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Empathy for Pain and Touch in the Human Somatosensory Cortex

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Although feeling pain and touch has long been considered inherently private, recent neuroimaging and neurophysiological studies hint at the social implications of this experience. Here we used somatosensory-evoked potentials (SEPs) to investigate whether mere observation of painful and tactile stimuli delivered to a model would modulate neural activity in the somatic system of an onlooker. Viewing video clips showing pain and tactile stimuli delivered to others, respectively, increased and decreased the amplitude of the P45 SEP component that reflects the activity of the primary somatosensory cortex (S1). These modulations correlated with the intensity but not with the unpleasantness of the pain and touch ascribed to the model or the aversion induced in the onlooker by the video clips. Thus, modulation of S1 activity contingent upon observation of others' pain and touch may reflect the mapping of sensory qualities of observed painful and tactile stimuli. Results indicate that the S1 is not only involved in the actual perception of pain and touch but also plays an important role in extracting somatic features from social interactions.

Keywords: mirror systems, primary somatosensory cortex, simulation theory, social cognition, somatosensory-evoked potentials

Introduction

Current neuroscientific models of empathy postulate that a given motor, perceptual, or emotional state of an individual activates corresponding representations and neural processes in another individual observing that state (Preston and de Waal 2002; Gallese 2003; Decety and Jackson 2004). Thus, the classical notion of empathy, based on the ability to understand the emotional experiences of others, has been extended to include also the ability of an onlooker to share feelings and sensations of a model (Preston and de Waal 2002; Gallese 2003, Decety and Jackson 2004; Avenanti and Aglioti 2006; Decety and Grezes 2006). Until the last decade, no plausible mechanism explained how this resonant mapping between self and other might occur. However, the discovery of neurons in the monkey premotor and parietal cortex that become active during execution of a given action and observation of the same action performed by another human or monkey agent (mirror neurons) suggests that the primate nervous system is capable of mapping observed actions of others onto its own motor system (Gallese et al. 1996; Fogassi et al. 2005). In humans, evidence for shared neural representations between self and others was first reported in the domains of action (Rizzolatti et al. 2001) and emotion (Carr et al. 2003; Wicker et al. 2003). In the past few years, however, research has shown the role of shared representations in the domains of pain (Morrison et al. 2004; Singer et al. 2004, 2006; Avenanti et al. 2005, 2006; Botvinick et al. 2005; Jackson et al. 2005; Minio-Paluello et al. 2006; Saarela et al. 2007) and touch (Keysers et al. 2004; Blakemore et al. 2005; Schaefer et al. 2006) processing.

It is widely held that the actual experience of pain involves sensory discriminative (e.g., intensity, duration, localization of noxious stimuli) and affective-motivational (e.g., unpleasantness) components that are mapped in 2 distinct but overlapping nodes of a complex neural network referred to as the "pain matrix" (Melzack 1999). Whereas the sensory dimension of pain is mainly coded in parietal sensorimotor neural structures, including the somatosensory cortices (Porro et al. 1998; Bushnell et al. 1999; Peyron et al. 2000), the affective component of the pain experience mainly relies upon neural activity of the anterior cingulate cortex (ACC) and anterior insula (AI) (Peyron et al. 2000). The neural segregation of sensory and affective components makes pain an interesting model for testing theories of empathy based on the notion of shared neural representations.

Most of the neuroimaging studies carried out so far indicate that only the affective component of the pain matrix is called into play during empathy for pain. For example, Singer et al. (2004) showed that knowing via symbolic visual cues that the beloved person was going to receive an impending painful stimulus elicited neural activity mainly in ACC and AI, which correlated with emotional empathy scores. Affective neural responses to others' pain were also found in observational situations in which subjects were presented with static pictures implying pain (Jackson et al. 2005, 2006; Ogino et al. 2006), videos showing facial pain-related behavior (Botvinick et al. 2005; Saarela et al. 2007), or light pinpricks (Morrison et al. 2004).

Empathy, however, is a complex construct consisting not only of emotional but also of cognitive and somatomotor components (Davis 1996; Preston and De Waal 2002; Gallese 2003; Decety and Jackson 2004; Avenanti and Aglioti 2006). Thus, it is entirely possible that empathy may also rely on basic resonant mechanisms that allow to map others' sensation onto one's own sensorimotor system.

