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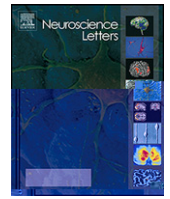
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Perspective taking modulates event-related potentials to perceived pain

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ABSTRACT

Recent event-related brain potential (ERP) study disentangled an early automatic component and a late top-down controlled component of neural activities to perceived pain of others. This study assessed the hypothesis that perspective taking modulates the top-down controlled component but not the automatic component of empathy for pain by recording ERPs from 24 subjects who performed pain judgments of pictures of hands in painful or non-painful situations from either self-perspective or other-perspective. We found that, relative to non-painful stimuli, painful stimuli induced positive shifts of ERPs at frontal–central electrodes as early as 160 ms after sensory stimulation and this effect lasted until 700 ms. The amplitudes of ERPs at 230–250 ms elicited by painful stimuli negatively correlated with both subjective ratings of others' pain and self-unpleasantness in both self-perspective and other-perspective conditions. Neural response to perceived pain over the central–parietal area was significantly reduced at 370–420 ms when performing the pain judgment task from other-perspective compared to self-perspective. The results suggest that shifting between self-perspectives and other-perspectives modulates the late controlled component but not the early automatic component of neural responses to perceived pain.

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Empathy – the capacity to understand and share others' feelings and thoughts – plays a crucial role in human social communication and interactions [6] and has been proposed to mediate development and acquisition of appropriate social behaviors such as helping and cooperation [8]. Recent brain imaging research has examined neural processes involved in empathy by scanning subjects during perception of visual displays that depict body parts in painful and non-painful situations [4,10,12–14]. Perception of painful stimuli applied to others induced increased activations in brain areas involved in the processing of both affective (e.g., the insula and anterior cingulate cortex (ACC)) [10,13,14,16,19,20] and sensory (e.g., the primary somatosensory cortex and parietal operculum) [1,3] aspects of the first-person pain experience.

Recent work further investigated temporal dynamics of neural responses to perceived pain by recording event-related brain potentials (ERPs) in association with perception of painful and non-painful stimuli applied to others [9,11]. Frontal ERP components differentiated between painful and neutral stimuli as early as 140 ms after sensory stimulation. Moreover, ERPs differentiating painful and non-painful stimuli were disentangled into two stages since the modulation of ERP amplitudes at 140–380 ms by perceived pain was independent of top-down attention to painful cues in stimuli and the amplitudes correlated with subjective ratings of perceived pain and self-unpleasantness. The modulation

of ERP components after 380 ms by perceived pain, however, was weakened when top-down attention was withdrawn from painful cues. It appears that an early automatic component and a late top-down controlled component are involved in neural responses to perceived pain.

This study further assessed this model by examining whether the early and late neural responses to perceived pain are modulated by shifting between self-perspectives and other-perspectives in a pain judgment task. Human beings are able to take a position regarding another person's mental life. This top-down controlled process, i.e., perspective taking, is critical for empathy as one has to adopt others' psychological view in order to understand and simulate others' emotional states [6,7]. A prior functional magnetic resonance imaging (fMRI) study found that judgment of perceived pain from self-perspective resulted in higher subjective ratings of perceived pain and enhanced activity in the secondary somatosensory cortex, posterior part of the ACC, and insula relative to judgment of perceived pain from other-perspective [13]. Similar modulations of neural responses to perceived pain in mid ACC and insula by perspective taking were observed when judging perceived painful facial expression [16]. Given the low temporal resolution of fMRI signals, the time course of the influence of perspective taking on neural responses to perceived pain remains unclear. Because perspective taking reflects a top-down controlled process to shift between perspectives of self and others, perspective taking may affect the top-down controlled processes of perceived pain. We tested this hypothesis by recording ERPs to pictures showing hands in painful or non-painful situations and asked

