Abstract

Previous neuroimaging studies have identified a neural circuit that is involved in empathy for pain. However, the temporal dynamics of neural activities underlying empathic processes remains poorly understood. This was investigated in the current study by recording event-related brain potentials (ERPs) from healthy adults who were presented with pictures or cartoons of hands that were in painful or neutral situations. Subjects performed a pain judgment task that required attention to pain cues in the stimuli or a counting task that withdrew their attention from these cues. The ERP results showed early differentiation between painful and neutral stimuli over the frontal lobe at 140 ms after sensory stimulation. A long-latency empathic response was observed after 380 ms over the central–parietal regions and was more salient over the left than right hemispheres. The early and late empathic responses were, respectively, modulated by contextual reality of stimuli and by top-down attention to the pain cues. Moreover, the mean ERP amplitudes at 140–180 ms were correlated with subjective reports of the degree of perceived pain of others and of self-unpleasantness. The ERP results support a model of empathy for pain consisting of early emotional sharing and late cognitive evaluation.
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1. Introduction

Successful social interactions require the capacity to understand emotional and sensory experience of other individuals. In addition, appropriate social communications and behaviours need vicarious experiencing of emotions congruent with those of others while being aware of the distinction between the self and others (Decety & Jackson, 2004; Decety & Lamm, 2006). This ability, referred to as empathy, has epistemological significance because it provides direct estimate of other's possible behaviours and the knowledge about potential properties of environments (De Vignemont & Singer, 2006).

A traditional approach to the understanding of psychology of empathy relies on subjective ratings of empathic emotion (Batson, 1987) and self-report questionnaires that measure empathy as a trait (Bryant, 1987; Davis, 1996). While this approach helps to comprehend subjective emotional reaction to others' feeling, the results of these studies could be influenced by intention of self-presentation and social desirability. Early researchers tried to obtain physiological measures of empathic responses by recording heart rate or galvanic skin response (Craig & Lowery, 1969; Orr & Lanzetta, 1980) and electromyography (EMG) (Lanzetta & Englis, 1989; Vaughan & Lanzetta, 1980). However, the subjective reports and physiological measures manifest the final outcome of neural responses to emotions of other individuals but tell little about the cognitive and neural processes of empathy.

Recent studies used functional magnetic resonance imaging (fMRI) to explore the neural substrates of empathy-related processes by manipulating representation of others' affective state and provided evidence that certain brain areas are engaged in shared representation of one's own and others' emotional states. For example, observing disgust faces and feeling disgust oneself activated the same sites in the anterior insula and anterior cingulate cortex (ACC) (Wicker et al., 2003), which were also activated when participants viewed faces with painful expression (Botvinick et al., 2005). Moreover, insula and ACC activities

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induced by painful faces were correlated with subjects' estimates of intensity of observed pain whereas magnitudes of the insula and left inferior frontal activities correlated with subjects' self-rated empathy (Saarela et al., 2007). Perception of pain stimulation applied to hands or feet also generated increased insula and ACC activation that was correlated with subjective estimation of pain intensity (Jackson, Meltzoff, & Decety, 2005; Jackson, Brunet, Meltzoff, & Decety, 2006; Morrison, Lloyd, di Pellegrino, & Roberts, 2004). Empathy-related neural activity has also been investigated in conditions simulating real social contexts. Singer et al. (2004) scanned female volunteers who either experienced painful stimuli themselves or watched symbols indicating application of painful stimuli to their partners. The authors found that both noxious stimuli applied to the subjects and perception of symbols indicating the partners' pain resulted in activation in the insular and ACC. Because ACC is involved in coding the affective dimension of pain such as subjectively perceived unpleasantness (Rainville, Duncan, Price, Carrier, & Bushnell, 1997), Singer et al. (2004) proposed that empathizing with pain is mediated by activation of re-representations of the affective dimension of pain. The sensorimotor cortex can be also involved in empathic responses because the amplitudes of motor-evoked potentials induced by transcranial magnetic stimulation (TMS) over the motor cortex were reduced when subjects observed others' hands being pricked relative to when observing objects such as a tomato being pricked (Avenanti, Bueti, Galati, & Aglioti, 2005; Avenanti, Paluello, Bufalari, & Aglioti, 2006). Viewing video clips of painful stimuli delivered to others increased the amplitudes of somatosensory-evoked potentials elicited by nonpainful electrical stimulation to the observers' wrist (Bufalari, Aprile, Avenanti, di Russo, & Aglioti, in press). These findings support the existence of a shared neural network for one's own emotional or sensory experience and the observation of others' similar states.

Researchers have tried to understand empathy as a process with which an observer perceives others' emotional states and generates a similar mental state in the self. Such approach decomposes the process of empathy into components that are automatically elicited by mere perception of others' emotional states (i.e., bottom-up process) and that depend upon top-down controlled processes. Preston and de Waal (2002) suggest that involuntarily triggered processes such as emotion contagion or imitation play a key role in understanding and sharing others' emotion. This view is supported by the neuroimaging findings that a shared neural network is engaged in perception of others' emotional states and in generation of one's own emotional experience (Botvinick et al., 2005; Jackson et al., 2005; Saarela et al., 2007; Singer et al., 2004). It has also been suggested that empathy is based on an unconscious and automatic simulation of the subjectivity of others through the function of mirror neurons (Gallese & Goldman, 1998). In agreement with this, neuroimaging studies observed empathy-related neural activities in association with others' pain regardless the relationship between an observer and the one being observed (e.g., loved ones in

and amygdala activations induced by facial expressions of pain were greatly reduced when subjects performed pain irrelevant task (e.g., gender judgment).

More recently, Gu and Han (2007) found that attention to pain cues in the stimuli modulate the neural activities linked to empathy. They designed two tasks to manipulate top-down attention to pain cues in the stimuli in which hands were in painful or neutral situations (see Fig. 1), i.e., rating the intensity of pain felt by a model that required focused attention to the pain cues or counting the number of hands in the stimuli that drew attention away from others' feeling. Gu and Han found that, relative to counting neutral stimuli, rating pain intensity of painful pictures induced increased activation in part of the pain matrix including ACC/paracingulate, insula, and the left middle frontal gyrus. However, these neural activities were evident in the pain judgment task but not in the counting task, indicating that empathic responses strongly depended upon top-down attention to the emotional cues. In addition, they found that empathy-related neural activities were also modulated by the contextual reality of stimuli. By transforming the painful pictures into cartoons so as to degenerate the realism of stimuli, Gu and Han (2007) found that, relative to rating pain intensity of painful pictures, rating pain intensity of painful cartoons failed to activate the insula and produced weaker ACC activity.

