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Autonomic responses to heat pain: Heart rate, skin conductance, and their relation to verbal ratings and stimulus intensity

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ABSTRACT

In human pain experiments, as well as in clinical settings, subjects are often asked to assess pain using scales (eg, numeric rating scales). Although most subjects have little difficulty in using these tools, some lack the necessary basic cognitive or motor skills (eg, paralyzed patients). Thus, the identification of appropriate nonverbal measures of pain has significant clinical relevance. In this study, we assessed heart rate (HR), skin conductance (SC), and verbal ratings in 39 healthy male subjects during the application of twelve 6-s heat stimuli of different intensities on the subjects' left forearm. Both HR and SC increased with more intense painful stimulation. However, HR but not SC, significantly correlated with pain ratings at the group level, suggesting that HR may be a better predictor of between-subject differences in pain than is SC. Conversely, changes in SC better predicted variations in ratings within a given individual, suggesting that it is more sensitive to relative changes in perception. The differences in findings derived from between- and within-subject analyses may result from greater within-subject variability in HR. We conclude that at least for male subjects, HR provides a better predictor of pain perception than SC, but that data should be averaged over several stimulus presentations to achieve consistent results. Nevertheless, variability among studies, and the indication that gender of both the subject and experimenter could influence autonomic results, lead us to advise caution in using autonomic or any other surrogate measures to infer pain in individuals who cannot adequately report their perception.

1. Introduction

In human studies involving some form of pain assessment, often subjects are asked to assess their pain by expressing ratings on various scales, such as the visual analogue scale (VAS) or numeric rating scale (NRS). This psychophysical method of pain quantification has been extensively used for decades by researchers and clinicians as a tool to monitor the effects exerted on pain by a wide variety of factors (eg, pharmacological [15] or psychological [21,22] manipulations, gender [31], ethnic background [44], personality traits [37], presence of disease [23], genetic mutations or polymorphisms [46]), and has proved to be extremely valuable, particularly for its ease of use and reliability [32]. However, although most subjects have little or no difficulty in learning how to rate their pain, using a VAS/NRS scale presupposes certain basic cognitive and motor skills which certain individuals could be lacking, either because these skills are not yet developed (eg, in preverbal children) or because they are altered because of aging or disease (eg, in elderly patients with motor difficulties, or in patients with dementia or paralysis patients).

Since the identification of accurate nonverbal measures of pain could potentially bypass this issue, several investigators have generated qualitative descriptors of pain behaviors to be used in these populations [3,17,24–26,30,43]. Although some of these indices have been shown to have specificity and reliability, they still rely on some form of motor response (eg, facial expressions), which makes them not usable in paralyzed patients. Thus, many researchers assess subjects' autonomic response to pain, most frequently by monitoring skin conductance or heart rate [1,4,6–8,11,19,20,

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33,34,38–40]. A number of studies have in fact shown that the application of pain stimuli induces the activation of the sympathetic system, which results in increased heart rate [12,16,18,27,41], as well as increased skin conductance [9–11,13,36].

Despite the plethora of studies documenting a pain-related increase in either heart rate or skin conductance, the majority have tested only 1 of these measures in isolation (therefore not allowing for a direct comparison), has applied stimuli of only 1 intensity, or has not compared autonomic response with ratings of pain. The latter point is important as it is currently unknown whether (1) autonomic response is more closely associated with the physical intensity of the noxious stimulus or the perceived intensity of the pain, and whether (2) heart rate or skin conductance has a stronger predictive value for pain rating than the other.

In the present study, we added to the growing literature on autonomic responses to pain by directly assessing heart rate and skin conductance, as well as VAS ratings, in response to brief calibrated heat stimuli of different intensities. By taking advantage of the naturally occurring interindividual variability in the magnitude of the pain responses evoked by noxious stimuli of constant intensity, we were able to perform a direct comparison between autonomic measures, numeric pain ratings and intensity of noxious stimulation.

2. Methods

2.1. Subjects

A total of 39 male subjects between the ages of 19 and 34 years (mean ± SD = 24.6 ± 4.3 years) completed the study. Subjects were recruited through advertisements posted on university classified advertisements. Written informed consent was obtained from each subject. Exclusion criteria were chronic and acute pain, neurological disease, serious cardiovascular disease (ie, any type of disease involving the heart or blood vessels that might result in life-threatening medical emergencies, eg, arrhythmias, infarct, stroke), and current use of drugs. Ethical approval was obtained through the McGill University Faculty of Medicine Institutional Review Board.