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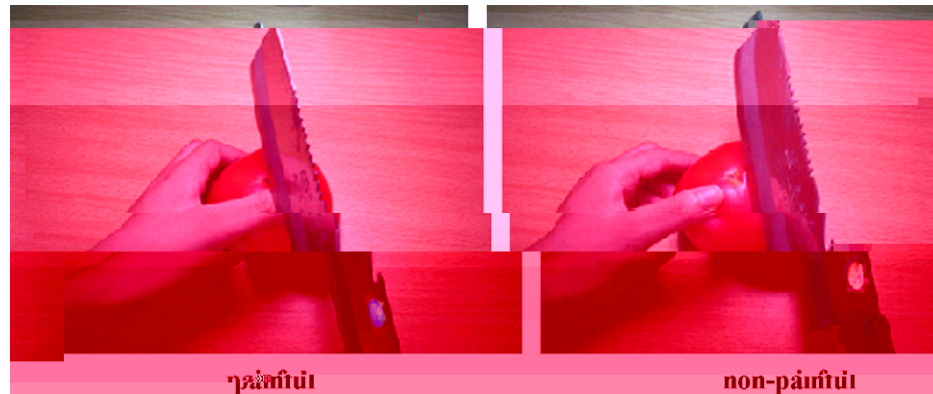


Fig. 1. Illustration of painful and non-painful stimuli used in this study.

participants to perform a pain judgment task from self-perspective or other-perspective. Neural responses to perceived pain were identified by examining the pain effect (i.e., ERPs differentiating painful and non-painful stimuli) and the influence of perspective taking on neural responses to perceived pain was assessed by comparing the pain effect when subjects imagined that hands in stimuli were their own or unfamiliar others'.

Twenty-four healthy adults (12 males and 12 females, mean age = 23.21 ± 2.65) participated in the study. All were right-handed (assessed using Edinburgh Inventory), had normal or corrected-to-normal vision, and were not color blind. Informed consent was obtained prior to the study.

Similar to the previous studies [7–9], visual stimuli consisted of 40 color pictures showing hands in painful situations and 40 color pictures of hands in non-painful situations (Fig. 1), which were repeatedly used in different blocks of trials. Painful pictures included situations such as a hand trapped in a door or cut by scissors. Each painful picture was matched with a non-painful picture. Each stimulus was presented in the center of a grey background of a 21-inch color monitor and subtended a visual angle of 2.58×3.43 (width $\times$ height) at a viewing distance of 100 cm.

On each trial a picture was presented for 200 ms, followed by a fixation cross with a duration varying randomly between 800 and 1600 ms. Painful and non-painful stimuli were presented in a random order. Subjects had to judge painful vs. non-painful pictures on each trial. The assignment of the left or right index finger to painful and non-painful stimuli and the order of perspectives were counterbalanced across subjects. Each subject participated in 8 blocks of 80 trials. Each block started with the presentation of instructions for 3 s that defined perspectives from which subjects performed the pain judgment task, i.e., self-perspective ("Imagine that hands shown in the picture are your own") in 4 blocks or the perspective of a specific but unfamiliar person ("Imagine that hands shown in the picture are unfamiliar others") in 4 blocks.

After the electroencephalography (EEG) recording session, subjects were asked to rate the intensity of perceived pain and the related self-unpleasantness from self- or other-perspectives when they observed each stimulus using the Face Pain Scale-Revised (FPS-R) adapted from the Faces Pain Scale [2] (an 11-point scale with 0=no pain, 10=very much painful, or 0=not unpleasant, 10=very much unpleasant). Individual differences in empathy ability were measured using the Interpersonal Reactivity Index (IRI) Scale [5] that contains four subscales related to empathic concern, perspective taking, fantasy scale and personal distress.

The EEG was recorded from 62 scalp electrodes that were mounted on an elastic cap in accordance to the extended 10–20 system and were referenced to the average of the left and right mastoid electrodes. The electrode impedance was kept less than 5 k Ω . Eye blinks and vertical eye movements 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 0.1–100 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 1000 ms. Trials contaminated by eye blinks, eye movements, or muscle potentials exceeding $\pm 50 \mu V$ at any electrode were excluded from the average. 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 amplitudes of each ERP component were calculated 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), response accuracies and subjective rating scores were subjected to a repeated measure analysis of variance (ANOVA) with pain (painful vs. non-painful stimuli) and perspective (self vs. other) as within-subjects independent variables. The mean ERP amplitudes were subjected to ANOVAs with the factors being pain, perspective, and hemisphere (electrodes over the left and right hemisphere) as within-subjects independent variables. Statistical data were reported at the electrode that showed the most conservative results (frontal electrodes: FC3–FC4; central electrodes: CP3–CP4; parietal electrodes: P3–P4).