These findings suggest that the neural correlates of empathy are strongly modulated by social relations between individuals, by the voluntary effort to understand others' emotion, and by the prior knowledge of contextual reality of stimuli. Preston and de Waal (2002) proposed that early on, automatic processes cause the state of individuals who experience an emotional state to elicit a similar or relevant state in the observers. Top-down controlled processes may then inhibit or facilitate this vicarious emotional state. Decety and Lamm (2006) suggest that empathy involves both emotion sharing (bottom-up information processing) and executive control to regulate this experience (top-down information processing), underpinned by specific and interacting neural systems. However, it is unclear at which stage of empathic processing the top-down controlled mechanisms (e.g., attention and evaluation of social relations and behaviours) are involved in modulation of empathic response. De Vignemont and Singer (2006) suggest two models to account for the modulation of vicarious affective responses towards others' emotion. The late appraisal model proposes that empathic responses are automatically activated by the perception of emotional cues while contextual information is processed in parallel so as to be involved to modulate the empathic responses at a later stage. The early appraisal model, however, suggests that emotional cues are first evaluated in a context of external and internal information. The outcome of the contextual appraisal processes determines whether empathic responses take place at a later stage. Nevertheless, previous research failed to distinguish between these two models because blood oxygen dependent (BOLD) signals recorded in fMRI studies have a low temporal resolution.

The current study investigated several issues regarding the cognitive and neural mechanisms underlying empathy for pain. First, we investigated the temporal dynamics of neural mechanisms underlying empathy for pain by recording event-related brain potentials (ERPs) elicited by pictures of hands in painful or neutral situations (Fig. 1). Empathic responses to pain of other individuals were indexed by the difference between ERPs to painful and neutral stimuli, similar to that in previous fMRI studies (Gu & Han, 2007; Jackson et al., 2005). Of particular interest were the temporal features of the ERP differentiation between painful and neutral stimuli.

Secondly, we studied whether and how empathic responses are modulated by top-down attention to pain cues. Similar to our previous fMRI study (Gu & Han, 2007), we manipulated attention to pain cues by asking subjects to judge pain intensity supposedly felt by the model or to count the number of hands in the stimuli. The effects of task demands on empathic responses help to distinguish between the automatic and top-down controlled process of empathy for pain. Specifically, the automatic process is indexed by the responses that are not influenced by task demands, whereas the top-down controlled process is reflected in the responses that depend upon task manipulations. Although the responses in ACC and insula were observed in the pain judgment task but not in the counting task (Gu & Han, 2007), such fMRI results do not necessarily mean that all empathic neural responses depend upon task demands or that there are no automatic empathic responses. It is possible that BOLD signals with low temporal resolution, particularly in the studies using box-car design (Gu & Han, 2007; Jackson et al., 2005, 2006; Singer et al., 2004), mainly reflect sustained neural activity related to empathy and are not efficacious to reveal automatic empathic neural responses that are essentially transient and occur early and rapidly. The slow sustain empathic neural responses revealed by fMRI studies may conceal the rapid transient empathic neural responses.

Third, we investigated to what degree the automatic and controlled processes of empathy for pain are modulated by prior knowledge of contextual reality of stimuli. We recently found that, although the knowledge of contextual reality of stimuli modulated empathic neural responses, this effect was different from that produced by top-down attention (Gu & Han, 2007). Particularly, empathy-related insula activity to painful cartoons was eliminated and ACC activity was weakened when perceiving pain in cartoons compared with that in pictures. However, the right frontal activity was not influenced by the contextual reality of stimuli. As mentioned above, if brain areas such as ACC and insula underpin the automatic "affective sharing" process (Jackson et al., 2005, 2006; Singer et al., 2004; Wicker et al., 2003), it may be hypothesized, on the ground of Gu and Han's observation, that the prior knowledge of contextual reality of stimuli should modulate early automatic processes of empathy for pain. To assess this hypothesis, we compared neural activities differentiating painful versus neutral pictures and painful versus neutral cartoons, similar to our previous fMRI research (Gu & Han, 2007). We expected weaker neural responses related to empathy for pain shown in cartoons than in pictures.

Finally, we explored ERP correlates of subjective feeling about others in pain and subjective feeling of one's own unpleasantness. While previous fMRI studies showed correlation between ACC/insula activity and subjective ratings of pain

of other individuals (Jackson et al., 2005; Saarela et al., 2007) and between ACC/insula activity and individual differences in empathy as measured with empathic concern scale (Singer et al., 2004), we know little about the relationship between electrophysiological activity and subjective feeling of empathy for pain. Specifically, it is unknown whether the automatic or controlled process of empathy for pain is more closely related with subjective feeling of others' pain and self-unpleasantness.

2. Methods

2.1. Subjects

Thirty-one healthy undergraduate and graduate students (16 males and 15 females) from Peking University participated in the study as paid volunteers. Five of the subjects (3 males and 2 females) were excluded from data analysis because of excessive artifacts during EEG recording. The behavioural and EEG data were reported from 26 subjects (13 males, 13 females, aged between 18 and 25 years, mean age $\pm$ S.D. = 20.96 $\pm$ 1.87). All subjects had no neurological or psychiatric history. All were right-handed, had normal or corrected-to-normal vision, and were not color blind. Informed consent was obtained from each subject before the study. This study was approved by a local ethic committee at the Department of Psychology, Peking University.

2.2. Stimuli and procedure

Visual stimuli consisted of 40 digital color pictures showing one hand or two hands in painful and neutral situations, similar to those in our previous fMRI study (Gu & Han, 2007). The pictures were shot from the first-person perspective and described accidents that may happen in everyday life, as illustrated in Fig. 1. Painful pictures included situations such as a hand trapped in a door or cut by scissors. Twenty pictures showed hands in painful situation (1 hand in 8 painful pictures and two hands in 12 painful pictures). The left and right hand was, respectively, involved in the painful situations in half of the painful stimuli. Each painful picture was matched with a neutral picture that showed one or two hands in situations that, although similar in contexts, did not imply any pain. The pictures were transformed into a set of cartoons using "filter → artistic → poster edge" tool of the software "Photoshop". Thus the cartoons were similar to the picture stimuli in presentation of painful and neutral situations but lacked the colors and textures that were necessary for representation of visual reality. The stimuli were presented in the center of a grey (128 cd/m^2) background of a 21-inch color monitor. Each stimulus was 7 cm $\times$ 5.5 cm (width $\times$ height), subtending a visual angle of 4° $\times$ 3.15° at a viewing distance of 100 cm.

Each subject participated in 16 blocks of trials that varied in stimuli and tasks. In each four blocks of trials, subjects (1) judged pain versus no-pain for hands in painful and neutral pictures; (2) counted the number of hands in painful and neutral pictures; (3) judged pain versus no-pain for hands in painful and neutral cartoons; or (4) counted the number of hands in painful and neutral cartoons. Each block 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 at the center of the screen, which was followed by a fixation cross with a duration varying randomly between 800 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 pressing using the left or right index finger.

