Sex differences in temporal characteristics of descending inhibitory control

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Abstract
The aim of this study was to investigate sex differences in temporal characteristics of descending noxious inhibitory control (DNIC). Recordings were obtained from 20 healthy volunteers (10 M, 10 F) and sensory as well as pain thresholds over the orofacial region and the finger were measured. Pain threshold were recorded before (baseline), during and after the activation of DNIC by means of a cold pressor test (CPT), which involved immersing an upper limb in cold water (1-3 ºC). The subjects’ perceived intensity and unpleasantness of the painful sensation induced by the CPT was rated on a numeric rating scale (NRS) as well as with the PainMatcher. The baseline electrical pain threshold (EPT) over the finger was significantly higher in the males. In general pain thresholds were increased during CPT, but decreased 5 minutes after CPT compared to baseline, but had normalized 15 minutes after CPT. However, the EPT in the orofacial region was significantly increased during CPT compared to 5 minutes after CPT in the females, but was significantly higher 5 minutes after the CPT in males compared to females. The subjects’ perceived rating of pain with the PainMatcher during the CPT was significantly higher in males. To summarize, our findings suggest an increase in pain thresholds in healthy subjects after activation of DNIC. This pain inhibitory effect was gender-specific in the response to electrical stimulation of the orofacial region that was larger in the males 5 min after CPT.

Introduction
Pain is an introspective, unpleasant experience with varying degrees of intensity in different individuals. With the help of category scales and psychophysical methods it is possible to characterise, measure and compare pain perception within and among groups of different individuals in given situations. Results from clinical and experimental pain studies provide consistent evidence of sex differences in pain perception, with women demonstrating lower pain tolerance levels, reporting more clinical pain and having a higher incidence of musculoskeletal pain than men. This knowledge of gender differences in medicine has gained increasing interest during the last 10-15 years and consequently inspired the research community to experimentally explore these differences. Various studies have shown that there are several mechanisms that lead to these gender differences. These include psychosocial factors (1), such as beliefs regarding one’s ability to control and tolerate pain (2), anxiety (3), and biological factors, such as different sex-related hormones (4), resting blood pressure (5), genetic influences (6) as well as descending noxious inhibitory control (DNIC) (7).

In the experimental situation there are also factors that influence the induction of pain, for instance the type of stimulus used to induce pain (8). Some of the pain receptors (nociceptors) can be activated by different types of stimulus, while other nociceptors are activated by a specific type of stimulus. For instance, many mechanoreceptors also act as nociceptors since they induce pain if the stimulus is of sufficient intensity. Also the duration of the stimulus plays an important role in pain perception, as well as the number of nociceptors and their
localisation. Depending on the localisation in the body, the pain perception differs because different parts of the body are differently presented in the somatosensory cortex. In one study it was shown that an experimental systemic treatment with granisetron, which is a selective 5-HT receptor antagonist, significantly increased the pressure pain threshold (PPT) in the trapezeus- and tibialis anterior muscels, but not in the masseter- and temporalis anterior muscles (9). This could be explained with the fact that the orofacial regions are very largely presented in the somatosensory cortex. This latter knowledge has great importance in the process of understanding the nature of craniofacial pain.

It should also be mentioned that the pain perception is experimentally influenced by which pain parameter that is investigated, i.e. pain intensity, pain threshold or pain tolerance. Females have in experiment shown lower pain thresholds and pain tolerance levels as well as higher experienced pain intensity to a certain stimulus, compared to males. These differences between genders are partly explained by psychological factors. In experimental stress studies women have shown to produce less cortisol than men (10). Since cortisol has a pain reducing effect this leads to a lower pain tolerance. Furthermore, during depression and anxiety conditions the regulatory system of serotonin (5-HT) levels is defected. This finding is also seen in individuals with increased pain perception, which is mostly represented by women (11). Furthermore, pain thresholds vary between groups of women depending on the menstruation cycle and the levels of sex-hormones. Women have experimentally shown to have higher pain threshold during the follicular phase of the menstruation cycle (day 5-12) when the progesterone levels are relatively low (12).

There is evidence that some chronic pain conditions occur more commonly and aggressively in women than men, such as migraine, fibromyalgia, rheumatic, trigeminal neuralgia and some cardiac pain contitions. In addition, treatments including opioids and non-steroidal anti inflammatory drugs (NSAID) exhibit different pain relieving effects between the sexes. Administration of the µ opioid-agonist morfin has in experiments on rats and humans shown a higher analgesic effect in men compared to women (13). In contrast administration of the kappa-opioid such as pentazocine induced better analgesic effect on women (14). This could indicate that women have different receptor profiles than men. Some NSAIDs also seem to have different effects depending on the gender (15).

