this study was to investigate the association between experimental pain sensitivity and selected genetic variants.

Method:

In this cross sectional study 377 subjects (251 low back pain patients and 126 healthy controls) was genotyped and underwent experimental pain assessments. The experimental pain assessment consisted of test for heat pain thresholds, heat pain tolerance thresholds, pressure pain thresholds, conditioned pain modulation, temporal summation, offset analgesia and secondary hyperalgesia. Single nucleotide polymorphisms of COMT (rs46480), OPRM1 (rs1799971) and HLA (rs2395185, rs927312, rs3916765) were included in a linear regression model.

Results:

No significant associations was found between the five selected genetic variants and the seven different test for assessment of experimental pain, except from HLA rs2395185 and heat pain tolerance threshold.

Conclusion:

Of our selected genetic variants, only HLA rs2395185 was associated with experimental pain sensitivity (heat pain tolerance threshold).

The distribution of chronic pain conditions in a psychiatric outpatient population

Løvås, I, Borchgrevink, PC, Thorsvik, D, Butler, SH, Woodhouse, A

Tiller CMHC, St. Olavs hospital, Trondheim, Norway

Aims:

The aim of this study is to gain basic knowledge about chronic pain conditions in a psychiatric outpatient population by establishing the distribution of chronic pain diagnoses through clinical examinations performed. We know that both chronic pain and psychiatric disorders are associated with a major loss of work capacity and decrease in self- reported health and functioning. However, chronic pain characteristics have rarely been studied or clinically examined in patients with psychiatric disorders.

Method:

A sample of 154 consecutively recruited patients from psychiatric outpatient units participated in this descriptive cross-sectional study consisting of self-reported questionnaires and a structured physical examination by a doctor and a physiotherapist. Inclusion criteria were having a diagnosed psychiatric disorder and chronic pain. We classified chronic pain with the International Classification of Disease (ICD-10). The psychiatric outpatient units performed the psychiatric assessments pre-participation, also using ICD-10 criteria.

Results:

The sample consisted of 123 females and 31 males, average age was 36. 45% received benefits as work assessment allowance, whilst 15% was working. The most frequent psychiatric disorders were anxiety disorders 29%, PTSD 21% and mood disorders 21%. A total of 43% met criteria for chronic widespread pain (ACR 1990), and 33% met criteria for M79.7 fibromyalgia (ACR 1990). Fibromyalgia was significantly higher in females than males (p=.002). The most frequent local pain diagnoses was M54.5 "low back pain" and M54.2 "cervicalgia". Headache was reported by 79% and 20% met criteria for irritable bowel syndrome.

Conclusion:

These investigations of chronic pain give unique information in terms of clinical and detailed data on the pain condition; the type, severity and functional limitations caused by pain. This is essential in gaining a better understanding of chronic pain in psychiatric disorder and towards developing efficient health care services and management programs both in primary and secondary healthcare service

The Association of Age at Menarche and Chronic Pain: The Tromsø Study

Lund, Cl¹, Rosseland, LA^{1, 2}, Stubhaug, A^{3, 4}, Nielsen, CS^{3, 5}

- 1. Department of Research and Development, Division of Emergencies, and Critical Care, Oslo University Hospital, Oslo, Norway
- 2. Division of Clinical Care, University of Oslo, Oslo, Norway
- 3. Department of Pain Management and Research, Oslo University Hospital, Oslo, Norway
- 4. Institute of Clinical Medicine, University of Oslo, Oslo, Norway
- 5. Division of Mental and Physical Health, the Norwegian Institute of Public Health, Oslo, Norway

Aims:

Chronic pain is more prevalent in women compared to men. Hormonal modulation of pain may possibly be a cause accounting for sex differences. Early menarche is a marker for increased long-term estrogen and is associated with enhanced risk of chronic lower back pain and breast cancer. This study aims to examine the association between age at menarche and chronic pain in the general population.