By using single-pulse transcranial magnetic stimulation (TMS), we demonstrated that viewing needles deeply penetrating specific body parts of a stranger model brought about a selective corticospinal inhibition of the model's penetrated muscle. Importantly, the inhibition correlated with the intensity but not the unpleasantness of the pain ascribed to the model (Avenanti et al. 2005, 2006; Minio-Paluello et al. 2006). Although these results support the view that others' pain elicits a resonant mapping of sensory qualities of pain (intensity, localization), single-pulse TMS alone cannot provide direct information about the sensorimotor structures involved in this mapping. Theoretically, parietal sensorimotor cortices may participate in the

extraction of the sensory qualities of others' pain. Indeed, 2 recent functional magnetic resonance imaging (fMRI) studies indicate that viewing static pictures of potentially painful situations and imagining to feel the pain of the model activates the parietal operculum and secondary somatosensory cortex (Jackson et al. 2006; Ogino et al. 2006). Moreover, observing facial expressions of pain induced neural activity in the inferoparietal lobule that correlated with the intensity of pain attributed to the models (Saarela et al. 2007). Somatosensory neural structures play also a role in shared touch representations. Indeed, observation of tactile stimuli delivered to other individuals induced activity in the onlookers' somatosensory cortical areas (Keysers et al. 2004; Blakemore et al. 2005). Crucially, these areas are typically involved in the personal experience of being touched as well as in the personal experience of pain (Porro et al. 1998; Ploner et al. 2000; Timmermann et al. 2001; Bingel et al. 2004), and they code the intensity of sensation.

Here we sought to determine whether the primary somatosensory cortex (S1) is involved in pain and touch shared representations by recording somatosensory-evoked potentials (SEPs) during the direct observation of painful and nonpainful stimuli delivered to a human model's hand. The SEP recording technique allows for noninvasive, high temporal resolution assessment of subcortical and cortical activities along the somatosensory pathways following electrical stimulation of peripheral nerves. To specifically explore whether observation of pain and touch stimuli modulates neural activity in S1, we focused on changes in amplitude and latency of the SEP components that are likely generated in different subareas of S1 (Allison et al. 1991, 1992; Valeriani et al. 2001).

Methods

Participants

Eighteen healthy volunteers (10 males, 8 females) aged between 19 and 29 years (mean = 23.8 standard deviation [SD] = 2.4) participated in the study. All subjects were right handed according to a standard handedness inventory (Oldfield 1971), had normal or corrected vision, and were naive as to the purposes of the experiment. Participants gave their written informed consent and were paid €10/h for their participation in the study. The procedures were approved by the local ethics committee and were in accordance with the ethical standards of the 1964 Declaration of Helsinki.

Stimuli

Subjects were presented with video clips projected in the center of a 21-inch dark screen located approximately 57 cm away from them. The video clips depicted 4 different observational conditions: 1) a needle penetrating the dorsal view of a male right hand (Pain); 2) a Q-Tip moving over and pressing the same region of the hand (Touch); 3) a static dorsal view of the same right hand (Hand); and 4) a fixation cross located in the center of a white rectangle (Baseline). The hands depicted in the video clip were presented in an egocentric first person perspective. Observing action activates the motor mirror system (Rizzolatti et al. 2001), which in turn may modulate the activity of S1 and secondary somatosensory cortex (Avikainen et al. 2002; Rossi et al. 2002). To avoid this modulatory effect in the present study, we carefully checked that the holder of the syringe or the Q-Tip was not visible in any of the videos. Moreover, we know from previous TMS research that observation of similar dynamic visual stimuli does not bring about any sign of motor facilitation (Avenanti et al. 2005, 2006; Minio-Paluello et al. 2006). Speed, trajectory, and angle of the different moving stimuli were matched. To minimize any possible habituation effect, we used 3 differently sized syringes, each filled with a different colored liquid, and 3 differently colored Q-Tips. Each syringe/Q-Tip could penetrate/touch the hand in 3 different places. Thus, for each dynamic observation condition, 9 slightly different penetrations/touches were presented.

Procedure

The experiment lasted approximately 3 h and included 3 sessions. In the pretest session, participants became familiar with the experimental setup and were provided with instructions about the subsequent SEP recording sessions. In particular, they were requested not to blink or move the eyes, to watch attentively the events shown on the video clips, and to disregard the electric stimulation applied to their hand for evoking somatic potentials. Participants were also requested to focus on what the model in the movies may have felt.

In the SEP sessions, Electroencephalographic (EEG) activity was recorded during the 4 observation conditions described above (Pain, Touch, "Hand", and Baseline). A schematic representation of the experimental design is provided in Figure 1.