The mean rating scores (standard deviation) of IRI questionnaire were perspective taking scale = 17.29(4.20), fantasy scale = 17.38(5.60), empathic concern scale = 19.00(4.26), and personal distress scale = 15.21(4.69). Table 1 shows mean RTs and response accuracies in each condition. ANOVAs of RTs showed a significant interaction of pain $\times$ perspective ($F(1, 23) = 7.409$, $p < 0.05$) because subjects responded faster to painful than non-painful stimuli in self-perspective condition ($t(23) = 3.058$, $p < 0.01$), but not in other-perspective condition ($t(23) = 0.401$, $p > 0.05$). ANOVAs of response accuracy also showed a significant interaction of pain $\times$ perspective reached significance ($F(1, 23) = 9.10$, $p < 0.01$). Response accuracies were higher to non-painful than painful

Table 1

Mean RTs (ms) and response accuracy (%) (standard deviation) in each perspective condition.

	Self-perspective	Other-perspective
RTs		
Painful	687(87.0)	707(82.8)
Non-painful	714(99.6)	712(111)
Accuracies		
Painful	85.0(10.9)	80.8(15.7)
Non-painful	85.8(9.50)	87.5(8.94)

Table 2
Mean FPS-R scores (standard deviation) in each perspective condition.

	Self-perspective	Other-perspective
Painful stimuli		
Pain	5.95(2.04)	5.46(2.04)
Unpleasantness	5.94(1.89)	5.54(1.90)
Non-painful stimuli		
Pain	0.17(0.29)	0.14(0.36)
Unpleasantness	0.85(0.88)	0.44(0.56)

stimuli in other-perspective condition ($t(23)=2.153$, $p<0.05$), but did not differ between painful and non-painful stimuli in self-perspective condition ($t(23)=0.358$, $p>0.05$).

ANOVAs of rating scores of pain intensity showed significant main effects of Pain ($F(1,23)=186.85$, $p<0.001$) and perspective ($F(1,23)=4.529$, $p<0.05$, Table 2). Although the interaction of pain $\times$ perspective did not reach significance ($F(1,23)=3.566$, $p>0.05$), separate analysis suggested that the scores of pain intensity were significantly higher in the self-perspective than other-perspective conditions ($t(23)=2.077$, $p<0.05$), whereas there was no significant difference in the scores of self-unpleasantness between the conditions ($t(23)=1.506$, $p>0.05$). The scores of pain intensity positively correlated with those of self-unpleasantness in both the self- ($r=0.846$, $p<0.001$) and other-perspective conditions ($r=0.792$, $p<0.001$).

Fig. 2 illustrates grand-averaged ERPs to painful and non-painful stimuli and the voltage topographies of specific ERP components. Stimuli in all conditions evoked a negative component between

80 and 120 ms (N110) over the frontal area, which was followed by a positive deflection at 140–180 ms (P160) and a negative wave peaking at 220–270 ms (N240) over the frontal/central areas. There was a long-latency negativity at 310–350 ms (N320) over the frontal–central area and a positivity at 340–740 ms (P3) with the maximum amplitude over the central area.

ANOVAs of the mean ERP amplitudes showed a significant main effect of pain at 160–180 ms (parietal electrodes: $F(1,23)=9.128$, $p<0.01$), 230–250 ms (frontal electrodes: $F(1,23)=14.024$, $p<0.01$; central electrodes: $F(1,23)=7.547$, $p<0.05$), 290–360 ms (frontal electrodes: $F(1,23)=7.902$, $p<0.01$), 370–420 ms (frontal electrodes: $F(1,23)=13.699$, $p<0.01$; central electrodes: $F(1,23)=13.308$, $p<0.01$; parietal electrodes: $F(1,23)=9.045$, $p<0.01$), 420–500 ms (frontal electrodes: $F(1,23)=13.709$, $p<0.01$; central electrodes: $F(1,23)=19.182$, $p<0.001$; parietal electrodes: $F(1,23)=15.154$, $p<0.001$), 500–580 ms (frontal electrodes: $F(1,23)=10.55$, $p<0.01$; central electrodes: $F(1,23)=22.794$, $p<0.001$; parietal electrodes: $F(1,23)=20.252$, $p<0.001$), 630–700 ms (frontal electrodes: $F(1,23)=4.518$, $p<0.05$; central electrodes: $F(1,23)=9.619$, $p<0.01$; parietal electrodes: $F(1,23)=9.296$, $p<0.01$). Painful stimuli induced positive shift of the ERP components in these time windows relative to non-painful stimuli. The main effect of perspective was not significant ($ps>0.05$). Interestingly, ANOVAs of the mean ERP amplitudes showed significant interactions of pain $\times$ perspective at 370–420 ms at electrodes over the central–parietal area (central electrodes: $F(1,23)=5.485$, $p<0.05$; parietal electrodes: $F(1,23)=5.985$, $p<0.05$), suggesting that the pain effect in this time window was modulated by shift of perspectives between self and

