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Original experimental

Painful heat attenuates electrically induced muscle pain in men and women

Maria Gullander[a,b], Stein Knardahl[b], Dagfinn Matre[b,*]

[a] Norwegian University of Life Sciences, Ås, Norway
[b] Dept of Work Psychology and Physiology, National Institute of Occupational Health, Oslo, Norway

HIGHLIGHTS

- Is gender differences in pain inhibition the reason for high prevalence of pain in women?
- Muscle pain was inhibited by heat pain conditioning in both men and women.
- Women were investigated in the menstrual phase with highest pain inhibition.
- No gender differences in pain inhibition was found.

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ABSTRACT

Background and purpose: Women exhibit higher prevalence of most painful disorders. Several explanations have been proposed for this discrepancy, one being that endogenous pain modulatory pathways, which affect incoming nociceptive signals, act differently in men and women. A less efficient pain inhibitory system has been proposed as a contributing factor to explain why women exhibit higher prevalence of most painful disorders. The present study determined whether muscle pain, induced experimentally by electrical stimulation, is inhibited by a painful heat stimulus. This conditioned pain modulation (CPM) paradigm was used to determine whether women show signs of reduced inhibition compared to men.

Methods: Forty self-reported healthy individuals (20 female, 20 male) participated in a cross-over design with painful and non-painful heat as a conditioning stimulus. Test stimuli were painful intramuscular electrical stimulation of the tibialis anterior muscle at two intensities; low (1.1 × pain threshold) and high (1.6 × pain threshold). Painful conditioning was contact heat (45–49 °C) to the contralateral forearm. Non-painful conditioning was contact heat at 35 °C. Ten test stimuli were delivered in three blocks (before, during and after conditioning) in two sessions (painful and non-painful conditioning). The women were tested during days 12–14 of the menstrual cycle. This interval corresponds to the ovulatory phase of the menstrual cycle, the interval during which women are reported to show the largest inhibitory effects.

Results: Test stimuli were rated significantly lower during painful conditioning, compared with before conditioning. This was found for both low and high test stimulus intensities. A nonspecific attenuation was seen during non-painful conditioning for the low test stimulus intensity. Test stimuli were rated significantly lower also 3 min after conditioning, compared with before conditioning. The inhibitory effects were not different between men and women. Similar findings were obtained also if six non-CPM-responders (subjects rating test stimuli higher during conditioning than before conditioning) were excluded.

Conclusions and implications: The present findings indicate that painful contact heat inhibits electrically induced muscle pain and that inhibition was not different between men and women, when women were tested in the interval 12–14 days after their last menstruation. Some inhibition of muscle pain was seen during non-painful conditioning, indicating that nonspecific inhibitory effects were triggered. Also the nonspecific inhibitory effects were similar in men and women.

1. Introduction

Women exhibit higher prevalence of most painful disorders [1,2]. Several explanations have been proposed for this discrepancy, one being that endogenous pain modulatory pathways, which affect incoming nociceptive signals, act differently in men and women. An imbalance between activation of descending

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* Corresponding author at: National Institute of Occupational Health, PB 8149 Dep, 0033 Oslo, Norway. Tel.: +47 23 19 52 15; fax: +47 23 19 52 00.
E-mail addresses: dagfinn@stami.no, dagfinn.matre@gmail.com (D. Matre).

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facilitatory and inhibitory pathways in women may facilitate pain transmission [3,4].

The pain modulatory pathways may be triggered by several factors. One example is expectations during which inert pain-reducing or pain-enhancing treatments lead to reduced or enhanced pain, respectively [5,6]. Distracting the attention away from the painful stimulus is another example that is known to reduce pain [7,8]. Pain inhibition may also be triggered by a somatic stimulus such as a concomitant non-painful [9] or painful stimulus [10,11]. Generally, in this 'pain-inhibits-pain' phenomenon, a painful heterotopic conditioning stimulus (CS) attenuates a painful test stimulus (TS). The phenomenon through which the conditioning stimulus affects the test stimulus is termed 'conditioned pain modulation' (CPM) [12]. Hence, the efficacy of the pain inhibitory system may be assessed by quantifying to what extent a painful CS inhibits a painful TS [10,12]. This is termed the CPM effect.