2.3. ERP data recording and analysis

The electroencephalogram (EEG) was continuously recorded from 62 scalp electrodes that were mounted on an elastic cap in accordance to the extended 10–20 system (see Fig. 2), with the addition of two mastoid electrodes. The electrode at the right mastoid was used as reference. The electrode impedance was kept less than 5 kohms. Eye blinks and vertical eye movements were monitored with electrodes located above and below the left eye. The horizontal
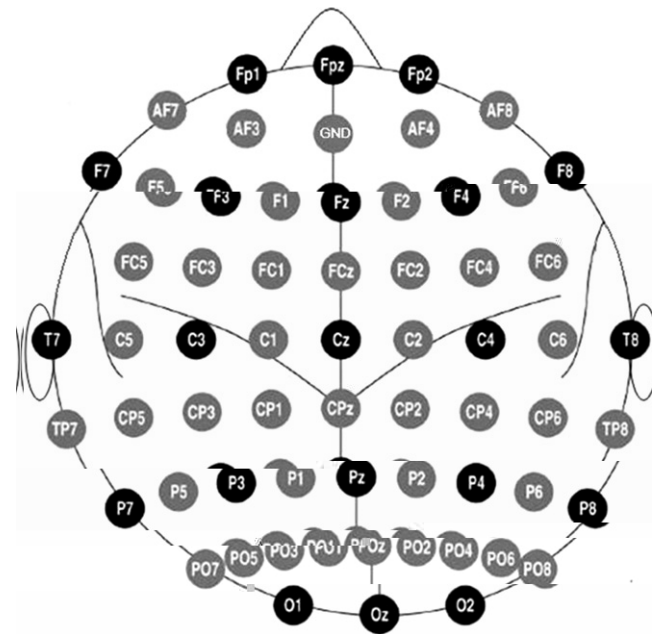

Fig. 2. The diagram of 62-channel scalp montage used in the present study. GND, the ground electrode.

electro-oculogram was recorded from electrodes placed 1.5 cm lateral to the left and right external canthi. The EEG was amplified (band pass 0.1–100 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 $\pm$50 μV at any electrode were excluded from the average. 8.89% of the trials were excluded due to artifacts (pictures: pain judgment = 9.0%; counting = 9.3%; cartoons: pain judgment = 8.5%; counting = 8.8%).

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 was 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), Stimulus Reality (picture vs. cartoon) as within-subject independent variables. The mean ERP amplitudes were subjected to ANOVAs with the factors being Pain, Task, Stimulus Reality, Hemisphere (electrodes over the left or right hemisphere) as within-subject independent variables. 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.

2.4. Measurement of subjective reports

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 their own unpleasantness 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, Reeve, Champion, Addicoat, & Ziegler, 1990), which contained six photocopied faces showing neutral to extremely painful expression.

Table 1
Mean RTs (ms) and response accuracy (%) (standard deviation) in each stimulus condition

	Picture		Cartoon	
	Pain judgment	Hands counting	Pain judgment	Hands counting
RTs				
Painful	609.05 (51.56)	469.83 (40.04)	596.13 (43.52)	463.17 (38.66)
Neutral	613.52 (58.33)	466.33 (38.06)	604.21 (49.57)	461.55 (37.37)
Accuracies				
Painful	75.95 (11.85)	96.15 (2.84)	81.47 (9.23)	96.25 (2.40)
Neutral	84.77 (6.39)	97.02 (1.83)	87.19 (6.10)	96.97 (1.96)

3. Results

3.1. Behavioural performance

The mean RTs and response accuracies in each condition are shown in Table 1. ANOVAs of RTs showed significant main effects of Task ($F(1,25) = 307.12$, $p < 0.001$) and Stimulus Reality ($F(1,25) = 10.42$, $p < 0.01$). RTs were longer in the pain judgment task than in the counting task. Subjects responded slower to picture than to cartoon stimuli. The ANOVAs performed on response accuracies showed significant main effect of Pain ($F(1,25) = 13.02$, $p < 0.01$), Task ($F(1,25) = 157.39$, $p < 0.001$), and Stimulus Reality ($F(1,25) = 74.32$, $p < 0.001$). Response accuracy was higher to the neutral than painful stimuli, higher in the counting than pain judgment tasks, and higher to cartoon than to picture stimuli. There was a reliable interaction of Pain × Task ($F(1,25) = 9.07$, $p < 0.01$), suggesting the difference in response accuracy between painful and neutral stimuli was larger in the pain judgment task than in the counting task.

3.2. Electrophysiological data

Grand-averaged ERPs to pictures and cartoons were computed separately for each stimulus condition and are illustrated in Figs. 3 and 4. Stimuli in all conditions evoked a negative component between 90 and 130 ms (N110) over the frontal–central area. The N110 was followed by a positive deflection between 140 and 200 ms (P180) over the central area and a negative wave peaking between 200 and 280 ms (N240) over the frontal region. There was another negative deflection peaking at 340 ms (N340) over the frontal area followed by a long-latency positivity between 360 and 800 ms (P3) with the maximum amplitude over the parietal area. ERPs over the occipito-temporal area were characterized with a positivity wave between 80 and 140 ms (P1), a negative wave between 140 and 200 ms (N170), and a positive wave between 200 and 450 ms (P320). A long-latency negative deflection was also observed over the occipito-temporal electrodes. The voltage topographies in Figs. 3 and 4 show the scalp distribution of each ERP component.

3.2.1. ERPs to picture stimuli
3.2.1.1. Automatic versus controlled processes of empathy. ANOVAs of the mean ERP amplitudes recorded at the frontal–central electrodes showed a significant main effect of Pain at 140–200 ms ($F(1,25) = 14.832$, $p < 0.01$), 200–280 ms

($F(1,25) = 16.457$, $p < 0.001$), 280–360 ms ($F(1,25) = 15.095$, $p < 0.001$), and 360–660 ms ($F(1,25) = 30.384$, $p < 0.001$). Relative to the neutral stimuli, painful stimuli elicited a positive shift of the ERPs in these time windows. The main effect of Task was significant at 100–280 ms over the frontal–central area ($F(1,25) = 15.061$, $p < 0.001$), suggesting that the pain judgment task induced a positive shift in this time window relative to the counting task. There was also a significant main effect of Task at 460–820 ms over the frontal–central area ($F(1,25) = 116.442$, $p < 0.001$), because the P3 was of larger amplitude in the pain judgment task than that in the counting task.

To examine whether the effects of Pain were modulated by the tasks, we analyzed the interaction of Pain × Task. There was a reliable interaction of Pain × Task at 380–500 ms over the frontal–central area ($F(1,25) = 6.604$, $p < 0.05$), suggesting that the painful stimuli elicited larger amplitudes at the ascending phase of the P3 component than the neutral stimuli when subjects performed the pain judgment task ($F(1,25) = 29.846$, $p < 0.001$) but not when they performed the counting task (380–460 ms, $F(1,25) = 3.257$, $p > 0.05$).

The ERPs recorded at the occipito-temporal electrodes showed a significant main effect of Pain between 420 and 660 ms ($F(1,25) = 9.408$, $p < 0.01$), due to the fact that the painful stimuli elicited larger amplitudes of the descending phase of the P320 relative to the neutral stimuli. There was a significant main effect of Task over the occipito-temporal area at 80–320 ms ($F(1,25) = 18.383$, $p < 0.001$) and at 460–780 ms ($F(1,24) = 73.497$, $p < 0.001$), suggesting that pain judgment elicited a positive shift at 80–320 ms relative to the counting task, whereas the counting task evoked a larger long-latency negativity at 460–780 ms.