Method:

Cross-sectional analysis was performed on responses from the 6th Tromsø Study questionnaire. Participants reported about chronic pain ("Do you have persistent pain that has lasted three months or longer?"); women reported age at menarche. Body mass index (BMI), a major predictor of age at menarche, was calculated from onsite measurements of height and weight. Chi-square test examined between sex differences of chronic pain prevalence. Logistic regressions were performed to test the effects of age at menarche on chronic pain, pre and post-adjustment for BMI.

Results:

In total, 6,054 men and 6,928 women participated in the study (response rate 66%). Complete data on all study variables were available for 6,035 men, 6,571 women. Chronic pain was reported by 28.7% of males and 40.6% of females (p < 0.001). Among the women, age at menarche was associated with chronic pain (OR 0.92, p < 0.001 pre-adjustment; OR 0.95, p<0.01 post-adjustment for BMI). Prevalence of chronic pain monotonically decreased with increasing age at menarche. 26.2% of the women with age at menarche above 16 years old reported chronic pain.

Conclusion:

Early menarche is associated with higher prevalence of chronic pain in women. Adjustment for BMI has a negligible impact on results indicating no confounding effects of obesity on this association. Prevalence of chronic pain among women with late menarche is comparable to men. It suggests that gonadal hormones may have a role in modulating chronic pain.

Screen time, sleep and pain in healthy youth and patients with prolonged pain or juvenile idiopathic arthritis

Marttinen, MK, Vuorimaa, H, Hintikka, J, Kauppi, MJ, Pohjankoski, H

- 1. Faculty of Medicine and Heath Technology, University of Tampere, Finland
- 2. Päijät-Häme Central Hospital, Lahti, Finland
- 3. Department of Anesthesiology, Intensive Care and Pain Medicine, University of Helsinki, Finland

Aims:

Screen time has been suggested to adversely associate with sleep outcomes and development of physical and cognitive abilities in children (Hale et al. 2015, Domingues-Montanari et al., 2017). An independent association of screen time with backache and headache in adolescents from Nordic countries has been presented (Torsheim et al. 2010).

The aim of the present study was to examine screen time in relation to pain and sleep disturbances in healthy high-school students in comparison to patients with prolonged pain or juvenile idiopathic arthritis. To the best of knowledge, no previous study has presented results from such study setting or examined screen time and pain in juvenile pain patients.

Methods:

Prospective case-control study. Questionnaire-based data from 60 high-school students, 40 patients with juvenile idiopathic arthritis and 33 children with prolonged pain was collected in years 2015-2019. The questionnaire consisted of questions regarding screen time, pain, days absent from school due to pain, depressive symptoms, sleep, Child Health Assessment Questionnaire —based abilities in everyday life, and exercise.

Results:

Results regarding patients are indefinitely uncomplete. According to the preliminary results regarding students, vast majority of subjects had reported extremely high percentage of social media related and only a little school task related screen time in the school days. Majority had reported cell phone use just before falling asleep and only a few feeling brisk in the school mornings. Almost all students had reported some pain during the past one week, and headache during the past three months.

Conclusion:

Ever growing proportion of school tasks have been encouraged to be executed with computers, however, adolescents seem to use the screen time prediominantly for other than school related things. Results regarding the prevalence of pain and morning tiredness emerged alarming.

Pain, opioid drug effects and post-operative analgesic consumption in day surgery patients: A prospective pilot study

Meir, R, Ørstavik, N, Eikemo, M, Ernst, G, Leknes, S

University of Oslo/Leknes Affective Brain Lab

Aims:

This was a pilot, prospective study exploring the potential for pre-operative measures of nervousness, pain, pain interference, and other affective measures to predict post-operative analgesic use.

