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The modulation of pain by attention and emotion: A dissociation of perceptual and spinal nociceptive processes

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ABSTRACT

Emotions and attention have been shown to influence the perception of pain and several psychophysiological studies have suggested an implication of descending modulatory mechanisms to explain these effects. However, the specificity of the neurophysiological mechanisms underlying the emotional and attentional modulation of pain still remains unclear. In order to differentiate the supra-spinal and spinal mechanisms involved in emotional and attentional modulation of pain, we measured pain perception (self-ratings) and the RIII reflex in healthy volunteers during the presentation of pleasant, unpleasant and neutral pictures, as well as during a baseline condition with no visual distractor (Experiment 1). In a second experiment, we manipulated the emotional arousal induced by pleasant and unpleasant pictures in order to compare more directly the effects of distraction and arousal. Whereas emotional valence influenced pain and the amplitude of the RIII reflex in the same direction (negative > positive), distraction by neutral pictures reduced pain but *increased* the RIII reflex relative to baseline. Increased arousal further potentiated the effects of negative valence on both pain and the RIII reflex and the effects of positive emotions on pain, as previously reported. However, arousal did not potentiate the inhibitory effect of positive pictures on the RIII and seems insufficient to account for the effect of distraction on the RIII. Overall, these data provide further evidence that attention and emotion modulate pain through partially dissociable neurophysiological mechanisms.

1. Introduction

In line with its fundamentally affective nature, pain can be easily influenced by emotions (Price, 2000). Pleasant emotions generally reduce pain while unpleasant ones tend to increase it. In a previous study, Rhudy and colleagues (2005) demonstrated that this effect was mediated in part by descending pain-modulatory pathways. Using emotional pictures from the International Affective Picture System (Lang, 1980), they showed that emotions modulated the amplitude of a spinally-mediated nociceptive reflex (nociceptive flexion reflex or RIII reflex; Sandrini et al., 2005).

However, the interpretation of these results in purely emotional terms is difficult, because changes in pain and RIII reflexes could also reflect in part attentional effects. Indeed, emotions are well known to influence the direction of attention (Ohman et al., 2001), including attention to pain (Keogh et al., 2001). It is therefore possible that the effects of emotion on pain may operate at least partly through a redirection of attention towards or away from pain (Janssen and Arntz, 1996; Villemure and Bushnell, 2002). Nonetheless, Villemure et al. (2003) did succeed in disentangling attentional and emotional effects on pain using an original factorial design in which these two factors were varied orthogonally. Based on these findings and on prior neurophysiological results (Bushnell et al., 1985), the authors suggested that attentional modulation of pain might preferentially engage descending pain-modulatory pathways, possibly funnelled through the periaqueductal gray matter (PAG) (Bantick et al., 2002; Tracey et al., 2002; Valet et al., 2004).

Yet, the evidence for a diminution in spinal nociception during distraction, as measured by the RIII reflex, is mixed. Although early studies suggested that directing attention away from the noxious stimulus attenuates the RIII reflex (Bathien and Hugelin, 1969; Bathien, 1971; Bathien and Morin, 1972; Willer et al., 1979), more recent studies have shown that performing a distractive mental arithmetic task reduces RIII thresholds (Petersen et al., 2001; Edwards et al., 2003, 2007) and increases RIII amplitudes (McIntyre et al., 2006). These increases in RIII

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responses during distraction appeared paradoxical because these were paralleled by decreases in pain ratings, suggesting a dissociation between spinal and supra-spinal nociception under these conditions. The reasons for these discrepancies across studies remain speculative, but some authors have pointed out that these might be explained by the possibly higher arousal induced by the distractive task in more recent studies (McIntyre et al., 2006).

In order to decipher the role of attention and emotion on spinal and supra-spinal nociceptive processing, we measured RIII reflexes and pain ratings to electrical stimulations delivered during the viewing of pleasant, unpleasant and neutral pictures, as well as during a control condition with no visual distraction. We hypothesised that the differences in pain responses during the presentation of neutral pictures compared with the fixation point would reveal the effects of distraction induced by simple picture viewing. In a second experiment, we further manipulated the arousal of emotional pictures along with their valence in order to compare the effects related to emotional arousal to those related to distraction.

2. Methods

2.1. Participants

A total of 33 healthy volunteers participated in the study (seventeen males and sixteen females; mean age: 24.2 years; SD: 4.1). All participants performed the two parts of the study. The Research Ethics Board of the "Centre de recherche de l'Institut de gériatrie de Montréal" approved the study. All participants gave written informed consent and received a compensation of 30$ for their participation. Four participants (two males and two females) were excluded because they did not tolerate the stimulus intensity required to reach 120% of the RIII threshold (see below).

2.2. Electrical stimulation

Transcutaneous electrical stimulation was delivered with a Grass-S48 stimulator (Astro-Med Inc., West Warwick, RI, USA) through a custom-made constant-current stimulus-isolation unit. The stimulation consisted of a 30 ms train of 10×1 ms pulse, delivered on degreased skin over the retro-malleolar path of the right sural nerve by means of a pair of custom-made 1 cm^2 surface electrodes. The intensity of the electrical stimulation was recorded (Biopac systems Inc., Goleta, CA, USA) and the intensity of the stimulation was adjusted individually at 120% of the reflex threshold using the staircase method (Willer, 1977). This intensity minimizes ceiling and floor effects, and induces a stable and moderately painful pin-prick sensation.

2.3. Affect Induction

2.3.1. Experiment 1

Ninety pictures that evoked pleasant (ex.: erotica, skydiving), unpleasant (ex.: mutilated bodies, attack scenes) or neutral (ex.: neutral faces, household objects) emotions were selected from the International Affective Picture System (Center for the Study of Emotion and Attention, 1999)[1]. Based on their normative ratings, 30 pictures were chosen within each category in order to maximize valence differences between pleasant and unpleasant pictures, while equating their arousal levels. Neutral pictures were of intermediate valence and of lower arousal than pleasant and unpleasant pictures. The lower arousal of the neutral pictures was due to the fact that, within the IAPS, the most pleasant and unpleasant pictures are also of high arousal, whereas the neutral pictures are never of high arousal. As a result, it is impossible to match neutral pictures on arousal when selecting the most pleasant and unpleasant pictures (Lang, 1995; Rhudy et al., 2005).