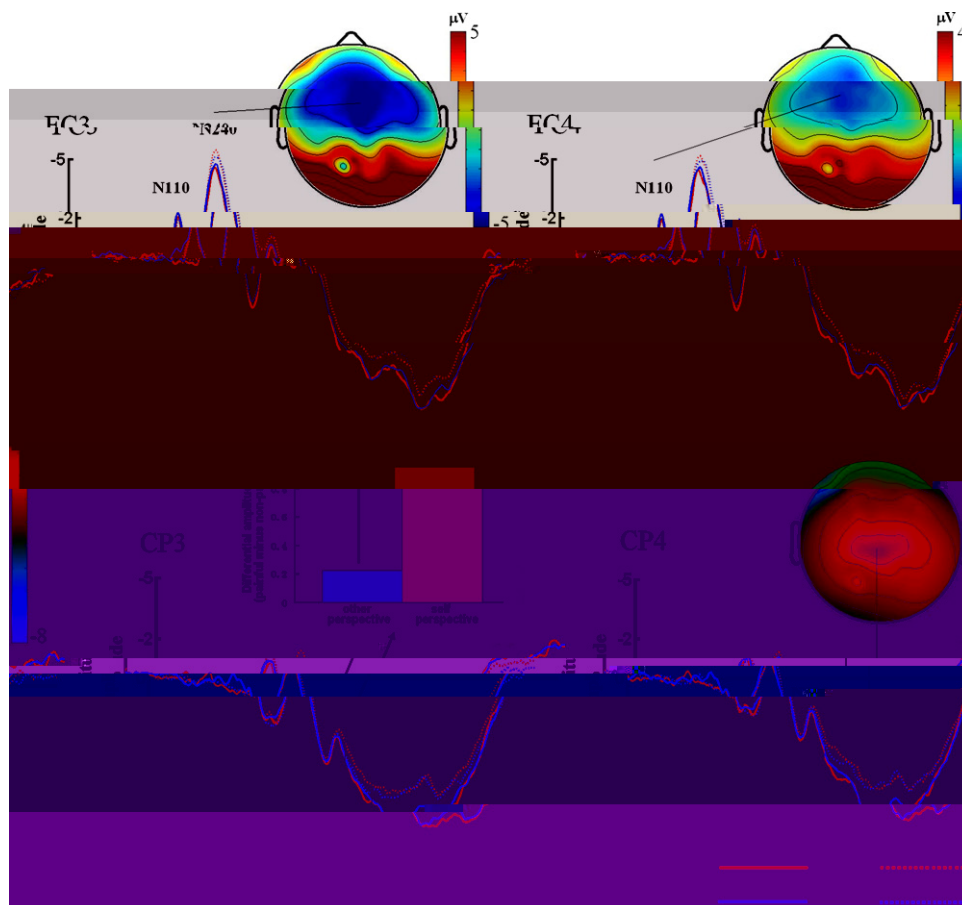


Fig. 2. Illustration of ERPs results in different stimulus conditions. ERPs recorded at FC3, FC4, CP3, and CP4 were plotted respectively to painful and non-painful stimuli in the self- and other-perspective conditions. Voltage topographies illustrate the locus of maximum amplitudes of N110, N240, and P3. The bar chart illustrated that the pain effect at 370–420 ms was greatly reduced in the other-perspective than self-perspective conditions.

