Expression of α_1 adrenergic receptor subtypes by afferent fibers that innervate rat masseter muscle

B.E. Cairns[a,b,*], J. Liu[b], H. Wong[b]

[a] *Center for Neuroplasticity and Pain, SMI, Department of Health Science and Technology Faculty of Medicine, Aalborg University, Frederik Bajers Vej 7D3, 9220 Aalborg East, Denmark*
[b] *Faculty of Pharmaceutical Sciences, University of British Columbia, 2405 Wesbrook Mallm, Vancouver, BC, Canada V6 T 1Z3*
E-mail address: bec@hst.aau.dk (B.E. Cairns).

Aims: In temporomandibular disorders sufferers, muscle pain is more severe in individuals who have undergone a traumatic stress. Why stress exacerbates masticatory muscle pain in these individuals is not known. One possibility is that under conditions of stress there is an interaction between the sympathetic and sensory nervous systems. This study investigated whether trigeminal ganglion neurons that innervate the masseter muscle express α_1 adrenergic receptor subtypes to identify whether a direct interaction between the sympathetic and sensory nervous systems is feasible.

Methods: Masseter muscle ganglion neurons were identified by injection of the fluorescent dye fast blue into the masseter muscle of 4 Sprague Dawley rats (2 male, 2 female). Trigeminal ganglion sections were stained for α_{1a}, α_{1b} or α_{1d} adrenergic receptors, as well as the transient receptor potential vanilloid 1 (TrpV1) receptor. Sections were examined with a Leica confocal microscope. The percent of masseter ganglion neurons expressing each receptor was calculated.

Results: Masseter muscle ganglion neurons expressed α_{1a} ($29 \pm 9\%$), α_{1b} ($34 \pm 4\%$) and α_{1d} ($19 \pm 13\%$) adrenergic receptors. Expression of all three α_1 receptor subtypes was higher in female rats than in male rats. Expression of α_{1b} receptors was more commonly found on larger diameter masseter ganglion neurons. Overall $11 \pm 3\%$ of masseter ganglion neurons expressed the TrpV1 receptor, which suggests they served a nociceptive function. The TrpV1 receptor was co-expressed by about ~10% of α_{1a} and α_{1b} receptor positive masseter ganglion neurons.

Conclusions: Afferent fibers that innervate the masseter muscle express all three α_1 adrenergic receptor subtypes. Agonists at the α_1 receptor have been previously shown to depolarize trigeminal ganglion neurons, which suggests that activation of these receptors on masseter muscle afferents would be excitatory. The expression of α_1 receptors by putative nociceptors that innervate the masseter may permit a direct interaction between the sensory and sympathetic system that contributes to pain in this muscle.

http://dx.doi.org/10.1016/j.sjpain.2017.04.010

Buprenorphine alleviation of pain does not compromise the rat monoarthritic pain model

M.S. Berke*, Klas S.P. Abelson

Department of Experimental Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark
E-mail address: mibe@sund.ku.dk (M.S. Berke).

Aims: This study investigated the effects of buprenorphine treatment on pain and welfare parameters and model specific parameters in a rat model of monoarthritis to eliminate unnecessary pain from this model.

Methods: 32 male Sprague Dawley rats were divided into four groups: (1) A negative control without arthritis receiving no analgesia. (2) A positive monoarthritic control group receiving no analgesia, but subcutaneous saline injections twice a day. (3) A positive control with monoarthritis receiving subcutaneous carprofen once a day and saline once a day. (4) A group with monoarthritis receiving subcutaneous buprenorphine twice a day. Monoarthritis was induced with an injection of 0.02 ml Complete Freund's Adjuvant intra-articularly in the left tibiotarsal joint. Treatment with analgesia was initiated at day 15 and the rats were euthanized at day 23.