Significant interactions of Pain × Task were observed over the occipito-temporal area at 220–300 ms ($F(1,24) = 5.378$, $p < 0.05$) and 420–580 ms ($F(1,24) = 6.691$, $p < (1,25) = 18.386$,
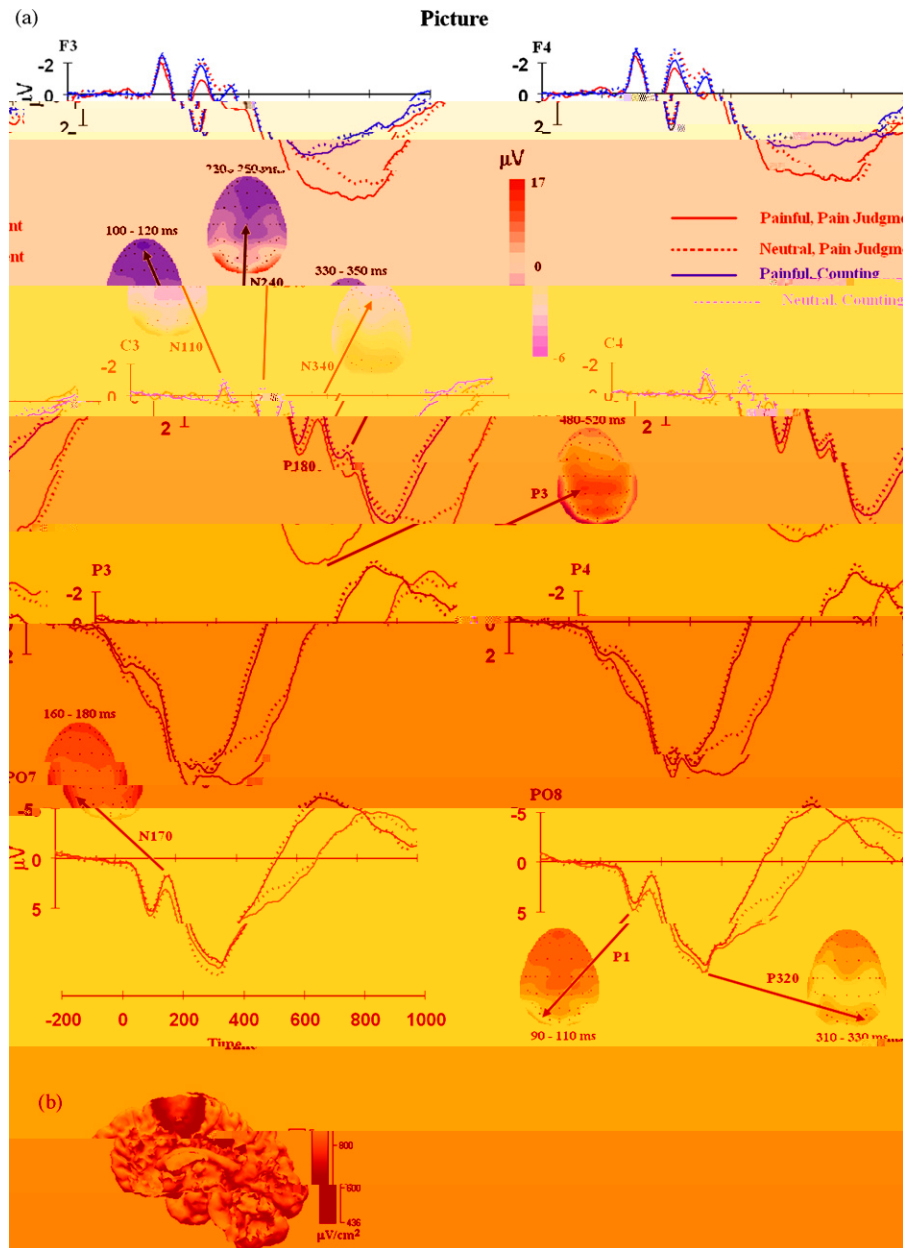
Fig. 3. (a) ERPs to picture stimuli in each stimulus condition. ERPs to the painful and neutral pictures recorded at F3–4, C3–4, P3–P4, and PO7–8 were illustrated. The voltage topographies illustrate the scalp distribution of each ERP component. (b) Current source density calculated from the difference wave obtained by subtracting ERPs to neutral stimuli from those to painful stimuli between 500 and 590 ms.

3.2.1.2. Hemispheric difference. A reliable main effect of Hemisphere was observed at 80–140 ms ($F(1,25) = 7.886$, $p < 0.01$), 220–360 ms ($F(1,25) = 8.518$, $p < 0.01$), and 660–820 ms ($F(1,25) = 6.530$, $p < 0.05$) at the frontal–central electrodes, suggesting that the N110, N240 and N340 were of larger amplitudes over the right than left hemispheres, and the descending phase of the P3 showed larger amplitudes over the left than right hemispheres.

There was a highly significant interaction of Pain × Hemisphere at 380–700 ms ($F(1,25) = 25.726$, $p < 0.001$) at the frontal–central–parietal area, suggesting larger difference in P3 amplitude between the painful and neutral stimuli over the left than the right hemispheres. Separate analysis showed that, over

the left hemisphere, there was a reliable main effect of Pain at 380–700 ms ($F(1,25) = 50.853$, $p < 0.001$), because the painful stimuli elicited a larger P3 relative to the neutral stimuli. However, over the right hemisphere, the main effect of Pain was significant at 380–540 ms ($F(1,25) = 12.200$, $p < 0.01$) but not at 540–700 ms ($F(1,25) = 0.551$, $p > 0.5$). These results suggest a longer differentiation between painful and neutral stimuli over the left than right hemispheres.

