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Sex differences in responsiveness to painful and non-painful stimuli are dependent upon the stimulation method

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Summary Sex differences in thermo- and electrocutaneous responsiveness to painful and non-painful stimuli were investigated in 20 women and 20 men. Heat pain, warmth, and cold thresholds were assessed on the hand and foot with a Peltier thermode system. In addition, subjects used magnitude estimation to judge the sensation intensity evoked by temperatures ranging from 38°C to 48°C applied to the forearm. To measure detection, pain, and tolerance thresholds of electrocutaneous sensitivity, electrical pulses were administered to the hand. Magnitude estimates of sensation intensity were assessed for stimuli ranging from 0.5 mA to 4.0 mA. There were no sex differences in heat pain, warmth and cold thresholds. There were significant sex differences in electrical detection, pain and tolerance thresholds, with lower thresholds in women. Correspondingly, magnitude estimates were similar in women and men when using thermal stimuli while women judged stimuli from 2.5 mA on as more intense than men when using electrical stimuli. Despite these discrepancies, the measures for pain responsiveness from the two stimulation methods correlated significantly. In contrast, no significant correlations between the methods were found when considering the responsiveness to non-painful stimuli. The findings help to clarify controversies in the pain literature about sex differences. Results affirming and denying such differences could be obtained within a single sample, with stimulation method as the critical variable.

Key words: Sex difference; Pain threshold; Sensory threshold; Magnitude estimation

Introduction

There is a long history of interest regarding sex differences in responsiveness to experimental pain. Despite many advances in stimulation techniques and psychophysical assessment methods, the issue of whether such differences exist has still not been resolved. The view that women are more likely to differ from men with respect to pain tolerance than with other measures of pain responsiveness appears to be the only one that receives widespread agreement (e.g., Goolkasian 1985).

One assumption inherent in many experimental studies of sex differences is that the method of pain induction (e.g., thermal, mechanical, electrical) is not particularly relevant. Based upon this assumption, previous results have been interpreted as being dependent on the pain dimension assessed (e.g., threshold or tolerance, sensory or affective component) and on higher-order variables such as anxiety, sex role, hormonal influences, and the like. This assumption needs to be examined.

There would be little debate about the existence of sex differences if only pressure pain were considered. Studies using constant pressure methods (Otto and Dougher 1985; Dubreuil and Kohn 1986) as well as ones using variable pressure techniques (Woodrow et al. 1972; Fischer 1987; Brennum et al. 1989; Jensen et al. 1992) have consistently found that women are more pain sensitive than men.

Most of the studies that have produced conflicting results have used either thermal or electrical stimulation. For example, Clark and Mehl (1971), applying radiation heat, found no differences in pain threshold

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between men and women, whereas Procacci et al. (1970) reported lower radiation heat pain thresholds in women than in men. Goolkasian (1980), also using radiation heat, observed a better discrimination ability in women than in men, but only if the women were in the ovulatory phase of their menstrual cycles. Testing pain tolerance at four body sites with a heat beam dolorimeter, Lipman et al. (1990) obtained lower tolerance values in women only for the breast, which was the sole site examined with a clear anatomical sex difference.

Using contact heat, two studies showed that detection as well as pain thresholds were similar in women and men (Kenshalo 1986; Lautenbacher and Strian 1991). In contrast, Feine et al. (1991) found that women rated temperature stimuli – delivered by a contact thermode and probably mostly above pain threshold – more strongly than did men.

Rollman and colleagues (Rollman and Harris 1984, 1987; Rollman et al. 1990) observed, in a series of studies with electrocutaneous stimulation, that women had lower detection, pain and tolerance thresholds. In contrast, Neri and Aggazani (1984) found no sex differences at all, while Robin et al. (1987) and Notermans (1966; Notermans and Tophoff 1967) found them only for tolerance but not for detection and pain thresholds. Harkins and Chapman (1977), using electrodental stimulation, obtained similar values for pain threshold, discrimination ability, and response bias in the two genders.

One possibility may be that sex differences in pain responsiveness are simply smaller for thermal and electrical stimulation than for mechanical pressure. Consequently, the influence of sample characteristics would be greater for the first two methods. To address the question of sample dependency, we planned a comparison of two stimulation methods which either had previously produced sex differences (Rollman and Harris 1984, 1987; Rollman et al. 1990) or had not (Lautenbacher and Strian 1991) in a single sample.

There have been some attempts (e.g., Larkin et al. 1986) to explain sex differences in somatosensation and pain sensitivity by body measure differences. These have only been partially successful (Rollman et al. 1990; Lautenbacher and Strian 1991, 1993). The idea underlying this concept is that the notion that women are more responsive than men can be replaced by the notion that small people are more responsive than large individuals. Intervening factors may be such things as skin thickness, receptor density, or length of the afferent pathways. Some of these may affect the temporal and spatial summation properties in second-order neurons by influencing the degree of simultaneous arrival of afferent impulses, a matter of particular importance when slowly conducting primary afferents, responding to noxious inputs, are involved.

TABLE I

SAMPLE DESCRIPTION FOR AGE, BODY MEASURES, ANXIETY (STAI-X1) AND REACTIVITY (RS) (mean ± S.D.)

P values of *t* tests on sex differences are given.

	Women	Men	*P* value
	n = 20	n = 20	
Age (years)	21.0 ± 4.8	20.6 ± 2.5	0.388
Height (cm)	165.0 ± 7.5	180.6 ± 6.0	< 0.001
Weight (kg) [a]	61.3 ± 7.0	73.6 ± 6.5	< 0.001
Body Mass Index [b]	22.6 ± 2.9	22.6 ± 2.4	0.499
Body Surface (cm^2)	16627.3 ± 1066.7	19191.2 ± 919.9	< 0.001
STAI	36.4 ± 6.2	33.2 ± 10.2	0.123
RS	78.6 ± 10.2	67.9 ± 12.6	0.003

[a] Weight with clothes.

[b] Weight (cm)/height (m)^2.

