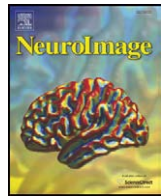




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Physicians down-regulate their pain empathy response: An event-related brain potential study

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ABSTRACT

Watching or imagining other people experiencing pain activates the central nervous system's pain matrix in the observer. Without emotion regulation skills, repeated exposure to the suffering of others in healthcare professionals may be associated with the adverse consequences of personal distress, burnout and compassion fatigue, which are detrimental to their wellbeing. Here, we recorded event-related potentials (ERP) from physicians and matched controls as they were presented with visual stimuli depicting body parts pricked by a needle (pain) or touched by a Q-tip (no-pain). The results showed early N110 differentiation between pain and no-pain over the frontal area as well as late P3 over the centro-parietal regions were observed in the control participants. In contrast, no such early and late ERP responses were detected in the physicians. Our results indicate that emotion regulation in physicians has very early effects, inhibiting the bottom-up processing of the perception of pain in others. It is suggested that physicians' down-regulation of the pain response dampens their negative arousal in response to the pain of others and thus may have many beneficial consequences including freeing up cognitive resources necessary for being of assistance.

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Introduction

Research in cognitive neuroscience using functional neuroimaging techniques reliably demonstrated that perceiving or even imagining other people in pain is associated with activation in a neural circuit involved in pain processing, including the somatosensory cortex, anterior insula, dorsal anterior cingulate cortex (dACC), anterior medial cingulate cortex (amCC), and periaqueductal gray (PAG), a major site in pain transmission and processing of fear and anxiety (e.g., Akitsuki and Decety, 2009; Jackson et al., 2006 for a review). These results suggest that attending to people in pain triggers a sort of empathic mimicry response in the observer. It is worth mentioning that the activation of this neural network reflects a general aversive response (Yamada and Decety, 2009). Indeed, this network of regions underpin a physiological mechanism that mobilizes the organism to react-with heightened arousal and attention-to threatening situations (Decety, in press-a). Pain itself signals a potential threat in the environment and urges individuals to escape or avoid its source (Williams, 2002).

When witnessing another person experience pain, the scope of observer's reaction can range from concern for personal safety, including feelings of alarm, fear and avoidance, to concern for the other person, including compassion, sympathy, and care-giving (Goubert et al., 2009). The somatic sensorimotor resonance in pain processing areas between other and self may trigger empathic concern and feelings of sympathy (e.g., Decety et al., 2008). But the same signals may also constitute a threat to the individual that can lead to personal distress (i.e., feelings of discomfort and anxiety) or even compassion fatigue. If not regulated, this distress can be costly, both physiologically and cognitively, impact on the individual's wellbeing, and can eventually conflict with their capacity of being of assistance to the other (Decety and Lamm, 2009).

This necessity of regulation is particularly relevant for physicians and other health care professionals who, by the very nature of their work, not only encounter people with various injuries in their everyday practice, but also often need to inflict pain in the course of their treatments. Being overly sensitive to other people's pain could thus be detrimental and cause a host of serious deleterious effects such as compassion fatigue or burnout in this population (Figley, 2002). It is therefore vital that physicians regulate their capacity to empathize with their patients so that their emotional reaction does not interfere with the efficacy of their treatment nor impact their wellbeing. However, active (conscious) regulation of negative emotions also has physiological and socio-psychological costs. For

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instance, research has shown that it can disrupt communication, reduce rapport and increase blood pressure (Butler et al., 2003). Without some powerful regulatory mechanisms, it is very likely that medical practitioners would experience personal distress and anxiety when facing other people in pain, and this negative arousal would interfere with their ability to heal.

Previous neuroimaging work showed that the perception of pain in others can be modulated by a host of factors including attentional demands (Fan and Han, 2008; Gu and Han, 2007), social relationship between individuals (Singer et al., 2006), cognitive appraisal (Lamm et al., 2007), and a priori attitudes towards others (Decety et al., 2009). Of special interest in the context of medical practitioners, an fMRI study conducted by Cheng et al. (2007) compared the brain hemodynamic response in a group of physicians and a group of matched control participants when they were exposed to short video clips depicting hands and feet being pricked by a needle (painful situations) or being touched by a Q-tip (non-painful situations). The results demonstrated activation of the pain matrix in the control participants when they attended to the painful situations relative to the non-painful ones. A different pattern of signal change and effective connectivity was detected in the physicians when they watched the painful procedures. Cortical regions underpinning executive functions, self-regulation (dorsolateral and medial prefrontal cortex), and executive attention (precentral, superior parietal and temporo-parietal junction) were activated, and unlike in the control group, no activation was detected in the dACC, anterior insula and PAG.