For each category, pictures were grouped in six blocks of five successive pictures presented during six seconds each (30 s per block). The pictures were presented on a computer screen (33 cm $\times$ 20 cm) situated approximately at 60 cm from the participants. A fourth condition consisting of a white fixation cross displayed in the middle of a black screen for 30 s served as an additional control with no picture.

2.3.2. Experiment 2

In the second part of the study, two categories of pictures were added in order to vary orthogonally the dimensions of valence and arousal. Therefore, 150 pictures that evoked pleasant-high arousal (ex.: erotica, extreme sports), pleasant-low arousal (ex.: babies, people smiling), unpleasant-high arousal (ex.: violent scenes), unpleasant-low arousal (ex.: pollution, sad faces) or neutral (ex.: neutral faces, household objects) emotions were selected from the International Affective Picture System (Center for the Study of Emotion and Attention, 1999)[2]. All the pictures were different from the ones used in Experiment 1. Based on the normative ratings, the pictures were selected so that the sets of pictures within the same valence category had comparable mean valence ratings, and that the sets of pictures within the same arousal category had comparable mean arousal ratings. As a consequence of this matching process, pleasant-high arousal and pleasant-low arousal pictures were a bit less pleasant or unpleasant than those used in Experiment 1. They were also slightly less arousing. Neutral pictures were of intermediate valence, but were of the same arousal level as the low arousal pictures. As in Experiment 1, pictures were grouped in six blocks of five pictures of the same category. The presentation length of each picture was of six seconds for a total of 30 s per block. Finally, a sixth condition consisting of a white fixation cross displayed in the middle of a black screen for 30 s served as an additional control with no picture.

2.4. Procedure

2.4.1. Experiment 1

All participants started with Experiment 1. Before the experiment began, the participants were installed in a comfortable chair and the electrical stimulation was adjusted at 120% of each partic-

[1] Images numbers were: pleasant (4607, 4608, 4652, 4658, 4659, 4660, 4664, 4666, 4670, 4681, 4687, 4689, 4800, 4810, 5260, 5450, 5621, 5629, 8030, 8034, 8080, 8180, 8185, 8186,8190, 8200, 8370, 8400, 8490, 8501), unpleasant (2352_2, 3005_1, 3030, 3053, 3060, 3063, 3064, 3068, 3069, 3071, 3100, 3102, 3110, 3120, 3130, 3140, 3150, 3266, 3500, 3530, 6313, 6360, 6540, 6560, 6570, 9252, 9410, 9635_1, 9910, 9921) and neutral (2190, 2393, 2480, 2570, 2840, 2880, 2890, 5510, 5740, 7000, 7004, 7006, 7010, 7020, 7035, 7041, 7050, 7080, 7090, 7100, 7161, 7175, 7179, 7185, 7187, 7217, 7233, 7235, 7491, 7950). Mean valence and arousal ratings across pictures set were: pleasant (valence: $M = 6.81$, arousal: $M = 6.58$), unpleasant (valence: $M = 1.64$, arousal: $M = 6.75$) and neutral valence: $M = 4.99$, arousal: $M = 2.54$).

[2] Images numbers were: pleasant-low arousal (2250, 5300, 8330, 2341, 7095, 8032, 4100, 2372, 2222, 8600, 5661, 2650, 2092, 8497, 7475, 2600, 2331, 1740, 7351, 5594, 2310, 1510, 8320, 7281, 2575, 1500, 8050, 7238, 4532, 2375_2), pleasant-high arousal (4669, 8178, 4677, 5626, 8192, 8470, 8161, 5920, 4656, 4683, 8191, 8160, 4651, 4800, 8341, 8116, 5470, 4611, 8300, 8179, 4690, 2208, 4676, 8251, 8090, 1650, 4672, 8193, 8170, 5950), unpleasant-low arousal (9110, 9000, 2399, 9561, 9290, 6010, 2722, 2375_1, 9280, 9090, 2590, 2276, 9342, 9265, 3300, 2205, 9331, 9220, 9041, 2900_1, 2490, 9045, 9415, 2750, 9190, 9330, 9001, 2753, 2455, 9830), unpleasant-high arousal (2683, 6370, 9620, 3550, 6570, 8485, 6242, 4664_2, 1525, 9630, 6550, 6211, 1300, 9622, 6840, 6210, 2981, 1201, 6834, 6530, 2688, 1090, 9400, 6831, 6200, 1052, 9250, 6830, 6250_1, 5971) and neutral (1945, 4230, 7920, 2410, 5532, 7590, 2780, 2487, 1935, 9635_2, 4613, 2749, 1240, 9401, 7211, 2702, 2230, 1230, 7182, 4233, 2220, 1121, 7830, 6570_2, 2690, 1112, 7595, 5535, 4000, 2635). Mean valence and arousal ratings across pictures set were: pleasant-low arousal (valence: $M = 6.13$, arousal: $M = 4.02$) pleasant-high arousal (valence: $M = 6.21$, arousal: $M = 6.03$), unpleasant-low arousal (valence: $M = 1.83$, arousal: $M = 4.09$) unpleasant-high arousal (valence: $M = 1.76$, arousal: $M = 6.11$) and neutral (valence: $M = 4.12$, arousal: $M = 3.98$).

ipant's RIII threshold following the staircase method (Willer, 1977). The first experiment consisted of 26 experimental trials. The time course of a trial is depicted in Fig. 1. Each trial consisted of a 30 s block of emotional pictures or fixation point. Blocks with emotional or neutral pictures included five images successively presented for six seconds each. Two electrical stimuli were delivered during each block of visual stimulation, always 300 ms before the end of a picture. The stimulations occurred pseudo-randomly according to six possible combinations of pictures: first and second, first and third, first and fourth, second and third, second and fourth or third and fourth pictures. The onsets of stimulations were balanced across the experimental conditions.

At the end of each block of images, participants had 8 s to rate the pain elicited by the electrical stimulations by moving a cursor on a visual analogue scale (VAS) displayed on the computer screen. The VAS was presented horizontally and included the verbal anchors "0 – no pain" and "100 – extremely painful" at the left and right extremities, respectively. After the participants had given their pain ratings, they were asked to rate the valence and arousal of the pictures (or fixation) blocks using a computerized version of the Self-Assessment Manikin (SAM) (Lang, 1980; valence: 1 = unpleasant, 9 = pleasant; arousal: 1 = low arousal, 9 = high arousal).