Results: The induced monoarthritis elicited a pronounced acute inflammation. Several parameters such as bodyweight, mobility, stance, joint-stiffness and lameness scores were affected. A marked mechanical hyperalgesia in the tarsal area was observed by Electronic Von Frey testing, but no severe compromise of the animal welfare was seen at any time. Signs of chronic development began to appear from day 10 after the monoarthritic induction. No significant change in serum cytokines and faecal corticosterone measurements was found after administration of buprenorphine. A minor decrease in body weight was seen, and a higher pain tolerance to mechanical stimuli was observed, indicating pain alleviation. The histological examination confirmed monoarthritic development in all monoarthritic rats and revealed periarticular lesions suggesting diffusion of adjuvant from intra-articular injection site to the periphery.

Conclusions: The study demonstrated that buprenorphine has an analgesic effect in the adjuvant induced monoarthritic rat model, without obvious interference with the development of arthritis.

http://dx.doi.org/10.1016/j.sjpain.2017.04.011

Association between pain, disability, widespread pressure pain hypersensitivity and trigger points in subjects with neck pain

Matteo Castaldo[a,b,c,*], Antonella Catena[a], Alessandro Chiarotto[d], Jorge Hugo Villafañe[e], César Fernández-de-las-Peñas[b,f], Lars Arendt-Nielsen[b]

[a] *Poliambulatorio FisioCenter, Collecchio, Parma, Italy*
[b] *SMI®, Department of Health Science and Technology, Faculty of Medicine, Aalborg University, Aalborg, Denmark*
[c] *University of Siena, Siena, Italy*
[d] *Department of Health Sciences, Faculty of Earth and Life Sciences, EMGO+ Institute for Health and Care Research, VU University, Amsterdam, The Netherlands*
[e] *IRCCS Don Gnocchi Foundation, Milan, Italy*
[f] *Department of Physical Therapy, Occupational Therapy, Physical Medicine and Rehabilitation, Universidad Rey Juan Carlos, Alcorcón, Spain*
E-mail address: matteo.castaldo@poliambulatoriofisiocenter.com (M. Castaldo).

Aims: Mechanical neck pain (MNP) and whiplash-associated disorders (WAD) represents two groups of subjects with a different pathogenesis, since current evidence supports that WAD subjects presents greater sensitization than MNP. Nevertheless, it is still unclear the relationship between neck pain, neck disability, widespread pressure pain hypersensitivity (sign of sensitization) and trigger points (TrPs) in these two groups of neck pain subjects. The aim of the current study was to investigate these associations in MNP and WAD subjects.

Methods: Forty-six MNP and fifty-one WAD subjects underwent the following examination: pressure pain thresholds (PPTs) in the upper trapezius and tibialis anterior muscles, TrP examination in

the upper trapezius, and collection of neck disability and neck pain intensity. The examination was performed by an assessor blinded to subjects' condition.

Results: A significant positive association between pain and disability ($P < 0.003$), pain and PPT in the upper trapezius ($P < 0.041$), pain and PPT in tibialis anterior ($P < 0.038$), disability and PPT in upper trapezius ($P = 0.006$) was found in both groups. Subjects with MNP showed significantly negative association between disability and PPT in the tibialis anterior ($P = 0.003$). Subjects with active TrPs in the upper trapezius exhibited significantly higher neck pain intensity and neck disability and lower PPTs (all, $P < 0.015$), than those with latent TrPs in both groups.

Conclusions: Our results suggest that the association between pain, disability, and PPTs is similar in subjects with neck pain and not influenced by the origin of neck pain. The presence of active TrPs in upper trapezius in neck pain patients was related to higher pain intensity, related-disability and lower PPTs, compared to neck pain patients with latent TrPs in upper trapezius. Future studies are needed to determine the clinical role of these associations.

http://dx.doi.org/10.1016/j.sjpain.2017.04.012

Association between widespread pressure pain hypersensitivity, health history, and trigger points in subjects with neck pain

Matteo Castaldo[a,b,c,*], Antonella Catena[a], César Fernández-de-las-Peñas[b,d], Lars Arendt-Nielsen[b]

[a] *Poliambulatorio FisioCenter, Collecchio, Parma, Italy*
[b] *SMI®, Department of Health Science and Technology, Faculty of Medicine, Aalborg University, Aalborg, Denmark*
[c] *University of Siena, Siena, Italy*
[d] *Department of Physical Therapy, Occupational Therapy, Physical Medicine and Rehabilitation, Universidad Rey Juan Carlos, Alcorcón, Spain*
E-mail address: matteo.castaldo@poliambulatoriofisiocenter.com (M. Castaldo).