Such an explanation, however, can be valid only if the influence of body measures on responsiveness holds within as well as across genders. We wished to investigate this issue further. The criteria for a valid explanation we set were the finding of a substantial body measure-responsiveness measure relation in both sexes examined separately and in the groups combined, as well as the finding of a significant difference between the sexes in this body measure. In a similar manner, we tested two psychological variables that have previously been shown to provide a possible basis for sex differences in pain perception: anxiety (Robin et al. 1987) and psychological reactivity (Dubreuil and Kohn 1986).

Methods

Subjects

Twenty women and 20 men took part in the study; all participants were undergraduate students. The description of both samples is given in Table I. The two groups were very similar in age. The body measure differences between genders were typical in that men were both taller and heavier; the equivalent body mass indices for the two groups indicates that each consisted of normal weight subjects. Women had only slightly higher scores on the state anxiety scale but significantly higher scores on the psychological reactivity scale.

Ten women served as subjects while they were in the menstrual and postmenstrual phases (days 1–12), 5 in the intermenstrual phase (days 13–17), and 5 in the premenstrual phase (days 17–28). Fifteen had natural periods and 5 were taking oral contraceptives. There is some evidence (Goolkasian 1980; Hapidou and de Catanzaro 1988) that pain responsiveness is greater during the inter- and premenstrual phases than during other times. If so, we had equal numbers of more and less pain responsive women in our sample.

The protocol was approved by an ethics committee; all subjects gave written informed consent. A single male experimenter conducted all testing sessions.

Apparatus and procedure

At the beginning of each session, subjects filled out the questionnaires measuring anxiety (STAI-X1, Spielberger et al. 1970) and psychological reactivity (RS, Kohn 1985).

Following this, psychophysical tests using thermal stimuli were administered. The stimulator was a temperature-controlled contact thermode with a stimulation surface of 1.6×3.6 cm^2, mounted on an articulated arm. Contact pressure could be adjusted and was held at 0.4 N/cm^2. The apparatus (PATH Tester MPI 100; for details see Galfe et al. 1990) also included a thermode controller with a microcomputer for managing thermal stimulation and a personal computer for controlling the procedures.

The protocols used by Lautenbacher and Strian (1991) were chosen for the assessment of thermal thresholds (warmth, cold) and heat pain thresholds in order to conduct a replication of their study. Sites of stimulation were the lateral dorsum pedis (right foot) and the thenar of the right hand, in that order. At each site, the detection thresholds for warmth and cold were first assessed. Starting at a temperature of 32°C, 7 warm and then 7 cold stimuli were administered. The rate of the temperature change was 0.7°C/sec. The subjects had to press a button as soon as they noticed a change in temperature. Following this, the temperature returned to the base value (1.5°C/sec). The mean differences between the base temperature and the peak temperature in the 2 sets of 7 trials were taken as the measures of the warmth and cold thresholds. The intertrial interval lasted 10 sec. The stimuli were delayed between 1 and 3 sec (pseudo-randomized intervals) after visual and acoustic warning signals for the start of a trial.

The heat pain threshold was then measured. Eight trials were run, each beginning at a temperature of 40°C, with a rate of temperature change of 0.7°C/sec. The subjects were instructed to press a button as soon as they felt pain. Each time they pressed the button, the temperature returned to the base value at a cooling rate of 1.5°C/sec. An upper limit was set at 52°C for safety reasons. The start of each trial was announced visually and acoustically, but the stimulus was presented with a pseudo-randomized delay of between 1 sec and 3 sec. The intertrial interval lasted 10 sec. The pain threshold was calculated as the mean of the peak temperatures of the last five trials.

Subjects then made magnitude estimates of non-painful and painful thermal stimuli applied to four sites at the right volar forearm. The forearm was chosen because it allowed site variations without sensitivity variations and guaranteed a plane contact surface at all sites. Forty-four stimuli (base temperature: 36°C; rate of temperature change: 1.5°C/sec; saw tooth shape) were given in four blocks of 11 each. In each block, all intensities ranging from 38°C to 48°C in steps of 1°C were used. The order of the stimuli was pseudo-randomized so that strong intensity differences between consecutive trials were avoided, by limiting the differences between them to 5°C or less. Such differences were balanced across intensity levels. This was thought to be necessary to control for adaptation level effects.

The subjects could stop the temperature increase at any time, if they felt that the stimulation produced undue discomfort, by pressing the response button. At the end of each block, the site of stimulation was changed. Each trial consisted of the stimulation interval lasting at least 10 sec and until the base temperature was reestablished, and the response interval of 10 sec, which also constituted the interstimulus interval. Both intervals were signalled with acoustic and visual cues.

Subjects estimated the perceived intensity of each stimulus by assigning a number to the sensation. To obtain interindividually comparable sensation estimates, a form of modulus was introduced by telling the subjects that they should use the number 50 for a 'barely painful sensation.' This variant of magnitude estimation has been successfully applied in experimental pain studies (Willer et al. 1984; Marchand et al. 1991). The first block was a practice one and was not considered in the evaluation. The average of the three magnitude estimates for each stimulus intensity was used as the corresponding sensation intensity.

In the next part of the study, psychophysical tests using electrocutaneous stimuli were conducted. After skin preparation (cleaning and abrading), two Grass silver electrodes were attached slightly proximal to the base joints of the thumb and index finger (cathode at thumb, anode at index finger). The stimuli were delivered by a constant-current stimulator (CCS-1, Frederic Haer and Company) and consisted of ten 1-msec monophasic square-wave pulses with an interval between pulse onsets of 20 msec (frequency: 50 Hz; total duration: 181 msec). The start of each stimulus was signalled by a light. First, detection, pain, and tolerance thresholds were measured in three ascending series with discrete steps of 0.15 mA. An upper limit was set at 7.5 mA for safety reasons. The average in the three series was taken as the corresponding threshold value.

For magnitude estimation, 44 stimuli with 11 intensities (0.5, 1.0, 1.5, 2.0, 2.5, 2.75, 3.0, 3.25, 3.5, 3.75, 4.0 mA) were applied using the same procedures for stimulation and magnitude estimation as those with the temperature stimuli. Subjects with a tolerance threshold below 4.0 mA were not run in the magnitude estimation experiment. The intensity range was based upon earlier studies (Rollman and Harris 1984, 1987) which indicated that a considerable portion of the subjects could be studied within these limits. The spacing of the intensities was chosen to provide 0.5-mA steps up to 2.5-mA and 0.25-mA steps from 2.5 mA to 4.0 mA in order to counterbalance the frequently observed increase of response variability at higher intensities with an increased density of data points.