Each model observation condition (Pain, Touch and Hand) was presented in one run, consisting of about 10 blocks (Fig. 1*a*). The "Baseline" condition was performed in two 5-block runs (Fig. 1*a*). Each block lasted approximately 63 s and included the presentation of 9 different video clips belonging to the same category of stimuli (Fig. 1*b*). Each video clip lasted 6 s and was followed by a 1-s blank

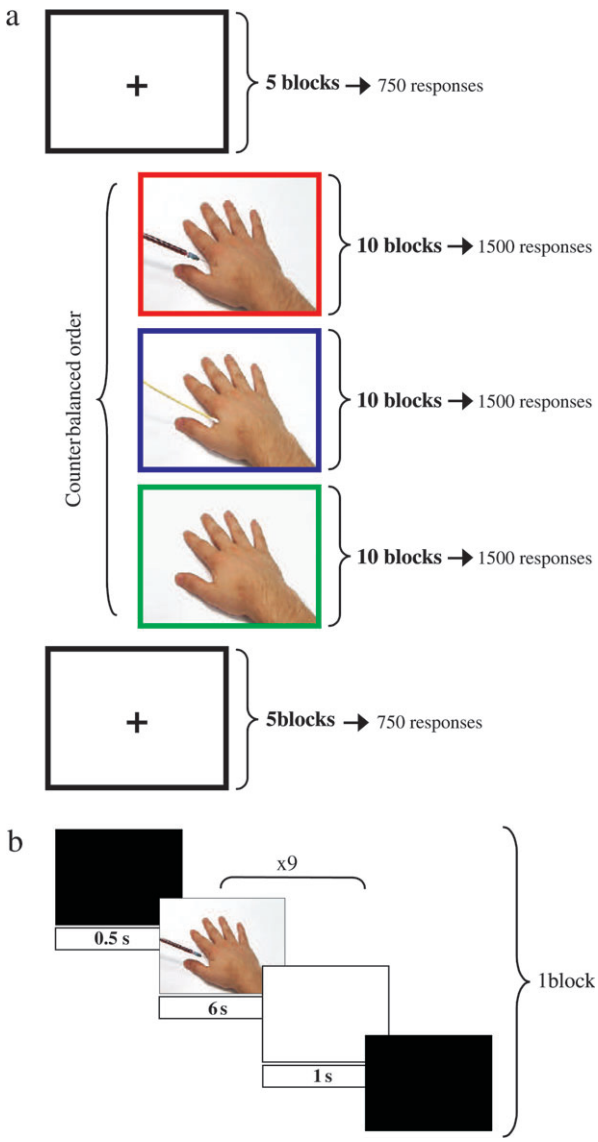

Figure 1. Schematic representation of the experimental design (*a*) and of the sequence of a typical experimental block (*b*).

screen (Fig. 1*b*). A dark screen signaled the end of each recording block. Pauses between blocks were commensurate to the subjects' fatigue. The order of the model observation runs was counterbalanced across subjects. The Baseline condition was presented at the beginning (5-blocks) and at the end (5-blocks) of the recording session (Fig. 1*a*).

The order of the different clips was pseudorandomized within each block for the "Pain" and "Touch" conditions to avoid the same colored syringe or the same stimulation location being repeated twice consecutively. At the end of each block, subjects were allowed to move and to relax for 2–3 min. During the break, the subjects were asked questions to ensure that they were following the instructions and were paying attention to the video clips (e.g., we asked: "Was it a right or a left hand? Was it a male or a female hand?" "How many syringes/Q-tips did you see?" "Were you able to disregard the electric stimulation?"). After the SEP session, the subjects were presented with all the movies and asked to judge the aversion induced by each movie ("self-oriented" emotional reactions) by marking a vertical, 10-cm visual analog scale (VAS) with 0 cm indicating "no effect" and 10 cm "maximal effect imaginable." VASs were also used to rate the Intensity (how much intense for the model was the stimulation shown in the clip?) and Unpleasantness (how much the stimulation shown in the clip bothered the model?) of the bodily sensation purportedly experienced by the model when being injected or touched on the hand ("other-oriented" measures of sensory or emotional pain dimensions).

SEP Recording

Subjects sat in an armchair in a warm, semidarkened room, in front of the movie screen. The SEPs were obtained by nonpainful electrical stimulation of the right median nerve at the wrist (square wave pulses, stimulus intensity just above the motor threshold, with a frequency of 3 Hz, duration 0.7 ms, and mean intensity of 11 mA). A panel was used so that the subjects could not see their hands. This allowed the experimenter to continuously check for thumb twitching induced by the electrical stimulation.