2.2. Procedure

Subjects were seated in an adjustable chair in a ventilated room and instructed about the procedures involved in the experiment. All subjects received the same series of 12 heat stimuli (4 temperatures: 42 °C, 44 °C, 46.5 °C, and 48 °C; 3 repetitions per temperature), which were pseudo-randomly applied on three regions of the left volar forearm using a 30 × 30-mm contact thermode (CHEPS, Medoc Ltd Advanced Medical System, Ramat Yishai, Israel). Each stimulus lasted 6 s (1 s to reach the target temperature, 4 s at plateau, and 1 s to return to the baseline temperature of 32 °C), and was presented 34 s after the previous one. Four seconds after the end of each stimulus, the thermode was removed from the skin, and subjects were asked to numerically rate the heat intensity and unpleasantness (Fig. 1A). The small delay between the return to baseline temperature and thermode removal/rating period was adopted in order to allow enough time to capture the heat-evoked skin conductance/heart rate responses, which exhibit a few seconds of delay from stimulus onset [5] (Fig. 1B and C) and to avoid contamination of the skin conductance/heart rate measurements by the expression of verbal ratings and the removal of the thermode from the skin (for the same reason, the thermode was placed on the next stimulation site at least 10 s before the onset of the subsequent stimulus). Using methods previously reported by our group [21,22,42] the ratings were expressed numerically using 200-mm visual analogue scales (VAS) as a reference (ie, the VAS were presented to the subjects who were asked to verbally report

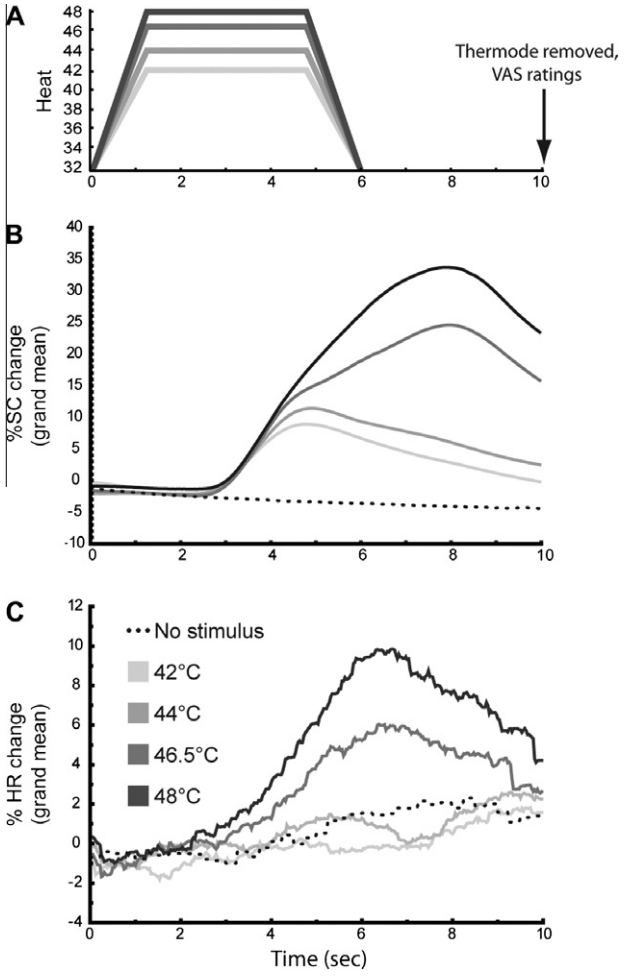

Fig. 1. Experimental design and average time course of autonomic responses to pain. Each of the 12 trials consisted of a 6-s stimulus (4 possible temperatures), followed by a rating period occurring 10 s after the stimulus onset (A); the interstimulus interval was 34 s. The delay between onset of the heat stimuli and the autonomic responses is apparent when comparing panel A with panels B and C. Dashed lines in panels B and C represent "baseline traces" (ie, autonomic activity in the absence of any stimulation). These values were calculated with the same methods used for the computation of the stimulus-induced % signal change in SC and HR, but using time epochs selected from a ~1-min period of resting state at the very beginning of the experimental session: for each subject, two 10-s ("pseudostimulation") epochs were expressed as percent signal change from their immediately preceding 10-s epochs ("pre-pseudostimulation") and then averaged.