Current models of empathy for pain emphasize that this phenomenon involves both an automatic component (bottom-up) based on the perception–action coupling that results in affective sharing, and an executive control (top-down) component subserved by the prefrontal cortex to regulate this experience (Decety, in press-b; Decety and Jackson, 2004; Decety and Moriguchi, 2007; Goubert et al., 2009). However, it is not known at what stage of information processing this regulation occurs in physicians. Because of the low temporal resolution of the blood oxygen dependent signals, which has a sensitivity of several seconds, functional MRI studies are not optimally suited to address this important question.

To investigate this issue, the current study used event-related potentials (ERP) to compare the time course of pain perception processing (and subsequent emotion regulation) in physicians (Physicians) and non-physicians (Controls), who were exposed to a series of static visual stimuli showing body parts either being pricked by a small needle or being touched by a Q-tip. The body parts pricked by the needle would actually activate the nociceptive system via sensory information conveyed by A-delta nerve fibers, which qualitatively differ from the second nociceptive input system conveyed by c-nociceptors.

According to the results of recent ERP studies in the domain of pain empathy, the temporal dynamics of perception of pain in others consists of two responses: (1) an early emotional sharing component (frontal N110); and (2) a late cognitive evaluation (centro-parietal P3) (Fan and Han, 2008; Han et al., 2008). Here, we hypothesized that the Physicians would demonstrate an early modulation of the emotion-sharing component that would reflect their acquired ability to down-regulate the bottom-up processing of negative stimuli. In this case, we anticipate no difference in ERP response between the stimuli depicting painful situations and the stimuli depicting non-painful situations in physicians. However, it may also be possible that the automatic resonance to pain is still present in the physicians and that the down-modulation of pain processing occurs at a later stage, as part of a cognitive re-evaluation. If this is the case, similar early ERP response between the Physicians and the Controls should be observed, with group differences occurring only at a later cognitive evaluative stage of pain-perception processing. The results of this investigation have a significant impact

on the neurophysiological and psychological models of emotion regulation.

Materials and methods

Participants

Thirty-three participants (17 females, mean age 35; SD 8 years) were enrolled in the study after providing written informed consent approved by the local Ethics Committee of Yang-Ming University. Three participants (2 males and 1 female) were excluded from data analysis because of excessive artifacts during EEG recording. According to their medical expertise, the participants were divided into two groups. One group ($N=15$; eight females) consisted of physicians (Physicians) from internal medicine. The other group, matched for age and level of academic education ($N=15$; eight females) was composed of participants with no medical or paramedical education or experience (Controls). None of the participants had any history of neurological or psychiatric disorders or were taking medication at the time of the testing. Participants received monetary compensation for their participation.

Visual stimuli

Participants were shown 120 static visual stimuli, consisting of pictures of different body parts (40 for mouth region, 40 for hand, and 40 for foot) that were previously used in a functional MRI study (Cheng et al., 2007). To minimize any possible habituation effect, we used at least ten different sites on each body part from two human actors. In half of the stimuli, the body parts were touched by a Q-tip (non-painful situations) and in the other half of the stimuli, the body parts were pricked by a small needle (painful situations). A white screen with a fixation cross was used as the baseline. The visual angle of the different stimuli was matched. The stimuli were presented in the center of a grey (128 cd/m^2) background of a 17-in. color monitor. Each stimulus was $8 \text{ cm} \times 6 \text{ cm}$ (width \times height), subtending a visual angle of $4.5^\circ \times 3.15^\circ$ at a viewing distance of 100 cm.

Experimental paradigm

One week before the ERP recording session, participants filled out a series of dispositional measures including the emotional contagion scale (ECS; Doherty, 1997), the interpersonal reactivity index (IRI; Davis, 1996; Siu and Shek, 2005), and the situational pain questionnaire (SPQ; Clark and Yang, 1983) to assess sensitivity to pain.

Before the ERP recordings, participants underwent a training session to become acquainted with the procedures. The ERP recordings consisted of a total of four sessions. Each session (~6 minutes) contained 75 trials. Each trial started with a picture presentation (1 s) followed by a fixation cross against a white screen with a duration varying randomly between 1.5 and 1.7 s. The order of the trial type (painful vs. non-painful) was randomized within each session. The order of the sessions was randomized and counter-balanced across participants.

To ensure that the participants were paying attention to the stimuli and their affective content, a pain judgment task was randomly interspersed among trials. Specifically, in 10% of the trials the static cross was replaced by a judgment task, in which participants were required to press a button to report the affective content of the stimuli (pain or no pain). These trials were excluded from the ERP analysis due to movement artifact.