Electrophysiological recordings were obtained from 64 tin electrodes following the 10–10 international system (Fp1, Fp2, AF3, AFz, AF4, F7, F3, Fz, F4, F8, FC5, FC3, FC1, FCz, FC2, FC4, FC6, T7, C5, C3, C1, Cz, C2, C4, C6, T8, M2, TP7, CP5, CP3, CP1, CP2, CP4, CP6, TP8, P7, P5, P3, P1, Pz, P2, P4, P6, P8, PO7, PO3, PO1, POz, PO2, PO4, PO8, O1, Oz, O2, I5, I3, Iz, I4, I6, SI3, SIz and SI4 and the left mastoid) by a BrainVision 64 channel system. The horizontal electroculogram (EOG) was recorded at right external canthi, and the vertical EOG was recorded using an electrode below the left eye. All scalp electrodes were referenced to an electrode on the right mastoid, ipsilateral to stimulation. The ground electrode was placed on a glabrous area of the forearm, ipsilateral to the stimulation side. Electrode impedances were kept below 5 kΩ, and all signals were filtered (1–2000 Hz), digitized (rate of 5000 Hz), and stored on disk for off-line averaging.

To avoid SEP contamination due to eye movements and blinks, semiautomatic artifact rejection was performed prior to signal averaging in order to discard epochs containing transients exceeding 65–90 μV at any recording channel. The artifact-rejection procedure was performed by an experimenter blind to the conditions. On average, about 15% of the trials in each condition were rejected due to the presence of artifacts. About 1500 artifact-free trials were collected for each condition. The EEG was segmented for each electrical stimulus giving epochs of 110 ms (−20 to 90 ms). The baseline was calculated from 20 to 1 ms before the electrical stimulus to avoid any stimulus artifact. The averages were digitally band-pass filtered between 2 and 200 Hz. 3-dimensional topographical maps of scalp voltage distribution were obtained using the BESA 2000 version 5.14 system.

Data Analysis

Grand averages of SEPs recorded in the different conditions were obtained. The typical SEP components were identified on the basis of their topographical distribution, by means of scalp voltage maps, and labeled on the basis of latency and polarity. SEP amplitudes were measured from the prestimulus baseline. The grand average waveforms in the fixation cross observation blocks recorded at the beginning and at the end of the experimental session were compared by series of paired *t*-tests. No significant difference for any component was found (all $t_{17} < 2.110$, not significant). Thus, these blocks were averaged and considered as Baseline. Because of the large interindividual variability in SEP amplitude, we expressed values for each hand observation condition (Pain, Touch, Hand) as percentages of the Baseline condition. These normalized values were used for the statistical analysis (McCarthy and Wood 1985). For each component, repeated measure 1-way analyses of variance (ANOVAs) with condition as factor (Pain, Touch, Hand) were conducted separately on normalized individual peak amplitude values. For each component, the mean of the 2 electrodes with greater amplitude was used. Selection of peak electrodes was guided by an evaluation of scalp topographies in group-averaged data. Peak electrodes are listed in Table 1. Moreover, for each component, peak latency values were analyzed by means of repeated 1-way ANOVAs with condition as factor (Pain, Touch, Hand, and Baseline). Post hoc analyses were carried out by means of the Newman–Keuls test. Subjects who did not show a clearly recognizable waveform or topography on a given SEP component were excluded from the statistical analysis relative to that component. The number of subjects included in each analysis is reported in Tables 1 and 2.

Subjective Reports and Correlation Analysis

The VAS subjective ratings of the Intensity and Unpleasantness supposedly experienced by the model when being injected or touched on the hand were analyzed by means of paired samples *t*-tests. A 1-way ANOVA for repeated measures with condition as main factor (3 levels, Pain, Touch, Hand) was conducted on subjective reports of VAS aversion. To explore whether SEP modulation contingent upon the observation of others' pain or touch was related to different aspects of the subjective experience of others' sensations (both other-oriented and self-oriented), we carried out a standard correlation analysis between these 3 scores and the only component (P45) in which a specific pain-related or touch-related modulation was found. Partial correlations were also computed to assess the possible contribution to significant standard correlations of the remaining variables. Thus, we computed both standard and partial correlations between the normalized amplitude of P45 during Pain condition and VAS Intensity, VAS Unpleasantness, and VAS Aversion judgments reported during Pain. In a similar vein, we computed standard and partial correlations between normalized amplitude of P45 during Touch and the corresponding VAS Intensity, VAS Unpleasantness, and VAS Aversion measures.

