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Research Report

Gender difference in empathy for pain: An electrophysiological investigation

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ABSTRACT

Our recent event-related brain potential (ERP) study disentangled the neural mechanisms of empathy for pain into an early automatic emotional sharing component and a late controlled cognitive evaluation process. The current study further investigated gender difference in the neural mechanisms underlying empathy for pain by comparing ERPs associated with empathic responses between male and female adults. Subjects were presented with pictures of hands that were in painful or neutral situations and were asked to perform a pain judgment task that required attention to the pain cues in the stimuli or to perform a counting task that withdrew their attention from the pain cues. We found that both males and females showed a short-latency empathic response that differentiated painful and neutral stimuli over the frontal lobe at 140 ms after stimulus onset and a long-latency empathic response after 380 ms over the central-parietal regions. However, females were different from males in that the long-latency empathic response showed stronger modulation by task demands and that the ERP amplitudes at 140–180 ms were correlated with subjective reports of the degree of perceived pain of others and of unpleasantness of the self. Our ERP results provide neuroscience evidence for differences in both the early and late components of empathic process between the two sexes.

1. Introduction

A widely held view, regarding the roles of males and females in social behaviour, is that men serve as a liaison between the family and society whereas women serve to facilitate interpersonal harmony within the family unit (Parsons and Bales, 1955; see Wood and Eagly, 2002 for recent review). The stereotype of females' social role assumes that women are more empathic than men. There are a number of ways with which psychologists studied gender difference in empathy (see Lennon and Eisenberg, 1987 for review). For example, researchers considered reflexive crying of infants as a primitive empathy response and found that females showed a tendency to display more reflexive crying than did males (Martin and Clark, 1982). Researchers also measured how children felt after they were exposed to picture/story stimuli (Feshbach and Doe, 1968). Meta-analysis of these studies suggests gender differences favouring females although the effect size was small (Eisenberg and Lennon, 1983). Another most widely used method to examine gender difference in empathy is to measure self-reports of empathy in simulated emotional situations. Self-report measures concern different aspects of empathy such as personal trait of empathy (Mehrabian and Epstein, 1972) or sympathetic concern (Davis, 1983). Most of

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the investigations measuring self-report of empathy found that females scored higher than males (Eisenberg and Lennon, 1983). A recent work also found that females scored higher than males on the Empathy Quotient that measures empathizing as a drive and an ability (Wheelwright et al., 2006). These results are consistent with the notion that females are more empathic than males (Baron-Cohen et al., 2005).

Nevertheless, as Lennon and Eisenberg (1987) noted, gender difference in empathy measured through subjective reports may be contaminated by social desires and a bias to confirm the sex-role stereotypes. Most importantly, such approach tells little about the cognitive and neural mechanisms underlying gender difference in empathic processes. Some early studies recording heart rate or galvanic skin response found that, relative to females, males showed stronger physiological responses associated with empathic induction (Craig and Lowery, 1969). However, modulations of such physiological activity reflect consequences of empathic responses rather than the empathic processes.

Recent neuroimaging studies have identified neural processes involved in empathy for pain. Functional magnetic resonance imaging (fMRI) studies that compared hemodynamic responses to painful versus non-painful stimuli showed increased activations in the brain areas such as the insula and anterior cingulate cortex (ACC) (Singer et al., 2004; Jackson

performed on RTs showed significant main effects of Task [$F(1,24)=289.297$, $p<0.001$] and Gender [$F(1,24)=6.403$, $p<0.05$]. RTs were longer in the pain judgment task than in the counting task. Females responded faster than males. Because there was a significant interaction of Pain × Gender [$F(1,24)=13.614$, $p<0.01$], post-hoc analysis was conducted and confirmed that males responded faster to painful than to neutral stimuli [$F(1,12)=7.250$, $p<0.05$] whereas a reverse pattern was true for females [$F(1,12)=6.365$, $p<0.05$]. In addition, ANOVAs showed a reliable interaction of Pain × Task × Gender [$F(1,24)=9.961$, $p<0.005$]. Separate analysis showed a reliable interaction of Pain × Task for males [$F(1,12)=18.106$, $p<0.005$], because males responded faster to painful than neutral stimuli in the pain judgment task [$F(1,12)=13.056$, $p<0.005$] but not in the counting task [$F(1,12)=1.213$, $p>0.1$]. In contrast, the interaction of Pain × Task was not significant for females [$F(1,12)=0.876$, $p>0.1$], suggesting that differential behavioral responses to painful and neutral stimuli did no differ between the two tasks for females.