DNIC is an endogenic system to reduce pain perception that can be defined as a supraspinally mediated physiological phenomenon. It has been found in animal studies to be a powerful and widespread inhibition of wide dynamic range (WDR) neurons at spinal as well as at trigeminal level (16-18). It has been suggested that this phenomenon has the same effects in humans. DNIC refers to the action of one noxious stimulus inhibiting the percept of pain produced by application of a second noxious stimulus. This phenomenon is a normal bodily event and is used in the medical science in many areas, e.g. injection of hypertonic saline to women in the act of birth in order to activate DNIC and thus reduce the pain of giving birth. DNIC can also be activated through physical training. This was shown in a study where healthy volunteers withheld a higher electrical pain threshold after physical training (19). DNIC attenuates spatial summation of second pain in normal males but not in normal females or fibromyalgia patients (20). Furthermore, females normally exhibit lower ability to recruit DNIC triggered by spatial summation from bilateral experimental trapezeus muscle pain (7). However, it is still unclear as to whether there are sex specific differences in temporal characteristics of DNIC. It could be anticipated that a sex specific weak or slow development of DNIC would also predispose women to the development of musculoskeletal pain.

Experimental studies have shown that DNIC has spatial characteristics with stimulation from the afferents of both skin and the muscles (7, 21) which allows different methods of
activation. In some experiments intramuscular injection of hypertonic saline into a specific muscle has been chosen to induce pain and thus activate the DNIC system. In other studies the activation of DNIC has been accomplished by immersion of the hand in cold water for several minutes, so called a Cold Pressor Test (CPT). Furthermore, in most studies regarding craniofacial regions mechanical stimulation has been used to investigate the pain thresholds to pressure (PPT) over the muscles and jaws. However as to our knowledge, no studies have yet been published regarding gender differences in sensory and pain thresholds to electrical stimulation of intra-oral regions, such as and pulpal tissue in healthy subjects.

The aim of this study was to investigate of the influence of DNIC on sensory and pain thresholds in healthy subjects and to evaluate whether any such effects are gender specific and to investigate if the effect is influenced by anatomical regions and type of stimuli. This was done by comparing recordings of PPT, electrical pain thresholds (EPT) and electrical sensory thresholds (EST) in the trigeminal region with those obtained in the finger before, during and after a CPT.

**Material and Methods**

**Subjects**

Our data were collected from 10 healthy men (mean (SD) age 24 (1,2) years) and 10 age matched healthy women (mean (SD) age 24 (1,2) years) recruited among the students of Karolinska Institutet.

The inclusion criteria for participating in the study were as followed: 1 – age between 20 and 40 years, 2 – no ongoing chronic pain, 3 – not pregnant, 4 – not currently using prescription analgesics, tranquilizers, antidepressants or other centrally acting agents.

Prior to participating in this experiment the subjects were provided with verbal and written information and gave their written consent. The female participants were furthermore asked about at which day in the menstruation cycle they were and use of birth control pills.

**General procedures**

The subjects were placed in a relaxed supine position. Before the experiment started the participants were subjected to an initial training session to familiarize them with the procedures. The experiment started with recording of baseline values of EST, EPT and PPT of the finger and orofacial region. All the recordings were made two-three times and the mean values were used in the analysis. The experiment was performed in a randomized manner concerning which side that was tested and which region that was tested first. All subjects received a patient number consecutively. Subjects with even subject numbers were tested on the right side and the recordings started in the orofacial region, while subjects with uneven subject numbers were tested on the left side and the recordings started with the finger. After recordings of baseline sensory and pain thresholds a CPT was performed. Thirty seconds after the subjects had immersed the hand in the cold water EPTs and PPTs were again assessed in the same order as during recordings of baseline values. To investigate any after sensations of the CPT the recordings of sensory and pain thresholds were repeated 5 and 15 min after the termination of the CPT.
Assessments of PPT