At the end of each session, the body measures (height, weight) were taken and the subjects were briefly interviewed about possible medications.

Evaluation

In some subjects, a threshold – especially the tolerance threshold for electrocutaneous stimulation – could not be obtained within the pre-set safety limits. In these cases, the threshold was assumed to be higher than the safety limit and ranked correspondingly. Therefore, non-parametric statistics (Mann-Whitney U test, Spearman rank correlation) were used in the part of the analysis dealing with thresholds. Otherwise, for simple group comparisons t tests were computed. A MANOVA with the group factor 'sex' and the repeated-measures factor 'stimulus intensity' was used to evaluate the magnitude estimation of sensation intensity. Only subjects with estimates at all stimulus intensity levels were included to avoid varying sample sizes over the intensity dimension. To obtain an over-all measure of perceived magnitude, the data of the different intensity levels were collapsed by summing all ratings of an individual across all stimulus intensities. As directed hypotheses were available, 1-tailed significance testing was chosen. Alpha was set to 0.05 with the exception of the correlation analyses where it was set to 0.01 to take into account the greater number of tests.

Results

Sex differences in thermo- and electrocutaneous thresholds

Fig. 1 shows the thermal detection thresholds for non-painful stimuli (warmth, cold) measured at the hand and foot for women and men. None of the sex comparisons reached significance (warmth at the hand: $U = 191.5$, $P = 0.409$; warmth at the foot: $U = 160.5$, $P = 0.143$; cold at the hand: $U = 167.0$, $P = 0.183$; cold at the foot: $U = 192.0$, $P = 0.414$). The same was true for the heat pain thresholds measured at the same two sites, as shown in Fig. 2 (hand: $U = 183.5$, $P = 0.328$; foot: $U = 189.5$, $P = 0.388$). In contrast, all three

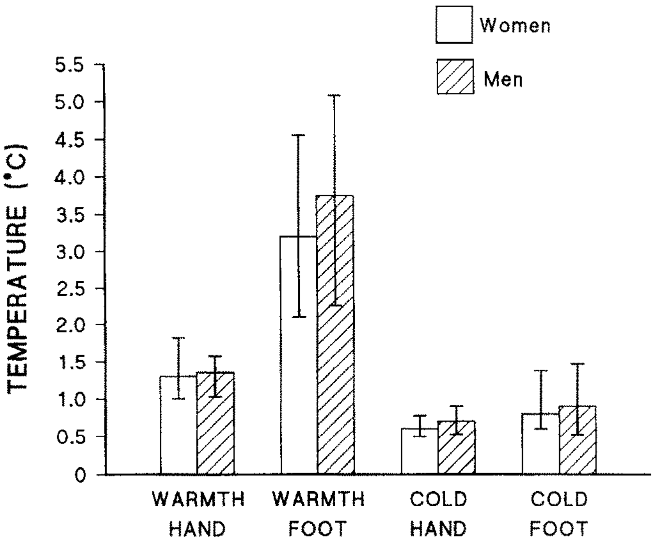

Fig. 1. Thermal detection thresholds for warmth and cold in women and men measured at the hand and foot (temperatures in °C relative to the base temperature of 32°C); median, quartile 1 and 3 are given for each measure; n = 20 in each group.

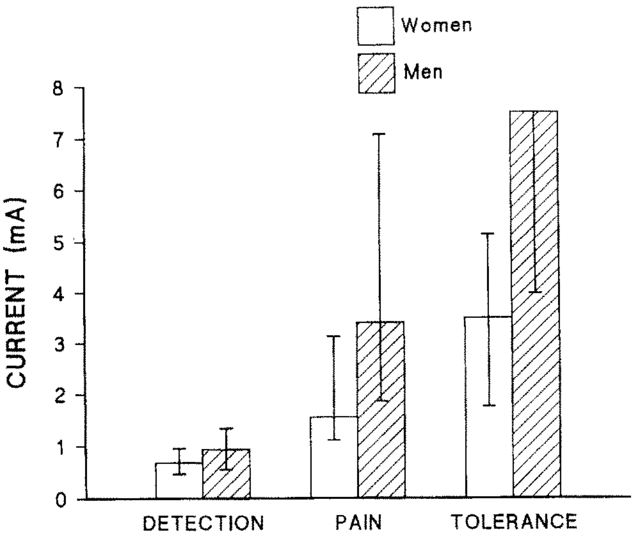

Fig. 3. Detection, pain and tolerance thresholds with electrical stimulation in women and men measured at the hand (current in mA); median, quartile 1 and 3 are given for each measure. Note that median and quartile 3 for the tolerance threshold of the men has the same value; n = 20 in each group.

thresholds with electrocutaneous stimulation at the hand were significantly lower in women than in men (detection: $U = 122.0$, $P = 0.017$; pain: $U = 107.5$, $P = 0.006$; tolerance: $U = 88.0$, $P = 0.001$) (Fig. 3). These findings point to a clear difference between thermo- and electrocutaneous stimulation in respect to sex differences.

Sex differences in magnitude estimation of thermo- and electrocutaneous stimuli

In the magnitude estimation experiment with thermal stimuli, 6 of the 20 women switched off the temperature increase before the pre-set maximum on one or more trials. All 6 women did so with 48°C stimuli, 5 with 47°C stimuli, 2 with 46°C stimuli and 2 with 44°C stimuli. None of the men stopped a trial. This alone suggests less willingness to tolerate painful heat stimuli in women than in men. These 6 observers were excluded from further evaluation to avoid missing data and to get equivalent data samples for each intensity level. (The problem of using selected samples is addressed in the Discussion). Fig. 4 shows the results. The effect of stimulus intensity was highly significant ($F = 133.2$, $df = 10, 320$, $P < 0.001$). There was no significant effect for the group factor 'sex' ($F = 0.1$, $df = 1, 32$, $P = 0.392$) or for the interaction 'sex by stimulus