The ANOVAs also showed a reliable interaction of Task × Hemisphere at 200–380 ms ($F(1,25) = 19.610$, $p < 0.001$) over the frontal–central–parietal area, indicating larger difference in the N240 and N340 amplitudes between the pain judgment and the counting task over the left than right hemi-
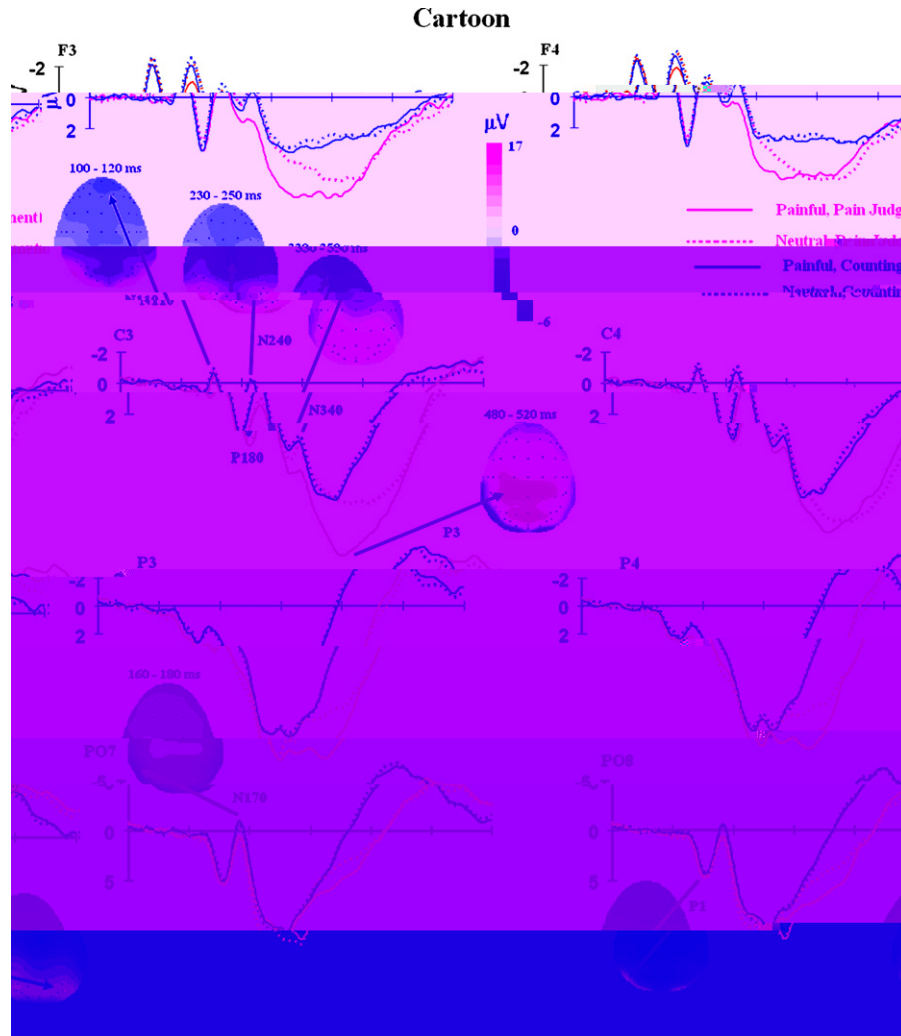
Fig. 4. ERPs to cartoons in each stimulus condition. ERPs to the painful and neutral cartoons recorded at F3–4, C3–4, P3–P4, and PO7–8 were illustrated. The voltage topographies illustrate the scalp distribution of each ERP component.

spheres. Separate analysis confirmed a reliable main effect of Task over the left hemisphere at 200–360 ms ($F(1,25) = 11.469$, $p < 0.01$) because the pain judgment task induced a positive shift of the ERPs relative to the counting task. In contrast, the main effect of Task was significant at 200–260 ms ($F(1,25) = 29.385$, $p < 0.001$) but not at 260–380 ms ($F(1,25) = 0.350$, $p > 0.5$) over the right hemisphere, suggesting a longer duration of the left hemispheric dominance in pain judgments.

Furthermore, ANOVAs showed a reliable interaction of Pain × Task × Hemisphere at 420–780 ms ($F(1,25) = 32.895$, $p < 0.001$) over the frontal–central–parietal area. Separate analysis showed that there was a reliable interaction of Pain × Hemisphere at 420–780 ms in the pain judgment task ($F(1,25) = 34.566$, $p < 0.001$). Further separate analysis showed that, in the pain judgment task, there was a significant main effect of Pain over the left hemisphere at 420–700 ms ($F(1,25) = 37.814$, $p < 0.001$), whereas such pain effect was evident only at 420–500 ms over the right hemisphere ($F(1,25) = 4.195$, $p < 0.05$). In contrast, the interaction of Pain × Hemisphere was not significant in the counting task

($F(1,25) = 0.853$, $p > 0.5$), although the main effect of Pain was significant at 460–660 ms ($F(1,25) = 7.852$, $p < 0.01$).

There was also a reliable interaction of Task × Hemisphere at 380–580 ms over the occipito-temporal area ($F(1,25) = 13.032$, $p < 0.01$), due to a larger effect of task over the right than left hemispheres. Separate analysis confirmed a main effect of Task at 420–580 ms over the right hemisphere ($F(1,25) = 22.056$, $p < 0.001$) and at 460–580 ms over the left hemisphere ($F(1,25) = 61.939$, $p < 0.001$), suggesting that both effects of pain cues in the stimuli and task demands were more salient over the left than right frontal–central–parietal areas. Such hemispheric asymmetry in the processing of empathy for pain was evident only when subjects performed the pain judgment task, suggesting that task demands for pain judgment is necessary for the left hemispheric dominance in empathetic processing of pain.

3.2.2. ERPs to cartoon stimuli

3.2.2.1. Automatic versus controlled processes of empathy.
The ANOVAs of the mean ERP amplitudes to cartoons

showed a main effect of Pain over the frontal–central area at 220–280 ms ($F(1,25) = 6.475$, $p < 0.05$), 280–360 ms ($F(1,25) = 9.894$, $p < 0.01$) and 360–620 ms ($F(1,25) = 28.382$, $p < 0.001$), reflecting the fact that, relative to the neutral stimuli, the painful stimuli elicited a positive shift of the ERPs in these time windows. The main effect of Task was significant over the frontal–central area at 180–260 ms ($F(1,25) = 15.163$, $p < 0.001$) and 460–820 ms ($F(1,25) = 75.401$, $p < 0.001$), suggesting that the pain judgment task induced a positive shift at 180–260 ms relative to the counting task, and the P3 was of larger amplitude in the pain judgment task than in the counting task.

There was a reliable interaction of Pain × Task over the frontal–central area between 320 ms and 540 ms ($F(1,25) = 10.528$, $p < 0.01$). Separate analysis confirmed that the painful stimuli elicited a larger P3 component than neutral stimuli in the pain judgment task ($F(1,25) = 31.404$, $p < 0.001$) but not in the counting task between 380 and 540 ms ($F(1,25) = 2.703$, $p > 0.1$).

Over the occipito-temporal area, the main effect of Pain was observed at 160–300 ms ($F(1,25) = 15.822$, $p < 0.001$) and 380–620 ms ($F(1,25) = 22.524$, $p < 0.001$), indicating that the painful stimuli evoked a positive shift relative to the neutral stimuli in these time windows. There was also a main effect of Task over the occipito-temporal area at 120–260 ms ($F(1,25) = 26.975$, $p < 0.001$), 280–340 ms ($F(1,25) = 5.609$, $p < 0.05$), and 420–780 ms ($F(1,25) = 54.291$, $p < 0.001$) because the pain judgment task elicited a positive shift in these time windows relative to the counting task.

Moreover, a significant interaction of Pain × Task was observed over the occipito-temporal area at 220–260 ms ($F(1,25) = 12.129$, $p < 0.01$) and 380–580 ms ($F(1,25) = 22.889$, $p < 0.001$). Separate analysis revealed that the painful stimuli evoked a smaller amplitude at the ascending phase of P320 than the neutral stimuli in the pain judgment task ($F(1,25) = 34.974$, $p < 0.001$) but not in the counting task ($F(1,25) = 2.664$, $p > 0.1$). However, the painful stimuli evoked a larger amplitude at the descending phase of P320 than the neutral stimuli in the pain judgment task ($F(1,25) = 31.030$, $p < 0.001$) but not in the counting task ($F(1,25) = 0.629$, $p > 0.5$).