The ANOVAs performed on response accuracies showed a significant main effect of Pain [$F(1,24)=15.860$, $p<0.005$] and Task [$F(1,24)=194.146$, $p<0.001$]. Subjects' accuracies were higher to neutral than painful stimuli, and higher in the counting than pain judgment tasks. There were reliable interactions of Gender × Pain [$F(1,24)=8.383$, $p<0.01$], Task × Pain [$F(1,24)=12.337$, $p<0.005$] and Gender × Task × Pain [$F(1,24)=6.540$, $p<0.05$]. Separate analysis revealed that, for females, response accuracy was higher to neutral than to painful stimuli in the pain judgment task [$F(1,12)=15.805$, $p<0.005$] but not in the counting task [$F(1,12)=3.872$, $p>0.1$]. In contrast, response accuracies did not differ between painful and neutral stimuli in both tasks for males [$F(1,12)=1.154$, $p>0.1$].

2.2. *Electrophysiological data*

Grand-averaged ERPs recorded at the central and lateral occipital electrodes in each stimulus condition are illustrated in Fig. 2 respectively for males and females. Both painful and neutral stimuli elicited a negative component at 90–130 ms (N110) over the frontal-central area, which was followed by a positive wave at 140–200 ms (P180) and a negative wave at 200–

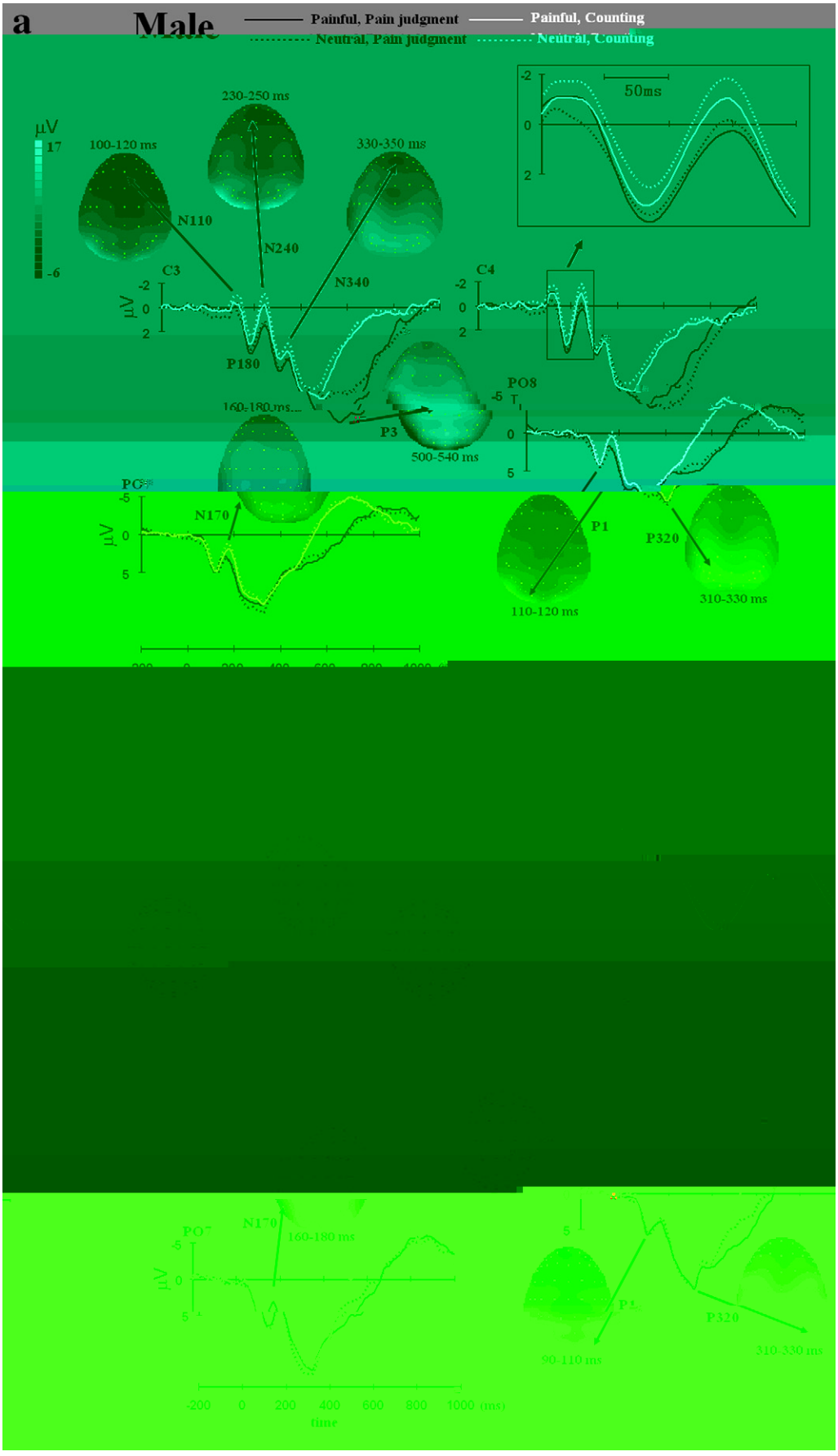
a
Male
Painful, Pain judgment
Painful, Counting
Neutral, Pain judgment
Neutral, Counting
μV
17
-6
100-120 ms
230-250 ms
330-350 ms
N110
N240
N340
50ms
C3
C4
P180
160-180 ms
P3
500-540 ms
PO8
N170
P1
P320
110-120 ms
310-330 ms
PO7
160-180 ms
90-110 ms
-200
0
200