a number indicating where they would place a mark on the VAS). The heat/pain intensity scale was anchored with 0 ("no heat") and 200 ("most intense pain tolerable") with a mid-point of 100 defined as "pain threshold"; the unpleasantness scale was anchored with −100 ("extremely unpleasant") and 100 ("extremely pleasant") with a mid-point of 0 ("neutral"). To allow subjects to distinguish sensory and affective components of pain, we stressed the differences between stimulus intensity and pleasantness/unpleasantness using explanations similar to those adopted by Price et al. [29]; to illustrate the dissociability of intensity and unpleasantness of a perceptual state, subjects were presented with a series of auditory metaphors (eg, a dripping faucet in the middle of the night, for which the intensity could be very low, while the unpleasantness could be very high). All of the experimental procedures, for all subjects, were performed by the same experimenter (male, white, 29 years old).

During the whole session skin conductance and heart rate were continuously recorded using Procomp+ and BioGraph Software

V2.0 (Thought Technology, Canada). The skin conductance was recorded in micro-Siemens (μS; sampling rate: 32 Hz) using 2 circular electrodes (1-cm diameter), positioned on the volar aspect of the distal phalanx of the index and middle finger of the left hand (ie, at least 10 cm away from the regions of the forearm receiving thermal stimulation). The heart rate was measured in beats per minute (BPM; sampling rate: 4 Hz) using 1 electrode placed under each clavicle and 1 electrode below the sternum.

2.3. Data processing and statistical analyses

All data preprocessing was performed with Excel 2002 (Microsoft, Redmond, WA) and statistical analyses were performed with Statistica 6.0 (StatSoft, Tulsa, OK), using an alpha level of 0.05.

All the SC or HR values (in μS for the skin conductance and in BPM for the heart rate) acquired during the stimulation period (0 to 10 s from stimulus onset; see below) and those acquired during the period immediately preceding the stimulus onset (−10 to 0 s from stimulus onset) were separately averaged, in order to obtain a "stimulation mean" and a "prestimulation mean" for each stimulus. The percent signal change in SC (%SC) or HR (%HR) for each stimulus was then calculated by expressing the difference between the relative "stimulation" and "prestimulation" means as a percentage of the "prestimulation" mean value (ie, % signal change = $(\text{mean}_{\text{STIM}} - \text{mean}_{\text{PRESTIM}}) * 100/\text{mean}_{\text{PRESTIM}}$). The stimulation mean values were calculated over a time window of 10 s starting with the stimulus onset (ie, lasting 4 s after stimulus offset), to allow enough time to acquire the autonomic responses to the stimuli. The prestimulation mean values were calculated over a 10-s window immediately preceding the stimulus onset.

2.3.1. Within-subject analyses

To assess the reliability of autonomic measures as predictors of pain at the single-subject level, correlation analyses were performed between individual verbal ratings and their relative %HR and %SC, for each subject (given the high correlation levels between intensity and unpleasant ratings, only the correlations with intensity ratings will be presented). These analyses were performed both on the responses to all 12 stimuli (ie, "*all-stimuli*" correlations), and on the responses to only the stimuli rated as painful (ie, associated with a pain intensity value greater than 100; "*pain-only*" correlations). The parametric Pearson product–moment correlation coefficients (R) were calculated for the all-stimuli correlations, whereas the nonparametric Spearman's rank correlation coefficients (ρ) were calculated for the pain-only correlations (as the number of events included into these analyses was too low for a parametric test, ie, as low as 6). To determine whether the verbal ratings were consistently most strongly correlated with HR or SC at the individual level, a paired t test was performed between the correlation coefficients (ie, R or ρ values calculated in the within-subject analyses for the 2 autonomic measures.

Furthermore, in compare the stability of %HR and %SC in response to multiple repetitions of the same stimulus (ie, over the three presentations of each of the 4 temperatures), a repeated-measures analysis of variance (ANOVA) was carried out on the within-subject coefficient of variations (CVs). The CV is a normalized measure of dispersion, defined as the ratio between the standard deviation and its relative mean, which allows the comparisons of variability between variables with different means [14]. For each subject, a CV was calculated for each of the 4 temperatures, and then log transformed to improve normality. A repeated-measures ANOVA was then carried on these values, including the factors Temperature and Measure (%HR versus %SC) as within subject variables. Post hoc pairwise comparisons were performed using the Tukey test.