3.2.2.2. Hemispheric difference. There was a significant main effect of Hemisphere over the frontal–central–parietal area at 220–360 ms ($F(1,25) = 6.343$, $p < 0.05$), because the N240 and N340 were of larger amplitude over the right than the left hemispheres. The main effect of Hemisphere was also observed at 660–820 ms ($F(1,25) = 8.463$, $p < 0.01$) suggesting larger ampli-
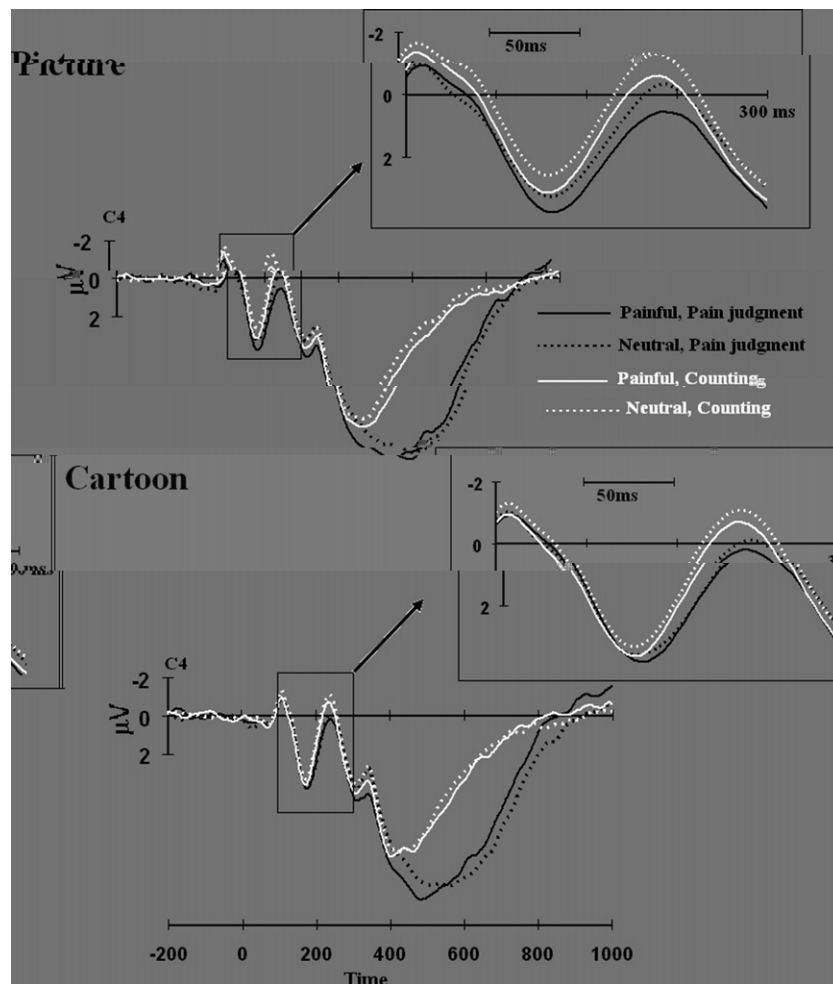

Fig. 5. Comparison between the early ERP pain effects induced by pictures and cartoons.

Table 2
Mean FPS-R scores (standard deviation) under each condition

	Painful stimuli		Neutral stimuli (other's pain)
	Other's pain	Self-unpleasantness	
Picture	4.36 (0.71)	4.30 (0.74)	1.17 (0.25)
Cartoon	4.30 (0.71)	4.23 (0.70)	1.22 (0.20)

tude of the descending phase of the P3 over the right than the left hemispheres.

There was a reliable interaction of Pain × Hemisphere over the frontal–central–parietal area between 380 and 740 ms ($F(1,25) = 21.955$, $p < 0.001$), suggesting a greater pain effect over the left than right hemispheres. Separate analysis indicate that the painful stimuli induced a larger P3 than the neutral stimuli over the left hemisphere (380–660 ms, $F(1,25) = 39.017$, $p < 0.001$) but not over the right hemisphere (500–660 ms, $F(1,25) = 1.998$, $p > 0.1$). There was also a reliable interaction of Task × Hemisphere over frontal–central area at 140–420 ms ($F(1,25) = 13.903$, $p < 0.01$) and 580–820 ms ($F(1,25) = 11.995$, $p < 0.01$), suggesting a larger task effect over the left than the right hemispheres. The task of pain judgment elicited a positive shift relative to the counting task in both time windows over the left hemisphere ($F(1,25) = 21.175$, $p < 0.001$). However, the effect of Task was significant only at 180–260 ms and 580–820 ms over the right hemisphere ($F(1,25) = 22.672$, $p < 0.001$).

3.2.3. Effects of stimulus reality

To confirm whether stimulus reality influenced the automatic and controlled process of empathy for pain, we examined the interaction of Pain × Stimulus Reality and found significant interaction at 200–240 ms ($F(1,25) = 4.394$, $p < 0.05$) over the frontal–central area. There was a significant main effect of Pain in this time windows for pictures ($F(1,25) = 16.457$, $p < 0.001$) but not for cartoons ($F(1,25) = 1.839$, $p > 0.1$). This indicates that the automatic process of empathy for pain was evident only for picture stimuli at this time window. Fig. 5 illustrates the difference in the early automatic process of empathy for pain between pictures and cartoons. A reliable interaction of Task × Stimulus Reality was found at 120–160 ms over the frontal–central area ($F(1,25) = 5.559$, $p < 0.05$), because the effect of Task in this time window was significant for pictures ($F(1,25) = 10.272$, $p < 0.01$) but not for cartoons ($F(1,25) = 0.572$, $p > 0.5$), suggesting that the task modulate early frontal–central activity only when subjects perceived picture stimuli.

3.2.4. Subjective reports and their correlation with neural activity

The mean scores and standard deviation of subjective reports of the degree of perceived pain and self-unpleasantness are shown in Table 2. The scores of pain intensity were subject to ANOVAs with Pain (painful vs. neutral) and Stimulus Reality (picture vs. cartoon) as main effect. There was only a significant main effect of Pain ($F(1,25) = 565.51$, $p < 0.001$), suggesting higher scores for painful than neutral stimuli. Paired-sample t-

test confirmed that there was no significant difference between the scores related to other's pain and self-unpleasantness (pictures: $t(25) = 0.545$, $p > 0.5$; cartoons: $t(25) = 0.503$, $p > 0.5$). Moreover, the scores of rating others' pain did not differ between pictures and cartoons ($t(25) = 0.782$, $p > 0.1$), nor did the scores of rating self-unpleasantness ($t(25) = 0.618$, $p > 0.5$). We also calculated the correlation between the scores of other's pain and self-unpleasantness and found a significant correlation between the two scores both when watching painful pictures ($r = 0.688$, $p < 0.001$) and cartoons ($r = 0.498$, $p < 0.01$).