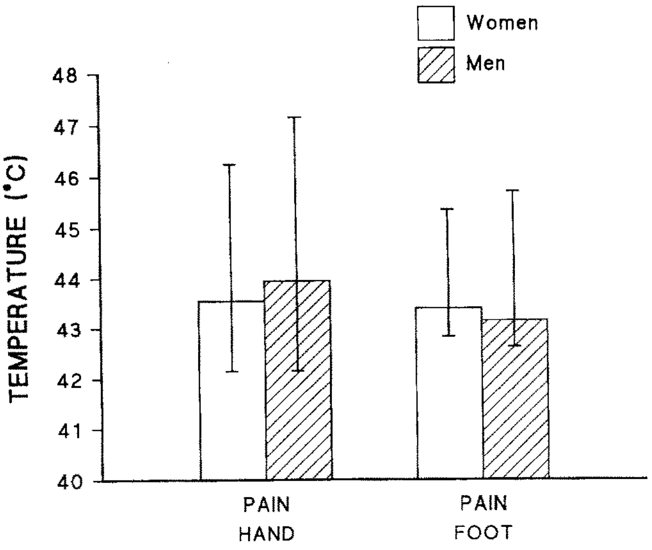

Fig. 2. Heat pain thresholds in women and men measured at the hand and foot (absolute temperatures in °C); median, quartile 1 and 3 are given for each measure; n = 20 in each group.

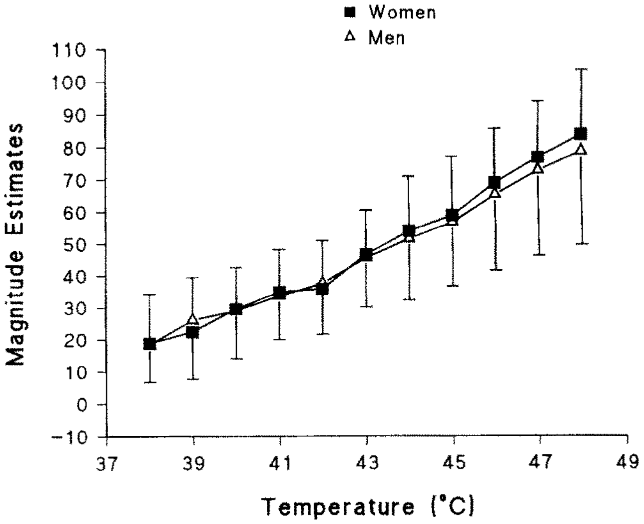

Fig. 4. Magnitude estimates of temperature stimuli applied to the forearm ranging from 38°C to 48°C in women and men; mean and 1 S.D. are given; n = 14 for women and n = 20 for men.

intensity' ($F = 0.5$, $df = 10, 320$, $P = 0.449$). Hence, no sex-related differences could be demonstrated by magnitude estimation of thermal stimuli at non-painful and painful intensity levels.

Because of the drop-out of the 6 female subjects, who may have been especially pain responsive, examining the magnitude judgments of the remaining women might possibly have led us to underestimate potential sex differences. In order to decrease the likelihood of such an error, a second analysis was conducted which included all observers. Since quadratic polynomial regressions on individual data resulted in an excellent goodness of fit for the 34 subjects who had no missing data (median of $r^2 = 0.977$), missing values for the remaining 6 subjects were replaced by estimates based upon quadratic polynomial regressions of their available data. Again, an excellent goodness-of-fit was achieved (median of $r^2 = 0.976$). Consequently, the estimates of the missing values (22.7% of the data points for the female dropouts) could be based upon reasonably good statistical models.

The second analysis of variance, now with 20 subjects in each group, corroborated the first. Neither the group factor 'sex' ($F = 0.3$, $df = 1, 38$, $P = 0.305$) nor the interaction 'sex by stimulus intensity' ($F = 0.3$, $df = 10, 380$, $P = 0.487$) became significant. While an element of uncertainty remains, these results make a sex difference in the magnitude estimation of the thermal stimuli very unlikely.

Nine women and 5 men could not be included in the magnitude estimation experiment with electrical stimuli because their tolerance thresholds were too low to enable them to receive the full stimulus range of 0.5–4 mA. Fig. 5 presents the magnitude estimation results.

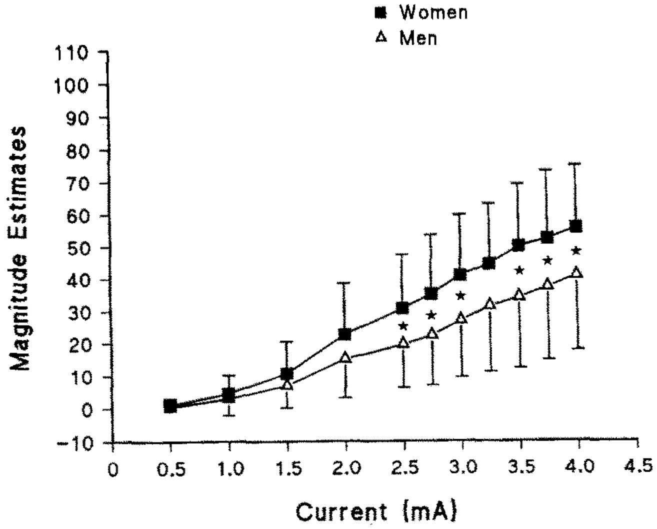

Fig. 5. Magnitude estimates of electrical stimuli applied to the hand ranging from 0.5 mA to 4 mA in women and men; mean and 1 S.D. are given; n = 11 for women and n = 15 for men. Significant sex differences at an intensity level are shown by stars (all $P \leq 0.05$).

