The perception of pain in others suppresses somatosensory oscillations: A magnetoencephalography study

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Accumulating evidence demonstrates that similar neural circuits are activated during the first-hand experience of pain and the observation of pain in others. However, most functional MRI studies did not detect signal change in the primary somatosensory cortex during pain empathy. To test if the perception of pain in others involves the primary somatosensory cortex, neuromagnetic oscillatory activity was recorded from the primary somatosensory cortex in 16 participants while they observed static pictures depicting body parts in painful and non-painful situations. The left median nerve was stimulated at the wrist, and the poststimulus rebounds of the ~10-Hz somatosensory cortical oscillations were quantified. Compared to the baseline condition, the level of the ~10-Hz oscillations was suppressed during both of the observational situations, indicating the activation of the primary somatosensory cortex. Importantly, watching painful compared to non-painful situations suppressed somatosensory oscillations to a significant stronger degree. In addition, the suppression caused by perceiving others in the painful relative to the non-painful situations correlated with the perspective taking subscale of the interpersonal reaction index. These results, consistent with the mirror-neuron system, demonstrate that the perception of pain in others modulates neural activity in primary somatosensory cortex and supports the idea that the perception of pain in others elicits subtle somatosensory activity that may be difficult to detect by fMRI techniques.

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Introduction

Empathy, the ability to experience and understand what other people feel without confusion between self and others, plays a fundamental role in social interaction and moral development (Decety and Jackson, 2004; Decety and Lamm, 2006; Decety and Moriguchi, 2007; Hodges and Wegner, 1997). It is generally assumed from evolutionary (de Waal and Tompson, 2005) and developmental (Eisenberg et al., 2006) reasons that the initial component that precedes the full blown human empathic ability draws on somatic mimicry, i.e., the tendency to automatically and unconsciously mimic and synchronize facial expression, vocalization, postures, and movements with those of another person, and consequently to converge emotionally (Hatfield et al., 2003). This motor mimicry mechanism, which leads to shared emotional experience between self and other, is supported by the direct link between perception and action (Preston and de Waal, 2002). The discovery of sensory-motor neurons (a.k.a. mirror-neurons) in the monkey premotor and posterior parietal cortices provides direct evidence for the biological underpinning of the direct matching between perception and behavior (Rizzolatti and Craighero, 2004). In humans, shared circuits between perception and action are well documented from neurophysiologic and functional neuroimaging studies (e.g., Fadiga et al., 1995, 2006; Hari et al., 1998; Grèzes et al., 2003; Keysers et al., 2004; Lawrence et al., 2006; Cheng et al., 2005, 2006, 2007a; Lamm et al., 2007).

There is also some evidence to suggest that similar neural circuits are recruited when humans experience emotions and when they perceive others expressing emotions. For instance, a subset of common activated clusters was detected in the anterior insula in response to the sight of disgusted facial expressions of others as well as by the first-hand experience of disgust (Wicker et al., 2003). One fMRI experiment demonstrated that when participants are required to observe or to imitate facial expressions of various emotions, increased neurodynamic activity was found in the superior temporal...
sulcus, the anterior insula and the amygdala, as well as in areas of the premotor cortex corresponding to the representation of faces (Carr et al., 2003). Another study showed that the observation of everyday hand and face actions performed with emotion recruits regions involved in the perception and the experience of emotion and/or in communication (Grosbras and Paus, 2006). The authors of that study speculated that, in addition to inducing resonance in the motor program necessary to execute an action, watching an action performed with emotion induces a resonance in the emotional system responsible for the affective modulation of the motor program. Such a mechanism could also be a key to understanding how the other person feels, and to her associated intentions. Further support for this mechanism is provided by the finding of activation in the somatosensory cortex and the amygdala when participants imagine everyday life situations that elicit social emotions (Ruby and Decety, 2004). Another neuroimaging study indicates that the specific recruitment of emotion-related regions depends in large part on how well the participant can relate to the situation of the other. When participants selected the non-personal story that they could relate to the most, there were no statistically significant differences between areas recruited for personal and non-personal imagery (Preston et al., 2007).