To investigate whether the electrophysiological activity elicited by the painful stimuli was correlated with subjective evaluation of other's pain and the self-unpleasantness, we calculated the correlation between the mean amplitudes of ERPs elicited by painful stimuli in each time window and the FPS-R scores, as illustrated in Fig. 6. When subjects performed the pain judgment task, the mean ERP amplitudes at 140–180 ms related to the painful pictures was significantly correlated with both the score of other's pain ($r(1,25) = -0.485$, $p < 0.05$) and the score of self-unpleasantness ($r(1,25) = -0.464$, $p < 0.05$). However, the mean ERP amplitudes evoked by painful cartoons at 140–200 ms during the pain judgment task was significantly correlated with the score of other's pain ($r(1,25) = -0.641$, $p < 0.001$) but not with the score of self-unpleasantness ($r(1,25) = -0.152$, $p > 0.1$). No reliable correlation between the rating score and ERP amplitudes was observed in the counting task for both pictures and cartoons.

4. Discussion

The present study utilized ERPs to investigate temporal dynamics of neural activity underlying empathy for pain. Our ERP data analysis focused on when neural activities started to differentiate between perception of painful and neutral stimuli and whether such differential activity was modulated by task demands so as to identify the automatic and controlled components of empathy-related activity. We also tested the hypothesis that empathic neural responses are modulated by contextual reality of stimuli using cartoons to manipulate stimulus realism.

4.1. Sustained neural activity underlying the pain judgment task

The mean response accuracy was high for both pain judgment and counting tasks, although the former was lower than the latter. Consistent with the results of response accuracy, subjects responded slower in the pain judgment task than in the counting task, suggesting that pain judgment took more time for evaluation of the pain cues in the stimuli relative to the counting task. The ERPs differentiating the pain judgment and counting tasks reflected sustained neural activity associated with the task demand. The early task effect occurred at 120 ms as indexed by a positive shift at 120–280 ms over the anterior frontal–central electrodes induced by the pain judgment relative to the counting task. The pain judgment task was also characterized with larger P3 amplitudes over the posterior parietal area. Most of the previous fMRI studies of empathy for pain compared neu-
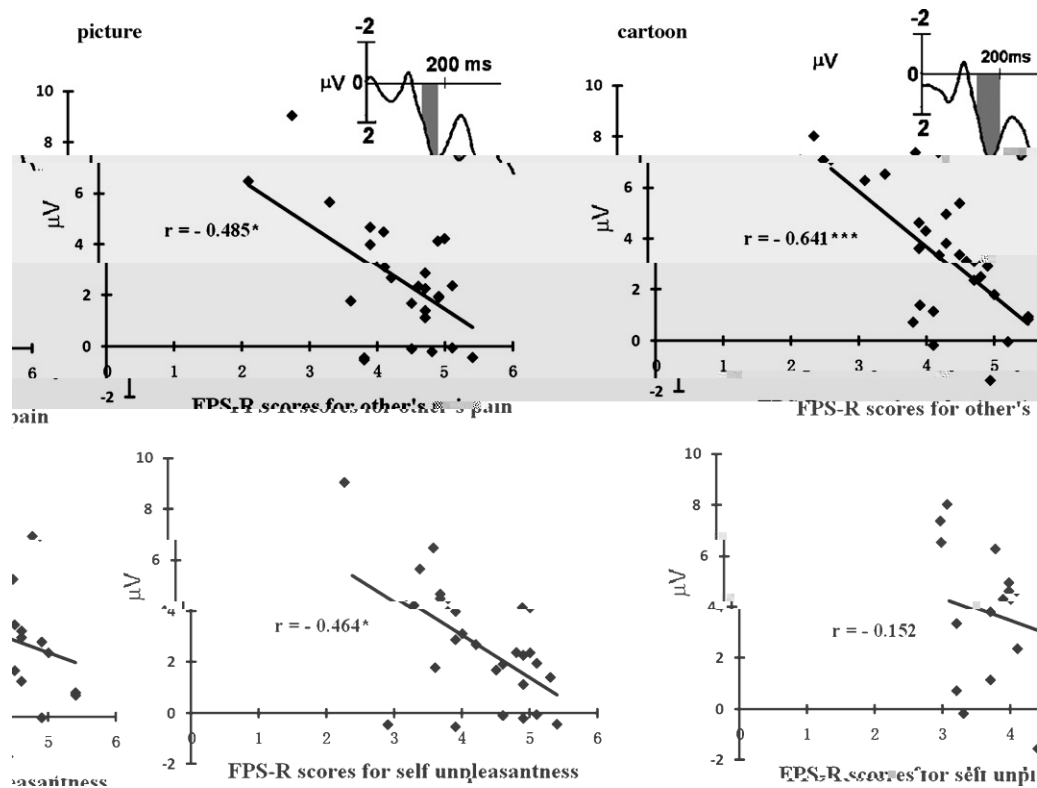
Fig. 6. Correlation between the ERP amplitudes and the FPS-R scores for other's pain and the FPS-R scores for self-unpleasantness.

ral activities elicited by observations of painful and nonpainful stimulation applied to others (Botvinick et al., 2005; Gu & Han, 2007; Jackson et al., 2005, 2006; Morrison et al., 2004; Singer et al., 2004) and found evidence for the involvement of a neural network including the insula, ACC, and thalamus in empathic processes for pain. The observed activations in these neural structures were related per se to both perception of painful stimulation and the task of pain judgment or evaluation. Gu and Han (2007) examined the stimulus-independent neural correlates of pain judgment by comparing pain judgment of painful stimuli and hand-number counting of painful stimuli. Because the visual stimuli (both visual features and emotional cues) were identical in both conditions, the brain activations observed in the contrast between the two tasks (e.g., bilateral ACC/Paracingulate, the right insula and inferior frontal gyrus, right putamen, and right middle frontal gyrus) mainly manifest the neural activity underlying the pain judgment task itself. However, activation of these brain areas was also observed in the contrast between pain judgment of painful stimuli and hand-number counting of non-painful stimuli. These results indicate that the neural network identified in the fMRI studies possibly mediates both the cognitive processes and emotional responses related to empathy for pain. Our ERP results complement the fMRI findings by providing evidence that the neural activities related to pain-judgment can be divided into an early component over the frontal–central area and a late component over the parietal area. The ERP voltage topographies suggests that the early and late components of the activities associated with pain-judgment may arise from distinct brain areas, i.e., the early response possibly with an anterior

frontal source whereas the late response possibly with a posterior parietal source. In addition, our ERP data demonstrated larger difference in neural activities at 200–380 ms between the pain judgment and counting tasks over the left than right hemispheres, suggesting a left hemispheric dominance in pain judgment in this time window.