Method:

We tested 88 patients scheduled for outpatient surgery at Kongsberg Hospital. Patients were measured at four timepoints, in which we collected a variety of affective measures. T1 was a few weeks before surgery, T2 was a few hours before surgery, T3 was on the operating table, and T4 was the day after surgery. Pain intensity and pain interference were measured at T1, T2, and T4. At T3, we measured acute effects of the opioid drug remifentanil immediately before and after one minute of administration. Patients were administered equipotent doses of remifentanil. At discharge, patients received paracetamol and 1-5 Oxynorm pills for post-operative pain relief. We compared ratings of pain and drug effects between patients who chose to ingest opioids at home after surgery with those who used only NSAIDS.

Results:

Of our sample, 31% of patients consumed opioids at home post-operatively. The subset of patients who took opioids post-operatively reported significantly higher levels of pain interference before and after surgery as compared to patients who did not. They also reported significantly less ability to cope with their pain at T4. There was no significant difference between the two groups in measures of nervousness. Responses to pre-surgery remifentanil also did not significantly differ between these subgroups.

Conclusion:

Our results suggest pain interference may be a significant predictive factor for determining which patients will take post-operative opioids. This pilot study also illustrates that a larger prospective study combining trait measures, acute opioid drug effect measures and post-surgery medication measures is feasible and may provide valuable insights on the complex relationships between pain, affect and prescription analgesia use in relatively healthy day surgery patients.

Alzheimer's Disease and Pain Sensitivity – A Mendelian Randomization Study

Melum, TA, Winsvold, B, Zwart, JA, Stubhaug, A, Mathiesen, EB, Nielsen, CS

University Hospital of North Norway, Tromsø, Norway

Aims:

Pain is processed by a widely distributed brain network. Diffuse brain damage by diseases such as Alzheimer's disease (AD) is therefore likely to affect the perception of pain. The aim of this pilot study was to test whether there is a causal relationship between AD and pain sensitivity through Mendelian randomization.

Method:

Analysis was performed of 5,402 subjects from the population-based Tromsø Study who had been tested with the cold pressure test (3°C, maximum time 106s) and where genotype information was available. Subjects where classified as pain tolerant it they could endure the full 106 seconds of the cold pressure test, and pain sensitive if not. Subjects were classified as having high or low genetic risk for AD based on their APOE genotype. The high-risk e4/e4 variant (OR = 20.6) and the moderate-risk e3/e4 variant (OR = 5.5) were combined into a high-risk group (AD+). Remaining variants were combined to a low-risk group (AD-). Group differences in pain sensitivity were tested with Chi-squared. Since AD typically manifests in old age, separate analyses were performed for subjects \leq 70 years (n = 4,434) and subjects > 70 years (n = 968).

Results:

Among subjects \leq 70 years, 32.1% of the AD+ group versus 32.0% in the AD- group were pain sensitive (chi2=0.002, p=0.964). Among subjects > 70 years, 40.7% of the AD+ group versus 34.5% in the AD- group were pain sensitive (chi2 = 3.42, p = 0.065).

Conclusion:

These findings suggest that genetic risk of AD is associated with pain sensitivity in older subjects. The findings are consistent with the hypothesis that AD increases sensitivity to pain, which, if true, has important clinical implications. Confirmation of the findings in a larger sample awaits further genotyping of the Tromsø Study in the near future.

Comparison of opioid naïve patients to opioid tolerant patients referred to the Acute Pain Service

Nordrik, T, Rygh, LJ

Haukeland University Hospital, University of Bergen

Aims:

The organization of the acute pain service (APS) has changed since the concept of a formal APS was first suggested in 1988 by Brian Ready. It is however not obvious what are the optimal size and participants of the APS and neither which patients should be or should not be treated by the APS. Recently a national quality registry for pain treatment (SmerteReg) was established in Norway with a purpose of collecting data for use in both clinical quality improvement and research. SmerteReg includes in-hospital patients referred to the APS at the major hospitals in Norway. These patients are neither diagnosis- nor procedure-specific, but they represent a selected group of challenging pain patients. One subgroup of these pain patients are those that are opioid tolerant. We want to investigate how these patients separate from opioid naïve pain patients in the registry.