Aims: Health history (medical conditions, comorbid musculoskeletal pain, surgical operation, long term intake of medications) may contribute to central sensitization. The duration and the number of the peripheral nociceptive input seem to play a crucial role in the development and maintenance of sensitization. No study has previously investigated these relationships. Our aim was to investigate the association between pressure pain thresholds (PPTs) and health history in patients with neck pain, and the role of active trigger points (TrPs) on PPTs.

Methods: Thirty-four subjects with mechanical neck pain and 34 with whiplash-associated neck pain participated. They underwent an assessment of PPTs over upper trapezius, extensor carpi radialis longus, and tibialis anterior muscles, and were screened for the presence of active TrPs in upper trapezius muscle. Further, patients fulfilled a questionnaire investigating health history outcomes number and duration.

Results: Significant negative correlations between all PPTs and the duration of health history outcomes were found in both groups (all, $P < 0.02$), with no correlations between PPTs and the number of health history outcomes (all, $P > 0.15$). Significant lower PPTs over upper trapezius, extensor carpi radialis longus, and tibialis anterior (all, $P < 0.01$) muscles were found in subjects with active TrPs as compared to those with latent TrPs.

Conclusions: Widespread pressure pain hypersensitivity was associated with the duration, but not the number, of health history outcomes suggesting that long-lasting health complains may act as triggering factor driving sensitization in individuals with neck pain regardless the origin of neck pain. Patients with active TrPs in the upper trapezius muscle showed higher widespread pressure sensitivity than those with latent TrPs. These data should be included in the assessment of neck pain subjects, as they may be useful for planning the management of their symptoms.

http://dx.doi.org/10.1016/j.sjpain.2017.04.013

Neuromas in patients with peripheral nerve injury and amputation - *An ongoing study*

N.S. Buch[a,b,*], E. Qerama[c], N.B. Finnerup[b], L. Nikolajsen[a,b]

[a] *Department of Anesthesiology and Intensive Care, Aarhus University Hospital, Denmark*
[b] *Danish Pain Research Center, Aarhus University Hospital, Denmark*
[c] *Department of Neurophysiology, Aarhus University Hospital, Denmark*
E-mail address: nina.buch@clin.au.dk (N.S. Buch).

Background and aims: Injury to peripheral nerves associated with trauma, amputation, or surgery may lead to the formation of neuromas that can cause severe pain. Unfortunately, neuromas are frequently refractory to medical and surgical treatment. This ongoing study examines whether neuromas are more frequent in patients experiencing pain after peripheral nerve injury or amputation than in patients without pain.

Methods: In this observational cohort study, 80 patients with peripheral nerve injury or amputation will be recruited. Patients will answer pain questionnaires and undergo a clinical examination with quantitative sensory testing performed within the area of spontaneous pain, including areas of brush-evoked allodynia and pinprick hyperalgesia. Neuromas are identified using ultrasound.

Results: Patient inclusion is ongoing. At present, fourteen amputees have participated in the study: nine males and four females, aged 38–77 years. Six patients had no neuromas. Stump pain in this group ranged from 0 to 8 and phantom pain from 0 to 10 on a numerical rating scale, 0–10. Eight patients had neuromas. Stump pain in this group ranged from 0 to 7 and phantom pain from 0 to 8. Further results will be presented at the congress.

Conclusions: Because of a limited number of patients included, it is not yet possible to conclude if neuromas are more frequent in patients with pain.

Hopefully, this study will increase our understanding of the role of neuromas in patients with pain after peripheral nerve injury and amputation.

http://dx.doi.org/10.1016/j.sjpain.2017.04.014