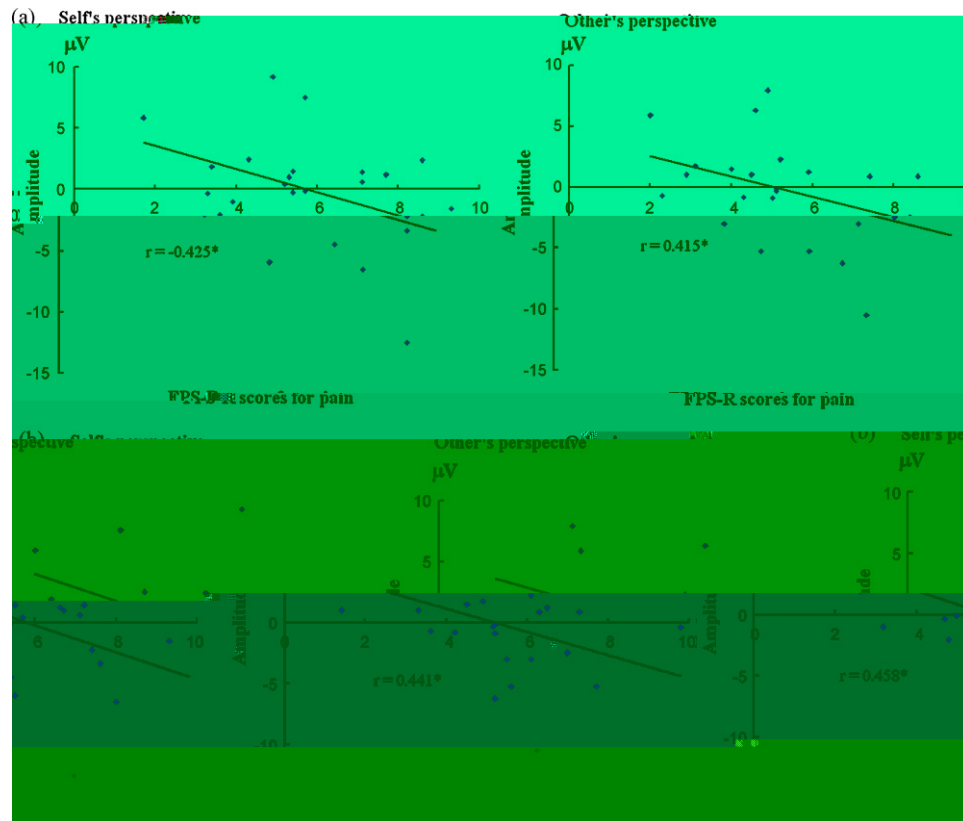


Fig. 3. (a) Correlation between the ERP amplitudes at 230–250 ms and FPS scores of the degree of perceived pain in the self- and other-perspective conditions. (b) Correlation between the ERP amplitudes at 230–250 ms and FPS scores of the degree of self-unpleasantness in self- and other-perspective conditions.

others. Further analysis confirmed that painful stimuli induced positive shift of the ERP amplitude in this time window compared to non-painful stimuli in the self-perspective condition (central electrodes: $t = -3.851$, $p < 0.01$; parietal electrodes: $t = -3.888$, $p < 0.01$) but not in the other-perspective condition (central electrodes: $t = -0.768$, $p > 0.05$; parietal electrodes: $t = -0.785$, $p > 0.05$).

We calculated the correlation between the FPS-R scores and the mean amplitudes of ERPs elicited by painful stimuli in each time window. We found that the mean ERP amplitudes at 230–250 ms related to painful stimuli negatively correlated with both the rating scores of perceived pain (self-perspective: $r = -0.425$, $p = 0.038$; other-perspective: $r = -0.415$, $p = 0.044$, Fig. 3a) and the rating scores of self-unpleasantness (self-perspective: $r = -0.458$, $p = 0.024$; other-perspective: $r = -0.441$, $p = 0.031$, Fig. 3b).

Our study investigated the temporal dynamics of neural mechanisms underlying modulations of empathic response to perceived pain by perspective taking. Specifically, we tested the hypothesis that perspective taking modulates the top-down controlled component but not the automatic component of empathy for pain. We showed evidence for modulations of behavioral and neural responses to perceived pain by shift of perspectives between self and other. Subjects responded more quickly to painful than non-painful stimuli when taking self-perspective but not when taking other-perspective. Moreover, subjects rated higher the intensity of perceived pain when taking self-perspective compared to taking other-perspective. These are consistent with the observation of previous research [13] and suggest that taking self-perspective increased subjective feeling of perceived pain and induced faster reactions to perceived pain, possibly because more extensively cognitive-related brain areas engaged in the other-perspective condition whereas enhanced responses in the emotion-related regions were involved in the self-perspective condition [13].

