follow up, after the patients had taken part in a CBT-ACT based 4 weeks in-hospital pain rehabilitation program (PRP).

Methods: Blood samples were collected from 52 well characterized chronic pain patients. Plasma from matched healthy blood donors were used as controls. At one year after the treatment program, 28 of the patients were available for follow up. Instead of only analyzing single inflammation-related substances, we used a new multiplex panel enabling the simultaneous analysis of 92 inflammation-related proteins, mainly cytokines and chemokines (Proseek Inflammation, Olink, Uppsala, Sweden). Multivariate statistics were used for analysis.

Results: Clear signs of increased inflammatory activity were detected in the pain patients. Accepting a false discovery rate (FDR) of 5%, there were significant differences in 43 of the 92 inflammatory biomarkers. The expression of 8 biomarkers were 4 times higher in patients compared to controls. Three biomarkers, CXCL5, SIRT2, AXIN1 were more than 8 times higher. The conventional marker for inflammation, CRP, did not differ. Of the 28 patients available for follow up one year after the intervention, all showed lower levels of the inflammatory biomarker initially raised.

Conclusions: The results indicate that CPP suffer from a low grade of chronic systemic inflammation, not detectable by CRP analysis. This may have implications for the general pain hypersensitivity, and other symptoms, often described in this group of patients. We conclude that inflammatory plasma proteins may be measureable molecular markers to distinguishes CPP from pain free controls, and that a CBT-ACT pain rehab program seem to decrease this inflammatory activity.

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Fixed or adapted conditioning intensity for repeated conditioned pain modulation

M. Hoegh[a,*], K.K. Petersen[b], T. Graven-Nielsen[a]

[a] *Center for Neuroplasticity and Pain (CNAP), SMI, Aalborg University, Aalborg, Denmark*
[b] *SMI, Department of Health Science and Technology, Faculty of Medicine, Aalborg University, Aalborg, Denmark*
E-mail address: msh@hst.aau.dk (M. Hoegh).

Aims: Conditioned pain modulation (CPM) is used to assess descending pain modulation through a test stimulation (TS) and a conditioning stimulation (CS). Due to potential carry-over effects, sequential CPM paradigms might alter the intensity of the CS, which potentially can alter the CPM-effect. This study aimed to investigate the difference between a fixed and adaptive CS intensity on CPM-effect.

Methods: On the dominant leg of 20 healthy subjects the cuff pressure detection threshold (PDT) was recorded as TS and the pain tolerance threshold (PTT) was assessed on the non-dominant leg for estimating the CS. The difference in PDT before and during CS defined the CPM-effect. The CPM-effect was assessed four times using a CS with intensities of 70% of baseline PTT (fixed) or 70% of PTT measured throughout the session (adaptive). Pain intensity of the conditioning stimulus was assessed on a numeric rating scale (NRS). Data were analyzed with repeated-measures ANOVA.

Results: No difference was found comparing the four PDTs assessed before CSs for the fixed and the adaptive paradigms. The CS pressure intensity for the adaptive paradigm was increasing during the four repeated assessments ($P < 0.01$). The pain intensity was similar during the fixed (NRS: 5.8 ± 0.5) and the adjusted paradigm (NRS: 6.0 ± 0.4). The CPM-effect was higher using the fixed condition compared with the adaptive condition ($P < 0.05$).

Conclusions: The current study found that sequential CPM paradigms using a fixed conditioning stimulus produced an increased CPM-effect compared with adaptive and increasing conditioning intensities.

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Combined treatment (Norspan, Gabapentin and Oxynorm) was found superior in pain management after total knee arthroplasty

M.B. Jensen*, M.M. Andersen, B. Boesen, M.B. Jørgensen, O. Simonsen
E-mail address: mikkel.jensen@rn.dk (M.B. Jensen).

Background: Gabapentin (GAB) has recently been introduced for postoperative pain treatment in orthopedic surgery. As persistent postoperative pain is still a major problem in total knee arthroplasty (TKA), studies on the effect and side effects of Gabapentin in addition to the commonly used morphine (MOR), Oxynorm (OXY) and Norspan (NOR) are highly warranted. In the present study, four relevant treatment algorithms, gabapentin and morphine (GAB/MOR), gabapentin and Oxynorm (GAB/OXY), Oxynorm (OXY) and Gabapentin, Oxynorm and Norspan (GAB/OXY/NOR) were examined.