Several studies have found support for a reduced CPM effect in women compared to men [13]. A common CS in CPM studies is the cold pressor test in which a hand (or a foot) is submerged in painfully cold water. Using the cold pressor test as a conditioning stimulus, test stimuli of several different modalities (pressure pain, the spinal R-III reflex, contact heat pain) has been shown to be inhibited less in women than in men [14–16]. A difference between men and women is also seen when a painful hot water bath is used as conditioning to inhibit repeated heat stimuli delivered to the thenar surface of the hand [17] or when saline-induced trapezius muscle pain inhibits pressure pain [18].

Although several studies indicate that the CPM effect is stronger in men than in women, contradictory findings also exist; see e.g. [19–22]. Tousignant-Laflamme and Marchand [22] found that when the women were tested in a fixed interval relative to the first day of their last menstrual cycle (days 12–14), the CPM effect did not differ between men and women. This indicates that the efficacy of the pain modulatory systems vary across the menstrual cycle.

The CPM literature is dominated by studies during which test stimuli are delivered to the skin [10]. The musculoskeletal pain prevalence in the general population is reported to be 10–35% depending on body location [2,23]. Data from animal studies indicate that muscle nociception is likely to be influenced to a much stronger degree by endogenous inhibitory systems than skin nociception [24]. Taken together this call for more studies of how endogenous pain modulatory systems affect muscle pain.

The aim of the present study was to determine whether inhibition of a painful *muscular* test stimulus is different in women and men when contact heat was used as the conditioning stimulus. In order to control for a potential variation in the efficacy of the pain modulatory systems across the menstrual cycle, the female participants were tested during days 12–14 relative to their last menstruation.

2. Methods

2.1. Design

The experiment was a single-blind cross-over study with two sessions, a test session with painful conditioning and a control session with non-painful conditioning. Half of the subjects participated in the test session first followed by the control session. In the other half, the order of the sessions was reversed. Subject gender was balanced between the groups. The second session started 30 min after the first session was finished. In each session electrical test stimuli (TS) were delivered in three blocks (before CS, during CS and 3 min after CS). In the test session a painful contact heat stimulus was delivered as a conditioning stimulus (CS) simultaneously with the electrical TS in the second block. In the control session no CS was delivered.

2.2. Subjects

Forty subjects (20 females/20 males) participated in the study. Mean age was 23.6 ± 2.7 years (male) and 25.2 ± 2.7 years (female; $p = 0.08$). All participants responded to an announcement at the homepage of the National Institute of Occupational Health, Norway or to flyers posted at universities and colleges in Oslo. All participants were paid 150 NOK/hour (≈$25). Inclusion criteria were age between 18 and 45 years and self-reported good health. Exclusion criteria were diagnosis of any somatic or psychiatric disease Furthermore, individuals who used prescription drugs for blood pressure, sedatives, antidepressants, or allergy medication, and smokers were excluded. Subjects were instructed not to drink any alcohol during the last 24 h before the experiment. An informed consent was obtained from each individual. The experimental protocol was approved by the regional ethical committee and was conducted according to the Helsinki Declaration.

2.3. Menstrual cycle

At inclusion, the women reported the first day of their last menstruation (=day 1). All women were tested during days 12–14 in reference to this day. Days 12–14 is referred to as the ovulatory phase by Tousignant-Laflamme and Marchand [22]. If more than 14 days had elapsed since the last menstruation, the subject was asked to report back on the first day of their next menstruation.

2.4. Procedures

2.4.1. Test stimulation (TS)

Intramuscular electrical stimulation of the tibialis anterior muscle served as TS. Each stimulus consisted of a brief (25 ms) train of five unipolar 1-ms electrical square-wave pulses at 200 Hz. At the start of each session, the individual pain threshold was determined by a ladder regime consisting of five ascending series of stimuli. Starting at sub-detection intensities, the stimulus intensity was increased until the subject reported it as being painful [25]. The mean of the five mA-values perceived as painful was defined as the pain threshold (PT). The number of stimuli used to determine the PT was usually between 20 and 30. The inter stimulus interval was 10–15 s. Test stimuli (TS) were administered at two painful intensities, one slightly above pain threshold (1.1 × PT = low TS intensity) and one that was aimed to be moderately painful in order to mimic a clinically relevant pain intensity (1.6 × PT = high TS intensity).