400
600
800
1000 (ms)
time

Table 2 – Mean FPS-R scores (standard deviation) of others' pain and self unpleasantness

	Male	Female
Painful stimuli		
Others' pain	4.32(0.52)	4.39(0.89)
Self unpleasantness	4.29(0.67)	4.30(0.84)
Neutral stimuli		
Other's pain	1.28(0.29)	1.07(0.13)

[$F(1,12)=18.351$, $p<0.01$], whereas no such difference was observed in males [$F(1,12)=2.361$, $p>0.1$]. Furthermore, there was a significant interaction of Pain × Task × Gender between 420 ms and 540 ms over the occipito-temporal area [$F(1,24)=6.272$, $p<0.05$]. Separate analysis showed a reliable interaction of Pain × Task at 420–540 ms in females [$F(1,12)=23.061$, $p<0.001$], suggesting that the descending phase of the P320 showed larger amplitude to the painful than neutral stimuli in the pain judgment task [$F(1,12)=15.887$, $p<0.01$] but not in the in counting task [$F(1,12)=0.343$, $p>0.5$]. For males, however, the interaction of Pain × Task was not significant [$F(1,12)=0.069$, $p>0.5$], although the main effect of Pain was significant in this time window [$F(1,12)=19.124$, $p<0.01$].

We also observed an interaction of Gender × Pain × Hemisphere at 140–300 ms over the occipito-temporal area [$F(1,24)=9.042$, $p<0.01$]. Separate ANOVAs showed a reliable interaction of Pain × Hemisphere at 160–300 ms for females [$F(1,12)=8.644$, $p<0.05$] but not for males [$F(1,12)=1.241$, $p>0.1$], suggesting a more salient effect of painful contents of the stimuli over the left than right hemispheres for females.