Because there is extensive knowledge about the neural mechanisms underlying the processing of nociception and the first-hand experience of pain is ubiquitous across individuals, studying pain perception in others constitutes a valuable and ecologically valid paradigm for investigating the neural underpinning of human empathy. In recent years, a growing number of functional neuroimaging studies demonstrated that brain areas that belong to the pain matrix, notably the anterior insula and the anterior cingulate cortex, implicated in processing the affective and motivational aspects of pain also mediate the observation of pain in others (e.g., Singer et al., 2004; Morrison et al., 2004; Botvinick et al., 2005; Jackson et al., 2005, 2006b; Gu and Han, 2007; Lamm et al., 2007; Moriguchi et al., 2007; Saarala et al., 2007; Ogino et al., 2007). However, none of these studies detected significant signal change in the primary somatosensory cortex during the perception of pain in others (for a meta-analysis, see Jackson et al., 2006a). This result (i.e., lack of primary somatosensory activation) seems at odds with the perception–action–coupling mechanism (mirror-neuron system) that underlies the automatic resonance between self and others. The somatosensory cortex/posterior dorsal insula contributes to the sensory discriminative dimension of pain as demonstrated by various neuroimaging studies (e.g., Symonds et al., 2006). However, two recent studies indicate involvement of the sensorimotor cortex during the perception of pain in others. These studies used transcranial magnetic stimulation (TMS) and found changes in the corticospinal motor representations of hand muscles in individuals observing needles penetrating hands or feet of a human model (Avenanti et al., 2005, 2006). Using electroencephalography (EEG), another study found a modulation of the primary somatosensory cortex activity contingent upon the observation of others’ pain (Bufalari et al., 2007). Two possibilities can explain the discrepancy between EEG/TMS and fMRI studies. One is that the TMS and EEG methods can sense subtle changes in the sensorimotor cortex that are below the significance threshold in fMRI measures. The other possibility is that attending to a specific body part elicits somatosensory activity in the corresponding brain region. This has been demonstrated in a positron emission tomography study in which participants were instructed to focus their attention either on the unpleasantness or on the location of the noxious stimuli delivered on the participants’ hands (Kulkarni et al., 2005), with the latter condition resulting in increased regional cerebral blood flow in the contralateral primary somatosensory cortex.

To address the question of whether the perception of others in pain can elicit activity in the primary somatosensory of the observer, we used rhythmic magnetoencephalographic (MEG) oscillations with a frequency of around 10 Hz as indicators of primary somatosensory cortex activity. Spontaneous oscillatory activity at frequencies around the ~10 Hz (alpha) and ~20 Hz (beta), also termed mu rhythm, has been consistently observed over the primary sensorimotor cortex (e.g., Hari and Salmelin, 1994; Niedermeyer, 1999). Mu rhythm can be attenuated by observation of action (Hari et al., 1998) as well as limb movements (Hari and Salmelin, 1997; Pfurtscheller, 1999). Furthermore, several lines of evidence indicate that the ~10-Hz oscillations concentrate predominantly in the posterior bank of the central sulcus while the ~20-Hz rhythms originate in the precentral gyrus (Hari and Salmelin, 1994, 1997; Pfurtscheller, 1999). Both the spatial distribution and reactivity demonstrate that this oscillatory activity is related to the functional state of the nervous system. Increased amplitudes of oscillation can be related to an idling state of a system whereas reduced amplitudes can be associated with activation of the system (Hari and Salmelin, 1997; Niedermeyer, 1999; Pfurtscheller, 1999; Lee et al., 2003). Mu suppression has been related to a higher degree of excitability in the sense of a thalamocortical gate, which can be opened by endogenous or exogenous events (Steriade and Llinas, 1988). The amplitude of the ~10-Hz oscillations decreases immediately after median nerve stimuli, increases above the prestimulus level within 500 ms afterward, and reaches the maximal rebound usually around 500–800 ms (Salenius et al., 1997a,b; Hari and Salmelin, 1997). In the current study, we expected the presence of mu suppression when participants are watching visual stimuli depicting body parts in painful versus non-painful situations. Moreover, we anticipated that observation of pain will suppress the ~10-Hz rhythms, as an index of primary somatosensory cortical functional state, to a stronger degree than during non-painful situations.