The electrical stimuli were delivered through two needle electrodes (9013R0272, Alpine BioMed, Skovlunde, Denmark) inserted 10–15 mm into the tibialis anterior muscle 10 cm distal to the lower edge of the patella, with approximately 1 cm between the electrodes. The proximal electrode served as the anode. The electrical stimulation was produced by a constant-current stimulator (Noxitest, Aalborg, Denmark) that received trigger pulses from a computer (custom made software; Labview, National Instruments, Texas, USA).

2.4.2. Pain rating

Participants rated the pain intensity of each TS on a 100-mm visual analogue scale (VAS) with anchor labels "no pain" (VAS = 0 mm) and "worst pain imaginable" (VAS = 100 mm). Each VAS rating was noted on paper by the experimenter.

2.4.3. Conditioning stimulus (CS)

The conditioning stimulus was contact heat delivered to the volar forearm on the side contralateral to the TS. Contact heat was produced by a 25 mm × 50 mm peltier thermode (MSA-II, Somedic AB, Solna, Sweden). The thermode was held in place by a cuff inflated to 15 mmHg in order to standardize pressure on the skin.

The painful CS intensity was calibrated to an intensity corresponding to VAS = 50 mm (pain-50), adapted to a procedure described by Granot et al. [16]. The non-painful CS intensity was equal to the baseline temperature (35 °C).

2.4.4. Administration of stimuli

Pain-50 was determined once, at the start of the experiment, using the forearm contralateral to the side that was to receive the first CS. The electrical pain threshold (PT) was determined twice (once for each tibialis anterior muscle) at the start of each session.

Test session (painful CS): The test session consisted of three blocks spaced by 3 min. Each block lasted around 2 min and consisted of 10 electrical TS (five at 1.1 × PT and five at 1.6 × PT) delivered in pseudorandom order at 10–15 s intervals. The thermode was attached to the contralateral forearm before the first block and removed after the third block. Including spacing between blocks, the thermode was attached for around 13 min. The temperature of the thermode was 35 °C, except during the second block, during which it increased to the pain-50 level (CS) thirty seconds before TS. Thus, the first block consisted of 10 electrical TS paired with contact heat at 35 °C (before CS), the second block consisted of 10 electrical TS paired with contact heat at the pain-50 level (during CS), the third block consisted of 10 electrical TS paired with contact heat at 35 °C (3 min after CS).

Control session (non-painful CS): The control session was identical to the test session except for the contact heat stimulus, which was maintained at 35 °C during all blocks (including the 3-min breaks between blocks). I.e., no conditioning stimulus was given. The control session served as a non-painful control to the test session, incorporating the inhibitory effects of habituation, attention and other nonspecific effects.

2.5. Instructions to participants

The subjects were informed that the purpose of the study was to test their sensitivity to electrical stimulation of the tibialis anterior muscle. They were informed that three blocks, each consisting of 10 painful electrical stimuli, would be given to each leg in two separate sessions. They were further told that a metal element warmed to 35 °C would be attached to their opposite forearm. Before the second block in both sessions, the subjects were told that the temperature of the heating element would be increased to the pain-50 intensity. Note that the same instruction was given in both sessions, regardless of whether it was a test session or a control session. A written manuscript used by the experimenter (MG) ensured that identical oral information was given to all subjects.

2.6. Data analysis and statistics

Due to non-normal distribution, the electrical PT and TS pain ratings were log-transformed. Paired *t*-tests were performed to determine if the electrical PT was different between sessions, and to determine if pain ratings in response to TS at 1.1 × PT were different from ratings of TS at 1.6 × PT. Data from the 'before CS' block in each session was used for this analysis. Gender differences in electrical PT and pain-50 were tested with independent *t*-tests.