2.3.2. Group analyses

Autonomic responses and verbal ratings were averaged, for each subject, across the 3 trials for a given stimulus temperature. The effects of temperature on VAS ratings of heat intensity and unpleasantness, as well as the %SC and %HR, were then evaluated using a repeated-measures ANOVA, including the factor temperature as a within-subject variable. Post hoc pairwise comparisons were performed using the Tukey test. Group–level correlation analyses between VAS ratings and autonomic measures were performed independently for each temperature level by calculating the Pearson product–moment correlation coefficients.

3. Results

3.1. Within-subject analyses

The coefficients of the within-subjects correlations between the intensity ratings and autonomic responses are shown in Fig. 2. A paired t test revealed that the coefficients for the correlations between intensity ratings and %SC were significantly higher than those for the correlations with %HR when all stimuli were analyzed ("all-stimuli" correlations: $t(38) = 5.24$, $P < .001$), with a similar trend when only the painful stimuli were analyzed ("pain-only" correlations: $t(38) = 2.54$, $P = .061$). The "all-stimuli" correlations (left panel) with %SC had uncorrected P values lower than .05 for 31/39 subjects (34/39 if trends with P values <.1 are included); those with %HR had uncorrected P values <.05 for 12/39 subjects (17/39, if trends are included). Although a few subjects exhibited negative correlations between pain ratings and heart rate, none reached statistical significance (only 1 subject reached trend levels, $P = .06$). The "pain-only" correlations (right panel) with the %SC had uncorrected P values <.05 in 16/39 subjects (22/39 with trends); those with %HR in 7/39 (10/39 with trends). In a few subjects, correlations with %HR or %SC were negative (statistically significant in 1 subject for SC, $P < .01$, and trending toward significance in another subject for HR, $P = .08$).

The repeated-measures ANOVA on the coefficient of variations (Fig. 3) yielded a significant Temperature * Measure interaction, $F(3, 114) = 3.38$, $P < .05$. Post hoc pairwise comparisons revealed that the CVs for %HR were not statistically different across temperatures ($P > .16$), but those for %SC at the 2 highest temperatures were statistically smaller than both those at the 2 lowest temperatures ($P < .05$), and than those of %HR at all temperatures ($P < .05$, except for %SC at 46.5 °C versus %HR at 48 °C, $p = .08$).

3.2. Group analyses

Fig. 4A and B, respectively, show the group-averaged intensity and unpleasantness ratings (±SD) elicited by the 4 different temperatures. As previously observed (although on the back of the hand rather than the volar forearm [21]), the 42 °C and 44 °C stimuli rated, on average, as nonpainful (although some subjects rated these temperatures as slightly above the pain threshold: 6 for 42 °C and 13 for 44 °C), whereas the 46.5 °C and 48 °C stimuli were rated as painful by all of the subjects. The ANOVAs revealed a highly significant effect of temperature on both intensity ratings [$F(3, 114) = 430.6$, $P < .001$] and unpleasantness ratings [$F(3, 114) = 224.2$, $P < .001$]. Post hoc pairwise comparisons across different heat levels were all statistically significant ($P < .001$, except for the 42 °C versus 44 °C unpleasantness ratings, $P < .05$). The intensity and unpleasantness ratings were all significantly correlated (42 °C: $r = 0.35$, $P < .05$; 44 °C: $r = 0.47$, $P < .01$; 46.5 °C: $r = 0.82$, $P < .001$; 48 °C: $r = 0.78$, $P < .001$).

Temperature also had a highly significant effect on both skin conductance [$F(3, 114) = 58.8$, $P < .001$] (Fig. 4C), and heart rate [$F(3, 114) = 19.2$, $P < .001$] (Fig. 4D). Post hoc pairwise comparisons