PPT was recorded using an algometer, which has been reported to reflect mainly pressure pain sensitivity of deeper tissues. (22). The algometer (Somedic Sales AB, Höör, Sweden) consisted of a pistol grip and a rod with a pressure-sensitive strain gauge at the tip (diameter 10 mm), connected to a power supply, an amplifier and a display. The display showed the pressure (kPa) and a scale indicating the rate of pressure force increase. A pressure rate of 30kPa/s was used. The scale enables the examiner to keep a constant rate of pressure increase. The subjects were instructed to push a button as soon as the pressure sensation became painful. This was first performed over the soft tissue close to the base of the thumb on the dorsal side of the hand, in order to accustom the subjects to the procedures. In the orofacial region the recordings of PPT (PPTO) were made over the most prominent part of the superficial masseter muscle with the muscle at rest by holding the algometer perpendicular to the skin surface. The PPT over the finger (PPTF) was recorded over the tip of the middle finger with the aid of a pinch handle attached to the algometer. The pinch handle allows the finger tip to be pressed against the handle by the probe during recording, i.e. the finger tip is squeezed between the pinch handle and the probe. Recordings of PPT were made three times at baseline, twice during the CPT and again three times after the CPT.

Assessment of EST and EPT

EST and EPT in the orofacial region were recorded over one of the central maxillary incisors (ESTO and EPTO, respectively) with an electrical pulp tester (Vitality scanner, Analytic Technology, Redmond; Washington U.S.A.). It consisted of a probe, through which electrical impulses fire towards the tooth. To achieve this there has to be a closed circuit between the device, the operator and the subject. The probe is connected to a power supply, an amplifier, a rate controller and a display. The subjects were instructed to say “stop” when they started to feel any sensation in the tooth (EST) or when the sensation started to become painful (EPT). As soon as the test stopped the numbers froze on the display and the examiner recorded the value.

EST and EPT over the finger tip (ESTF and EPTF, respectively) were recorded using the PainMatcher (PainMatcher AB, Lund, Sweden; score 0-60). Pain Matcher is a microprocessor controlled constant-current electrical stimulation unit that provides rectangular pulses with a frequency of 10 Hz and 10mA pulse amplitude to electrodes held by the subjects between their thumb and index finger (23). It creates an eventually noxious stimulus with increasing intensity. The increase of the stimulation is obtained by increasing the pulse width from 0 to a possible maximum of 450 ms in increments of 7.5 ms, i.e. 60 steps in all. The PainMatcher records the scores as soon as the subject releases the electrodes and the score is then displayed for the operator.

Cold pressor test

During the CPT the subjects immersed their entire hand in a cold water bath (1-3 ºC) as long as they could endure, but not more than 4 minutes. The subjects were instructed to circulate the in the cold water during the test to avoid warming up the water in the close vicinity of the hand by the body temperature. The subjects could remove their hand at any time if the pain became intolerable. The CPT tolerance time was recorded, as well as the water temperature after CPT.
Assessments of pain

During CPT the subjects were asked to score the intensity and unpleasantness of the painful sensation on a 0-10 numerical rating scale graded from 0 = no pain to 10 = unbearable pain. In addition, they were also asked to use the PainMatcher to match their perceived pain intensity/unpleasantness during CPT with a similar level induced by the PainMatcher.

Statistics

The significance of the differences between genders in age and base-line pain thresholds were tested with Students unpaired *t*-test. Two-way repeated measures ANOVA was used to test the significance of the differences in pain threshold during the experiment for each stimuli and region separately. The factors used were gender with two levels; males and females, and condition with four levels; baseline, during CPT, 5 minutes after CPT, and 15 minutes after CPT. The Holm-Sidak all-pairwise multiple comparison procedure was used as post-hoc test. Additional two-way repeated measures ANOVAs were used to test if the changes in pain thresholds during and after CPT were influenced by which side that was tested (right or left) or by the order of test sites, i.e. if the finger or orofacial region was tested first. The data concerning gender differences in pain-tolerance time were analysed for statistical significance with unpaired *t*-test, while differences in pain intensity and pain unpleasantness were tested with non-parametric test, i.e. the Mann-Whitney *U*-test. The Spearman rank correlation test was used to test the significance of the correlations between pain scales (NRS vs. Pain Matcher) regarding pain intensity and pain unpleasantness. Statistical significance was accepted at *p* ≤ 0.05.

Results

Baseline sensory and pain thresholds

The base line sensory and pain thresholds are shown in Table 1. The EPTF was significantly higher in the males than in the females (*p* = 0.022). There was also a tendency to a higher PPTF in the males (*p* = 0.076). There were no significant differences between the genders regarding the other sensory and pain thresholds.
Changes in sensory thresholds after CPT

The EST_F differed significantly between genders (F = 4.770, p = 0.042), i.e. the change was significantly higher in the males compared to the females at all occasions (Fig. 1). There was also a significant difference in EST_F between conditions (F = 11.962, p < 0.001). The post hoc test showed that the EST_F was significantly increased at 5 and at 15 minutes after the CPT.
compared to baseline \((p = 0.05)\), but there was no difference between the EST\(_F\) 5 and 15 minutes after CPT (Table 2). The EST\(_O\) did not differ significantly with gender or condition.