To test the inhibitory effect of CS on TS pain ratings (CPM-effect), a 2-way repeated measures analysis of variance (RM-ANOVA) was performed for each TS intensity with block (before, during, after) as one repeated measures factor and session (test vs. control) as the other repeated measures factor. Gender was entered as a between subjects factor and allowed us to determine gender differences in TS pain ratings as well as gender differences in the CPM effect. Greenhouse-Geisser correction was used when non-sphericity was detected (Maunchly's test). The percentage of CPM-responders/non-responders was calculated. Subjects who did not have any inhibitory CPM effect during or after painful CS were defined as non-responders. Data were analyzed separately for all subjects and for CPM-responders. Correlations between the CPM effect, pain-50 and electrical pain thresholds were tested by Spearman's bivariate analysis. PASW 18.0 was used for all statistical analyses (IBM, Chicago, Illinois, USA) and $p < 0.05$ was considered significant.

3. Results

3.1. Session differences in electrical PT

The electrical PT was equal in the two sessions; 5.43 ± 0.98 mA (mean ± standard deviation) in the first session and 5.83 ± 1.24 mA in the second session ($t(39) = 0.005$, $p = 0.996$). Both genders were included in this analysis.

3.2. Gender differences in electrical PT and pain-50

The electrical PT did not differ significantly between genders. The electrical PT averaged across the two sessions was 6.55 ± 6.52 mA for men and 4.71 ± 6.43 mA for women ($t(38) = 1.65$, $p = 0.106$).

The intensity of the painful conditioning stimulus (pain-50) differed between genders. Pain-50 was 47.8 ± 0.6 °C for men and 46.9 ± 0.8 °C for women ($t(38) = 3.7$, $p = 0.001$).

3.3. The effect of painful and non-painful CS on TS

3.3.1. CPM effects during CS

For the high TS intensity there was a significant interaction between session (painful CS vs. non-painful CS) and block (before CS, during CS, after CS), indicating stronger CPM effect during painful CS than during non-painful CS ($F(1,38) = 4.43$, $p = 0.042$). Table 1 shows the TS pain ratings before, during and after conditioning for all subjects and for the 34 responders. Fig. 1 shows the CPM-effect during CS, relative to before CS. For the low TS intensity, there was an inhibitory CPM effect during both painful CS and during non-painful CS ($F(1,38) = 4.62$, $p = 0.038$). As expected, the interaction between session and block was stronger with only responders included ($F(1,32) = 7.52$, $p = 0.01$).

Subjects with large inhibitory effects during painful CS also exhibited large inhibitory effects during non-painful CS. This was tested by correlation analyses, which were significant for the high TS intensity (Pearson's $r = 0.68$, $p < 0.001$), but not for the low TS intensity (Pearson's $r = 0.22$, $p = 0.17$).

Order was not a significant between-subjects factor neither for the low TS intensity ($F(1,36) = 0.017$, $p = 0.897$) nor for the high TS intensity ($F(1,36) = 0.002$, $p = 0.967$).

3.3.2. CPM effects after CS

TS pain ratings after CS were significantly lower than before CS regardless of whether painful or non-painful conditioning had been delivered in the previous block (during CS). This was consistent for the low TS intensity ($F(1,38) = 4.6$, $p = 0.038$) and for the high TS intensity ($F(1,38) = 4.2$, $p = 0.047$) (Table 1). The effect was more pronounced when only CPM-responders were included in the analysis ($F(1,32) = 9.38$, $p = 0.004$ and $F(1,32) = 8.46$, $p = 0.007$; low and high TS intensity, respectively). There was no effect of gender ($F(1,38) = 0.12$, $p = 0.7$).

3.4. Gender differences on the CPM effect

In the RM-ANOVA assessing the effect of session and block on TS pain ratings, gender was not a significant factor ($F(1,38) = 0.45$, $p = 0.5$). To determine whether non-responders contributed to the

Table 1
Test stimulus (TS) pain ratings (VAS) before, during and after painful and non-painful conditioning stimulus (CS). Data are mean ± standard deviation.