Each series of stimulation started with two control trials with only the fixation point. These trials, allowed for the RIII reflex to stabilize, controlled for potential habituation effects, and were not included in data analysis. The following 24 trials were presented in a pseudo-random order consisting of six consecutive cycles, comprising each of the four experimental conditions. These cycles were ordered so that no experimental condition was presented twice consecutively. Two orders of presentation were created (order 2 inverse of order 1) and their administration was counterbalanced across participants.

2.4.2. Experiment 2

After the first experiment, participants took a 5-min break before starting the second experiment. The procedure of the two experiments was exactly the same, except for the pleasant-low arousal and unpleasant-low arousal conditions added in Experiment 2. Therefore, Experiment 2 comprised 38 experimental trials, each including 2 electric shocks. As in Experiment 1, the first two trials were control trials with only the fixation point, and the remaining 36 trials were arranged in six pseudo-random cycles, comprising each of the six experimental conditions. Two orders of presentation were created (order 2 inverse of order 1) and their administration was counterbalanced across participants.

2.5. RIII reflex recording

Electromyographic (EMG) activity of the biceps femoris was recorded with Ag–AgCl surface electrodes (Type EL-508, Biopac systems Inc., Goleta, CA, USA) with an inter-electrode distance of 2 cm. Electromyographic (EMG) activity was amplified, band pass filtered (100–500 Hz), digitized and sampled at 1000 Hz (MP150, Biopac systems Inc., Goleta, CA, USA). EMG data were analysed using Acknowledge 3.8 (Biopac systems Inc., Goleta, CA, USA). The raw EMG data were filtered off-line (120–130 Hz) and transformed using the root mean square. The resulting signal was integrated between 90 and 180 ms post-stimulus onset to quantify the RIII reflex to each shock.

2.6. Data analysis

2.6.1. Manipulation checks

To confirm that the pictures elicited the target emotion, mean ratings of valence and arousal were averaged for each experimental condition and compared using multiple pairwise *t*-tests thresholded at $p = 0.05$ (Bonferonni corrected for the multiple tests).

2.6.2. Pain ratings and RIII reflex

Pain ratings and RIII reflex amplitudes were first standardised within participants by converting them into *z*-scores in order to reduce inter-subject variability and normalise the distribution of the data (as in Rhudy et al., 2005). The resulting scores were then averaged for each condition and compared through analyses of variance (ANOVA) with the experimental condition as a within-subject factor. Pairwise differences between conditions were then considered with the appropriate follow-up contrasts.

2.6.3. Sex differences

Although this study was not designed specifically to assess sex-related differences, the potential interaction between this variable and the effects of experimentally-induced emotions on pain was tested post hoc by adding sex as a between-subject factor in all analyses. All significant effects of sex are reported in their corresponding sections.

3. Results

3.1. Experiment 1

3.1.1. Manipulation checks

The ratings confirmed that the different blocks of emotional pictures effectively induced the intended emotions (Table 1). Pleasant pictures were the most pleasant, neutral pictures and the fixation

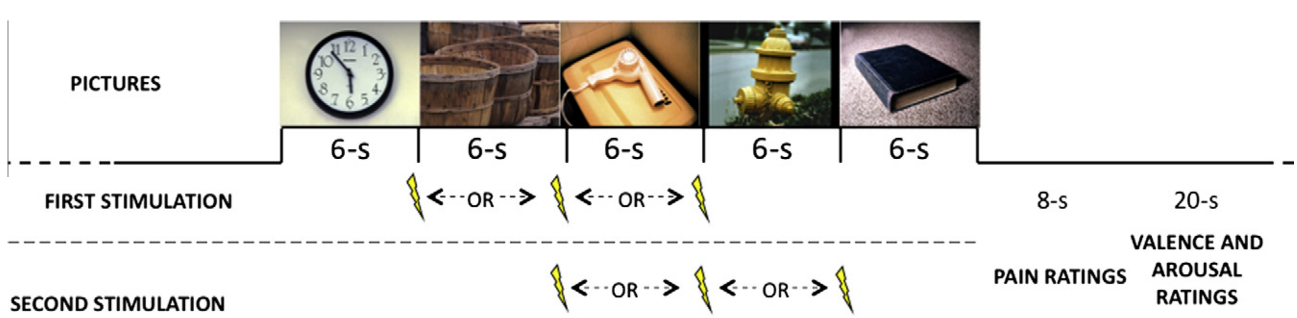

Fig. 1. *Time course of a typical experimental trial.* Each trial starts with the presentation of a 30-s long block of five 6-s long pictures of the same category. Neutral pictures are displayed here as an example. Two electrical stimulations were delivered, either during the first, second or third picture for the first stimulation and the second, third or fourth stimulation for the second stimulation. After the block of pictures, participants rated the pain of the electrical stimulations and the emotions induced by the pictures.

point were of intermediate valence, and unpleasant pictures were the most unpleasant. There was no significant difference between the valence of the neutral pictures and the fixation point. On the arousal scale, unpleasant pictures were found to be slightly more arousing than the pleasant pictures, and both were judged as more arousing than neutral pictures. Finally, the neutral pictures were rated as only slightly more arousing than the fixation point. There was a main effect of sex on arousal ratings ($F(1, 26) = 7.08$, $p < 0.05$), with men rating all pictures as more arousing than women (mean arousal rating for men = 4.93; mean arousal rating for women = 4.03).

3.1.2. Pain ratings and RIII reflex

Normalized pain ratings and RIII reflex amplitudes are reported for each experimental condition in Fig. 2 (non-normalized pain ratings and RIII reflex amplitudes are reported in supplementary Table S1. See the online version at 10.1016/j.ejpain.2010.11.013). There was a significant effect of the experimental condition on pain ratings ($F(3, 81) = 26.25$, $p < 0.001$). Planned follow-up contrasts showed that pain ratings were lower during pleasant than neutral pictures ($t(28) = 3.96$, $p < 0.01$) and higher during unpleasant than neutral pictures ($t(28) = 5.01$, $p < 0.001$). Moreover, pain ratings also decreased during the presentation of neutral pictures compared with the fixation point ($t(28) = 2.96$, $p < 0.01$).

The RIII was also significantly modulated by the experimental conditions ($F(3, 81) = 14.53$, $p < 0.001$). Planned follow-up contrasts showed that the RIII reflex was increased during the viewing of unpleasant pictures compared to the pleasant and neutral pictures ($t(28) = 4.90$, $p < 0.001$). However, there was no significant difference between pleasant and neutral pictures ($t(28) = 0.90$, p = ns.). In contrast to the effect found on ratings, the amplitude of the reflex was *increased* during the presentation of neutral pictures compared to the response produced during fixation ($t(28) = 2.13$, $p < 0.05$).