Patients and methods: A total of 241 patients were followed systematically during one month following TKA in four consecutive series: 60 patients were treated with GAB/MOR, 62 patients with GAB/OXY, 59 patients with OXY, and 60 patients with GAB/OXY/MOR. On the day before surgery and on postoperative day 1, 14, and 30, pain during rest, pain during walking and side effects (constipation, dizziness, and nausea) were reported (VAS).

Results: After 30 days, pain greatly decreased in all groups, with a superior effect of GAB/OXY/NOR for pain during rest and only slightly more side effects at day 1.

Conclusions: In management of postoperative pain following TKA, data indicated that GAB/OXY/NOR was superior, compared to GAB/MOR, GAB/OXY, and OXY.

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Effects of conditioned pain modulation on the withdrawal pattern to nociceptive stimulation in humans – Preliminary results

F.A. Jure[a,*], F.G. Arguissain[b], J.A. Biurrun Manresa[a,c], O.K. Andersen[a]

[a] *Center for Neuroplasticity and Pain (CNAP), SMI®, Department of Health Science and Technology, Aalborg University, Denmark*
[b] *Hammel Neurorehabilitation and Research Centre, Aarhus University Hospital, Hammel, Denmark*
[c] *Centro de Investigaciones y Transferencia de Entre Ríos (CITER), CONICET-UNER, Entre Ríos, Argentina*
E-mail address: faj@hst.aau.dk (F.A. Jure).

Aims: Conditioned pain modulation (CPM) is a paradigm employed to assess descending control of spinal nociception.

Previous studies have shown that CPM affects the nociceptive withdrawal reflex (NWR) threshold (RTh), typically assessed in one muscle. However, the NWR activates not one but a group of synergistic muscles, which are recruited by common neural commands to achieve the limb withdrawal. In this regard, synergy analysis can provide the minimum coordinated recruitment of groups of muscles with specific activation balances that describe a movement. The aim was to assess how CPM modulate the global withdrawal strategy of the lower limb expressed by synergy analysis.

Methods: Sixteen healthy subjects received electrical stimulation in the arch of the foot at 2× RTh intensity assessed at the biceps femoris muscle, to elicit the NWR at three time points: before, during and after immersion of the hand in cold water at 2.6 ± 0.4° (cold pressor test, CPT) to trigger CPM. Electromyographic signals (EMG) were recorded from 2 distal muscles (tibialis anterior, soleus) and 2 proximal muscles (biceps femoris, rectus femoris). Muscle synergies were identified by a non-negative matrix factorization algorithm for the EMG envelope in the 60–180 ms post-stimulus interval. Data were analyzed by a point-by-point Wilcoxon test using a permutation strategy.

Results: The overall withdrawal pattern was explained by two main synergies (Syn1 and Syn2). Syn1 mainly contributes to EMG of distal muscles, whereas Syn2 contributes to EMG of proximal muscles. During CPT, the magnitude of Syn2 was reduced in the 160–180 ms post-stimulus interval ($p < 0.05$), whereas no changes were found for Syn1.

Conclusions: At least two synergies are required to explain the NWR. Furthermore, results suggest that CPM might differentially affect proximal and distal muscles. Further analysis is needed to provide additional information about the behavior of the individual muscles.

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Application of miR-223 onto the dorsal nerve roots in rats induces hypoexcitability in the pain pathways

A. Legfeldt[a,b,*], D.P. Jacobsen[a,b], J. Gjerstad[a,b]

[a] *National Institute of Occupational Health, Oslo, Norway*
[b] *Department of Bioscience, University of Oslo, Norway*
E-mail address: Anna.Legfeldt@stami.no (A. Legfeldt).

Aims: Lumbar radicular pain is often associated with increased local and systemic synthesis of inflammatory mediators. This process can be modulated by specific microRNAs (miRs). Here, in the animal model, we investigated the effect of miR-223 on the spinal nociceptive signaling and local gene expression.