	Painful CS		Non-painful CS	
	Low TS intensity (mm)	High TS intensity (mm)	Low TS intensity (mm)	High TS intensity (mm)
All subjects (*n* = 40)				
Male				
Before CS	22.9 ± 16.6	29.1 ± 17.4	25.4 ± 17.6	30.9 ± 20.6
During CS	20.7 ± 14.2	25.9 ± 18.2	23.0 ± 17.0	29.0 ± 21.1
After CS	21.8 ± 16.9	27.5 ± 18.6	21.9 ± 15.9	28.8 ± 17.5
Female				
Before CS	31.2 ± 19.8	37.8 ± 21.5	25.0 ± 15.5	33.6 ± 18.8
During CS	27.4 ± 19.5	32.8 ± 22.1	22.4 ± 15.3	30.9 ± 18.7
After CS	29.0 ± 22.9	34.9 ± 25.2	20.5 ± 13.2	29.8 ± 18.6
Responders (*n* = 34)				
Male				
Before CS	24.2 ± 17.3	30.7 ± 18.0	26.4 ± 17.6	32.1 ± 20.4
During CS	21.1 ± 14.8	26.5 ± 19.4	22.7 ± 15.6	29.2 ± 20.3
After CS	22.3 ± 18.1	27.8 ± 19.9	20.8 ± 14.8	28.4 ± 16.9
Female				
Before CS	33.3 ± 20.2	39.7 ± 21.2	26.2 ± 16.4	33.2 ± 18.6
During CS	28.0 ± 20.6	33.1 ± 22.1	24.0 ± 16.1	30.9 ± 19.9
After CS	29.6 ± 23.7	35.8 ± 25.7	20.5 ± 14.1	29.2 ± 19.5

negative effect on gender, the analyses were repeated on the 34 CPM-responders. However, gender was still not a significant factor in the analysis ($F(1,32) = 0.3$, $p = 0.6$).

An additional comparison of the CPM effect between men and women was made by performing independent *t*-tests on the CPM effect (during CS minus before CS) for the session with painful CS. There was no difference between men and women for the low TS intensity ($t(38) = 0.95$, $p = 0.35$) or for the high TS intensity ($t(38) = 0.21$, $p = 0.84$) when all subjects were included or when only CPM-responders were included (low TS intensity: $t(32) = 1.0$, $p = 0.31$; high TS intensity: $t(32)$ $t = 0.23$, $p = 0.82$). Taken together, this indicates that the CPM effect in the present study was not different in men and women.

3.5. Correlations between the CPM effect, pain-50 and electrical pain thresholds

Correlations between the CPM effect, the conditioning stimulus (pain-50) and electrical pain thresholds were tested on the 34 CPM-responders. No significant correlations were found between