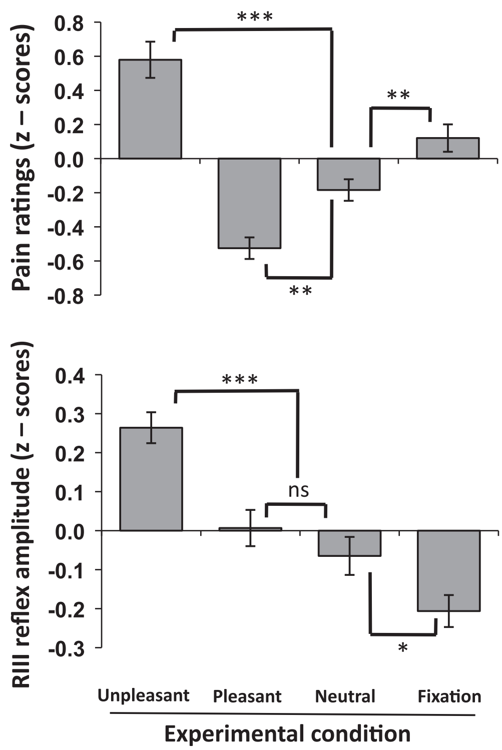

Fig. 2. Mean pain ratings and RIII reflex amplitudes (*z*-scores) for the four experimental conditions of Experiment 1. Significant differences are marked by asterisks ($^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$).

3.2. Experiment 2

3.2.1. Manipulation checks

The ratings confirmed that the different blocks of emotional pictures effectively induced the intended emotions (Table 2). Pleasant-high arousal and pleasant-low arousal pictures were judged as the most pleasant pictures, neutral pictures and the fixation point were of intermediate valence, and unpleasant-low arousal and unpleasant-high arousal pictures were judged as the most unpleasant pictures. Most crucially, there were no differences between the valence of high arousal and low arousal pictures within each valence category. Neutral pictures and the fixation point were also judged as equally pleasant.

On the arousal scale, the high arousal pictures were judged as more arousing than the low arousal pictures, within each valence category. Moreover, there were no differences in arousal between the pleasant-high arousal and unpleasant-high arousal pictures and between pleasant-low arousal and unpleasant-low arousal. However, unpleasant-low arousal pictures were not judged as less arousing than the pleasant-high arousal pictures. Thus, the arousal of unpleasant-low arousal pictures appeared to lie between the arousal of pleasant-low arousal and pleasant-high arousal pictures. Pleasant-low arousal and neutral pictures were found to be equally arousing. Finally, neutral pictures were judged as slightly more arousing than the fixation point.

3.2.2. Pain ratings and RIII reflex

Mean Normalized pain ratings and RIII reflex amplitudes are reported for each experimental condition in Fig. 3 (non-normalized pain ratings and RIII reflex amplitudes are reported in supplemen-

Table 1
Mean (±SD) valence and arousal ratings and results of statistical tests for Experiment 1 results of statistical tests.

	SAM ratings	Pleasant	Unpleasant	Neutral	Fixation
Valence[a]					
Pleasant	7.16(±1.30)	–	$t(28) = 14.86^{***}$	$t(28) = 9.16^{***}$	$t(28) = 15.14^{***}$
Unpleasant	1.91(±0.86)	–	–	$t(28) = 15.14^{***}$	$t(28) = 7.98^{***}$
Neutral	4.80(±0.70)	–	–	–	$t(28) = 1.05$
Fixation	4.53(±1.43)	–	–	–	–
Arousal					
Pleasant	6.04(±1.40)	–	$t(28) = 4.18^{**}$	$t(28) = 9.12^{***}$	$t(28) = 10.22^{***}$
Unpleasant	6.85(±1.30)	–	–	$t(28) = 11.24^{***}$	$t(28) = 12.19^{***}$
Neutral	2.89(±1.46)	–	–	–	$t(28) = 4.11^{**}$
Fixation	2.16(±1.55)	–	–	–	–

[a] Neutral valence = 5.00.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$, Bonferonni-corrected for multiple comparison.

Table 2
Mean (±SD) valence and arousal ratings and results of statistical tests for Experiment 2 results of statistical tests.

	SAM ratings	Pleasant-high arousal	Pleasant-low arousal	Unpleasant-high arousal	Unpleasant low arousal	Neutral	Fixation
Valence[a]							
Pleasant-high arousal	6.81(±1.14)	–	$t(28) = 2.26^{‡}$	$t(28) = 12.31^{***}$	$t(28) = 12.26^{***}$	$t(28) = 9.15^{***}$	$t(28) = 9.86^{***}$
Pleasant-low arousal	6.38(±0.62)	–	–	$t(28) = 12.39^{***}$	$t(28) = 13.49^{***}$	$t(28) = 9.56^{***}$	$t(28) = 8.41^{***}$
Unpleasant-high arousal	2.95(±0.96)	–	–	–	$t(28) = 2.75^{‡}$	$t(28) = 9.71^{***}$	$t(28) = 5.52^{***}$
Unpleasant-low arousal	3.27(±0.75)	–	–	–	–	$t(28) = 9.36^{***}$	$t(28) = 4.66^{***}$
Neutral	4.75(±0.80)	–	–	–	–	–	$t(28) = 0.85$
Fixation	4.55(±1.10)	–	–	–	–	–	–
Arousal							
Pleasant-high arousal	5.70(±1.50)	–	$t(28) = 6.38^{***}$	$t(28) = 0.81$	$t(28) = 2.48^{‡}$	$t(28) = 6.43^{***}$	$t(28) = 9.75^{***}$
Pleasant-low arousal	4.05(±1.32)	–	–	$t(28) = 5.00^{***}$	$t(28) = 3.08^{‡}$	$t(28) = 0.72$	$t(28) = 7.23^{***}$
Unpleasant-high arousal	5.95(±1.45)	–	–	–	$t(28) = 5.81^{***}$	$t(28) = 11.26^{***}$	$t(28) = 8.46^{***}$
Unpleasant-low arousal	4.97(±1.35)	–	–	–	–	$t(28) = 3.85^{*}$	$t(28) = 6.91^{***}$
Neutral	4.20(±1.17)	–	–	–	–	–	$t(28) = 7.34^{***}$
Fixation	2.35(±1.58)	–	–	–	–	–	–