2.3. *Correlation between subjective rating and ERP amplitudes*

After the EEG recording procedure, subjects were asked to evaluate the pain intensity felt by the model in painful and neutral stimuli and to report subjective feeling of their own unpleasantness when watching others in pain. The mean scores and standard deviation of the subjective reports are shown in Table 2. The ratings of others' pain were subject to ANOVAs with Pain (painful vs. neutral) and Gender as main effect. There was only a significant main effect of Pain [$F(1,24)=470.330$, $p<0.001$], suggesting higher scores for painful than neutral stimuli.

We calculated the correlation between the mean amplitudes of ERPs elicited by painful stimuli in each time window and the FPS-R scores (see Fig. 3). The mean ERP amplitudes at 140–180 ms associated with the painful stimuli was significantly negatively correlated with both the score of other's pain [F3: $r(1,13)=-0.748$, $p<0.01$; FC3: $r(1,13)=-0.715$, $p<0.01$; C3: $r(1,13)=-0.616$, $p<0.05$; F4: $r(1,13)=-0.723$, $p<0.01$; FC4: $r(1,13)=-0.623$, $p<0.05$; C4: $r(1,13)=-0.689$, $p<0.01$] and the score of self unpleasantness [F3: $r(1,13)=-0.810$, $p<0.01$; FC3: $r(1,13)=-0.816$, $p<0.01$; C3: $r(1,13)=-0.736$, $p<0.01$; F4: $r(1,13)=-0.804$, $p<0.01$; FC4: $r(1,13)=-0.803$, $p<0.01$] for females. The larger the ERP amplitudes in this time window, the lower perceived pain intensity and the weaker subjective feeling of unpleasantness induced by the perception of others' pain. However no reliable correlation was observed for males between the mean ERP amplitudes at this time window and the subjective reports score of other's pain [all $p>0.5$] and score of self unpleasantness [all $p>0.5$].

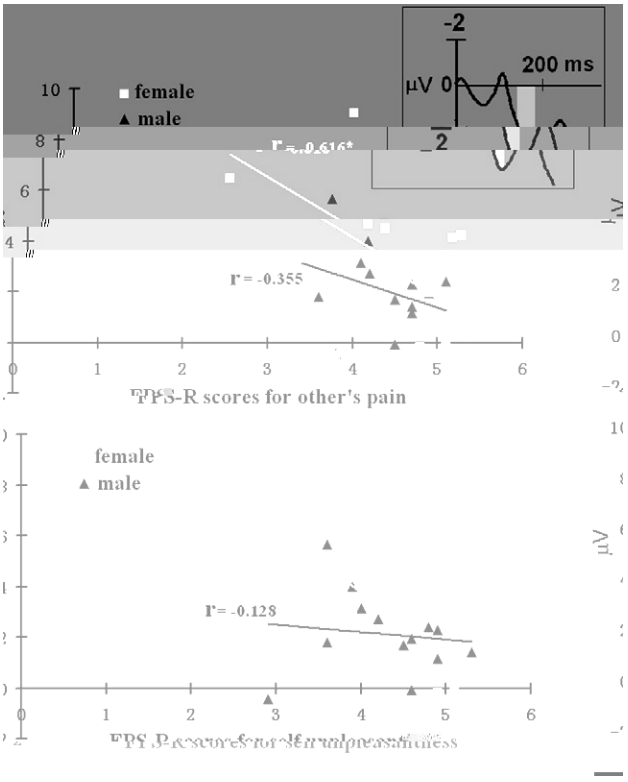

Fig. 3 – Correlation between the amplitudes of ERPs evoked by painful pictures and the FPS-R scores of both other's pain (upper panel) and self-unpleasantness (lower panel). The up-right panel shows the ERPs before 300 ms and the white area shows the time window (140–180 ms) during which the ERP amplitudes showed significant correlation with subjecting ratings. The *p*-values equivalent of * and ** are 0.05 and 0.01, respectively.