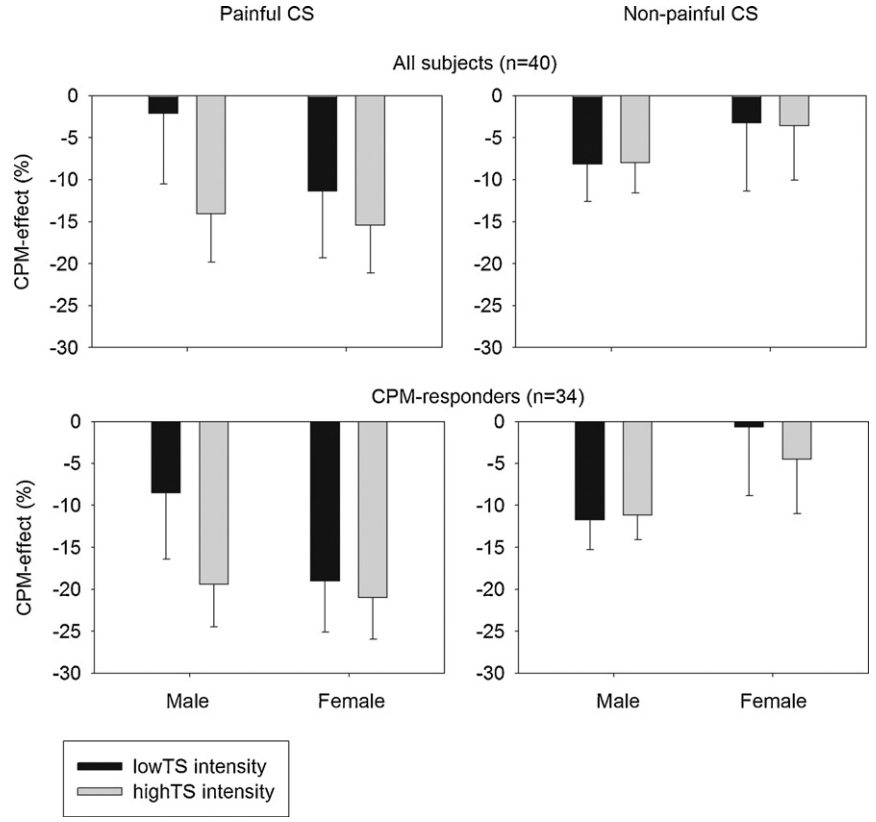

Fig. 1. Conditioned pain modulation (CPM)-effects during painful and non-painful conditioning stimulation (CS) in all subjects ($n = 40$; upper panels) and in CPM-responders only ($n = 34$; lower panels). The statistical analysis showed a significant CPM-effect during CS across both sessions, genders and intensities (see Section 3.3.1), but no effect of gender. Values are mean ± SEM.

the CPM effect and pain-50 (Spearman's rho < 0.179, $p > 0.31$) or between the CPM effect and the electrical PT (rho < 0.282, $p < 0.106$).

4. Discussion

The present findings indicate that painful contact heat inhibits electrically induced muscle pain. Inhibition was not different between men and women. Women were tested in the time interval 12–14 days after their last menstruation. An inhibition of muscle pain was also seen during non-painful CS, indicating that nonspecific inhibitory effects were activated. The nonspecific inhibitory effects were similar in men and women.

4.1. Gender differences in pain modulation

Differences in activation of endogenous analgesic systems in men and women have been investigated in several studies during the last decade. Recently two reviews were published. Popescu et al. [13] performed a meta-analysis of 17 articles, quantifying the CPM effect in each study. They report that CPM (or DNIC) was 1.7 times less efficient in females than in males. Van Wijk and Veldhuijzen [26] report that seven studies demonstrated more efficient pain inhibition in men than in women and six studies showed no gender difference.

Two previous studies on gender differences controlled for the menstrual cycle, testing women in the follicular phase. Serrao et al. [14] found that ice water induced greater inhibition of the nociceptive withdrawal reflex in men than in women. Baad-Hansen et al. [20] did not find any difference between men and women when ice water inhibited ratings of painful intraoral capsaicin. Different definitions of the follicular phase may explain the divergent findings. The women were tested during days 8–10 of the menstrual cycle in the study by Serrao and co-workers, while they were tested during days 3–9 in the study by Baad-Hansen and co-workers, both studies defining the respective time window as the follicular phase. However, methodological variations such as the duration and strength of the applied stimuli and the anatomical region tested make it difficult to generalize across studies of pain inhibitory mechanisms [10].

The women participating in the present experiment were tested during days 12–14 relative to the self-reported first day of the last menstruation. This particular interval was selected since Tousignant-Laflamme and Marchand [22] found that women during this interval have comparable CPM efficacy to men. Since no confirmatory hormonal or temperature measurements were performed we cannot be certain that all the women were indeed tested in the ovulatory phase. Although the start date of the last menstrual period can be reliably obtained from self-report [27], it is difficult to exclude irregular cycling base on only self-report [28]. Still, it seems reasonable to take the present findings as support for the conclusion posed by Tousignant-Laflamme and Marchand [22]; that during certain periods of the menstrual cycle, the efficacy of the descending inhibitory systems is as effective in women as in men.

4.2. The effect of painful conditioning stimulation on muscle pain

The mean inhibitory CPM-effects on experimentally induced muscle pain during painful CS in the present study was somewhat lower compared to other studies that tested painful heat as CS in combination with an electrically induced test stimulus. In the present study, the maximum CPM-effect was ca 20% (obtained when only responders were analyzed on high TS intensity scores). CPM effects of 80% and 43%, respectively, were obtained in two studies measuring the electrocutaneous pain threshold [29,30]. The pain intensity (VAS) during electrical tooth stimulation was inhibited by 33% [31].

