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.

http://dx.doi.org/10.1016/j.sjpain.2017.04.036

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

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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.

http://dx.doi.org/10.1016/j.sjpain.2017.04.037

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

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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.

http://dx.doi.org/10.1016/j.sjpain.2017.04.038

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

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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

heat pain (HP) stimuli were assessed by visual analogue scale (VAS) and adjusted to elicit approximately 70/100 mm. Alternately pulse stimulations (pulse duration of 40 s; 0.025 Hz) which consisted of CP, HP, or neutral temperature (32 °C) were applied. Four conditions were tested and subjective sensations were assessed: (1) one QTSD was applied to non-dominant forearm and cold-heat pulse stimulation was applied.

Two QTSDs were applied to (2) non-dominant ipsilateral forearm with 5 cm apart, (3) non-dominant and contralateral forearms, (4) non-dominant forearm and ipsilateral thigh, respectively. In conditions of (2)–(4), CP-neutral pulse stimulation (C-Neutral) and neutral-HP pulse stimulation (Neutral-H) were applied simultaneously with opposite phase, respectively.

Results: CP and HP were 3.9 ± 1.0 °C (mean ± SD) and 43.6 ± 0.9 °C (mean ± SD), respectively. The VAS values for CP and HP were 73.4 ± 2.0 mm (mean ± SD) and 76.4 ± 4.8 mm (mean ± SD), respectively. Some subjects could not discriminate cold or heat sensation and some felt cold as heat (paradoxical sensation). The number of subjects with such paradoxical sensation in (1), (2), (3), (4) were 9 (45%), 2 (10%), 0 (0%) and 3 (15%), respectively.

Conclusions: In healthy volunteers, simultaneous alternately cold-heat pulse stimulation on one site triggered paradoxical thermal sensation, which to a much less degree is triggered when C-Neutral and Neutral-H were applied to different dermatomes. This suggests that the mechanism is primarily triggered peripherally.

Acknowledgements: This work was supported by Grants-in-Aid for Scientific Research (No. 15K20975 and 15K20972) from the Japan Society for the Promotion of Science. There is no conflict of interest.

http://dx.doi.org/10.1016/j.sjpain.2017.04.039

Assessing Offset Analgesia through electrical stimulations in healthy volunteers

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Background and aims: Offset Analgesia (OA) is a disproportionally large decrease of pain perception evoked by a slight decrease of a painful cutaneous heat stimulus, resulting in a lower pain perception compared to a simple constant stimulus at the same temperature. This study aimed to investigate the possibility of evoking the same disproportional analgesic effect by applying electrical stimuli.

Methods: 24 subjects underwent two control-trials of 30 s constant intensity by applying either heat stimulation at 48 °C or an electrical stimulation at 150% of the individual electrical Pain Detection (ePD) on the volar forearm. OA-trials consisted of a 30 s stimulation, divided into three periods: T1 (5 s), T2 (5 s), and T3 (20 s), with stimuli intensities of 48 °C, 49 °C and 48 °C or 150% of ePD, 180% of ePD, and 150% of ePD.

Subjects were asked to rate the pain intensity on an electronic Visual Analog Scale (VAS; 0: no pain; 10: worst imaginable pain), and were categorized as responders if they showed more than 30% lower VAS at heat OA-trials compared to heat control-trial. Repeated measures Analysis of Variance was applied to investigate the difference in pain intensity to the electrical OA-trials, compared with the electrical control-trials.

Results: Responders to the heat OA-trial also responded to the electrical OA-trial compared to the electrical control-trial, with an analgesic effect of 3.3 ± 0.5 VAS points ($P < 0.001$). However, when analyzing all subjects, no difference was found comparing the electrical OA-trial (VAS 3.8 ± 0.5) to the electrical control-trial (VAS 6.2 ± 0.4; $P > 0.5$).

Conclusions: This study suggests that responders to the heat OA-paradigm also respond to the electrical OA-paradigm.

http://dx.doi.org/10.1016/j.sjpain.2017.04.040

Metastatic lung cancer in patient with non-malignant neck pain: A case report

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Background: Symptoms from disseminated cancer can develop very slowly. This could be very difficult to distinguish those symptoms from chronic disabilities and nuisances in patients with chronic non-malignant pain.

Objective: In this report, the case of a woman with both non-malignant pain and cancer is presented.

Case report: A 54 years old woman was referred by a general practitioner to Multidisciplinary Pain Center. The diagnosis was chronic non-malignant neck pain on the basis of degenerative columnar disease. The patient was also suffering from osteoporosis. During the first visit in the Center, the patient complained of shooting pains in the neck and had tingling sensations in the fingers – most of his right hand. Moreover, the patient experienced shooting pains in the hips, lower back and spine. The multidisciplinary treatment with medication, physical therapy, TENS and cognitive behavioral therapy was offered. Paracetamol together with gabapentin was used. The patient experienced relief of pain. The doses of gabapentin was escalated up to 2400 mg daily without significant side effects. Afterwards, the dose was gradually increased to 3600 mg daily and the patient experienced fatigue, mild headache and dizziness. These symptoms were initially interpreted as side effects of gabapentin. However, the tingling sensations in the fingers were almost disappeared. The doses of gabapentin was reduced, but without relief of symptoms. Within 2 weeks, the patient developed partial paresis of the right upper limb and aphasia. The patient was urgently referred to the neurologic inpatient clinic. CT- and MR-scans showed multiple cerebral metastases. Under the diagnostic workup the lung tumor was found. The biopsy showed pulmonary adenocarcinoma.

Conclusions: The symptoms of lung cancer with cerebral metastases can mimic side effects of gabapentin.

http://dx.doi.org/10.1016/j.sjpain.2017.04.041