After the ERP recording, participants were presented with the same set of pictures again and asked to rate the pain intensity and unpleasantness experienced by the model using computerized visual-analogue scales (VAS scales: left = no pain/no unpleasantness, right = extreme pain/unpleasantness; 10-point).

Apparatus and recordings

The EEG was continuously recorded from 32 scalp electrodes mounted on an elastic cap according to the extended 10-20 system in addition to two mastoid electrodes. The electrode at the left mastoid was used as the reference. The electrode impedance was kept below 5 Ω . Eye blinks and vertical eye movements were monitored with electrodes located above and below the left eye. The horizontal electro-oculogram (EOG) was recorded from electrodes placed 1.5 cm lateral to the left and right external canthi. The EEG was amplified in a 0.1–50 Hz band pass and digitized at a sampling of 500 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 $\pm 50 \mu\text{V}$ at any electrode were excluded from the average.

Statistical analysis

The mean voltage of a 200 ms pre-stimulus interval was used for the baseline correction of ERP measurements. The mean ERP voltages was obtained from each grand average peak (± 30 ms), starting from the onset of each stimulus and continuing 800 ms post-stimulus. To investigate expertise-induced effects, statistical analysis was examined through repeated-measure ANOVAs with two within-subject factors [stimulus type (needle vs. Q-tip) \times electrode (Fz, Cz, Pz, Oz)] and one between-subject factor [group (Physicians vs. Controls)]. The dependent variable was the mean ERP amplitude of each ERP component at each electrode. Degrees of freedom were corrected using the Greenhouse–Geisser method for correlated measures. Scheffé's test was conducted only when preceded by significant main effects.

Finally, regression analyses were computed to assess whether the Physicians differed from the Controls in the correlation between the extent of subjective ratings of pain intensity and unpleasantness and the cortical activity changes elicited by the stimuli. To this aim, the differential ERP amplitudes between painful and non-painful stimuli were used as an explanatory variable from the pain ratings between the groups. Fisher tests were performed to compare the *r*-values between groups.

Electrophysiological source analysis

For source reconstruction, the subtractions of ERP traces between painful and non-painful stimuli, as well as between Physicians and Controls, were assessed using the standardized Low Resolution Brain Electromagnetic Tomography (sLORETA) with the Curry 5.0 software (Neuroscan). sLORETA enables the computation of statistical maps from EEG data that indicate the locations of the underlying source processes with low error (Pascual-Marqui, 2002). Unlike usual dipole-based methods, sLORETA does not require a priori hypotheses regarding field distribution of active sources. Brain areas were considered as active when the signal value exceeded the mean pre-stimulus baseline by at least 3 standard deviations. The analytic process included the three following steps: (1) creation of a boundary element method (BEM) model, including cortical and skin, with about 5000 nodes from magnetic resonance imaging (MRI) data; (2) selection of an instant of time with large deflection in the subtracted ERP; and (3) a location-wise inverse weighting from the Minimum Norm Least Square (MNLS) analysis with estimated variances. Thereafter, a current source reconstruction map was obtained.

Results

Behavioral measures

No difference was found in the dispositional measures between the two groups ($F_{1, 28} = 0.032$, $P = 0.859$) (Table 1). However, one-

Table 1

Dispositional measures of empathy and subjective ratings of pain intensity and unpleasantness in the Physician and Control groups.

| Measure | Physicians (N = 15) | | Controls (N = 15) | |
|-----------------|---------------------|------|-------------------|------|
| | Mean | SD | Mean | SD |
| ECS | 27.93 | 4.75 | 27.93 | 5.63 |
| IRI (FS) | 16.26 | 4.83 | 16.93 | 5.47 |
| IRI (EC) | 20.86 | 4.24 | 21.33 | 4.15 |
| IRI (PT) | 18.93 | 4.99 | 18.00 | 3.04 |
| IRI (PD) | 12.26 | 4.26 | 13.40 | 4.56 |
| SPQ | 5.85 | 1.38 | 5.53 | 1.34 |
| Pain intensity* | 3.28 | 1.06 | 6.56 | 1.35 |
| Unpleasantness* | 3.02 | 1.14 | 6.33 | 1.21 |

Abbreviations: Emotional contagion scale (ECS), interpersonal reactivity index (IRI), fantasy (FS), empathic concern (EC), perspective taking (PT), personal distress (PD), situational pain questionnaire (SPQ). Subjective ratings of pain intensity and unpleasantness were significantly different between the Physicians and Controls (* $P < 0.001$).

way ANOVAs calculated on the subjective pain ratings showed a significant difference between the groups for pain intensity ($F_{1, 28} = 54.359$, $P < 0.001$) and unpleasantness ($F_{1, 28} = 63.777$, $P < 0.001$), such that the control participants reported significantly higher pain intensity and unpleasantness ratings than did the physicians. All participants correctly reported the pain cues on the judgment task when watching the visual stimuli during the ERP recording sessions.