Again, the effect of stimulus intensity was highly significant ($F = 89.5$, $df = 10, 240$, $P < 0.001$). However, the effect of sex ($F = 3.39$, $df = 1, 24$, $P = 0.039$) and, to a stronger degree, the interaction 'sex by stimulus intensity' ($F = 2.59$, $df = 10, 240$, $P = 0.003$) were also significant. Subsequent t tests for sex differences at each stimulus intensity level revealed that the significant interaction was based on significant sex differences from the intensity of 2.5 mA on, the intensity of 3.25 mA being the only exception (0.5 mA: $t = 0.9$, $P = 0.181$; 1.0 mA: $t = 0.6$, $P = 0.220$; 1.5 mA: $t = 1.4$, $P = 0.124$; 2.0 mA: $t = 1.9$, $P = 0.092$; 2.5 mA: $t = 3.6$, $P = 0.034$; 2.75 mA: $t = 3.8$, $P = 0.032$; 3.0 mA: $t = 3.8$, $P = 0.032$; 3.25 mA: $t = 2.8$, $P = 0.053$; 3.5 mA: $t = 3.7$, $P = 0.033$; 3.75 mA: $t = 3.0$, $P = 0.047$; 4.0 mA: $t = 3.0$, $P = 0.047$). According to the t values, the sex differences, once established, did not increase in size with increasing stimulus intensity.

A comparison of the magnitude estimates shown in Figs. 4 and 5 indicates that the pre-set electrical stimulus intensities were not rated as painful as the pre-set thermal stimulus intensities (as a reminder, a 'barely painful sensation' was to be rated as 50). More subjects had to be excluded from magnitude estimation with electrical stimuli than from magnitude estimation with thermal stimuli to avoid undue discomfort. Had we abandoned ethical considerations and forced all subjects to rate all of the presentations in the full stimulus range, it is likely that the perceived magnitudes at the upper end of the physical scale would have been similar for the electrical and thermal stimuli.

Correlations between thermo- and electrocutaneous responsiveness measures

The findings point to a clear difference between thermo- and electrocutaneous stimulation in demonstrating sex differences. Therefore, it was of interest to look at the relationship between the two groups of measures. The corresponding correlational analysis is presented in Table II. It is evident that when non-painful levels are involved there was almost no relation between thermal and electrical measures (with the exception of the implausible but significant correlation between the collapsed magnitude estimates with electrical stimulation at the hand and the warmth threshold at the foot). In contrast, the two heat pain thresholds (hand, foot) correlated significantly with the electrical pain threshold measured at the hand. Similar cross-modal consistency in pain responsiveness was reported by Harris and Rollman (1983). A tendency to site specificity was found, since the pain measures determined at one site correlated more strongly with each other than those determined at different sites.

The collapsed magnitude estimates of the thermal stimuli correlated significantly and negatively with the electrocutaneous pain threshold and tolerance. That is,

TABLE II

SPEARMAN RANK CORRELATIONS FOR THE RELATION BETWEEN THERMO- AND ELECTROCUTANEOUS MEASURES OF SENSITIVITY

n = 40 for all correlations with the exception of those where magnitude estimates are involved, here n = 24.

Thermal Stimulation	Electrical Stimulation (Hand)			
	Detection	Pain	Tolerance	Mag. Est.
Warmth				
Hand	r = 0.06	r = 0.07	r = 0.11	r = −0.06
Foot	r = 0.02	r = 0.20	r = 0.09	r = −0.50 *
Cold				
Hand	r = 0.14	r < 0.01	r = 0.05	r = −0.18
Foot	r = 0.13	r = 0.18	r = 0.13	r = −0.21
Pain				
Hand	r = 0.33	r = 0.64 **	r = 0.56 **	r = −0.37
Foot	r = 0.10	r = 0.42 *	r = 0.33	r = −0.36
Magnitude Estimates				
Forearm	r = 0.06	r = −0.68 **	r = −0.53 *	r = 0.62 **

* $P \leq 0.01$, ** $P \leq 0.001$.

subjects with low electrical pain thresholds and tolerance levels rated strong thermal stimuli as more intense than did those with high thresholds.

However, the collapsed magnitude estimates of the electrical stimuli, while in the appropriate direction, did not significantly correlate with the heat pain thresholds (hand, foot). This may be a consequence of the finding that the ratings of the thermal stimuli were clearly higher and more strongly reflect painful sensations (see foregoing paragraph).

The sizable relation between experimental pain measures across induction methods was all the more meaningful because the magnitude of these correlations is comparable to the values obtained for correlations within a modality. For thermal stimulation, pain threshold on the hand correlated with that on the foot ($r = 0.86$). The collapsed magnitude estimates for the 11 temperature levels correlated with hand ($r = -0.75$) and foot ($r = -0.68$) heat pain thresholds. All correlations had a $P \leqq 0.001$. For electrocutaneous stimulation, pain threshold and tolerance had a correlation coefficient of 0.67. Collapsed magnitude estimates for the 11 current levels correlated significantly with pain threshold ($r = -0.88$) and tolerance ($r = -0.59$). Again, $P \leqq 0.001$.

Taken together, the correlational analysis suggests that the responsiveness measures of both stimulation methods are indicators of a common perceptual process at painful levels but not at non-painful ones.

Correlations between responsiveness measures and covariates (body measures, anxiety, reactivity)

In order to test the assumption that sex differences in the responsiveness measures can be explained by other variables, we looked for significant correlations in the two sexes separated and in the samples combined. None of the covariates presented in Table I met this criterion. There were some examples of relations which appear significant when the two sexes are combined, but not for males or for females separately. Height, for example, correlated significantly with the electrical detection threshold ($r = 0.50$, $P < 0.001$), pain threshold ($r = 0.37$, $P = 0.009$) and tolerance threshold ($r = 0.40$, $P = 0.005$) only in the combined sample. Similarly, body surface area correlated significantly with the electrical pain threshold ($r = 0.37$, $P = 0.009$) and tolerance threshold ($r = 0.43$, $P = 0.003$) in the combined sample.

We consider these to be pseudo-relations; ones which emerge because size and responsiveness data for women tend to cluster together in one group and those for men in another. There is no indication of a relationship between responsiveness and height or body area when the data for males alone or females alone are examined.

In addition to such pseudo-relations, some inexplicable correlations appeared although we had set an alpha of 0.01 for the correlational analysis. We mention them in passing: for the combined sample, STAI-X1 × warmth threshold at the foot, $r = -0.42$, $P = 0.003$; for the group of women, age × electrical tolerance threshold, $r = 0.54$, $P = 0.008$; STAI-X1 × cold threshold at the hand, $r = -0.68$, $P = 0.001$; RS × heat pain threshold at the foot, $r = -0.54$, $P = 0.007$; body mass index × electrical detection threshold, $r = -0.55$, $P = 0.006$.