Methods:

SmerteReg collects data via a purpose-made and web-based software system (OpenQReg) and the data set includes demographics, reason for admission, pain diagnosis, analgesics including opioids at admission, the type and duration of in-hospital pain treatment. Opioid tolerant and opioid naïve patients will be compared with respect to pain intensity, sleep quality, level of anxiety, depression and catastrophizing and number of visits performed by the APS. The data will be analyzed using "R", a software environment for statistical computing and graphics.

Preliminary results:

By the end of January 2019, a total of 553 patients have been included in the registry. 335 patients were on opioid treatment (considered opioid tolerant) and 218 patients did not receive opioid treatment (considered opioid naïve) at the time of admission. The data are currently being analyzed, and the results will be presented at the poster session.

Group based physiotherapy and patient education in women with chronic pelvic pain - a randomized controlled trial

Nygaard, AS, Stedenfeldt, M, Lindsetmo, RO, Rydningen, MB, Larsen, M, Haugstad, GK, Øian, P

University Hospital of North Norway

Aims:

Chronic pelvic pain (CPP) in women is a complex condition of which clinical guidelines recommend physiotherapy as part of a broad approach. The aim of this parallel group randomized controlled trial was to investigate the efficacy of a group based physiotherapy and patient education program (intervention group) compared with usual physiotherapy (comparator group) in women with CPP.

Method:

Norwegian-speaking women aged 20-65, with CPP ≥6 months, referred to physiotherapy by a medical specialist were eligible. Sixty-two participants were allocated to intervention or comparator group by concealed telephone randomization.

Baseline and 12 months measurements were made at the University Hospital of North Norway, from March 2015 to January 2018. Primary outcome was change in mean pain intensity measured on the Numeric Rating Scale (NRS, 0-10). Secondary outcomes were changes in movement patterns (posture, active movements, gait, sitting posture, respiration) measured with the Standardized Mensendieck Test (SMT, 0-7), and fear of movement-related pain measured with the Tampa Scale for Kinesiophobia (TSK-13, 13-52). The assessor of the SMT-test was blinded to treatment group. Complete case analyses were performed with linear regression.

Results:

Of the 62 included women data on 51 (26 and 25 in the two groups) were available. Reduction in mean pain intensity was 1.8 (SD 2.0) points in the intervention group and 0.5 (SD 1.9) points in the comparator group, resulting in a significant difference in mean reduction of pain (beta: -1.3, 95% CI [-2.3, -0.2], p=0.03). Adjusting for baseline pain intensity did not change the outcome (beta: -1.2, 95% CI [-2.2, -0.1], p=0.03). There were significant differences in change in favor of the intervention group for posture, respiratory patterns and fear of movements.

Conclusion:

The intervention group was superior to the comparator group in terms of improvement in pain intensity, movement and respiration patterns, and fear of movement-related pain.

Registered in clinicaltrials.gov February 5, 2015 (NCT02356796).

Social stress up-regulates expression of Nr3C1 in the pituitary gland and IL-6 in the spleen

Nymoen I, Rajalingam D, Jacobsen DP, Eriksen MB, Gjerstad J

National Institute of Occupational Health, Norway / University of Oslo, Department of Biosciences, Norway

Aims:

Persistent social stress may lead to changes in the hypothalamus-pituitary-adrenal (HPA)-axis and the neuro-immune interface that may be maladaptive. The purpose of this study was to generate new knowledge about the underlying mechanisms behind this association.

Method:

The resident-intruder paradigm where male Sprague Dawley rats (intruders) were exposed to male Long Evans rats (resident) one hour daily for a week, was used. Alterations in the gene expression in the pituitary gland and the spleen was examined by qPCR. A social interaction test was used to observe changes in behavior.