[a] Neutral valence = 5.00.
[*] $p < 0.05$.
[**] $p < 0.01$.
[***] $p < 0.001$, Bonferonni-corrected for multiple comparison.
[‡] $p < 0.05$, uncorrected.

tary Table S2. See the online version at 10.1016/j.ejpain.2010.11.013; mean normalized pain ratings by experimental condition and sex are reported in supplementary Fig. S1. See the online version at 10.1016/j.ejpain.2010.11.013). Pain ratings were lower during the pleasant compared to the unpleasant pictures (Main effect of valence: $F(1, 27) = 52.16$, $p < 0.001$). Moreover, this effect was modulated by arousal (valence × arousal interaction: $F(1, 27)) = 12.54$, $p < 0.001$). Indeed, within each valence category, high arousal pictures had more effects than low arousal ones. As a result, the increase in pain ratings was more pronounced for unpleasant-high arousal than unpleasant-low arousal pictures ($t(28) = 2.51$, $p < 0.05$) and the decrease in pain ratings was more important for pleasant-high arousal than pleasant-low arousal pictures ($t(28) = 1.80$, $p = 0.08$, $p < 0.05$, one-tailed). There was no main effect of arousal (Main effect of arousal: $F(1, 27) = 031$, $p =$ ns.). Finally, there was no significant difference between the pain ratings obtained during the neutral pictures condition and the fixation point ($t(28) = 0.43$, $p =$ ns.).

There was an interaction between arousal and sex ($F(1, 27) = 4.77$, $p < 0.05$). Whereas there was no significant difference between men's and women's pain ratings in the high arousal conditions (men = −0.10, women = 0.02; $t(27) = 0.74$, $p =$ ns.), there was a marginally significant difference between men's and women's pain ratings in the low arousal conditions (men = 0.05, women = −0.15; $t(27) = 1.83$, $p = 0.08$). Because women's pain ratings were lower than men's ratings in both pleasant and unpleasant-low arousal conditions, high arousal appeared to have a lower effect on the hypo-algesic effects of pleasant pictures, and a stronger effect on the hyper-algesic effects of unpleasant pictures for women than for men (Fig. S1). Indeed, although the three-way interaction between sex, valence and arousal was not significant ($F(1, 27) = 0.39$, $p =$ n.s.), arousal seemed to have a larger influence on women's than men's pain ratings for unpleasant pictures(women, unpleasant-low arousal: 0.17; women, unpleasant-high arousal: 0.49; men, unpleasant-low arousal: 0.28; men, unpleasant-high arousal: 0.37), whereas arousal appeared to have a smaller influence on women's than men's pain ratings for pleasant pictures (women, pleasant-low arousal: −0.47; women, pleasant-high arousal: −0.46; men, pleasant-low arousal: −0.19; men, pleasant-high arousal: −0.56).

The RIII was reduced during the viewing of pleasant as compared to unpleasant pictures (Main effect of valence: $F(1, 27) = 5.08$, $p < 0.05$). In contrast, arousal had no statistically significant effects on the RIII reflex (Main effect of arousal: $F(1, 27) = 2.16$, $p =$ ns.; valence × arousal interaction: $F(1, 27) = 0.71$, $p =$ ns.). Nonetheless, visual inspection of the mean RIII amplitude suggests that, within each valence category, high arousal pictures increase the reflex compared to low arousal ones. As a result, pleasant-low arousal and unpleasant-high arousal pictures were the only picture conditions to show differences in RIII reflex amplitude ($t(28) = 2.71$, $p < 0.05$). Finally, the reflex was found to be stronger during the presentation of neutral pictures than the fixation point ($t(28) = 2.77$, $p < 0.01$).

4. Discussion

The results of the present study largely replicate those obtained in a prior study (Rhudy et al., 2005), using a similar paradigm and showing that the emotional modulation of pain affects the spinal nociceptive flexion reflex. The present results extend these previous findings further by demonstrating that emotion and attention differentially involve cerebral and cerebro-spinal processes, as manifested in perceptual measures (self-rating) and RIII responses. While arousing negative emotions increased both pain and the amplitude of the RIII, the attentional effect induced by the simple presentation of neutral pictures *reduced* pain in Experiment 1 (consistent with distraction analgesia) and *increased* RIII amplitudes in both Experiments 1 and 2. Furthermore, high arousal enhanced the hypo- and hyper-algesic effects of positive and negative emotions on pain ratings, respectively (Experiment 2), but did not significantly influence the effects of positive and negative emotions on RIII reflexes.

4.1. Effects of emotional valence and arousal on pain ratings and RIII reflexes

In Experiment 1, pain ratings showed a typical effect of picture valence, with pain ratings being higher during the presentation of unpleasant pictures, intermediate during the presentation of neutral pictures, and lower during the presentation of pleasant pictures. These ratings were paralleled by higher RIII reflexes during the viewing of unpleasant pictures compared with pleasant and neutral pictures. However, we did not replicate the reduction in RIII reflex amplitude reported by Rhudy et al. (2005) during the presentation of pleasant as compared to neutral pictures. This lack of effect could be attributed to differences in the selection of pleas-