We found that painful stimuli elicited a positive shift of the ERP waves relative to non-painful stimuli from 160 to 700 ms, showing evidence for modulations of neural activity by perceived pain in others that covered both the early automatic and late top-down controlled components of neural responses to perceived pain identified in our previous work [9,11]. The modulation of ERPs by perceived pain is different from that associated with first-person pain experience and negative emotion. For example, painful electrical stimuli elicited larger N150 (more negative) and enlarged P260 (more positive) than non-painful stimuli [15]. Relative to perception of neural expressions, perception of fearful expression enhanced the N2 component (more negative) when stimuli were below the threshold for conscious detection but enlarged the P3 (more positive) when stimuli were above the threshold for conscious detection [17]. Apparently, these ERP effects are different from the modulation of ERPs by perceived pain observed in our study that was characterized by sustained positive shift of ERPs to visual painful than non-painful stimuli.

Given the different patterns of ERPs to perceived pain and painful electrical stimuli and the fact that the amplitude of ERPs related to painful stimuli negatively correlated with both the rating scores of perceived pain and self-unpleasantness in the same time window (230–250 ms), we suggested that the pain effect on ERPs reflected neural activity in association with empathy for pain rather than the process of general negative emotions. Moreover, the correlation results were observed regardless of whether subjects took self-perspective or other-perspective during the pain judgment task. The results are in favor of the idea that the early automatic neural responses underlie the emotional components of empathizing [9] and occur independently of the perspective taken by observers. The ERP results are consistent with fMRI findings that perception of others in pain increased neural activity in the brain areas (e.g., ACC and anterior insula) associated with affective

processing of empathy when subjects took both self-perspective and other-perspective during the task of pain rating [7].

Most important, we showed that the ERP amplitudes at 370–420 ms to painful stimuli were significantly modulated by perspective taking. Specifically, relative to non-painful stimuli, painful stimuli induced positive shift of the ERPs in this time window when subjects took self-perspective during the pain judgment task. This pain effect, however, was eliminated during the pain judgment task when taking other-perspective. The modulation of the neural responses to perceived pain took place in the time window of top-down controlled process of empathy identified in the previous ERP studies [9,11]. Our ERP results compliment previous fMRI findings [13] by showing the time course of modulation of neural responses to perceived pain by perspective taking. As perspective taking is a top-down controlled process, it is then reasonable to expect that perspective taking interacts with the top-down controlled process of perceived pain. However, while the fMRI research identified modulation of neural responses to perceived pain by perspective taking in the brain areas such as the secondary somatosensory cortex, the ACC, and the insula [13], it is difficult to identify the source of the modulation of neural responses to perceived pain by perspective taking in the current work because of the ambiguity of the number of sources and the low spatial resolution of ERPs.

As previous fMRI studies have shown that taking self-perspective or other-perspective modulates activities in the ACC and insula in association with the judgment of perceived pain [13,16] and our current work suggests modulation of the top-down controlled process of empathy by shift of perspectives, one may ask whether the brain regions such as the ACC and insula are involved in top-down controlled processes even though these brain areas mediate the affective component of empathy [19]. Our recent fMRI study [8] that examined how top-down attention to painful cues in visual displays modulated empathic neural responses showed that increased activations in the ACC and insula linked to perceived painful compared to non-painful stimuli applied to hands were observed when subjects performed the pain judgment tasks but not when they counted the number of hands in the stimuli. These findings indicate that even the brain areas engaged in affective processing during empathy are possibly involved in the top-down process related to attention to the emotional cues in the stimuli. Thus the prior fMRI studies [13,16] implied that the ACC and insula may contribute to the controlled process of shifting between self-perspectives and other-perspectives during empathy.

Taken together, our ERP results suggest that neural mechanisms underlying empathy for pain are modulated by perspectives taking during judgments of perceived pain, although people are fundamentally egocentric and have difficulty in getting beyond their own perspective when understanding others' mind [18]. The brain imaging results support that adopting subjective perspective of others helps to understand and share their emotional states [6,7]. Moreover, our ERP results indicate that taking other-perspective reduced neural responses to perceived pain, consistent with the proposal that, besides helping to overcome our usual egocentrism, perspective taking intervenes in the regulation of aversive emotions arising

from empathy [6] so that consequent altruistic behaviors during empathy can be conducted efficiently. Future research may further clarify the exact relationship between perspective taking and altruistic behaviors.

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