**Changes in pain thresholds during and after CPT**

The changes in pain threshold during and after CPT are shown in Table 2 and Fig. 2. In general, the pain thresholds were increased during CPT, but decreased 5 minutes after CPT. Fifteen minutes after CPT the pain thresholds was similar to base-line levels.

*Table 2.*

Changes (%) in mean pain thresholds (SD) to electrical and mechanical stimulation of the finger and orofacial region in 20 healthy subjects during and 5 min as well as 15 min after a cold pressor task (CPT). The values are normalized to baseline.

<table>
<thead>
<tr>
<th></th>
<th>During CPT</th>
<th>5 min after</th>
<th>15 min after</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Electrical sensory threshold</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finger (0-60)</td>
<td>n.a.</td>
<td>104 (22)*</td>
<td>103 (22)*</td>
</tr>
<tr>
<td>Incisor (mV)</td>
<td>n.a.</td>
<td>107 (25)</td>
<td>97 (24)</td>
</tr>
<tr>
<td><strong>Electrical pain threshold</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finger (0-60)</td>
<td>149 (26)*</td>
<td>79 (20)*</td>
<td>98 (15)</td>
</tr>
<tr>
<td>Incisor (mV)</td>
<td>107 (22)*</td>
<td>102 (20)*</td>
<td>96 (15)</td>
</tr>
<tr>
<td><strong>Pressure pain threshold (kPa)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finger</td>
<td>120 (20)*</td>
<td>83 (21)*</td>
<td>99 (15)</td>
</tr>
<tr>
<td>Superficial masseter muscle</td>
<td>154 (34)*</td>
<td>72 (19)*</td>
<td>100 (13)</td>
</tr>
</tbody>
</table>

\(* = \text{significant difference to baseline (repeated measures ANOVA with Holm-Sidak post-hoc test,}\ (p < 0.05). \text{EST during CPT was not assessed (n.a.).})

There was no significant difference between genders regarding changes of EPT\(_F\) (Fig. 2A), but a significant difference with condition \((F = 47.082, p < 0.001)\). The post hoc test showed that the EPT\(_F\) was significantly increased during CPT, but significantly decreased 5 minutes after CPT compared to baseline (Table 2).

There were no significant differences in EPT\(_O\), between genders or condition in general, but a significant interaction between them \((F = 4.718, p = 0.005)\). The post hoc test showed that the EPT\(_O\) was significantly increased during CPT \((p < 0.05)\) in the females, while there were no differences in the EPT\(_O\) with condition in the males. In addition, there was a significant difference in EPT\(_O\) between genders during and 5 minutes after CPT (Fig. 2C).

Neither the PPT\(_F\) or PPT\(_O\) differed significantly between genders (Fig. 2B and 2D), but differed significantly with condition \((F = 25.523; p < 0.001\) and \(F = 13.541; p < 0.001\), respectively). The post-hoc test showed that for both regions the PPT was significantly increased during CPT and significantly decreased 5 minutes after CPT compared to baseline (Table 2).
Fig. 2: The changes to baseline (%) on the electrical and pressure pain thresholds (EPT and PPT, respectively) of the finger tip and in the orofacial region during and 5 as well as 15 minutes after a cold pressor task in 10 healthy males and 10 age matched healthy females. The dotted line represents values at baseline. A) The EPT over the finger tip B) PPT over the finger tip C) EPT over the central maxillary incisor and D) PPT over the superficial masseter muscle. * = Significant difference between genders (p < 0.05).

Neither side or anatomical region influenced the results, i.e. there was no significant difference between subjects tested on the right or left side and no differences between subjects that depended on the sequence of testing, i.e. if the finger or orofacial region was tested first.

Pain during CPT

The CPT quickly induced pain of high intensity in all subjects. The tolerance time, i.e. the time that the subjects could tolerate to immerse their hand in the cold water varied between xx min y sec and 3 minutes and 55 seconds. There were no differences in the tolerance time with respect to gender.