Electrophysiological analysis

The Grand-average ERP at the midline electrodes was shown for the needle and Q-tip stimuli in the Physicians and Controls (Fig. 1). In line with previous ERP reports (Fan and Han, 2008; Han et al., 2008), both the observation of painful and non painful stimuli elicited an early negative component between 90 and 120 ms (N110) over Fz and

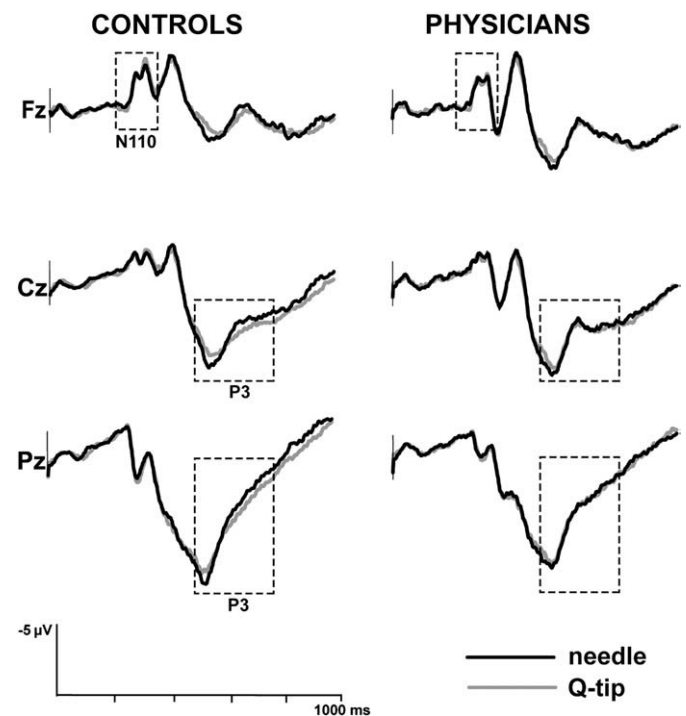


Fig. 1. Cortical responses to painful and non-painful stimuli in Physicians and Controls. The ERP response to body parts pricked by a needle (black solid traces) and to body parts touched by a Q-tip (gray solid traces) is shown in the Controls (left) and in the Physicians (right). Note that amplitude differences (dashed squares) occurred around 120–160 ms post-stimulus at Fz and 340–400 ms at Cz and Pz in the Controls, but not in the Physicians.

Cz, which was followed by a positive deflection between 140 to 200 ms (P180) over Cz and a negative wave peaking between 210 and 270 ms (N240) over Fz and Cz. There was another negative deflection peaking at 340 ms (N340) over Fz. A long-latency positivity (P3) around 360 and 400 ms with the maximum amplitude occurred over the Cz and Pz. In addition, ERP over the Oz was characterized with a positivity wave between 90 and 120 ms (P1), a negative wave between 140 and 200 ms (N170), and a positive wave between 300 and 450 ms (P320). There was also a long-latency negative deflection found over the Oz.

For the N110 component, the ANOVA found a reliable main effect of the stimulus type ($F_{1, 28} = 25.234, P = 0.005$), which was produced by a positive shift for the painful stimuli compared to the non-painful stimuli across all electrodes. There was a reliable significant interaction (stimulus type \times group \times electrode: $F_{3, 84} = 66.452, P = 0.009$; stimulus \times group: $F_{1, 28} = 9.358, P = 0.006$). For the P3 component, the ANOVA disclosed a reliable main effect in the stimulus type ($F_{1, 28} = 36.234, P = 0.001$), which was caused by larger P3 amplitudes for the painful compared to the non-painful stimuli across all electrodes. There was also a significant interaction (stimulus type \times group \times electrode: $F_{3, 84} = 76.443, P = 0.006$; stimulus \times group: $F_{1, 28} = 30.213, P = 0.005$).