3. Discussion

Previous studies investigated gender difference of empathy by measuring subjective reports and found evidence favored females (Eisenberg and Lennon, 1983; Wheelwright et al., 2006). The current work extends the previous research by examining gender difference in the neural processes underlying empathy for pain by recording ERPs from male and female

Fig. 2 – (a) ERPs to picture stimuli recorded at the frontal-central and occipito-temporal electrodes (C3–C4, PO7–PO8) from males. The up-right panel illustrates the early pain effect between 100 and 300 ms after stimulus delivery. (b) ERPs to picture stimuli recorded at the frontal-central and occipito-temporal electrodes (C3–C4, PO7–PO8) from females. The up-right panel illustrates the early pain effect between 100 and 300 ms after stimulus delivery.

healthy adults. In particular, we investigated gender difference in the early automatic and late controlled processes of empathy for pain that were indexed by differential neural activity elicited by painful and neutral stimuli (Fan and Han, in press).

Our ERP results indicate that the painful and neutral stimuli were differentiated as early as 140 ms after sensory stimulation over the frontal-central areas. In addition, the tasks of pain judgment or counting did not influence the differentiation between the painful and neutral stimuli until 380 ms over the frontal-central area and 220 ms over the occipito-temporal sites. These ERP results provide evidence for an early neural response at 140–340 ms over the frontal-central area that was elicited by observation of others in pain and independent of the task demand, suggesting an early automatic component of empathy for pain (Fan and Han, in press). In contrast, the later stage of the processing of others' pain depended upon the task demands. The differentiation between the painful and neutral stimuli indexed by the P3 was evident in the task of pain judgment but not in the counting task, suggesting that a controlled process of empathy for pain over the posterior parietal region occurred later than the automatic process of empathy for pain that focused over the anterior frontal-central areas. Our ERP results appear to parallel previous ERP studies that also observed an early fronto-central modulation of ERPs elicited by facial expressions at 120 ms (e.g., Eimer and Holmes, 2002) and a late positive potential at 350–750 ms that is involved in the processing of affective components of stimuli (e.g., Schupp et al., 2000). Based on their ERP findings, Fan and Han (in press) proposed a two-stage model of empathic responses consisting of early emotional sharing and late cognitive evaluation. This model may be applied to the processing other types of visual stimuli with emotional contents. However, both the ERP empathy effects observed in the current work and the ERP emotion effects observe in other research (e.g., Eimer and Holmes, 2002; Schupp et al., 2000) occurred much earlier than the ERP correlates of understanding others' belief, i.e., the theory-of-mind ability, which was linked to the modulation of a late slow wave ERP component over the frontal cortex that could start as early as 300 ms after sensory stimulation (Liu et al., 2004; Sabbagh and Taylor, 2000). These ERP results indicate dissociation in time course between the processing of emotion and belief contents in others' mind.

Of particular interests, we found that the early ERP pain effect (i.e., the positive shift at 140–320 ms elicited by the painful relative to neutral stimuli at the fronto-central electrodes) did not differ between male and female participants. As the pain effect in this time window was independent of the task demands, the results indicate that the early automatic process of empathy for pain is comparable for males and females. However, although the early ERP pain effect indexing the automatic process of empathy for pain did not show significant gender difference, subjective ratings were correlated with the ERP amplitudes in an early time window (140–180 ms) for females whereas no such correlation was observed for males. These results first imply that subjective feelings of both others' pain and self-unpleasantness are determined by the early automatic process of empathy. In addition, it may be further proposed that subjective feelings of both others' pain and self-unpleasantness are more strongly determined by the early automatic process of empathy in females than in males. The correlation between the early ERP amplitudes and subjective ratings, which reflected conscious awareness of others' pain and one's own unpleasantness, suggest that there might be a linkage between the early ERP component and subjective experience of affective contents of awareness or the "affective consciousness" in terms of Panksepp (2005), although further evidence is required for these propositions.