Discussion

The major finding of the present study was that different stimulation methods (thermo- and electrocutaneous) with a single set of observers produced different outcomes with respect to sex differences in responsiveness to non-painful and painful stimuli. Therefore, the assumption that the conflicting results of our previous electrical (Rollman Harris 1984, 1987; Rollman et al. 1990) and thermal (Lautenbacher and Strian 1991) studies were only due to sample differences could be rejected. With both stimulation techniques the earlier findings were replicated, demonstrating their reliability.

In the replication of Lautenbacher and Strian's (1991) study, again there were no sex differences in heat pain thresholds measured at the hand and foot. In the present investigation, the sample consisted of Canadians instead of Germans, and the mean age was 20.8 years instead 37.7 years. The findings of these two studies were akin to those of Kenshalo (1986), having applied a similar stimulation method (contact heat) for the assessment of pain thresholds at comparable sites in a group of young subjects and a group of elderly subjects. The present study and the earlier ones also demonstrated that there are no sex differences for the detection of non-painful cold. The only measure that produced conflicting findings in the three studies was the detection threshold for non-painful warmth. In Lautenbacher and Strian's (1991) study, women were more responsive than men to a small degree at the hand and to a large degree at the foot, whereas the present study showed no sex differences at either site. Kenshalo observed lower thresholds at the foot for young women, compared to men of similar age, but not for older women.

The present study expanded the methods to include magnitude estimation of sensation level for temperatures ranging from non-painful (38°C) to painful levels (48°C). The subjects were told that they could switch off the temperature increase at any time in order to avoid undue discomfort. Only women (30%) did so, mainly with temperatures clearly above pain threshold. This can be interpreted as less willingness of women than of men to experience supra-threshold heat pain. We excluded those women who withdrew on any of the trials from further evaluation. There was no indication that the remaining women rated the temperatures, both at non-painful and painful levels, differently from men.

Several points ought to be made. First, data from all the women and all the men went into the threshold comparisons. No gender differences emerged. Second, magnitude estimates reflect data from all the men and the majority of women (70%). Again, no differences were found. Had the excluded women been willing to endure higher temperatures, it is possible that the estimates for women would have been somewhat elevated within the upper pain range. The analysis based upon replacement of missing data with estimates obtained from individual psychophysical functions, however, strongly reinforced the original conclusions. The evidence clearly indicates that the majority of women have a similar responsiveness to both non-painful and painful temperatures as men.

Our findings contrast with the results of the study conducted by Feine et al. (1991) who also used a contact thermode and a magnitude estimation procedure. Feine et al. found that women gave appreciably higher ratings with the same temperatures than men. These differences occurred even at the lower end of their temperature range where the stimuli seem to be around the pain threshold level. It is unlikely that sample differences were the cause for the differing results, since young Canadians were the subjects in both studies. The sex of the experimenter is also unlikely to account for the differences. Feine et al. found that their sex differences occurred irrespective of the experimenter's gender. Moreover, the same male experimenter ran all sessions of this study, yet the sex of the subject was only significant for the electrical pulses.

The most likely reason for the different outcomes in this study and that of Feine et al. seems to be the thermal stimulation parameters. The present study applied temperatures from 38 – 48°C to the forearm with a 5.8 cm^2 thermode and a rate of temperature change of 1.5°C/sec. The corresponding parameters for the Feine et al. study were 45 – 50°C applied above the subject's upper lip, 0.8 cm^2 and 6°C/sec.

The fact that we were unable to administer the upper end of our temperature scale to all subjects, while in the Feine et al. study even higher temperatures could apparently be used without any problems, suggests that the same temperatures were felt as less intense in that investigation than in our own. This cannot be easily explained by the different heating slopes, because it has been demonstrated that higher rates of temperature change lead to higher sensation intensities (Yarnitsky and Ochoa 1990). It is also unlikely that the sites used accounted for the difference.

The smaller size of the thermode in the Feine et al. study, however, could well be critical. Douglas et al. (1992) and Price et al. (1989) presented persuasive evidence for spatial summation of heat pain within the range of areas under discussion. Hence, one might speculate that the degree of spatial summation was the critical difference between the two studies. If spatial summation mechanisms are stronger and reach a ceiling sooner in women than in men, sex differences may occur with small thermodes but not with large ones. This analysis would also account for the finding of no sex differences for heat pain thresholds in the study of Kenshalo (1986) who also used a large thermode (7.1 cm^2).

It might be argued that the difference in heating slope between the Feine et al. study and our own was still the crucial factor accounting for the contrasting findings on sex differences, but for affective and motivational reasons rather than sensory ones. Feine et al.'s higher slopes may have lead to greater levels of anxiety specifically related to the stimulation, influencing the rating of sensation magnitude. These anxiety levels may be different in the two sexes.

The results of the present study were also in agreement with the earlier findings of Rollman and coworkers (Rollman and Harris 1984, 1987; Rollman et al. 1990) regarding sex differences with electrocutaneous stimulation. Again, lower detection, pain, and tolerance thresholds were obtained in women than in men. The magnitude estimation outcomes corroborated the results for the thresholds. From a simulation intensity of 2.5 mA on, quite stable sex differences emerged, with women being more responsive than men. This contrasts with some other studies that used electrocutaneous stimulation, where either no sex differences (Neri and Aggazani, 1984) or differences only for tolerance threshold (Notermans and Tophoff 1967; Robin et al. 1987) were obtained.

A closer comparison of the present study with that of Robin et al. (1987) is particularly interesting, since similar samples (young subjects) and similar psychophysical procedures (method of limits with ascending series for the measurement of detection, pain, and tolerance thresholds) were used. In the Robin et al. study, the mean threshold values were similar for the detection threshold, lower for the pain threshold, and clearly lower for the tolerance threshold when compared with the present study. Different stimulation parameters may account for the differences. Here, ten 1-msec pulses were applied with a frequency of 50 Hz through electrodes with a size of 0.5 cm^2 to the dorsal hand; Robin et al. used fifteen 10-msec pulses with a frequency of 10 Hz and electrodes of 4.5 cm^2 at the finger pads.