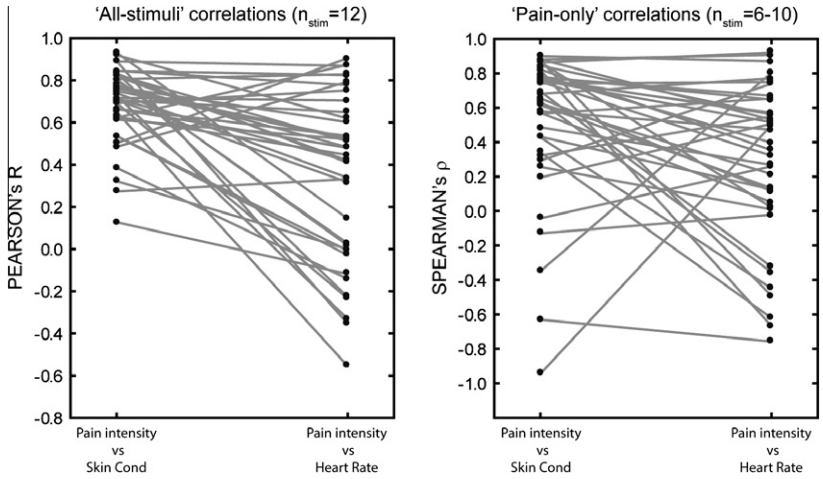

Fig. 2. Within-subject correlation analyses. All 12 stimuli (left panel) or only the stimuli rated as painful (6–10, depending on the subject; right panel) were correlated with the subjects' autonomic measures at the single subject level. Plots show coefficients for the correlations between pain intensity ratings and skin conductance (gray) or heart rate (black).

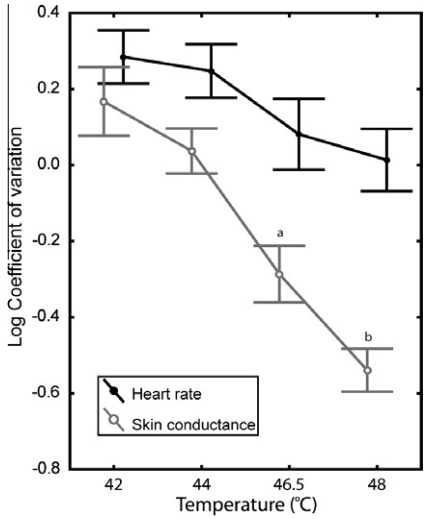

Fig. 3. Within-subject coefficients of variation. At the 2 highest temperatures the within-subject variability for %SC was significantly smaller than that for %HR. Whiskers represent mean ± SEM. [a]Statistically less than %SC at 42 °C and 44 °C, and than %HR at 42 °C, 44 °C, and 46.5 °C. [b]Statistically less than %SC at 42 °C and 44 °C, and than %HR at all temperatures.

revealed that the %SC and %HR responses to 46.5 °C and 48 °C were statistically different from each other and from those elicited by nonpainful stimuli (%SC: $P < .001$ for all comparisons; %HR: $P < .001$ for 46.5 °C and 48 °C versus 42 °C and for 48 °C versus 44 °C, $P < .05$ for 48 °C versus 46.5 °C and for 46.5 °C versus 44 °C), but those elicited by nonpainful stimuli were not different from each other (%SC: $P = .54$; %HR: $P = .62$). As a sizable portion of our subjects (33%) on average rated the 44 °C stimulus above the pain threshold, we also reanalyzed our dataset, including a categorical descriptor distinguishing subjects who rated this temperature as painful from those who did not. We observed neither main effects of this categorical predictor nor interactions between the predictor and the temperature level, for both heart rate (main effect: $F(1, 111) = 0.03$, $P = .87$; interaction: $F(3, 111) = 0.10$, $P = .96$), and skin conductance (main effect: $F(1, 111) = 0.06$, $P = .81$; interaction: $F(3, 111) = 0.59$, $P = .62$). This indicates that the relationship between autonomic measures and stimulus intensity was not statistically different between subjects who rated 44 °C as painful and those who did not.

The %SC and %HR were significantly correlated with each other only for the moderately painful stimulus (46.5 °C: $r = 0.38$, $P < .05$), but neither for the intensely painful stimulus (48 °C: $r = 0.27$, $P = .09$) nor for the on-average nonpainful stimuli (42 °C: $r = 0.29$, $P = .068$; 44 °C: $r = 0.24$, $P = .14$).

When the autonomic responses were correlated with the verbal ratings at the group level, we observed that neither %SC nor %HR predicted ratings of the 42 °C and 44 °C stimuli, ie, the stimuli on average rated as non painful ($.26 \leqslant P \leqslant 1$); the lack of statistically significant correlations between ratings and autonomic measures at 44 °C was also confirmed by repeating these analyses only on the subjects who rated those stimuli as nonpainful ($P > .15$), or only on those who rated them as painful ($P > .866$). However, although %SC did not predict ratings of 46.5 °C and 48 °C either ($.15 \leqslant P \leqslant .95$), %HR did predict both intensity and unpleasantness ratings ($0.40 \leqslant r \leqslant 0.46$; $.003 \leqslant P \leqslant .011$; Table 1).