The effects of pain-judgment task were observed over the occipito-temporal area as well. A positive shift was evident at 80–320 ms over the occipito-temporal electrodes to the pain judgment task compared with the counting task. The ERP components in this time window included early visual activities such as the P1 that showed maximum amplitudes over bilateral occipital areas. Because the P1 component evoked by visual stimuli arises from the lateral extrastriate cortex (Hillyard & Anllo-Vento, 1998; idonided sti,such

4.2. Automatic versus controlled processes of empathy for pain

A main purpose of the current ERP study was to isolate the automatic process from the controlled process of empathy for pain under the assumption that the automatic empathic responses may not be modulated by task demands whereas the top-down controlled empathic processes depend greatly upon task requirements. Our ERP results showed a salient pain effect in a long time window from 140 to 660 ms, i.e., painful stimuli elicited a positive shift of the ERP waves relative to the neutral stim-

1981; Duncan-Johnson & Kopell, 1981; McCarthy & Donchin, 1981). The P3 component with largest amplitudes over the

tal states by contextual reality of stimuli. However, a recent fMRI study using cartoons depicting emotional social contexts found empathy-related activity in ACC, paracingulate, and the amygdala (Völlm et al., 2006). Gu and Han (2007) observed increased activation in the ACC/paracingulate induced by painful cartoons, similar to those observed in the studies using painful pictures of body parts (Jackson et al., 2005, 2006) or faces (Botvinick et al., 2005; Saarela et al., 2007). However, painful cartoons failed to activate the insula and induced weaker ACC activation relative to painful pictures. Because it has been supposed that the ACC and insula underlies the affective component of empathy for pain (Singer et al., 2004), Gu and Han's fMRI results indicate that lack of contextual reality of stimuli may reduced the affective empathic responses.

As discussed above, the early ERP pain effect observed in the current work possibly mediated the affective component of empathy for pain such as emotional sharing. Thus our ERP results are in agreement with the implications of the fMRI findings because the early rather than the late pain effects induced by painful cartoons were decreased relative to those related to painful pictures. Furthermore, the results of correlation analysis indicate that the early neural activity evoked by painful cartoons contributed to the subjective ratings of pain intensity of others although the contextual reality of stimuli was reduced. Nevertheless, unlike the results of painful pictures, the early neural activity evoked by painful cartoons did not correlate with subjective feelings of self-unpleasantness when watching painful cartoons. This result has two implications, i.e., the early responses could be related to pain intensity judgment rather than to an emotional response from the observer when stimulus reality was destroyed and subjective feelings of others' pain could be dissociated from subjective feelings of self-unpleasantness. The modulation of empathic responses by manipulation of contextual reality of stimuli was different from that by manipulation of task demands. Task demands changed greatly the late controlled process whereas contextual reality of stimuli modulated the early affective component of empathy.

4.4. Conclusion

We found ERP evidence for an early empathic response over the frontal–central cortex that was independent of task demands but was modulated by the contextual reality of stimuli. The magnitude of the early neural activity was correlated with subjective feelings of both others' pain and self-unpleasantness, providing evidence for the functional role of the early empathic response in emotional sharing. We also found ERP evidence for a late empathic response over the central–parietal area that was modulated by task demands but independent of the contextual reality of stimuli. Given the frontal–central focus of the early ERP components and the correlation between the early ERP components and subjective feelings, it may be speculated that the early empathic ERP effect may arise from the brain areas such as ACC and insula that underlie the affective component of empathy for pain (Singer et al., 2004; Jackson et al., 2005). The cingulate and supplementary motor cortex might be engaged in the late

empathic response as suggested by the results of current source density analysis.

The ERP findings provide important implications for the models to account for the modulation of our vicarious affective responses towards others' emotion. According to De Vignemont and Singer (2006), while being confronted with an emotional context, the brain processes contextual information before or after the perception of emotional cues in the context. This in turn leads to modulations of empathic responses at either an early or later stage. Our ERP results indicate that modulations of empathy for pain may occur at both the early and late stages of empathic responses. The early modulation by contextual reality led to enhancement or weakening of subjective feelings of self-unpleasantness induced by perception of others in pain but did not to influence subjective ratings of pain intensity of other individuals. The late modulation by task demands altered the cognitive evaluation of others' pain. While previous fMRI studies suggest that empathic responses in the insula and ACC were modulated by the affective link between the empathizer and the person in pain (Singer et al., 2006) and by self-other differentiation and cognitive appraisal (Lamm, Batson, & Decety, 2007), the current ERP results demarcated the temporal course of modulation of empathic responses by contextual reality and top-down attention, both enhancing the previous fMRI results and fining the temporal neural mechanisms underlying empathy for pain.

References

Avenanti, A., Bueti, D., Galati, G., & Aglioti, S. M. (2005). Transcranial magnetic stimulation highlights the sensorimotor side of empathy for pain. *Nature Neuroscience*, *8*, 955–960.

Avenanti, A., Paluello, I. M., Bufalari, I., & Aglioti, S. M. (2006). Stimulus-driven modulation of motor-evoked potentials during observation of others' pain. *Neuroimage*, *32*, 316–324.

Batson, C. D. (1987). Physiological indices of empathy. In N. Eisenberg & J. Strayer (Eds.), *Empathy and its development* (pp. 356–360). New York: Cambridge University Press.

Bieri, D., Reeve, R. A., Champion, G. D., Addicoat, L., & Ziegler, J. B. (1990). The face pain scale for the self-assessment of the severity of pain experienced by children: Development, initial validation, and preliminary investigation for ratio scale properties. *Pain*, *41*, 139–150.

Botvinick, M., Jha, A. P., Bylsma, L. M., Fabian, S. A., Solomon, P. E., & Prkachin, K. M. (2005). Viewing facial expressions of pain engages cortical areas involved in the direct experience of pain. *Neuroimage*, *25*, 312–319.

Bryant, B. K. (1987). Critique of comparable questionnaire methods in use to assess empathy in children and adults. In N. Eisenberg & J. Strayer (Eds.), *Empathy and its development* (pp. 361–373). New York: Cambridge University Press.

Bufalari, I., Aprile, T., Avenanti, A., di Russo, F., & Aglioti, S. M. (in press). Empathy for pain and touch in the human somatosensory cortex. Cerebral Cortex.

Craig, K. D., & Lowery, H. J. (1969). Heart-rate components of conditioned vicarious autonomic responses. *Journal of Personality and Social Psychology*, *11*, 381–387.

Davis, M. H. (1996). *Empathy: A social psychological approach*. Boulder: Westview Press.

De Vignemont, F., & Singer, T. (2006). The empathic brain: How, when and why? *Trends in Cognitive Science*, *10*, 435–441.

Decety, J., & Jackson, P. L. (2004). The functional architecture of human empathy. *Behavioral and Cognitive Neuroscience Review*, *3*, 71–100.

Decety, J., & Lamm, C. (2006). Human empathy through the lens of social neuroscience. *Scientific World Journal*, *6*, 1146–1163.

Duncan-Johnson, C. C. (1981). P300 latency: A new metric of information processing. *Psychophysiology*, *18*, 207–215.

Duncan-Johnson, C. C., & Kopell, B. S. (1981). The stroop effect: Brain potentials localize the source of interference. *Science*, *214*, 938–940.