The interaction between stimulus type and group indicates how the effect of medical expertise modulates the perception of pain in others (Fig. 2). *Post-hoc* analysis found that the interaction ($F_{1, 28} = 9.358, P = 0.006$) in the N110 at Fz electrode was mainly driven by a more positive shift elicited by the painful stimuli relative to the non-painful stimuli ($F_{1, 14} = 3.563, P = 0.006$) in the control participants, whereas both types of stimuli elicited similar responses ($F_{1, 14} = -1.214, P = 0.281$) in the physicians. In addition, for the interaction in the P3 component at Cz ($F_{1, 28} = 11.427, P = 0.002$), *post-hoc*

analysis found significant P3 differences between the painful and the non-painful stimuli in the Controls ($F_{1, 14} = 5.453, P = 0.003$), but not in the Physicians ($F_{1, 14} = -1.234, P = 0.272$). Similarly, for the interaction of the P3 at Pz ($F_{1, 28} = 9.358, P = 0.005$), *post-hoc* analysis disclosed that the Controls ($F_{1, 14} = 3.561, P = 0.006$), not the Physicians ($F_{1, 14} = -2.214, P = 0.381$), differentiated the painful from the non-painful stimuli. These results indicate that only in the control participants, watching body parts being pricked by a needle relative to being touched by a Q-tip was associated with significant frontal N110 and centro-parietal P3. Conversely, participants with medical expertise seems to modulate the early ERP component associated with automatic emotion sharing as well as the late ERP component related to the cognitive evaluation of pain empathy.

Electrophysiological source analysis

The voltage topographies of N110 and P3 rendered with their scalp distributions are illustrated (Fig. 3a). Source analysis performed on the ERP data from time bins found significant changes in the group-by-stimuli (Fig. 3b). This method identified a small set of regions whose activity differed significantly from the perception of painful relative to non-painful stimuli between Controls and Physicians.

Correlation between subjective rating and ERP amplitudes

A significant positive correlation between the ratings of pain intensity and the differential N110 amplitudes at Fz was found in the Controls ($r = 0.83, P = 0.001$), but not in the Physicians ($r = 0.13, P = 0.526$) (Fig. 4a). A positive correlation also existed in all participants collapsed across groups ($r = 0.50, P = 0.005$). Further, Fisher test upon transformed r -value suggested that the correlation between the differential N110 amplitude and the subjective ratings of pain intensity was significantly larger for the Controls than the Physicians ($z = 2.59, P = 0.005$). These results indicate that larger differential amplitudes in the early emotional sharing component for the painful trials relative to non-painful trials were associated with higher ratings of pain intensity, and this correlation was mainly driven from the control participants.

The differential P3 amplitudes at the Cz electrode were positively correlated with the subjective ratings of unpleasantness in the Controls ($r = 0.85, P = 0.001$) whereas no correlation was found in the Physicians ($r = 0.15, P = 0.441$) (Fig. 4b). Such a positive correlation was also present in both groups together ($r = 0.55, P = 0.002$). Further, Fisher test used to compare the r -value between the groups found that the correlation was significantly stronger for the Controls than the Physicians ($z = 2.71, P = 0.003$). The larger differential ERP amplitudes of the late empathic response were related to the stronger subjective feelings of unpleasantness induced by the perception of others' pain, which mainly came out from the control participants.

Discussion

In sum, in line with previous ERP studies on pain empathy (Fan and Han, 2008; Han et al., 2008), the present study demonstrates a frontal N110 and a late centro-parietal P3 while the controls participants watched body parts pricked by a needle in comparison with body parts being touched by a Q-tip. In contrast, in the physicians, there was no such ERP differentiation, as well as lower subjective ratings of pain intensity and unpleasantness with respect to the controls' rating. The frontal N110 differential amplitude elicited by the painful stimuli relative to the non-painful stimuli was closely coupled with subjective ratings of pain intensity only in the controls. The central P3 differential amplitude was associated with ratings of unpleasantness only in the controls participants, not in the physicians.

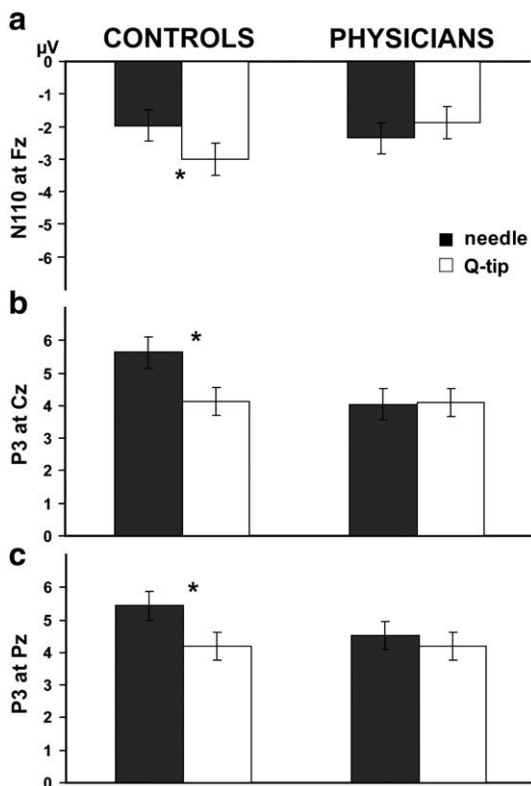


Fig. 2. Expertise effects on the cortical responses elicited by the perception of body parts pricked by a needle and body parts touched by a Q-tip. (a) N110 at Fz. (b) P3 at Cz. (c) P3 at Pz. The ERP responses are significantly different when the Controls watched the painful relative to the non-painful stimuli. No significant differences were detected in the Physicians. Values are expressed as mean \pm SE (* $P < 0.01$).