4. Discussion

Our findings show that graded intensities of painful cutaneous heat stimuli evoke graded increases in both heart rate and skin conductance. When correlations were run between pain ratings and autonomic responses at the single subject level (ie, between the autonomic and verbal responses to each individual trial, within each subject separately), or at the group level (ie, between the average verbal and autonomic responses to the same temperature, in all subjects simultaneously), a complex pattern emerged in our data. On 1 hand, within-subject analyses revealed higher and less scattered R values for the correlations with skin conductance (Fig. 2), demonstrating that SC is more sensitive to relative changes in perception (ie, on a trial-by-trial basis, an increase in pain is quite reliably associated with an increase in SC and less reliably by an increase in HR). The weakening of this effect observed when only stimuli rated as painful were considered, is likely due to the loss of statistical power that follows the inclusion in these analyses of a smaller number of observations (as low as 6).

Despite the stronger within-subject correlations, at the group level SC did not significantly correlate with each subject's pain rating, suggesting that this measure does not predict the absolute level of pain reported by the subject (ie, although an increase in SC

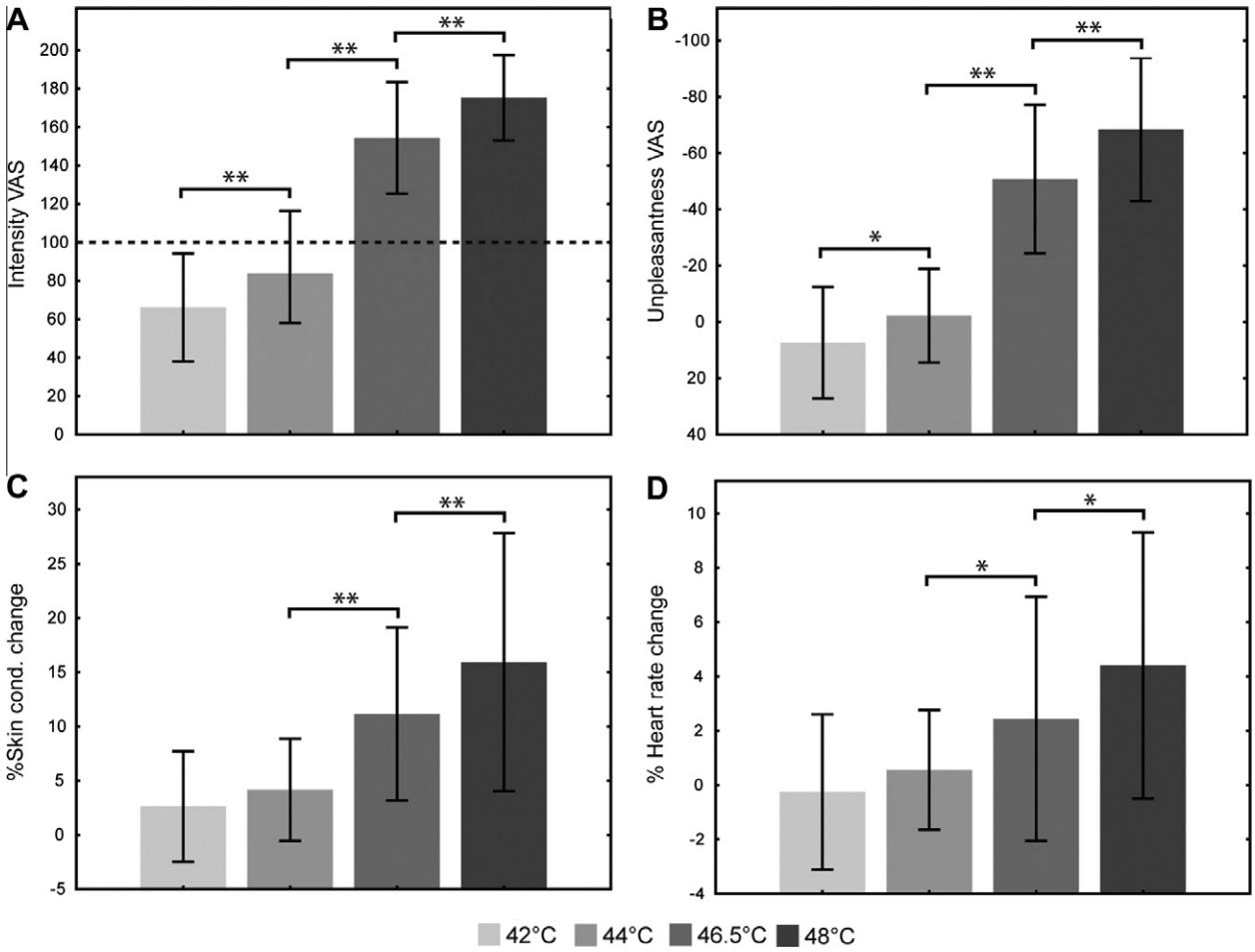

Fig. 4. Average verbal and autonomic responses to stimuli of different intensity. Subject ratings of intensity (A) and unpleasantness (B) significantly increased with increasing temperatures, for both the painful and nonpainful stimuli (dashed line represents pain threshold). Graded intensities of painful heat stimuli evoked graded increases in both heart rate (C) and skin conductance (D), whereas nonpainful warm stimuli did not evoke changes in either of these measures. Histograms represent mean ± SD. For consistency in the reported directionality of the effect, the *y*-axis of the unpleasantness graph is inverted, so that higher values mean worse pain (as for the intensity scale). $^{**}P < 0.001$, $^{*}P < 0.05$.

Table 1
Correlations between pain ratings and autonomic measures.

		Heat intensity				Heat unpleasantness			
		42 °C	44 °C	46.5 °C	48 °C	42 °C	44 °C	46.5 °C	48 °C
Skin conductance (%change)	42 °C	$r = 0.07$ $p = .65$				$r = 0.15$ $p = .37$			
	44 °C		$r = 0.09$ $p = .58$				$r = 0.00$ $p = .98$		