Our ERP data also showed evidence for gender difference in pain effects on neural responses in the time window of the controlled process. While the larger P3 amplitude at 340–540 ms to the painful than neutral stimuli was observed in both sexes, this pain effect was stronger for females than males. In addition, this differential pain effect was evident when participants performed the pain judgment task but not when they performed the counting task. Another way to analyze the gender difference in this time window suggests that task demands modulated the differentiation between the painful and neutral stimuli in females but not in males, because the pain effect in this time window was smaller in the counting task than in the pain judgment task only in females. Such gender difference could not simply arise from differential low-level sensory/perceptual processing of the painful and neutral stimuli. Potential differences in stimulus novelty and salience existed between the painful and neutral stimuli, which may result in distinct attentional involvement in the early sensory–perceptual processing and thus modulate the visual extrastriate activity (e. g., Martinez et al., 2001). However, the absence of differences in the occipital P1 and N1 amplitudes between painful and neutral stimuli suggests comparable effects of stimulus novelty and salience on the early sensory–perceptual processing of painful and neutral stimuli.

Nevertheless, the long-latency P3 results suggest a stronger top–down influence on the long-latency controlled process of empathy for pain in females than in males. There has been evidence that the P3 component reflects the process of stimulus evaluation and classification (Duncan-Johnson, 1981; Duncan-Johnson and Kopell, 1981; McCarthy and Donchin, 1981). Stimulus novelty also modulates the P3 amplitudes (Friedman et al., 2001). While our recent fMRI work (Gu and Han, 2007) showed that empathy-related activity in the ACC and insula decreased when top–down attention was withdrawn away from the emotional content of painful stimuli, the P3 empathy effect observed in the current work showed further ERP evidence for the dynamics of the top–down modulation of empathic responses to others' pain. Based on the cognitive functional roles of the P3 identified in the previous work (Duncan-Johnson, 1981; Duncan-Johnson and Kopell, 1981; McCarthy and Donchin, 1981; Friedman et al., 2001), Fan and Han (in press) suggested that the long-latency processes of empathy may function to provide extensive evaluation of painful stimuli because of their high stimulus novelty. Because the ERP results in the current work showed greater pain effect in the descending phase of the P3 component for females than males, it is likely that, relative to males, females intended to undergo more intensive evaluation of painful stimuli, as suggested by longer RTs to the painful than neutral stimuli in females. This is in agreement with females' social role of taking care of the

offspring (Vogel et al., 2003), which requires greater sensitivity to danger signals such as painful stimuli. While previous studies measuring subjective reports favored females in empathy (Eisenberg and Lennon, 1983; Wheelwright et al., 2006; Baron-Cohen et al., 2005), fMRI studies did not report such gender difference in empathy for pain (Jackson et al., 2005; 2006; Singer et al., 2004; Botvinick et al., 2005; Saarela et al., 2007; Gu and Han, 2007). The current work provided the first piece of ERP evidence for gender difference in the process of empathy for pain. Together with Singer et al.'s (2006) observation that males' empathic responses were more strongly influenced by social relationship, our current ERP results lend further support that males' and females' empathic responses are differentially modulated by top–down attention and social relationship.

Gender difference in neural activities elicited by the painful and neutral stimuli was also observed in ERP components recorded at the occipital electrodes. The early visual activity (i.e., the descending phase of the P1) at 100–140 ms varied as a function of task demands, being enhanced by the task of pain judgment relative to that observed in the counting task. However, this modulation of the visual activity was observed in females but not in males. One possibility is that, because females are more empathic or sympathetic than males (Eisenberg and Lennon, 1983; Wheelwright et al., 2006; Baron-Cohen et al., 2005), the pain judgment task generated enhanced attention to the stimuli in females than in males and thus induced stronger visual activity. This is consistent with the well established findings that increased visual attention enhances the activity of the visual cortex and results in facilitation of the early visual sensory–perceptual processing (Hillyard and Anllo-Vento, 1998; Mangun et al., 1998). Gender difference in the long-latency empathic responses over the occipito-temporal area was similar to that observed over the frontal-central area. For females, the descending phase of the P320 (420–540 ms) at the occipito-temporal electrodes was modulated by task demands, being of larger amplitude to the painful than neutral stimuli in the pain judgment task but not in the in counting task. However, the long-latency pain effects observed in males did not vary as a function of task demands. Given this similar pattern of the long-latency empathic responses over the anterior and posterior scalp sites, it may be assumed that these responses may