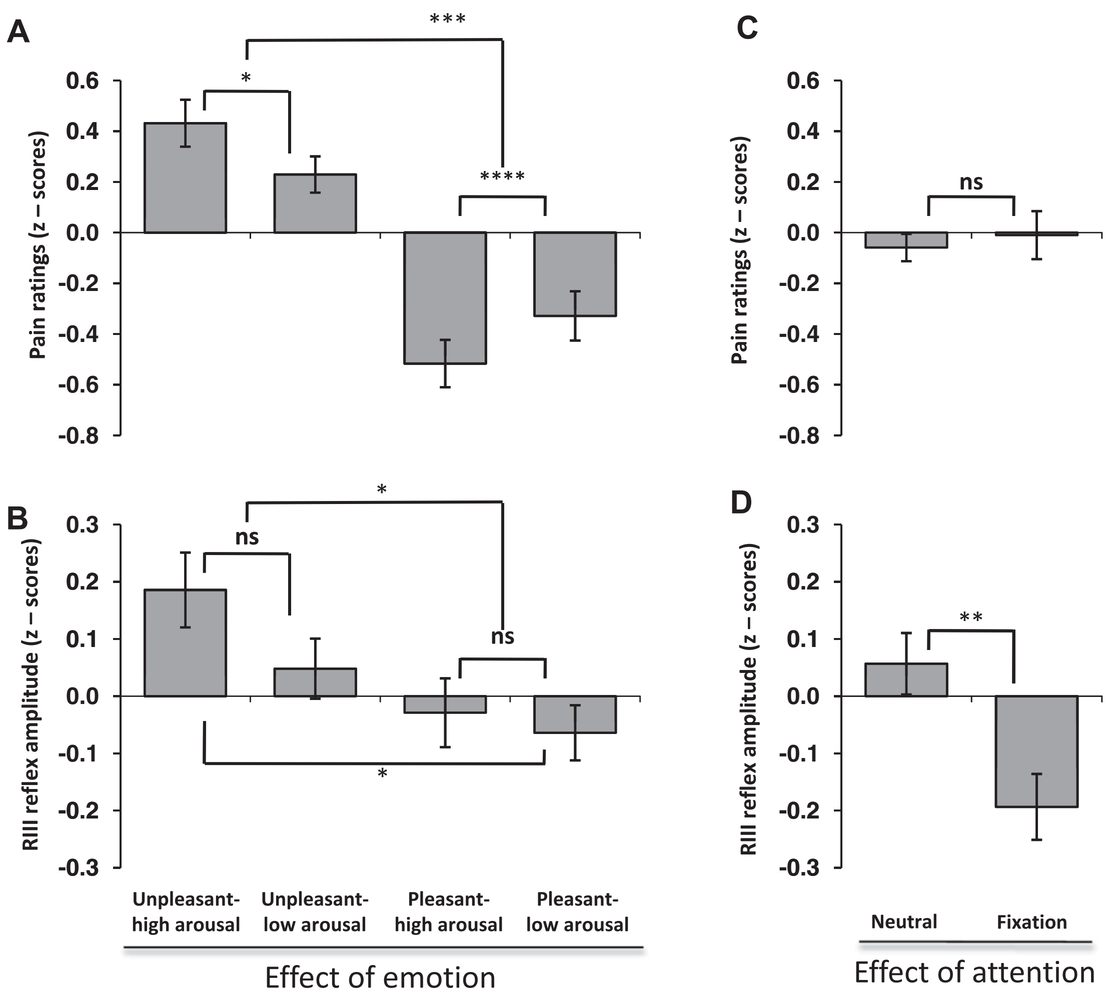

Fig. 3. Mean pain ratings and RIII reflex amplitudes (*z*-scores) for the six experimental conditions of Experiment 2. The effects of emotions on pain ratings (A) and RIII reflex amplitudes (B) are assessed by the valence and arousal effects of emotional pictures (pleasant-high arousal, pleasant-low arousal, unpleasant-high arousal and unpleasant-low arousal). The effects of distraction on pain ratings (C) and RIII reflex amplitudes (D) are assessed by the difference between the neutral picture condition and the fixation condition. Significant differences are marked by asterisks ($^*p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, $^{****}p = 0.08$ or $p < 0.05$, one-tail).

ant pictures. Whereas Rhudy et al. (2005) only selected erotic pictures, we selected pleasant pictures based solely on valence ratings, which led to the inclusion of outdoor sports pictures (ex.: rafting, skydiving), along with erotic pictures. Since outdoor sports pictures have previously been shown to produce effects similar to those generally associated with threat, such as enhanced startle reflex amplitude (Bernat et al., 2006), it is quite possible that they counteracted the effects of erotic pictures on RIII amplitude. This implies that positive valence may be insufficient to explain all effects of positive emotion on pain and spinal nociceptive processes.

In Experiment 2, we examined the influence of emotional arousal on pain more closely. First, the results of Experiment 2 replicated the main effect of emotional valence on pain perception observed in Experiment 1. In addition, high arousal amplified the effect of valence on pain ratings. Pain was stronger during unpleasant-high arousal than unpleasant-low arousal pictures, and lower during pleasant-high arousal than pleasant-low arousal pictures. These findings corroborate the results of a recent study also assessing the effects of arousal and valence of emotional pictures on pain (Rhudy et al., 2008). Moreover, this enhancement of valence effects by arousal fits with the motivational priming theory of Lang (1995), in which arousal is thought to determine the degree of activation of appetitive and defensive systems. The effects of arousal on pain ratings also interacted with the sex of the participants. Women's pain ratings were lower than men's in both pleasant and unpleasant-low arousal conditions. This result is consistent with the idea that, compared to low arousal pictures, highly arousing pleasant pictures tend to produce stronger hypo-algesic effects in men and highly arousing unpleasant pictures tend to produce stronger hyper-algesia effects in women (Rhudy and Williams, 2005).

The general interactive effect of arousal and valence on pain ratings was not paralleled by corresponding effects on RIII reflex amplitudes. Indeed, there were no significant differences in RIII reflex amplitude between pictures of different arousal. Nonetheless, visual inspection of the mean reflex amplitudes suggests that there was a trend towards increases in RIII reflex amplitude for highly arousing pictures, regardless of their valence. This is particularly clear on the pleasant pictures, for which the mean RIII reflex amplitude was larger during the pleasant-high arousal than pleasant-low arousal pictures, although the opposite was observed on pain ratings. Indeed, the only significant contrast between particular emotional picture conditions (i.e. unpleasant-high arousal vs pleasant-low arousal) combined the enhancing effects of negative valence and high arousal.

These results contrast with those of Rhudy et al. (2008), who observed that pleasant-high arousal pictures significantly reduced RIII reflex amplitudes compared with pleasant-low arousal pictures. Again, these differences might be related to the particular content of the pictures. Whereas Rhudy et al. (2008) used only erotic and food pictures as pleasant-high arousal and pleasant-low arousal stimuli, respectively, we selected our pictures based solely on valence and arousal normative ratings. Thus, in our study, outdoor sports pictures might have counteracted the effects of erotic pictures in our pleasant-high arousal condition, whereas the presence of low-arousal erotic pictures could have amplified the effects of our pleasant-low arousal condition. Although the question of which approach provides the best index of arousal remains debatable, picture content and arousal were confounded in both studies. Thus, the specific contribution of emotional arousal and picture categories to RIII reflex modulation remains to be assessed by varying arousal levels within strict categories and by systematically contrasting different categories with comparable arousal levels.