	46.5 °C			$r = 0.22$ $p = .18$				$r = 0.01$ $p = .95$	
	48 °C				$r = 0.24$ $p = .15$				$r = -0.02$ $p = .87$
Heat rate (% change)	42 °C	$r = 0.40$ $p = .80$				$r = 0.00$ $p = .99$			
	44 °C		$r = 0.00$ $p = 1$				$r = 0.18$ $p = .26$		
	46.5 °C			$r = \mathbf{0.46}$ $p = \mathbf{.01}$				$r = \mathbf{0.45}$ $p < \mathbf{.01}$	
	48 °C				$r = \mathbf{0.40}$ $p = \mathbf{.01}$				$r = \mathbf{0.45}$ $p < \mathbf{.01}$

Note: Heart rate was significantly correlated with both ratings of intensity and unpleasantness for painful stimuli, but not for nonpainful stimuli. Skin conductance was not significantly correlated with either ratings, for both nonpainful and painful stimuli. Statistically significant correlations are highlighted in bold.

does predict an increase in pain, the actual magnitude of the SC increase is not indicative of the magnitude of the pain increase).

The HR data reveal the opposite pattern: even though %HR did not reliably predict verbal responses to pain stimuli on a

trial-by-trial basis (Fig. 2), it did at the group level (ie, when the subjective *average* verbal and autonomic responses were correlated across subjects for each temperature separately; Table 1). The incongruity between within- and between subjects analyses suggests that HR, although genuinely affected by pain perception (as indicated by the between-subject analyses), is a very noisy measure, requiring averaging over several stimulations in order to yield reliable responses. In support of this hypothesis are the results of the analysis on the coefficients of variation, which demonstrate that the within-subject variability in %HR was significantly higher than that in %SC at the 2 highest temperatures. As averaging over multiple responses has the effect of enhancing the signal-to-noise ratio (SNR), it is likely that different results in the within- and between subjects analyses are due to different amount of averaging. In fact, although the within-subject analyses were carried out on the responses to each individual trial, the between-subjects analyses were carried out on "per-temperature" averages (ie, each datapoint was the average of three observations for a given temperature). This averaging is likely to have increased the SNR so that a positive correlation between %HR and verbal ratings, obscured in the single-subject analyses by the high levels of noise, became apparent.