Results:

Rats exposed to social stress in the resident-intruder paradigm showed reduced weight gain compared to controls. The social stress also increased the expression of the cortisol receptor Nr3C1 in the pituitary gland and increased the expression of the IL-6 in the spleen.

Conclusions:

The data showed that one week of repeated social defeat is a strong environmental stressor that may cause reduced weight gain and increased expression of Nr3C1 in the pituitary gland. Moreover, repeated social defeat appeared to increase the expression of IL-6 in the most important lymphoid organ, i.e. the spleen, suggesting that social stress induces a maladaptive inflammatory response. How this affects social interaction, fear and pain sensitivity remains to be investigated.

CSF Biomarkers of Inflammation in Trigeminal Neuralgia Patients Operated with Microvascular Decompression

Stiger, F, Ericson, H, Hamdeh, SA, Freyhult, E, Bäckryd E, Gordh, T, Kultima, K

Multidisciplinary Pain Center, Uppsala University Hospital

Aims:

Compression of the trigeminal root entry zone by a blood vessel can cause trigeminal neuralgia (TN). However, a neurovascular conflict does not explain all cases of TN and TN can exist without a neurovascular contact. A common observation during microvascular decompression (MVD) surgery to treat TN is arachnoiditis in the region of the trigeminal nerve. Thus, aberrant inflammatory mechanisms may be involved in the pathophysiology of TN but information about the role of inflammation in TN is scarce.

Method:

We used Proximity Extension Assay technology (PEA) to analyse the levels of 92 protein biomarkers related to inflammation in lumbar CSF from patients with TN (n=27) before and after MVD compared to individuals without TN. We aimed to obtain a general view of the pattern of inflammatory related proteins and to identify biomarker candidates or proteins improving our understanding of the pathophysiology of TN.

Results:

The main finding was that immunological protein biomarkers levels in the CSF from patients with TN decreased after surgery against levels observed in healthy controls. Two proteins appeared to be of specific interest for TN; TRAIL and TNF-b.

Conclusion:

Inflammatory activity might be one important mechanism in TN.

Latency of ACC and SI processing of noxious and non-noxious electrical stimulation

Tøttrup, L, Valencia, GAD, Lykholt, L, Jensen, W

Aalborg University

Different brain areas contribute in the processing of nociceptive and noxious stimuli, including the primary sensory cortex (SI) and the anterior cingulate cortex (ACC). While the SI primarily responds to sensory activation, the role of ACC is thought to be related to the subjective experience of pain. The purpose of this study was to investigate the differences in acute pain processing in the SI and ACC in relation to low and high intensity (i.e. noxious) electrical stimuli.

Five male Sprague-Dawley rats had a microelectrode array implanted with six electrodes in SI and six electrodes in ACC under isoflurane anesthesia. A cuff electrode implanted around the sciatic nerve in the contralateral hind leg was used for electrical stimulation. Every half hour the brain activity was recorded for three minutes under 2 Hz square pulse stimulation (0.1 ms pulse width). The intensity (i.e. amplitude) of the stimulation was individualized using two, four, and ten times movement threshold of the hind leg for each rat. The stimulation intensity was changed for each recording shuffling between the three intensities. The recorded spikes from both cortices were analyzed using time-frequency analysis.

The cortical response to the electrical stimulation in SI did not vary in regards to latency (~20 ms) between stimulation intensities. In ACC, the latency was in general prolonged (~50-150 ms) and the amplitude in the frequency domain decreased compared to SI. In addition, the cortical response in ACC varied between recordings and subjects.

This study has begun to identify non-subjective markers for pain. Additionally, this knowledge about how SI and ACC plays a role in processing of nociceptive stimuli can be used as a foundation for investigating the transition from acute to chronic pain in chronic pain models in animals.