Pulse duration may have been the crucial factor. If the electrode size were critical, the detection threshold should have been lower in the Robin et al. study than in ours (Higashiyama and Tashiro 1990). The lower frequency should have produced higher pain and tolerance thresholds in the Robin et al. study than in ours (Notermans 1966). Neither was the case. However, increases of the pulse duration above 1 msec seem to affect the pain threshold but not the detection threshold (Notermans 1966; Rollman 1969, 1975; Higashiyama and Tashiro 1983; Virtanen et al. 1987). Therefore, the difference in pulse duration between the two studies (1 msec vs. 10 msec) may play a role in accounting for the differing levels of the pain and tolerance thresholds and the partially divergent outcomes on sex differences. The hypothesis that sex differences become less likely with increasing temporal summation fits with the negative results of Neri and Aggazani (1984) and the partially negative results of Notermans and Tophoff (1967), both of whom used a pulse duration of 5 msec.

Alternatively, a more psychological explanation, similar to that posed for the results on thermal sensations, may be considered. Anxiety directly relevant to the stimulation can have an effect on pain sensitivity, while irrelevant anxiety does not (Al Absi and Rokke 1991). In the present study and in the former studies of Rollman's group (Rollman and Harris 1984, 1987; Rollman et al. 1990) shorter pulse trains were used than in the other studies mentioned above. Very brief shocks may evoke more anxiety, do this in a sex-related fashion, and thus influence the reported sensation intensity. General state anxiety neither differed between women and men nor correlated significantly with the responsiveness measures. Perhaps better measures of stimulation-relevant anxiety are needed.

Direct scaling methods proved to be useful additions to threshold procedures for the investigation of sex differences. However, because of the considerable individual differences in the stimulus intensities which produce pain, particularly for electrical stimulation, it was not possible to select a uniform range of pain stimuli for all subjects. This fact, recently also noted by Boureau et al. (1991), in a study with pain patients, deserves further consideration because the consequence is either having selected samples (as in the present study) or a decline in data quality with higher intensities due to an increasing amount of missing data.

Rollman and Harris (1987) noted that in selecting the stimuli to be used in magnitude estimation tasks, two approaches can be contrasted. The first is to present the same stimuli to all observers, while the second is to tailor the stimulus set to each individual's pain sensitivity range. The first more readily permits comparisons across groups and was utilized here.

Our correlational analysis showed that there was almost no relation between thermo- and electrocutaneous responsiveness at non-painful levels. This finding confirms that different neural systems are activated by weak thermal and electrical stimuli. Non-painful thermal stimuli trigger neural activity in small-diameter nerve fibers (Aδ and C) (Darian-Smith 1984). Electrical pulses directly activate large A-fibers (Reilly 1992; Rollman 1975). The different fibers, different spinal transmission systems, and different central processing mechanisms which are engaged by the two stimulus modalities apparently give rise to independent levels of somesthetic sensitivity.

In contrast, substantial correlations were found between the responsiveness measures of the two methods at painful levels. This provides further evidence that various forms of noxious stimulation can activate a common pain system (Harris and Rollman 1983; Melzack and Casey 1968). The close relation was preserved although the two stimulation methods differed clearly in their outcomes regarding sex differences.

None of our covariates (body measures, anxiety, psychological reactivity) appeared to be able to explain the observed sex differences because none of them met the criterion of correlating significantly with the responsiveness measures both in the two sexes separated and in the sample combined and of differing significantly between the sexes.

The present study clearly showed that the finding of sex differences in cutaneous responsiveness at non-painful and painful levels depends on the stimulation method used. Positive results were demonstrated with electrocutaneous stimulation; negative results occurred with thermocutaneous presentations. Moreover, it seems that within a single physical dimension (electrical, thermal, etc.), stimulus parameters may have a strong impact on the sex difference outcome. One critical factor may be the degree to which spatial and temporal summation are engaged by a stimulation method. The summation mechanisms may differ between the sexes and may, as a result, produce sex differences in the responsiveness measures. An alternative assumption may be that the stimulus characteristics of duration, onset time, and the like determine the amount of stimulus-related anxiety, the level of which may differ between the sexes.

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References

Al Absi, M. and Rokke, P.D., Can anxiety help us tolerate pain?, Pain, 46 (1991) 43-51.

Boureau, F., Luu, M. and Doubrère, J.F., Study of experimental pain measures and nociceptive reflex in chronic pain patients and normal subjects, Pain, 44 (1991) 131-138.

Brennum, J., Kjeldsen, M., Jensen, K. and Jensen, T.S., Measurements of human pressure-pain thresholds on fingers and toes, Pain, 38 (1989) 211-217.

Clark, W.C. and Mehl, L., Thermal pain: a sensory decision analysis of the effect of age and sex on d′, various response criteria, and 50% pain threshold, J. Abnorm. Psychol., 78 (1971) 202-212.

Darian-Smith, I., Thermal sensibility. In: I. Darian-Smith (Ed.), Sensory Processes. II. Handbook of Physiology, Sect. 1, Vol. 3., American Physiological Society, Bethesda, MD, 1984, pp. 879-913.

Douglas, D.K., Carstens, E. and Watkins, L.R., Spatial summation in human thermal pain perception: comparison within and between dermatomes, Pain, 50 (1992) 197-202.

Dubreuil, D.L. and Kohn, P.M., Reactivity and response to pain, Pers. Indiv. Diff., 7 (1986) 907-909.

Feine, J.S., Bushnell, M.C., Miron, D. and Duncan, G.H., Sex differences in the perception of noxious heat stimuli, Pain, 44 (1991) 255-262.

Fischer, A.A., Pressure algometry over normal muscle: standard values, validity and reproducibility of pressure threshold, Pain, 30 (1987) 115-126.

Galfe, G., Lautenbacher, S., Hölzl, R. and Strian, F., Diagnosis of small fibre neuropathy: computer-assisted methods of combined pain and thermal sensitivity determination, Hospimedica, 8 (1990) 38-48.

Goolkasian, P., Cyclic changes in pain perception: a ROC analysis, Percept. Psychophys., 27 (1980) 499-504.