The observation that the group correlations between verbal ratings and autonomic measures were not statistically significant for the lower temperature stimuli (42 °C and 44 °C) supports the concept that innocuous (or, possibly, even mildly painful) stimuli are not salient enough to induce the activation of an arousal response. The lack of an effect for the stimuli on average rated as nonpainful, together with the presence of an effect for the stimuli rated as painful by all subjects, corroborates the hypothesis that changes in heart rate reflect perceived intensity of the pain per se, rather than the physical intensity of the noxious stimulus. In an effort to provide further support for this claim, we reanalyzed our data grouping of the subjects based on whether they rated 44 °C as painful or not painful. These analyses did not yield significant differences from the analyses on the whole sample of participants, perhaps because the ratings of the subjects who perceived these stimuli as above the pain threshold might have been indicative of too low of a pain response to induce reliable increases in autonomic responses, or more simply for reasons of statistical power. Future experiments will need to evaluate this hypothesis.

The finding that skin conductance and heart rate were significantly increased during pain confirms a wide range of previous studies that have observed this relationship with either heart rate, skin conductance, or both, using experimental heat pain [1,9,18,27,36,39], cold pain [7,8,12,13,38,40], electric shock [2,6,33–35], evoked back pain [39], evoked muscle pain [4], evoked esophageal pain [28], heal prick in infants [10], and postoperative pain [19,20].

A few studies have directly compared skin conductance during painful and nonpainful stimuli and have found a significantly greater response during pain [9,10,36], suggesting that skin conductance could possibly serve as a surrogate measure of pain. Other studies have observed differential heart rate responses between noxious heat and nonpainful warm stimuli [18,27], as well as nonpainful cool and noxious cold stimuli [16], suggesting that heart rate could also serve as a surrogate measure of pain. Our findings show that both heart rate and skin conductance respond differentially between heat pain and innocuous warmth. Furthermore, they both differentiate between levels of heat pain (46.5 °C versus 48 °C), temperatures that subjects differentiate perceptually. Thus, it appears that both skin conductance and heart rate not only differentiate between pain and no pain, but also can discriminate levels of experimental pain, so that both of these measures could provide a possible surrogate for pain perception. Nevertheless, our data go further, by showing that each of these variables has different predictive value; whereas skin conductance is a more sensitive within-subject measure of changes in perception, heart rate (if averaged over the course of several stimulations) better predicts the absolute level of pain.

A number of studies have examined both skin conductance and heart rate in response to pain, and results of these studies are variable. Some find greater increases in skin conductance [6,7,12], others find stronger effects for heart rate [1,34,38], and some find similar changes for both measures [2,28,33,35,39,45]. Nevertheless, most of these studies do not include pain ratings [2,12,28,33,35], so they do not speak to the relationship between these measures and pain perception.

Only a few studies have directly correlated pain perceptual ratings with both skin conductance and heart rate. Using both male and female subjects and pain evoked by electrical stimulation, 1 of these studies found that skin conductance was a better predictor of pain ratings than was heart rate [6], whereas another found that heart rate accounted for more of the subjects' variation in pain ratings than did skin conductance [34]. The 1 study using heat pain to correlate perceptual ratings with heart rate and skin conductance found a significant correlation for heart rate but not skin conductance, but only for male subjects when they were being tested by a male experimenter [1]. Because, in our study, we used male subjects and a male experimenter, the findings of the latter study corroborate our results. Most studies do not report the gender of the experimenter, but there is other evidence that gender of the subject is important in heart rate and skin conductance responses to pain. Tousignant-Laflamme et al. [39,41] found that male subjects showed substantial changes in heart rate in response to both heat pain and evoked clinical low back pain, whereas female subjects showed less reliable changes. Thus, the gender of the subject and of the experimenter may be important factors in determining the autonomic response to pain.

All of these observations, together with the modest entity of the statistically significant group correlations here reported ($0.40 \leqslant R \leqslant 0.46$), as well as the sizable individual variability in the within-subject correlations (with some subjects displaying negative correlations, see also Chapman et al. [6]), suggest that autonomic measures should not be considered highly reliable predictors of pain, and could perhaps provide more interpretable results when considered in conjunction with a series of other indexes (where available).

In conclusion, it appears that both skin conductance and heart rate can distinguish between painful and nonpainful stimulation, as well as between levels of pain. For male subjects, our study and others provide evidence that skin conductance may be more sensitive to detect within-subject perceptual changes, but, when data are averaged over several stimulus presentations, overall heart rate may be a better predictor of pain perception than is skin conductance. Nevertheless, the variability observed in our experiment as well as in other studies and the indication that gender of both the subject and experimenter could influence the autonomic results lead us to advise caution in using autonomic or any other surrogate measures to infer pain in individuals who cannot adequately report their perception.

Conflict of interest statement

The authors have no conflicts of interest or competing financial interests to declare.

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