The pain intensity and pain unpleasantness assessed on the numeric rating scale (NRS) did not differ between genders (Fig. 3A), but was significantly higher in the males when assessed with the PainMatcher (p < 0.049 and p = 0.045, respectively; 3B).
Fig. 3: Sex differences in pain intensity and pain unpleasantness assessed with a numeric rating scale (NRS, 0-10) and the PainMatcher (0-99) respectively. A) Pain assessed with NRS B) Pain assessed with the PainMatcher. There was a significant gender difference in pain intensity as well as pain unpleasantness with the PainMatcher.

* = Significant difference between genders (p = 0.045).

There was a significant correlation between the pain unpleasantness assessed with the NRS and the PainMatcher (rs = 0.583, n = 20, p = 0.012), but no significant correlation regarding pain intensity (Fig. 4).

Fig. 4: The correlation between pain assessed with a numerical rating scale (NRS) and the PainMatcher. A) pain intensity and B) pain unpleasantness. There was a significant correlation between pain unpleasantness assessed with the NRS and the PainMatcher (rs = 0.583, n = 20, p = 0.012), but no significant correlation regarding pain intensity.
Discussion

The main results of the present study showed that the pain threshold increased during CPT and decreased 5 min after termination of the CPT for most of the stimuli used and for both regions, but that there were no gender differences in the response. However, in the orofacial region there was a significant difference between genders for electrical stimulation during CPT and 5 min after. In addition, the male subjects assessed the pain-intensity and pain-unpleasantness induced by the CPT significantly higher than the females on the PainMatcher, but not on the NRS.

Sex differences at baseline

Sensibility in general is well developed in the craniofacial region and other senses such as smell and taste are better developed in males than in females according to previous studies (24). However our study did not show any sex differences concerning EST in the craniofacial region at baseline. This indicates that sensory threshold is not gender specific. This is in concordance with a study that used a similar methodology to record the EST over the mentalis nerve (25).

The results of the present study did not show any sex differences at baseline regarding the pain threshold to mechanical stimuli over the finger or orofacial region, although there was a tendency to a difference between genders for the PPT over the finger. Neither was there any gender differences regarding the pain threshold to electrical stimulation in the orofacial region. In contrast, the EPT over the finger was significantly higher in the males than in the females. A number of studies using various stimuli indicate that there are gender differences in pain sensitivity to noxious stimuli (7, 8,15). Most studies have shown that females generally have lower pain thresholds than men. This is in agreement with the results regarding the pain threshold to electrical stimulation and the pain threshold to mechanical stimulation of the finger in the present study, but contradicts the results from the orofacial region. In most studies regarding craniofacial regions, mechanical stimulation, i.e. recording of PPT has been used to investigate pain thresholds over the muscles and jaws. Some studies have reported lower PPT over the temporalis anterior and masseter muscles in females than in males (9, 26) while other studies did not report any sex differences in PPT over either the masseter muscle or the temporal muscle (27-29). The study by Jensen et al. 1992 (26) included a large number of subjects, while most studies that did not show gender differences included few subjects. A recent review showed that most studies that have not show gender differences in PPT have included a too low number of subjects to reach statistical significance (30). This indicates that the results regarding the PPT over the orofacial region in the present study might be due to a type II error, i.e. that too few subjects were included. To our knowledge no studies have yet been published regarding gender differences in pulpal pain thresholds to electrical stimulation. Future studies including a larger number of subjects are needed to address this question.

DNIC is induced by CPT in both groups

Various studies have indicated that DNIC is less able to inhibit pain in females than in males. These studies have mostly concerned temporal summation of pain using thermal, electrical and mechanical stimuli and have shown a greater temporal summation in women suggesting an up-regulation of central processing of nociceptive inputs in females compared to males (20, 31-35). These findings can be seen as an indirect support for the hypothesis that endogenous analgesic mechanisms are functionally hypoactive in women, leading to an increased predisposition to chronic painful conditions (36, 37). The inhibitory effects of
DNIC observed in our study was somewhat different compared to these studies. During CPT the pain thresholds to electrical as well as mechanical stimulation increased in both groups, but 5 min after the CPT the pain thresholds were decreased compared to baseline. After 15 minutes the pain thresholds were normalized. This means that the inhibitory effects of DNIC were only active during CPT. Although the pain thresholds increased during CPT sex differences were observed only regarding EPTO during and 5 minutes after CPT. However, during CPT the increase of EPTO was greater in the women than in the men, which is a finding in contrast with previous research (35, 38), but 5 minutes after CPT the results were the opposite, i.e. the EPTO was increased in the males but not in the females. One explanation to the different results could be different methodology, but perhaps also that differences occur due to anatomical region. However, the most probable explanation is that too few subjects were included, i.e. a type-II error.