Methods: In anaesthetized Lewis rats, extracellular single unit recordings of spinal nociceptive activity and qPCR were used to explore the effect of miR-223 application onto the dorsal nerve roots (L3–L5).

Results: A significant decrease in the C-fiber response was observed following application of miR-223 onto the dorsal nerve roots. In addition, the gene expression of interleukin-6 (IL-6) was increased in the spinal cord.

Conclusions: Our data suggest that miR-223 may influence nociceptive signaling in the pain pathways, possibly by modulating the expression of inflammatory mediators.

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Acute muscle pain alters corticomotor output of the affected muscle stronger than a synergistic, ipsilateral muscle

Dennis Boye Larsen[a,*], Thomas Graven-Nielsen[a], Rogerio Pessoto Hirata[b], Shellie A. Boudreau[a]

[a] *Center for Neuroplasticity and Pain (CNAP), SMI, Department of Health Science and Technology, Aalborg University, Aalborg, Denmark*
[b] *SMI, Department of Health Science and Technology, Aalborg University, Aalborg, Denmark*
E-mail address: sboudreau@hst.aau.dk (S.A. Boudreau).

Aims: Muscle pain affects corticomotor areas representing the affected muscle, by changing the size of representation and reduces the corticospinal output as assessed by transcranial magnetic stimulation (TMS). Less work has been done to understand how pain in one muscle group may affect synergistic ipsilateral muscles distal to the pain. This study aimed to explore the effects of acute extensor carpi radialis (ECR) muscle pain on TMS motor-evoked potentials (MEPs) of the ECR and the first dorsal interosseus (FDI) muscle, which are known to strongly overlap within the corticomotor area.

Methods: Eight healthy volunteers (1 woman) were injected with hypertonic saline (5.8%, 0.5 mL) into the ECR muscle. Pain intensity was assessed by the visual analogue scale (VAS) every minute for 10 min. TMS was applied at 120% of ECR resting motor threshold, and MEPs were acquired from the ECR and the FDI muscles. At baseline, 10 TMS pulses were delivered. Temporal mapping of ECR and FDI MEPs over 10 min duration was performed by delivering 100 single-pulses of TMS, at 6 s interstimulus-interval. The MEPs for each muscle were averaged at baseline, peak-pain (1–2 min epoch), and 10 min post-injection

Results: Pain intensity reduced significantly at 10 min post-injection as compared to peak-pain ($P = 0.011$). Further, one-way repeated measures analysis of variance revealed that ECR MEPs were altered at peak-pain compared to baseline ($P < 0.05$), but not 10 min post-injection ($P > 0.05$). Baseline and 10 min post-injection of ECR MEPs did not differ significantly ($P = 0.67$). The MEPs of the FDI muscle did not show a similar alteration over time ($P = 0.1$).

Conclusions: Despite the overlap between ECR and FDI representations, acute muscle pain of the ECR only significantly altered cortical excitability of the ECR muscle representation.

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The subjective sensation induced by various thermal pulse stimulation in healthy volunteers

Y. Oono[a,*], H. Kubo[a], T. Imamura[a], K. Matsumoto[a], S. Uchida[a], S. Takagi[a], P. Gazerani[b], K. Wang[b], L. Arendt-Nielsen[b], H. Kohase[a]

[a] *Division of Dental Anesthesiology, Department of Diagnostic and Therapeutic Sciences, Meikai University School of Dentistry, Sakado, Japan*
[b] *Center for Sensory-Motor Interaction (SMI), Department of Health Science and Technology, Aalborg University, Aalborg, Denmark*
E-mail address: yoono@dent.meikai.ac.jp (Y. Oono).

Aims: Novel quantitative thermal stimulator devices (QTSDs) have been developed to deliver thermal pulse stimulation with regulated constant temperatures (0–45 °C) with a Peltier element probe (16 cm^2). The aim of this study was to investigate subjective sensation induced by the interaction between simultaneously applied painful cold and heat stimuli in various sites.

Methods: Twenty healthy subjects (12 men and 8 women, age range: 25–45 years) participated. The intensity of cold pain (CP) and