Materials and methods

Participants

Sixteen right-hand healthy participants (12 females) aged 24.6 ± 4.0 were enrolled after providing written informed consent according to the declaration of Helsinki. The study was approved by the local Ethics Committee of Taipei City Hospital. All participants had no history of neurological or psychiatric disorders, and were free of medication. They received monetary compensation for their participation.

Stimuli

A series of 128 digital color pictures showing right hands and right feet in painful and non-painful situations were used. These stimuli were previously used and validated in two behavioral and two fMRI studies (Jackson et al., 2005, 2006b). All situations depict familiar events that can happen in everyday life. Various types of pain (mechanical, thermal, and pressure) were represented (Pain). For each situation, a neutral picture, which involved the same settings without any painful component (No-Pain), was also obtained. All pictures were edited to the same size (600×450 pixels).
Procedures

A week before the MEG recordings, each participant filled in a series of self-report dispositional measures including the empathy quotient (EQ) (Baron-Cohen and Wheelwright, 2004), the interpersonal reaction index (IRI) (Davis, 1996; Siu and Shek, 2005), and the emotional contagion scale (ECS) (Doherty, 1997).

MEG recordings were performed under three different conditions: (1) Baseline, with participants fixating a fixation cross; (2) No-Pain, participants watching pictures of right hands and feet in non-painful situations; and (3) Pain, participants watching pictures of right hands and feet in painful situations. An average of 120 stimuli was presented within a 4-min block. The interval between each block was at least 5-min to avoid electrical habituation. The order of the observation blocks was balanced across conditions and randomized across subjects. At the end of the session, the Baseline condition was repeated to assess the signal reproducibility. The pictures were presented at a distance of 100 cm in front of the participant, and their presentation was jittered with a 1.5-s mean duration followed by a mean 0.5-s black screen. The maximum duration was 1.7 s for the picture and 0.6 s for the black screen. The minimum duration was 1.4 s for the picture and 0.3 s for the black screen. The durations were jittered and randomized whereas the onset-to-onset interval of each picture stimulus was fixed as every 2 s. The continuous performance task was used in order to make sure that participants attended to the visual stimuli. Participants were requested to report at the end of each block how many stops they had seen in the stimuli (2–5 stops), which were randomly inserted within each block.

After the MEG recordings, participants were asked to rate pain intensity on the same set of stimuli that they had seen during the MEG recordings using a computerized visual analogue scale (VAS) ranging from no pain to extreme pain as the endpoints of the scale.

MEG data recording

During the MEG recording, the participants were comfortably seated in a magnetically shielded room with the head leaning against the helmet-shaped neuromagnetometer. They were instructed to keep eyes fixed forward and to ignore the median nerve stimuli. Cortical activity was continuously recorded with a 306-channel (102 sensor unit) whole-head neuromagnetometer (Vectorview® Neuro-mag Ltd., Helsinki, Finland). The locations of the coils with respect to anatomical landmarks on the head were determined with a 3-D digitizer (Isotrak 3S10002, Polhemus Navigation Sciences, Colchester, VT) to allow alignment of the MEG and magnetic resonance (MR) image coordinate systems. MR images of the subjects’ brains were acquired with a 1.5-T Siemens Magnetom scanner.

The median nerve was stimulated at the level of the left wrist with 0.3-ms constant current pulses once every 2.0 s. The onset timing of the median nerve stimulation coincided with the onset of each picture presentation. The stimulus intensity was adjusted during the Baseline condition. We first recorded somatosensory-evoked magnetic fields with a stimulus intensity clearly exceeding the motor threshold to elicit cortical responses with excellent signal-to-noise ratio. Then, the intensity of the stimulus was decreased (3–5 mA, mean 4 mA) to produce clear tactile sensation without any motor movement or painful sensation. A panel was used to avoid the participants from seeing their hands. The experimenters continuously checked each subject’s thumb twitching induced by the electrical stimulation.

For control purposes, the surface electromyograms (EMGs) were recorded from the right first interosseous and thenar muscles. EMGs were highpass filtered at 3 Hz and rectified. The background EMG levels were compared across conditions.