Goolkasian, P., Phase and sex effects in pain perception: a critical review, Psychol. Women Quart., 9 (1985) 15-28.

Hapidou, E.G. and DeCatanzaro, D., Sensitivity to cold pressor pain in dysmenorrheic and non-dysmenorrheic women as a function of menstrual cycle phase, Pain, 34 (1988) 277-283.

Harkins, S.W. and Chapman, C.R., Age and sex differences in pain perception. In: D.J. Anderson and B. Matthews (Eds.), Pain in the Trigeminal Region, Elsevier, Amsterdam, 1977, pp. 435-441.

Harris, G. and Rollman, G.B., The validity of experimental pain measures, Pain, 17 (1983) 369-376.

Higashiyama, A. and Tashiro, T., Temporal and spatial integration for electrocutaneous stimulation, Percept. Psychophys., 33 (1983) 437-442.

Higashiyama, A. and Tashiro, T., Electrocutaneous spatial integration at threshold: the effects of electrode size, Percept. Psychophys., 48 (1990) 389-397.

Jensen, R., Rasmussen, B.K., Pedersen, B., Lous, I. and Olesen, J., Cephalic muscle tenderness and pressure pain threshold in a general population, Pain, 48 (1992) 197-203.

Kenshalo, D.R., Somaesthetic sensitivity in young and elderly humans, J. Gerontol., 41 (1986) 732-742.

Kohn, P.M., Sensation seeking, augmenting-reducing and strength of the nervous system. In: J.T. Spence and C. Izard (Eds.), Motivation, Emotion and Personality, Proc. XXIII Congress of Psychology, Elsevier, Amsterdam, 1985, pp. 167-173.

Larkin, W.D., Reilly, J.P. and Kittler, L.B., Individual differences in sensitivity to transient electrocutaneous stimulation, IEEE Trans. Biomed. Eng., 33 (1986) 495-504.

Lautenbacher, S. and Strian, F., Sex differences in pain and thermal sensitivity: the role of body size, Percept. Psychophys., 50 (1991) 179-183.

Lautenbacher, S. and Strian, F., The role of body size in somatosensory testing, Electromyogr. Clin. Neurophysiol., 33 (1993) 113-118.

Lipman, J.J., Blumenkopf, B. and Lawrence, P.L., Normal and radiculopathic cutaneous pain tolerance levels evaluated by heat-beam dolorimetry, J. Neurosurg., 72 (1990) 883-888.

Marchand, S., Bushnell, M.C., Molina-Negro, P., Martinez, S.N. and Duncan, G.H., The effects of dorsal column stimulation on measures of clinical and experimental pain in man, Pain, 45 (1991) 249-257.

Melzack, R. and Casey, K.L., Sensory, motivational, and central control determinants of pain: a new conceptual model. In: D. Kenshalo (Ed.), The Skin Senses, CC Thomas, Springfield, IL, 1968, pp. 423-443.

Neri, M. and Agazzani, E., Aging and right-left asymmetry in experimental pain measurement, Pain, 19 (1984) 43-48.

Notermans, S.L.H., Measurement of the pain threshold determined by electrical stimulation and its clinical application. I. Method and factors possibly influencing the pain threshold, Neurology, 16 (1966) 1071-1086.

Notermans, S.L.H. and Tophoff, M.M.W.A., Sex differences in pain tolerance and pain apperception, Psychiat. Neurol. Neurochir., 70 (1967) 23-29.

Otto, M.W. and Dougher, M.J., Sex differences and personality factors in responsivity to pain, Percept. Mot. Skills, 61 (1985) 383-390.

Price, D.D., McHaffie, J.G. and Larson, M.A., Spatial summation of heat-induced pain: influence of stimulus area and spatial separation of stimuli on perceived pain sensation intensity and unpleasantness, J. Neurophysiol., 62 (1989) 1270-1279.

Procacci, P., Bozza, G., Buzzelli, G. and Della Corte, M., The cutaneous pricking pain threshold in old age, Gerontol. Clin., 12 (1970) 213-218.

Reilly, J.P., Sensory responses to electrical stimulation. In: J.P. Reilly (Ed.), Electrical Stimulation and Electropathology. Cambridge University Press, Cambridge, 1992, pp. 231-284.

Robin, O., Vinard, H., Vernet-Maury, E. and Saumet, J.-L., Influence of sex and anxiety on pain threshold and tolerance, Funct. Neurol., 2 (1987) 173-179.

Rollman, G.B., Electrocutaneous stimulation: psychometric functions and temporal integration, Percept. Psychophys., 5 (1969) 289-293.

Rollman, G.B., Behavioral assessment of peripheral nerve function, Neurology, 25 (1975) 339–342.

Rollman, G.B. and Harris, G., Rating and behavioral measures of pain threshold and tolerance: stressor, sex, and individual differences, Pain, Suppl. 2 (1984) 175.

Rollman, G.B. and Harris, G., The detectability, discriminability, and perceived magnitude of painful electrical shock, Percept. Psychophys., 42 (1987) 257–268.

Rollman, G.B., Hapidou, E.G. and Jarmain, S.H., Gender differences in pain responsiveness: contributing factors, Pain, Suppl. 5 (1990) 314.

Spielberger, C.D., Gorsuch, R.L. and Lushene, R.E, STAI - Manual for the State-Trait-Anxiety-Inventory, Palo Alto, CA, 1987.

Virtanen, A.S.J., Huopaniemi, T., Närhi, M.V.O., Pertovaara, A. and Wallgren, K., The effect of temporal parameters on subjective sensations evoked by electrical tooth stimulation, Pain, 30 (1987) 361–371.

Willer, J.C., Roby, A. and Le Bars, D., Psychophysical and electrophysiological approaches to the pain-relieving effects of heterotopic nociceptive stimuli, Brain, 107 (1984) 1095–1112.

Woodrow, K.M., Friedman, G.D., Siegelaub, A.B. and Collen, M.F., Pain tolerance: differences according to age, sex and race, Psychosom. Med., 34 (1972) 548–556.

Yarnitsky, D. and Ochoa, J.L., Studies of heat pain sensation in man: perception thresholds, rate of stimulus rise and reaction time, Pain, 40 (1990) 85–91.