Self-reported measures of arousal for unpleasant pictures were also generally slightly higher than the normative ratings on which the pictures were initially selected. This led to slightly higher arousal ratings for unpleasant than pleasant pictures in Experiment 1 and to similar arousal ratings for the pleasant – high arousal and unpleasant – low arousal ratings in Experiment 2. This could be due to the fact that participants had to provide an average rating for the five pictures composing each block. It is thus possible that these average ratings were influenced by the most salient pictures within each block, possibly leading to higher ratings for unpleasant blocks. However, it is unlikely that these small divergences between reported and normative arousal ratings contributed to the effects of valence reported in Experiment 1, as the difference in valence ratings were much larger than the small differences in arousal rating. Moreover, the effect of valence between pleasant and unpleasant pictures of high arousal was replicated in Experiment 2 without any difference in self-reported arousal, confirming the typical valence effect reported in previous studies (Rhudy et al., 2005). Likewise, the similarity of arousal ratings for the pleasant – high arousal and unpleasant – low arousal conditions in Experiment 2 does not affect the main interpretation of our results, which focuses on the effects of arousal within each valence category.

4.2. Effects of attention on pain

Pain was decreased, while the RIII reflex amplitude was increased, during the presentation of neutral pictures compared with the fixation point condition in Experiment 1. In Experiment 2, the same pattern of response was observed, except that the effect of attention on pain ratings was much weaker (and ns), while the effect on the RIII reflex appeared larger. The fragility of neutral picture viewing effects on pain ratings could be due to the fact that the distraction provided by the neutral pictures was minimal, as the participants had no task to perform on them in contrast to previous studies (Petersen et al., 2001; Edwards et al., 2003, 2007; McIntyre et al., 2006). Moreover, as Experiment 2 immediately followed Experiment 1, the loss of the hypo-algesic effect of neutral pictures on pain ratings might be due to habituation to the experimental procedures. However, the effects of the passive viewing of neutral pictures on RIII reflexes appears to be strong and reliable. Most importantly, the dissociation between RIII reflexes and pain ratings observed in Experiment 1 was replicated in Experiment 2, as the marked increases in RIII reflex amplitudes were not paralleled by any increase in pain ratings.

These results replicate the dissociation between pain ratings and spinal nociception during distraction observed in recent studies (Petersen et al., 2001; Edwards et al., 2003, 2007; McIntyre et al., 2006). However, the distractive tasks used in these studies also induced high levels of arousal: Petersen et al. (2001) and McIntyre et al. (2006) used a mental arithmetic task, while Edwards et al. (2003, 2007) had their participants play a computer game (Tetris®). Thus, the effects of the task in these studies could either be attributed to the redirection of attention away from the painful stimulation or to the physiological arousal induced by the cognitively demanding task. It is striking that in our experiment the simple presentation of neutral pictures was sufficient to produce the same phenomenon.

We cannot completely exclude the possibility that the slight differences in arousal induced by the neutral pictures compared to the fixation point contributed to our results, either directly by enhancing motor responses, or indirectly through increased baroreceptor activity and systolic inhibition of the RIII (McIntyre et al., 2006). However, it appears unlikely that neutral pictures evoke cardiovascular responses sufficient to induce detectable changes in blood pressure leading to robust changes in the RIII. Moreover, the difference in arousal ratings between the neutral and fixation condition, although significant, appeared much smaller than the observed effects of distraction on RIII amplitude. Indeed, it is unlikely that the passive viewing of neutral pictures induced much arousal. Nonetheless, this condition induced large increases in RIII amplitude, similar to those observed when performing difficult attentional tasks (Petersen et al., 2001; Edwards et al., 2003, 2007; McIntyre et al., 2006). Furthermore, the results of Experiment 2 indicate that arousal cannot totally explain the dissociation observed between pain ratings (no changes) and RIII reflex amplitudes (increased) during the presentation of neutral pictures compared to the fixation point. Indeed, in Experiment 2, the arousal of pleasant or unpleasant pictures did not have any significant effect on RIII reflex amplitudes. Moreover, the effects of arousal reported in a prior study (Rhudy et al., 2008) were in some cases opposite to the ones reported here. In that study, the interactive effects of valence and arousal showed a parallel pattern of modulation on pain ratings and RIII amplitudes, leading to lower RIII reflexes in the pleasant-high arousal (erotica) compared with the pleasant-low arousal (food) condition. Thus, in some cases, high arousal can even be associated with lower RIII reflex amplitudes, which is inconsistent with the systematically higher RIII reflex amplitudes observed here during the viewing of neutral pictures compared to the fixation point.

Thus, the involvement of arousal in distraction-induced increases in RIII appears questionable. Rather, it seems that distraction is the main factor involved in these increases of RIII reflex amplitude during neutral pictures viewing. This attentional effect can be due to a release from supra-spinal tonic inhibition of the RIII reflex during distraction, as can be observed in some participants during hypnotically-induced analgesia (Danziger et al., 1998), or, more drastically, during cervical spinal cordotomy (Garcia-Larrea et al., 1993). Similarly, the facilitation of non-nociceptive spinal reflexes, such as the stretch reflex (McIntyre et al., 2004), during distraction is a common finding. The function of this facilitation would be to promote automatic adaptive responses, such as withdrawal from pain, while the brain's higher-order attention processes are engaged in a distractive task. In this perspective, the facilitation of automatic responses would be accompanied by reduced pain sensitivity induced at higher-order levels of nociceptive processing to permit the execution of the distractive task.

The dissociation between pain ratings and RIII reflex amplitude during distraction suggests that the increased spinal excitability observed during distraction may not specifically reflect spinal nociceptive processes and may be due to an increased excitability of spinal motoneurones, as observed for other non-nociceptive reflexes (McIntyre et al., 2004). Alternatively, the fact that electrical stimulations also excite non-nociceptive Aβ fibers raises the possibility that the dissociation between pain ratings and RIII reflexes could be due to a selective modulation of a putative non-nociceptive component of the reflex. However, the long latency of the RIII reflex, which fits with the slow conduction velocities of nociceptive Aδ fibers, but not with the fast conduction velocity of non-nociceptive Aβ fibers (Sandrini et al., 2005), renders this possibility rather unlikely. Moreover, the transient disruption of Aβ afferences by ischemic blocks has been shown to produce increases in RIII amplitudes and pain ratings (Willer, 1977), suggesting inhibitory effects of non-nociceptive inputs on both RIII reflexes and ascending nociceptive projections in normal conditions. Thus, the dissociation between RIII reflexes and pain ratings observed here, does not seem to be consistent with a putative modulation of a non-nociceptive component activated by the shock stimulus.