The signals were bandpass filtered within 0.03–200 Hz and digitized at 600 Hz. The analysis period of 1000 ms included a prestimulus baseline of 200 ms. Epochs coinciding with signals exceeding 600 μV in the simultaneously recorded horizontal and vertical electrooculogram were automatically rejected from the analysis. Approximately 100 artifact-free epochs were acquired in each experimental condition.

<table>
<thead>
<tr>
<th>Sample (n = 16)</th>
<th>Empathy quotient</th>
<th>Interpersonal reactivity index (IRI)</th>
<th>Emotional contagion scale</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PT</td>
<td>EC</td>
<td>PD</td>
</tr>
<tr>
<td>Sample (n = 16)</td>
<td>32.81 (13.47)</td>
<td>16.81 (3.37)</td>
<td>18.56 (2.61)</td>
</tr>
<tr>
<td>Normative data</td>
<td>41.88/47.22 (11.28/10.22)</td>
<td>17.37 (4.79)</td>
<td>20.36 (4.02)</td>
</tr>
</tbody>
</table>

The table provides results for the sample investigated in our study.

Normative data derived from and transformed to sum scores from: EQ (Baron-Cohen and Wheelwright, 2004); IRI (Bellini et al., 2002); and ECS (Doherty, 1997). m Male sample. f Female sample.

PT = perspective taking; EC = empathic concern; PD = personal distress; FS = fantasy.
Maximal scores: each subscale of IRI=28; Empathy quotient=80; Emotional contagion scale=60.
MEG data analysis

Level of the ~10-Hz oscillations

The recorded signals were bandpass filtered within 8–12 Hz (~10 Hz), rectified, and segmented to obtain neuromagnetic rhythmic epochs. Each neuromagnetic rhythmic epoch was segmented, starting at the onset timing of median nerve stimulation and ending at poststimulus 1000 ms, from the whole raw data. Then, all epochs were averaged to obtain oscillatory activities (Salmelin and Hari, 1994). The ~10-Hz rebound of each condition was calculated (in a time window from 300 to 1000 ms) from the mean of the four MEG channels showing the strongest reactivity over sensorimotor regions in the Baseline condition (Järveläinen et al., 2004). Then, the ~10-Hz rebounds relative to the Baseline was defined as the ~10-Hz suppression. Statistical analysis of the results was performed by a two-way repeated-measures ANOVA on the ~10-Hz suppression using two within-subject factors [hemisphere (right, left) × condition (Pain, No-Pain)] followed by Tukey’s Honestly Significant Difference post hoc test. In addition, multiple regression analysis was conducted between the Pain relative to the No-Pain ~10-Hz suppression and the dispositional measures of each participant to test if the pain perception-related modulation of somatosensory rhythm was associated with behavioral measures.

Fig. 2. Time frequency representations (TFR) of spontaneous neuronal activity in one of the four channel with the strongest power over right sensorimotor region averaged across all trials and all subjects at each of the condition (Baseline, No-Pain, and Pain).

Fig. 3. Group mean locations and time courses of the somatosensory oscillations associated with empathy for pain. The source location of ~10-Hz oscillations is in the bilateral postcentral gyrus (upper, red colored). The time courses of the channels with the maximal power respectively over the left and right somatosensory cortex after left median nerve stimulations are demonstrated for the three different conditions (lower).
Origin of the ~10-Hz oscillations

The current dipole sources of the 8–12-Hz signals were identified in six subjects from data recorded during the Pain condition. The least-squares fit was based on signals picked up by a subset of 18 channels over the right sensorimotor area. Dipoles were accepted only if they accounted for at least 80% of the field variance. Fifty dipoles from different cycles of the ~10-Hz rhythm were superimposed on the surface rendition of each participant’s anatomical MRI. From the dipole locations in the MEG coordinate system, we first converted to the Talairach and Tournoux stereotaxic space (1988) for individual anatomical localization and to take to a median in a three-step procedure by (i) determining the coordinates of anterior and posterior commissures in the MEG coordinate system by visual inspection of the subject’s MR scans, (ii) determining the extent of the brain in three dimensions by visual inspection of MR scans, and finally (iii) applying translation, rotation, and scaling in a Matlab procedure.

