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Correlation and cluster analysis of sensory, pain, and reflex thresholds to various stimulus modalities in symptom-free subjects

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Abstract

Objective: In order to evaluate the possible relation between the psychophysical response and a motor reflex, sensory and pain thresholds to various stimuli were analyzed in combination with the occurrence threshold of the late masseteric exteroceptive suppression (ES2) period.
Methods: Twenty men and 20 women participated. The tactile detection threshold and the filament-prick pain detection threshold were measured on the cheek skin overlying the left masseter muscles. The pressure pain threshold and pressure pain tolerance threshold were measured at the left masseter muscle. The surface EMG was recorded from the left masseter muscle, while electrical stimuli with 13 fixed intensities were applied to the skin above the left mental nerve. The stimulation intensity at which the ES2 appeared for the first time and the lowest stimulus intensity at which the subjects reported to be painful were defined as the ES2 and pain threshold, respectively.
Results: There were significant positive correlations between the tactile detection threshold and the pain thresholds determined using the different stimulus modalities, and the ES2 threshold was also significantly correlated with the pain thresholds ($P < 0.05$). Cluster analysis could significantly discriminate two distinct groups with high versus low tactile, pain and ES2 thresholds ($P < 0.05$).
Conclusions: The present findings suggested that the ES2 reflex response has a relation with the individual sensory and pain sensitivity in symptom-free subjects.
Significance: Combined examination of sensory, pain, and ES2 thresholds might provide complementary information on the pathophysiology underlying orofacial pain.

Keywords: Sensory threshold; Pain threshold; Reflex threshold; Stimulation; Exteroceptive suppression period; Cluster analysis

1. Introduction

In the diagnosis of and for a better understanding of the underlying pathophysiology of pain, information on the processing of sensory stimuli is of importance. Methods used in quantitative sensory testing encompass mechanical, electrical, chemical, and thermal stimuli (Jacobs et al., 2002; Jaaskelainen, 2004; Svensson et al., 2004). Lautenbacher et al. (1994) found a correlation between pressure pain, heat pain, and electrical pain thresholds during a multi-method assessment in patients with fibromyalgia and healthy control subjects. The processing of nociceptive and non-nociceptive stimuli may differ between clinical pain conditions which then possibly reflects a different etiology of the sensory signs and symptoms, or a different

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interindividual processing of these stimuli. Kosek et al. (1996) described that fibromyalgia patients had higher pressure pain sensitivity compared to normal subjects, and also had increased sensitivity to light touch in the site of maximal pain compared to the homologous contra-lateral side. In laboratory conditions, Svensson et al. (1998a) measured the mechanical sensitivity in the pain area occurring after injection of hypertonic saline in the masseter muscle. The psychophysical ratings of high intensity Semmes–Weinstein monofilament stimulation at the site of infusion were significantly increased 12 min after the start as compared to baseline.

Electrical stimulation of the trigeminal nerve fibers elicits suppression of the voluntary contraction in the human masseter and temporalis muscles (Godaux and Desmedt, 1975), and this reflex has been called silent period (SP) or exteroceptive suppression (ES). In the human masseter muscle both an early (ES1) and a late (ES2) exteroceptive suppression period can be found (Desmedt and Godaux, 1976). ES1 is assumed to be a pontine di- or oligosynaptic reflex with an onset latency of 9–15 ms (Cruccu et al., 1984), while ES2 is considered a pontomedullary polysynaptic brainstem reflex with an onset latency of 40–60 ms (Ongerboer de Visser et al., 1989). Previously, ES has been suggested as a quantitative measure of pathophysiological processes, such as temporomandibular disorders (De Laat et al., 1985), headache (Bendtsen et al., 1996), and trigeminal neuralgia (Cruccu et al., 1987). However, the necessary reliability and validity of the reflex-parameters were not studied to the degree necessary for possible clinical application in these conditions (for review see De Laat et al., 1998). We reported earlier that for ES2 stimulus-response curves (S-R curves) could be built in a reliable way and that a gender difference was present regarding ES2 threshold (Komiyama et al., 2005a,b). These findings also illustrated the potential of studying possible associations between sensory thresholds and motor reflexes, using this methodology.

Since no reports are available that link sensory threshold, pain perception and the reflex response to a standardized stimulus, possibly illustrating interindividual differences, and in order to know whether the late masseteric exteroceptive suppression (ES2) could be used for the evaluation of individual variations in this relationship, the present study aimed at exploring the relation between the psychophysical responses to various sensory stimulus modalities, the report of pain and the ES2 reflex threshold to electrical stimuli, in healthy volunteers.

2. Method

2.1. Subjects

Subjects were recruited from university students and staff. All were Caucasian, and asymptomatic for pain in the head and neck region. This was defined as absence of jaw dysfunction and headaches, and absence of subjective pain or soreness of the masticatory muscles. Subjects could also not participate when they were currently taking medication or received other treatment that could not be interrupted for the study, if general health problems (e.g. metabolic disease, neurological disorders, vascular disease, etc.) or periodontal disease was present, or in case of a history of drug abuse, recent facial or cervical trauma. Since a previous study (Isselee et al., 2001) indicated that pressure pain thresholds were lower in the menstrual phase, women were not tested during their menstrual phase. Twenty men and 20 women (age range from 20 to 33 years) participated. The subjects were informed about the study in a standardized way and signed an informed consent form. The institutional ethics committee approved the study (ML2569).

2.2. Tactile detection threshold and tactile pain detection threshold

All measurements were taken in the same room, in which temperature and humidity were kept constant (Andrews, 1993).

The tactile detection threshold and the filament-prick pain threshold were measured on the cheek skin overlying the central part of the left masseter muscles midway between the upper and lower borders and 1 cm posterior to the anterior border. The test area was limited to a circle with 5 mm diameter. Semmes–Weinstein monofilaments with 20 different diameters were used (Premier Products, USA). The numbers of the filaments (1.65–6.65) correspond to a logarithmic function of the equivalent forces of 0.0045–447 g.

At first, the tactile detection threshold was examined. The subjects were instructed to close their eyes during the whole test procedure and to raise their hand as soon as they felt the stimulus in the test site. The filament was applied vertically on the test site and slowly pressure was applied until the filament bended. The time needed to bend the filament was standardized to approximately 1.5 s. The stimulus was maintained for approximately 1.5 s and then removed in 1.5 s. Quick applications and bouncing of the filaments against the skin were avoided. The test started with the No. 4.31 filament. If the subject raised his/her hand, it was considered a positive response, and the next filament applied was one step lower (No. 4.17). This procedure was repeated with decreased filament diameters until the subject no longer felt the pressure. This was considered as a negative answer. Again, the filament with a higher pressure was applied. This procedure continued until eight positive and eight negative peaks were recorded and the tactile detection threshold was calculated as the average of these values (number of the filament). If the subject still had a positive response while applying the lowest fiber (No. 1.65), this filament was considered the threshold. Two "null" (placebo) trials were performed after the 5th and 11th peak. During these control trials, the filament did not make contact with the skin. If the subject did not report a sensation during the blank stimuli, the test was