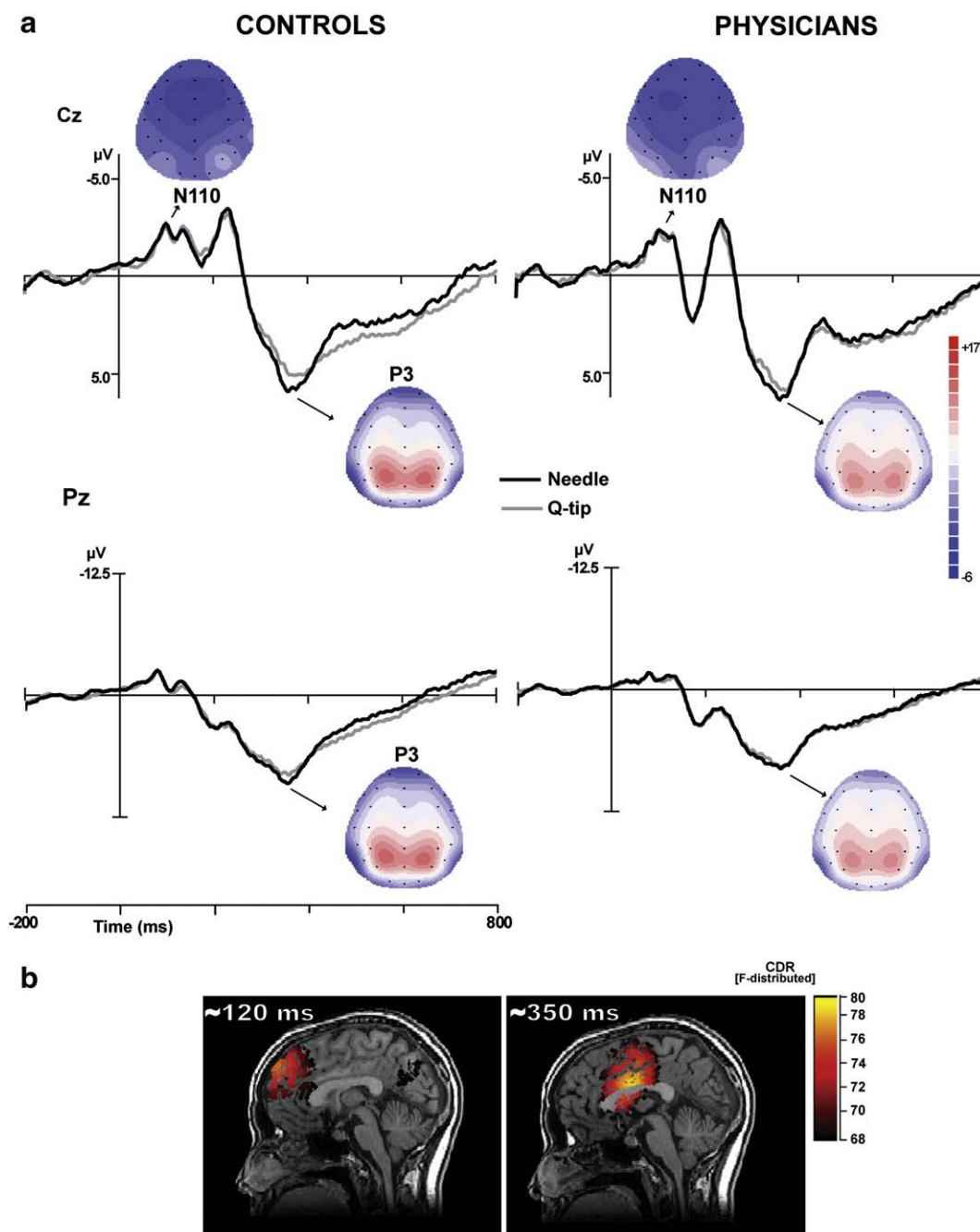


Fig. 3. (a) Voltage topographies illustrate the scalp distribution for the ERP components in the Control and Physician groups. (b) Current source density shows different waves obtained by subtracting ERP to the painful stimuli from the non-painful stimuli in the Controls around 120 ms and 350 ms.