Each subject participated in eight blocks of trials. In four blocks of trials subjects were required to judge pain vs. no-pain for hands in painful and neutral pictures. They were asked to count the number of hands in painful and neutral pictures in the other blocks of trials. Each block of trials started with the presentation of instructions for 3 s, which defined the task (i.e., pain judgment or counting the number of hands) for each block. There were 80 trails in each block. On each trial the stimulus display was presented for 200 ms in the center of the screen, which was followed by a fixation cross with a duration varying randomly between 800 ms and 1600 ms. The stimuli in each block of trials and the four tasks were presented in a random order for each subject. Subject responded to each stimulus by a button press using the left or right index finger. The assignment of the left or right index finger to the painful and neutral stimuli was counterbalanced across subjects.

4.3. *ERP data recording and analysis*

The electroencephalogram (EEG) was continuously recorded from 62 scalp electrodes that were mounted on an elastic cap according to the extended 10–20 system, with the addition of two mastoid electrodes. The electrode at the right mastoid was used as reference. The electrode impedance was kept at less than 5 kΩ. Eye blinks and vertical eye movement were monitored with electrodes located above and below the left eye. The horizontal electro-oculogram was recorded from electrodes placed 1.5 cm lateral to the left and right external canthi. The EEG was amplified (band pass 0.01–100 Hz) and digitized at a sampling rate of 250 Hz. The ERPs in each condition were averaged separately off-line with an epoch beginning 200 ms before stimulus onset and continuing for 1200 ms. Trials contaminated by eye blinks, eye movements, or muscle potentials exceeding ±50 μV at any electrode were excluded from the average.

ERPs at each electrode were re-referenced to the algebraically computed average of the left and right mastoids before further analysis. The baseline for ERP measurements was the mean voltage of a 200 ms prestimulus interval and the latency was measured relative to the stimulus onset. Mean voltage of ERPs were obtained (a) at 20-ms intervals starting at 80 ms after stimulus onset and continuing until 380 ms post-stimulus and (b) at 40-ms intervals from 380 to 820 ms post-stimulus. Statistical analysis were conducted at electrodes selected from the frontal (Fz, FCz, F3-F4, FC3-FC4), central (Cz, CPz, C3-C4, CP3-CP4), parietal (Pz, P3-P4), temporal (T7-T8, TP7-TP8, P7-P8), occipito-temporal (POz, Oz, PO3-PO4, PO7-PO8) regions.

Reaction times (RTs) and response accuracies were subjected to a repeated measure analysis of variance (ANOVA) with Pain (painful vs. neutral stimuli), Task (pain judgment vs. counting the number of hands) as within-subject independent variables, and Gender (male vs. female subjects) as a between-subject variable. The mean ERP amplitudes were subjected to ANOVAs with the factors being Pain, Task, Hemisphere (electrodes over the left or right hemisphere) as within-subject independent variables, and Gender as a between-subject variable. Because the ANOVAs of the ERP data showed similar results at anterior and posterior electrodes, we only reported the statistical results at electrodes C3–C4 and PO7–PO8.

4.4. *Measurement of subjective rating*

After the EEG recording session, subjects were asked to evaluate the intensity of pain supposedly felt by the model in the stimuli. Subjects were also asked to evaluate the unpleasantness felt by themselves when they observed the painful stimuli. The evaluations were measured using a 6-point scale (1=no pain, 6=very much painful, or 1=no unpleasantness, 6=very much unpleasant) with the Face Pain Scale-Revised (FPS-R) adapted from the Faces Pain Scale (Bieri et al., 1990), which contained six photocopied faces showing neutral to extremely painful expression.

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