Results

Dispositional and behavioral measures

Table 1 lists the results of the dispositional measures. The pain intensity ratings after MEG recordings indicate that participants rated the painful stimuli (Pain) significantly higher on the visual analogue scale (mean 6.3, SD = 1.6) than the non-painful ones (No-Pain) (mean = 1.2, SD = 0.4), validating their affective content (P < 0.001) (see Fig. 1). In addition, all participants correctly reported the number of stops across all conditions on the continuous performance task when watching the visual stimuli during the MEG recording.

~10-Hz oscillations

The time windows and frequency bands of pain perception-induced oscillatory activity were calculated. Global grand average temporal frequency representations at one of the four channels with the strongest rebounds over right sensorimotor cortex, controlateral to the left median nerve stimulation, across all trials and all subjects were illustrated for each condition (Fig. 2). The median nerve stimulation during the Baseline elicits ~10-Hz rebounds around 300 ms to 1000 ms. The observation of Pain and No-Pain stimuli is associated with suppression of the cortical oscillatory activity in the alpha-band (8–12 Hz).

The normalized values of the ~10-Hz suppression of the watching conditions were determined as mean ± SEM [Pain vs. No-Pain: (−1.48 ± 0.82) vs. (−1.24 ± 0.60) × 10⁻²⁵ (T/cm)² in left hemisphere; (−2.38 ± 1.02) vs. (−1.80 ± 0.92) × 10⁻²⁵ (T/cm)² in right hemisphere]. The statistic results showed a main effect in the condition [F(1,15) = 5.641, P = 0.031], neither in the hemisphere [F(1, 15) = 2.048, P = 0.173] nor their interaction [F(1, 15) = 0.451, P = 0.242]. After post hoc tests, the statistically differential suppression between Pain and No-Pain appears mainly driven from right hemisphere (P = 0.007) instead of left hemisphere (P = 0.342).

Somatosensory cortex origin of the ~10-Hz oscillations

In agreement with previous studies (e.g., Salmelin and Hari, 1994), the source of the ~10-Hz oscillations was located just posterior to the central sulcus (see Fig. 3, upper part). The localized dipole was accepted with the g value > 80%, the confidence volume ≤ 1 cm³, and the source amplitude ≥ 5 nAm. The Talairach coordinates for the median of all source locations were x = 31, y = −32, z = 51, thereby agreeing with the location of the primary somatosensory cortex (Talairach and Tournoux, 1988). In addition, the temporal spectral evolution of the ~10-Hz level at one of the four channels with the maximal power separately over left and right somatosensory cortex was also illustrated across all trials and all subjects (see Fig. 3, lower part). During the Baseline condition, the ~10-Hz rhythm was strongly enhanced after the median nerve stimulation, starting at about 300 ms and reaching its maximal level within 800 ms after the stimulus onset. Compared to the Baseline, the rebounds are clearly suppressed during the two observation conditions. Importantly, the Pain condition suppresses the ~10-Hz oscillations more strongly than the No-Pain condition.

Correlation between ~10-Hz oscillations and dispositional measures

The ~10-Hz suppression of the Pain relative to the No-Pain conditions correlated significantly with the scores from the perspective-taking subscale of the IRI (on scale 0–28, mean ± SD 16.8 ± 3.4, range 12–25) both in the right (r = 0.36, P = 0.014) (Fig. 4) and left hemispheres (r = 0.37, P = 0.013). By contrast, neither the measures of EQ, ECS, other subscales of IRI, nor the pain intensity ratings showed any significant correlations.