Empathy, the ability to share and appreciate the affective and emotional states of others is particularly important in patient–physician communication, and is associated with improved patient satisfaction and compliance with recommended treatment (Epstein et al., 2007). However, as Hodges and Biswas-Diener (2007) argued, there are costs to being too empathic. For instance, paying attention to other's suffering in the course of caring for patients experiencing trauma or pain can exhort a cost for medical practitioners, exhausting their emotional resources and ironically reducing their capacity for or their interest in bearing the suffering of others. Empathy may thus be viewed as a double-edged sword, facilitating caring and compassion but at the same time leaving the physician vulnerable (Figley, 2002; Sabo, 2006). It is therefore critical that physicians develop effective emotion appraisal and regulation processes in the context of providing care to their patients. Indeed, in order to cope with

repeated exposure to the suffering of others and minimize negative arousal, which would deplete executive functioning, physicians as well as other emergency service personnel learn to regulate their interpersonal sensitivity.

By using ERP to examine the temporal dynamics of pain empathy, the current study extends previous research to demonstrate that medical expertise modulates the sensory information processing both during the incoming sensory information as early as 110 ms post-stimulus at Fz, as well as during later cognitive evaluation after 380 ms at Cz and Fz. One previous EEG study found that perceiving pain and non-painful tactile stimuli delivered to others, respectively increased and decreased the amplitude of the P45 sensory evoked potential component, which reflects the involvement of primary somatosensory cortex (Bufalari et al., 2007). Magnetoencephalographic measurements have also demonstrated the engagement of the somatosensory

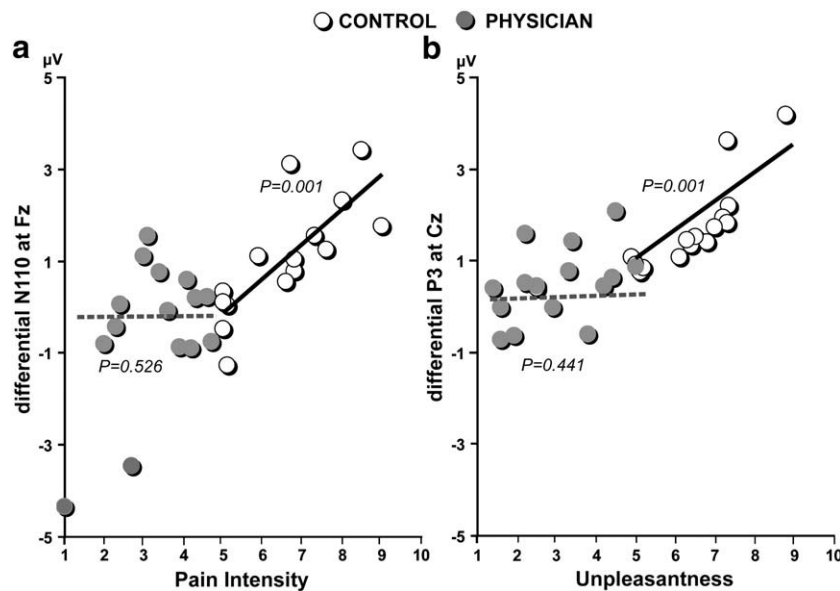


Fig. 4. Correlation between the differential ERP response to the painful stimuli versus the non-painful stimuli and the subjective pain ratings in each group. The y-axis depicts the differential amplitudes in the N110 at Fz and the P3 at Cz respectively. The x-axis represents the VAS ratings. (a) Frontal N110 and pain intensity are correlated in the control participants (white dots) (black solid line; $r = 0.83$, $P = 0.001$), but not in the physicians (gray dots) (gray dashed line; $r = 0.13$, $P = 0.526$). (b) Central P3 response and ratings of unpleasantness are significantly correlated in the controls ($r = 0.85$, $P = 0.001$), but not in the physicians ($r = 0.15$, $P = 0.441$).

cortex in pain empathy (Cheng et al., 2008). Two studies showed that watching someone's body parts in painful and non-painful situations elicited the early frontal N110 and late centro-parietal P3 (Fan and Han, 2008; Han et al., 2008). Here, the control participants showed a short-latency frontal N110 and a long-latency centro-parietal P3 response differentiating the painful from the non-painful situations whereas no such a differentiation occurred in the physicians. This result lends support to the notion that the temporal dynamics of empathy for pain comprise both an early vicarious component and a late cognitive evaluation, both of which seem to be suppressed by medical expertise or familiarization in physician participants.