Acknowledgements: Funded by Center for Neuroplasticity and Pain (CNAP). CNAP is supported by the danish national research fond

Anhedonia in Chronic Pain and Prescription Opioid Misuse

Trøstheim, M¹, Garland, EL^{2,3}, Eikemo, M¹, Leknes, S¹

- 1. Department of Psychology, University of Oslo, Norway
- 2. Center on Mindfulness and Integrative Health Intervention Development, University of Utah, USA
- 3. College of Social Work, University of Utah, USA

Aims:

Despite the high incidence of depression and prolonged prescription opioid use in chronic pain samples, little is known about the specific symptom of anhedonia in patients with chronic pain. In this observational study, we investigated anhedonia in chronic pain patients and its relationship with opioid use and misuse, pain severity, and depression.

Method:

Four hundred thirty-two opioid-treated chronic pain patients across three distinct samples completed the Snaith-Hamilton Pleasure Scale (SHAPS) and the Current Opioid Misuse Measure (COMM) along with other measures of opioid use, pain severity and depression. To estimate the typical level of anhedonia in healthy samples we used a meta-analytic approach, extracting SHAPS scores from 23 published studies totaling 1412 psychiatrically healthy participants. Anhedonia was compared between healthy samples and chronic pain samples with and without opioid misuse (COMM \geq 13). We also ran correlations and regressions within the chronic pain samples to address the contribution of depression, pain severity and opioid use to anhedonia.

Results:

Compared to the healthy samples, the chronic pain patients showed higher levels of anhedonia (M = 20.08, SE = 0.48 vs. M = 24.56, SE = 0.34, p < .001, two-tailed). Within the patient samples, neither opioid use duration, opioid dose nor pain severity alone was significantly associated with anhedonia. Depression explained $^{\sim}7\%$ of the variation in anhedonia in the chronic pain patients. Opioid misusers reported greater anhedonia than non-misusers (M = 26.28, SE = 1.12 vs. M = 23.15, SE = 0.55, p = .01, two-tailed). Opioid misuse remained a significant predictor of anhedonia even after controlling for pain severity, depression and opioid dose.

Conclusion:

The results from this study suggest that both chronic pain and opioid misuse contribute to anhedonia.

Representations of the body and peripersonal space during tool-use in CRPS

Vittersø, A, Halicka, M, Buckingham, G, Proulx, M, Wilson, M, Bultitude, J

University of Bath, UK; University of Exeter, UK

Aims:

Distorted representations of the body and its surrounding space (peripersonal space) are common in Complex Regional Pain Syndrome (CRPS), and may contribute to its aetiology. In pain-free people, representations of the body and space can be briefly distorted, and then normalised, when we interact with objects in our environment (e.g. during tool-use), or after limb immobilisation. We hypothesised that people with CRPS have problems with updating bodily and spatial representations, which thus contribute to the maintenance of the distorted experience by preventing normalisation.

Method:

36 people with unilateral CRPS (18 upper limb, 18 lower limb) and 36 pain-free controls completed a tool-use task known to alter peripersonal space and body representations (measured using a crossmodal congruency task [CCT] and tactile distance judgements [TDJs], respectively).

Results:

People with CRPS showed reaction time changes on the CCT that suggested a more pronounced updating of peripersonal space than controls. The felt distance between two points (TDJs) on the arm decreased after active tool-use for people with CRPS when their non-affected arm was tested, consistent with perceived arm lengthening (normal updating of body representation on this task). However, TDJs on the arm of the affected side of the body reflected perceived arm shortening following tool-use, for both upper and lower limb CRPS.

Conclusion:

Contrary to our predictions, people with CRPS showed a larger-than-normal adaptation of peripersonal space during active tool-use than controls. This might be due to an enhanced defensive awareness of their surroundings. Rather than reduced updating of body representation, people with CRPS showed updating in the opposite direction to normal for the arm of their CRPS-affected body side. We observed this in both upper and lower limb CRPS, suggesting that some alterations in neuropsychological processing might be specific to a side of the body, rather than selective for the CRPS-affected limb.