An argument for selecting a muscular test stimulus in the present study was that data from animal studies indicate that endogenous inhibitory systems are likely to influence muscle nociception to a stronger degree than skin nociception [24]. Comparing the present data with data from the above mentioned studies indicate that endogenous inhibitory systems influence skin nociception more strongly than muscle nociception. A recent study showed that the pressure pain threshold from the tibialis anterior was inhibited by 66.3% during cold pressor pain [32]. This show that weak inhibition of muscle nociception is not a general phenomenon and indicate that differences in outcome measures, body locations and experimental procedures may have a strong influence on these divergent findings. A paired study during which both muscular and skin nociceptive test stimuli are tested with the same conditioning stimulus is necessary in order to shed more light on this issue.

It has been uncommon to test several TS intensities in CPM studies. The two TS intensities tested in the present study were both perceived as mildly painful. It is possible that stronger CPM effects would have been detected if stronger TS intensities had been used. Oono et al. [31], who tested three TS intensities (mean ratings: 30, 41 and 59 of 100) reported inhibitory CPM effects for the two strongest TS intensities, but not for the weakest. There was also a tendency towards stronger CPM effect for the high TS intensity vs. the low TS intensity in the present study. Taken together, these and previous findings indicate that the CPM effect depends on TS intensity as well as on CS intensity.

Three minutes after CS the CPM effect was reduced, although it was still significant. This is in accordance with several previous studies [31,33–35] and indicates that activation of descending pain inhibitory mechanisms by a painful stimulus depends on an ongoing noxious input.

4.3. Nonspecific inhibitory effects

The present experiment demonstrated an inhibitory effect on TS also in the control session when a non-painful CS was applied. Although weaker than in the test session, this indicates that pain inhibitory mechanisms were activated by factors not related to nociceptive systems. Previous studies have shown inhibitory effects during non-painful heat (≈42 °C) [19,29,30,36,37] or during vibration [9,38].

In the present control session (non-painful CS) the thermode temperature remained at baseline level (35 °C) throughout the session (before, during, and after CS). Since no CS was actually given, pain inhibition activated by non-painful somatosensory input seems to be an unlikely explanation. A recent study found that habituation produced inhibitory effects of similar magnitude as a non-painful conditioning stimulus [39]. Habituation may explain some of the present effects. However, a higher TS responses 'after CS' than 'during CS' (for the high TS intensity) speaks against this explanation. A second explanation lays in the instructions given to the subjects. Before the second block in both sessions, subjects were told that they should expect that the forearm thermode temperature would increase to the pain-50 intensity. The wording was: "In the first series you will receive only electrical stimulations. In the second series you will receive electrical stimulations and heat stimulation at the pain-50 intensity. In the third series you will receive only electrical stimulations". Since pain-50 occurred in the test session only and not in the control session, one may speculate that the mere anticipation of a painful heat to the forearm resulted in inhibition of the TS [40,41]. Distraction from the TS while anticipating the noxious heat may also have contributed to reducing TS pain ratings [42].

4.4. Gender differences in pain perception

The present data indicated that women were more sensitive than men to suprathreshold heat pain. Increased pain perception in women is in accordance with several previous studies and seems to hold across several pain modalities [1,15,18,43–46]. Whereas most previous studies are based on pain threshold measurement, the present findings extend these findings by showing increased pain sensitivity in women also for suprathreshold stimuli.

There was no differences between men and women in pain perception when comparing ratings of suprathreshold intramuscular stimulation ($1.1 \times$ PT and $1.6 \times$ PT). Neither was there a difference when comparing intramuscular electrical PT, although women showed a tendency towards lower PT than men. In previous studies using electrocutaneous stimulation women reported greater pain than men [14,45]. The differences between the present study and the latter two studies may depend on type of stimulated tissue (muscle vs. skin).

4.5. Conclusion

The present findings indicate that painful contact heat inhibits electrically induced muscle pain and that inhibition was not different between men and women when women were tested in the time interval 12–14 days after their last menstruation. This interval corresponds to the ovulatory phase of the menstrual cycle. A weaker inhibition of muscle pain was seen during non-painful CS, indicating that nonspecific inhibitory effects were triggered. Also the nonspecific inhibitory effects were similar in men and women.

Conflict of interest

No funding sources were provided. The authors declare that no conflicts of interest exist.

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