Parallel to previous ERP studies of responses to affective stimuli (Eimer and Holmes, 2002; Fan and Han, 2008; Han et al., 2008; Schupp et al., 2000), a salient effect of the painful stimuli was detected in a broad time window from 120 ms to 400 ms: painful (needle) stimuli elicited stronger ERP amplitudes with respect to the neutral (Q-tip) stimuli. The dynamics of this evoked response are consistent with the two-stage model of empathy for pain, as evidenced by clear demarcations in the time course, scalp distribution, and functional in aspects of time course, scalp distribution, and functional significance (Decety, 2007; Decety and Lamm, 2006; Decety and Meyer, 2008; Fan and Han, 2008; Godinho et al., 2006; Goubert et al., 2005). It has been shown that the early automatic empathic responses over the anterior frontal area (N110) can be modulated by contextual reality of visual stimuli, whereas the late cognitive regulatory processes over the posterior parietal are greatly dependent upon task demands (P3) (Fan and Han, 2008; Han et al., 2008). The N110 with early frontal–central modulation, elicited by observation of others in pain, or facial expressions, implies automatic processes of pain empathy. The P3 with maximal amplitude over the central–parietal electrodes has been suggested to reflect the process of stimulus evaluation, which, in turn, is independent of response selection and execution to a certain degree (Duncan-Johnson and Kopell, 1981; McCarthy and Donchin, 1981; Olofsson et al., 2008). Our data seem to indicate that medical expertise affects both the early emotional sharing component as well as late cognitive evaluation of empathy for pain.

Importantly, negativity bias, attention allocation, and familiarity may have also contributed to the difference in the neural dynamics between the physicians and the controls noted here. First, early

frontal negativity, as indicated by the N110 at Fz, could account for negativity bias related to affective stimuli (Karayanidis and Michie, 1996; Taake et al., 2009). Given that the perception of body parts pricked by a needle elicited stronger affective arousal in the control participants than in the physicians, as shown by their subjective pain ratings, the physicians may have a reduced negativity bias to such painful situations. Second, attention allocation, as indicated by the P3 response, may reflect how the groups are engaging attention resources to process the stimuli, which may be driven from their previous experience (Johnson, 1988; Schupp et al., 2004). While the P3 component demonstrated increased amplitude for the painful stimuli, it is reasonable to assume that the physician participants did not differentially allocate attention resources whereas the control participants differentially engaged in this process. Finally, familiarity to the stimuli is known to affect attention allocation, which in turn modulates the P3 amplitude (Friedman et al., 2001). Given that the physicians had ample previous exposure to body parts being pricked by needles, the need for attention allocation may be lowered, thereby reducing the P3 amplitude. However, the differences between the two groups cannot be attributed to dispositional factors such as sensitivity to pain, empathy traits, or emotional contagion since these personality measures did not differ between the two experimental groups (Table 1).

Moreover, greater subjective evaluation of pain intensity and pain unpleasantness were correlated with larger frontal N110 and central P3 differentiation between the two classes of stimuli, respectively. Our previous fMRI study demonstrated that higher ratings of pain intensity and unpleasantness were positively correlated with increased signal in the anterior insula and anterior cingulate cortex but were inversely correlated with activation in the dorsolateral prefrontal cortex (Cheng et al., 2007). Other studies have found that the N110 at the Fz location is correlated with subjective ratings of pain of others (Fan and Han, 2008; Han et al., 2008), and that modulation of the somatosensory cortex activity is correlated with the intensity of the pain and touch ascribed to the model by the participants (Bufalari et al., 2007). Here we found that the N110 at Fz and the P3 at Cz elicited by viewing the needle relative to the Q-tip were associated with less pain intensity and unpleasantness, respectively, which is driven from the control participants.

In conclusion, our study demonstrates that medical expertise down-regulates the sensory processing elicited by the perception of pain in others. This down regulation occurs at an early stage (N110), which is thought to reflect the automatic emotional sharing component of empathy. Effective emotion regulation is essential for physicians exposed to the suffering of others because it dampens counterproductive feelings of alarm and fear and frees up processing capacity to be of assistance for the other. Unfortunately, however, there may be a price to pay in terms of concomitantly underestimating the pain that the other is feeling. Another important aspect to be elucidated is whether the down-regulation is the outcome of conscious inhibitory or unconscious inhibitory processing. A number of studies have shown that the former mode of emotional regulation (also called expressive suppression) may be particularly costly and disrupts multiple aspects of social exchange, creating stress for both the regulator and the interaction partner alike (Butler et al., 2003). Such suppression is accompanied by increased sympathetic and cardiovascular responding and reduces memory for social information (Gross and Levenson, 1993). Physicians face the challenge of devoting the right balance of cognitive and emotional resources to their patients' pain experience. They must try to resonate and understand the patient without becoming emotionally over-involved in a way that can preclude effective medical management.

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