The rms levels of surface EMG were decided by medians of the four 1-min segments per condition, averaged across thenar and interosseus EMGs. The Baseline EMG levels did not differ from those during viewing of the Pain nor the No-Pain situations.
Discussion

The present study investigated whether the perception of others in pain modulates the neural activity of primary somatosensory cortex in the observer by using MEG measurements. The results demonstrate that mere observation of others in pain modulates primary somatosensory oscillations. Observing body parts being in non-painful and painful situations was associated with activation of primary somatosensory cortex. These findings are in line with previous neuroimaging studies that reported similar results in individuals watching different body parts being touched (Keysers et al., 2005; Cheng et al., 2007). Importantly, in our study, the signal change over primary somatosensory cortex was significantly stronger when watching the painful situations than watching non-painful situations. This result supports previous TMS and EEG experiments that demonstrated somatic resonance during the mere perception of pain empathy (Avenanti et al., 2005, 2006; Bufalari et al., 2007). Moreover, the present MEG study provides a more direct mapping of primary somatosensory involvement with little attenuation from the generators to the sensors (Ioannides, 2006).

The strong suppression of the ~10-Hz oscillations during the observation of body parts in pain fits well with recent neurophysiological studies which showed that the perception of painful stimuli has a greater effect than the perception of tactile stimuli (Mouraux et al., 2003; Ohara et al., 2004; Ploner et al., 2006). The ~10-Hz oscillations, as one component of rolandic rhythm originating posterior to central sulcus, mainly reflect functional status of the primary somatosensory cortex (Salmelin and Hari, 1994). A higher amplitude of oscillatory activity reflects an idling state of a system, whereas a lower amplitude represents activation of a system (Hari and Salmelin, 1997; Niedermeyer, 1999; Pfurtscheller, 1999). The rolandic cortex of a relaxed human subject exhibits mu rhythm around 10 and 20 Hz, which can be detected non-invasively with EEG and MEG. Peripheral stimulation of median nerve transiently enhances mu rhythm, when it lends itself well to quantify the task-related changes with an advantage of better reproducibility and less variability than spontaneously occurring bursts of rhythmic activity (Salemius et al., 1997a,b). Accordingly, the current study adopted the power change of ~10-Hz oscillations as the window of pain perception in others.

It is worth noting that study participants scored higher on ratings on pain intensity to watching others in the painful situations than the non-painful situations. Accordingly, it is likely that the modulation of somatosensory oscillations is linked to increased attention to the stimulated hand induced by painful stimuli. However, all participants showed equally perfect performance on the continuous performance task when watching the painful and the non-painful stimuli. Moreover, non-specific attention effects can hardly explain the pattern of correlations between neurophysiological (i.e., suppression of somatosensory oscillations induced by the Pain relative to the No-Pain stimuli) and the dispositional measures (i.e., the perspective taking subscale of the IRI) found in the present study.

Interestingly, the ~10-Hz suppression induced by the Pain relative to the No-Pain significantly correlated to the perspective taking subscale of the IRI. The ~10 Hz oscillations, as one component of mu rhythms, appear to sensitive to cognitive and affective influences as well as echo somatosensory processing in the frontoparietal networks. Mu rhythm reflects downstream modulation of sensorimotor cortex derived from prefrontal mirror-neurons (Pineda, 2005). The IRI is probably the most widely used self-report measure of dispositional empathy. Its subscale of perspective taking assesses the ability to adopt the subjective perspective of others. A recent fMRI study demonstrated that the activity of the mirror-neuron system correlated with the scores of the IRI perspective-taking subscale (Gazzola et al., 2006). Here we found that individuals who scored higher in perspective-taking ability suppress the somatosensory oscillations to a stronger degree when watching others in painful relative to non-painful situations. This correlation lends support to a functional link between the mirror-neuron system and empathy.

Conclusion

The results of our MEG study indicate that empathy for pain modulates neural activity in primary somatosensory cortex and supports the idea that the mirror-neuron system is important for empathizing with others by simulating their actions onto one’s own sensory-motor representations. Furthermore, this MEG study shows that the perception of pain in others elicits subtle primary somatosensory activity that may be difficult to be detected by functional MRI techniques. Our results are also in line with a recent ERP study that demonstrated an early response to pain at 140 ms after stimulus onset (Fan and Han, 2008). Altogether, these new findings contribute to explain the discrepancy between TMS and functional MRI experiments. Finally, these data are in full agreement with the results and interpretation presented by Avenanti and colleagues (2006) who argued that the key variables modulating sensorimotor responses to others’ pain are mainly related to the visual features of the observed situations and not that much to the instructions given to the observers. Indeed in our study, no specific task was given to the participants.

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