None of the previous studies have investigated the effect of DNIC on pulp pain thresholds in healthy subjects. Hypothetically, the inhibitory effects of DNIC might have another impact in the orofacial region compared to other regions. There is evidence that the pain perception differs between different anatomical regions and different parts of the body are differently presented in the somatosensory cortex. The orofacial region has a very large presentation in the somatosensory cortex and the ability to recruit DNIC could thus be more efficient. The ESTF increased after CPT in both genders, while the ESTO remained unchanged. At baseline the ESTF was higher in males than in females. Unfortunately, due to limited time for the measurements we were not able to assess the EST during CPT. However, the results indicate that also the sensory detection threshold of the finger in contrast to the tooth pulp is influenced by DNIC. Further research is needed to address this question.

Several lines of evidence indicate that women’s sensitivity to pain changes across the menstruation cycle due to fluctuating levels of the hormones oestrogen and progesterone and that women are more sensitive to pain in the luteal phase than in the follicular phase (39). However this effect has been found to be reduced in women taking birth control pills (40). In the present study, 5 of the 10 females were in the follicular phase of the menstruation cycle and 5 in the luteal phase. Two female subjects took birth control pills. Therefore, we cannot exclude the possibility that differences in sex-hormone levels could have exerted some influence on the effects of DNIC.

There are theories which state that repeated painful experiences in the past can lead to greater pain sensitivity (41). An example of this is children who have suffered from repeated painful otitis media during their childhood, who are often more sensitive to pain compared to other children. This is believed to be due to a wind-up phenomenon (42). In our study 7 of the females and 4 of the males reported a single previous painful experience, but none reported repeated previous pain experiences. In theory, a single or only a few previous painful experiences, such as childbirth or bone fractures could increase the subject’s pain threshold, possibly by a more efficient activation of the DNIC. If our theory is correct, this could partly explain the lack of gender differences regarding DNIC in our study.

### NRS versus PainMatcher

Because of the inherent subjectivity, pain is very difficult to quantify. The ordered categorical scales, e.g. NRS are commonly used in the assessment of pain. These scales are however bounded by fixed endpoints and thus the range of measurement is limited. Furthermore, it is difficult to evaluate the individual subject’s rating of the intensity of his perceived pain, as these scales are influenced by personality variables and socio-cultural factors, which may be as strong as the ratings of pain intensity and unpleasantness itself (43). In the study of Lundeberg et al. 2001 (43) a solution to this problem was to introduce an additional painful
physical stimulus against which the subject could match his perceived pain. This was also
done in this study, by the PainMatcher.
This present study shows that there were no sex differences in rating of pain intensity and
pain unpleasantness with NRS. All the subjects in this study were mentally and physically
healthy. Thus these factors would not influence the ratings of pain. However, males assessed
both pain intensity and pain unpleasantness higher than females with the PainMatcher, which
was an unexpected finding. Previous studies have found the PainMatcher to be a valuable tool
to assess sensory- and pain thresholds in healthy volunteers (19). However, in the present
study most subjects experienced that the sensation induced by the PainMatcher was more
unpleasant than painful. This could explain the lack of correlation between NRS and
PainMatcher regarding pain intensity, in contrast to pain unpleasantness. This could indicate
that the PainMatcher might be a more valuable device in measuring the pain unpleasantness
rather than the pain intensity.
In conclusion, our findings suggest an increase in pain thresholds in healthy subjects after
activation of DNIC. This pain inhibitory effect was gender-specific in the response to
electrical stimulation of the orofacial region that was larger in the males 5 min after CPT.
However we were not able to find significant gender differences in the other parameters and
further research in this area is necessary, perhaps with a larger amount of subjects.

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   referred pain areas triggered by spatial summation of experimental muscle pain from

discussion 184-195.


Appendix

DNIC – descending noxious inhibitory control
EST – electrical sensory threshold
  EST\(_F\) – electrical sensory threshold finger
  EST\(_O\) – electrical sensory threshold orofacial
EPT – electrical pain threshold
  EPT\(_F\) – electrical pain threshold finger
  EPT\(_O\) – electrical pain threshold orofacial
PPT – pressure pain threshold
  PPT\(_F\) – pressure pain threshold finger
  PPT\(_O\) – pressure pain threshold orofacial
CPT – cold pressor test
NRS – numeric rating scale
PM – PainMatcher