The idea that distraction could cause a release from supra-spinal tonic inhibition of the RIII reflex is coherent with the findings of a recent study (Rhudy et al., 2006), showing that the predictability of shocks reduces RIII amplitudes. Thus, in our experiments, the tonic inhibition of the RIII reflex during the fixation point could reflect baseline levels of anticipation and orientation toward incoming shocks, which were disrupted by competing visual processing during the presentation of the pictures. The fact that the activation of descending mechanisms may vary across individuals (Danziger et al., 1998) may explain at least in part the discrepancies observed with prior studies conducted on experimented participants, or using slightly different paradigms (Bathien and Hugelin, 1969; Bathien, 1971; Bathien and Morin, 1972; Willer et al., 1979). Indeed, it is quite possible that some participants learned to actively dissociate themselves from the shocks during the baseline recordings, as suggested in Danziger et al. (1998), which would have led to enhanced RIII amplitudes during the baseline period. Accordingly, the performance of a distractive task may have competed with this active dissociation process and reduced the RIII. However this explanation remains highly speculative and further research is still needed to explore the specific conditions under which basic attention processes affect spinal nociceptive responses.

4.3 Summary

Overall, our results indicate that emotion and attention influence pain through different spinal and supra-spinal modulatory mechanisms. Whereas emotional valence modulates pain ratings and RIII reflexes in parallel, distraction by the passive viewing of neutral pictures reduces pain and enhances RIII reflexes. The parallel modulation of pain perception and RIII reflexes by emotional valence strongly supports the idea that descending modulatory mechanisms impacting on spinal nociceptive processes are involved in the effects of emotions on pain. However, the exact neurophysiological mechanisms underlying the dissociation between pain ratings and RIII reflexes during the attentional modulation of pain remain to be determined by future research.

The effects of emotional valence and attention were not only distinguished by their different effects on pain perception and RIII reflexes, but their respective effects also appeared to be independent and additive. Indeed, irrespective of their valence, all pictures in both experiments produced increases in RIII reflexes compared to the fixation condition, reflecting their distractive value. The more specific valence effects differentiating pleasant, unpleasant and neutral pictures only appeared to occur in addition to the general increase in RIII reflex amplitude related to picture viewing. Overall, these results further confirm that the distinct psychophysical effects of emotion and attention on pain (Villemure et al., 2003) are governed by distinct physiological mechanisms and support the idea that the effects of emotions on pain are at least partially independent from the effects of attention. This supports the use of emotion induction as a distinct and effective non-pharmacological intervention for the treatment of acute pain and reinforces the need to specifically consider emotional factors in the management of acute and chronic pain.

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Table S1
Mean (±SD) non-normalized pain ratings and RIII reflex amplitudes for Experiment 1.

	Experimental condition			
	Pleasant	Unpleasant	Neutral	Fixation
Pain ratings	37.61(±13.50)	51.73(±18.34)	41.31(±15.73)	45.96(±16.14)
RIII reflex (μv ∗ s)	3.69(±2.52)	4.23(±2.82)	3.44(±2.18)	3.18(±1.99)

Table S2
Mean (±SD) non-normalized pain ratings and RIII reflex amplitudes for Experiment 2.

	Experimental condition					
	Unpleasant-stimulating	Unpleasant-relaxing	Pleasant-stimulating	Pleasant-relaxing	Neutral	Fixation
Pain ratings	48.93(±17.05)	46.26(±17.69)	40.20(±14.62)	41.16(±14.12)	43.93(±14.84)	43.86(±16.94)
RIII reflex (μv ∗ s)	3.42(±2.26)	3.42(±2.26)	2.93(±1.78)	2.85(±1.61)	3.14(±1.84)	2.62(±1.46)

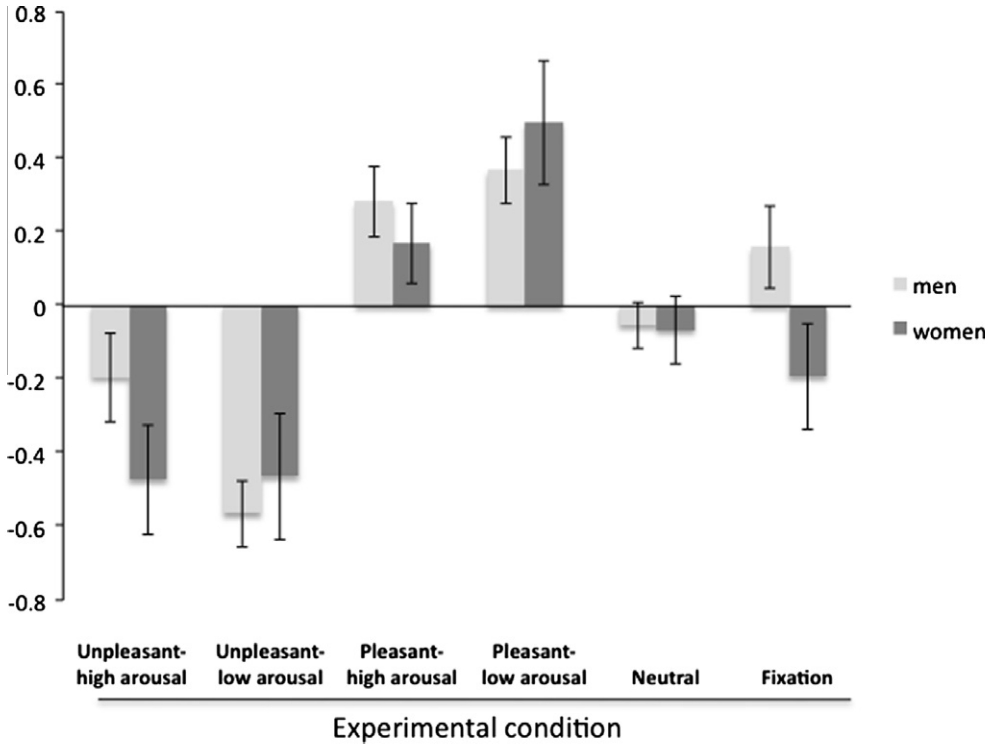

Fig. S1. Mean pain ratings (z-scores) by gender for the six experimental conditions of Experiment 2.