Results

Seven typical SEP components contralateral to the stimulation side were identified (Allison et al. 1991, 1992; Valeriani et al.

Table 1

For each component peak electrode, amplitude ratio values in the different observational conditions and associated values of *F* test (repeated measure 1-way ANOVA) are provided

SEP Component	Peak electrode	Condition	Amplitude	SD	*N*	*F*
P16	FC1	Pain	0.97	0.25	18	0.78
		Hand	0.95	0.26		
		Touch	0.91	0.35		
N20	P5	Pain	1.29	0.30	18	0.65
		Hand	1.20	0.18		
		Touch	1.25	0.29		
P22	C3	Pain	0.92	0.27	18	0.41
		Hand	0.95	0.29		
		Touch	0.93	0.24		
N24	Fz	Pain	1.15	0.24	13	0.12
		Hand	1.21	0.55		
		Touch	1.17	0.38		
N30	FC1	Pain	1.16	0.36	16	1.55
		Hand	0.99	0.28		
		Touch	1.26	0.50		
P45	CP3	Pain	1.09	0.29	17	8.86**
		Hand	0.99	0.21		
		Touch	0.92	0.30		
N60	FC1	Pain	0.94	0.71	15	0.71
		Hand	0.92	0.61		
		Touch	1.08	0.63		

Note: *N* indicates the number of subjects included in the statistical analysis. The only significant value is marked by 2 asterisks ($P \leq 0.001$).

Table 2
Mean latency values for each component in the different experimental conditions and associated values of *F* test (repeated measure 1-way ANOVA) are provided

SEP component	Condition	Latency	SD	*N*	*F*
P16	Baseline	15.1	0.98	18	0.53
	Pain	15.1	0.97		
	Hand	15.2	1.01		
	Touch	15.1	0.96		
N20	Baseline	19.9	0.99	18	0.18
	Pain	19.9	1.02		
	Hand	20.0	1.05		
	Touch	20.0	1.02		
P22	Baseline	21.9	0.90	18	0.24
	Pain	22.1	0.92		
	Hand	21.9	0.89		
	Touch	22.0	0.90		
N24	Baseline	23.5	0.89	13	1.30
	Pain	23.5	0.85		
	Hand	23.6	0.81		
	Touch	23.6	0.86		
N30	Baseline	32.2	2.49	16	0.84
	Pain	32.1	2.67		
	Hand	32.4	2.44		
	Touch	32.3	2.45		
P45	Baseline	42.5	2.67	17	1.76
	Pain	43.0	2.59		
	Hand	43.0	2.31		
	Touch	42.9	2.49		
N60	Baseline	60.0	4.44	15	0.88
	Pain	60.1	3.44		
	Hand	60.9	4.08		
	Touch	60.3	4.35		

Note: *N* indicates the number of subjects included in the statistical analysis.

2001). They showed the same spatiotemporal distribution in all the recording conditions. Figure 2 shows these components in the Baseline condition. Amplitude ratio values and peak latency of the different components in each observation condition and the results of the statistical analysis conducted on them are illustrated in Tables 1 and 2.

The first subthalamic SEP component called P16 consists of a widespread positivity peaking over the central electrodes about 15 ms after the stimulus (Buchner et al. 1995). The first cortical volley is a bipolar component called N20, generated by activity of area 3b in the S1 (Allison et al. 1991, 1992; Valeriani et al. 1998). This component consists of a large negativity peaking about 20 ms after the electrical stimulus over contralateral parietal sites (P5) and a smaller positive counterpart (P20) at medial frontocentral sites (FC1). The N20/P20 is followed by the radial component P22 recorded with maximum amplitude over contralateral central sites (C3) and is thought to be generated in the precentral (Desmedt et al. 1987) or postcentral sulcus (Valeriani et al. 1998). The component N/P24 shows a bipolar distribution with a frontal negativity (Fz) and a centro-parietal positivity (CP3). This component is supposed to be generated by the same source as that of the N20 (Garcia-Larrea et al. 1992; Valeriani et al. 1998). At about 30 ms, the N30 component consisted of a large negativity peaking with the maximum amplitude over the frontocentral electrodes (FC1). It is still controversial whether the N30 is generated by activity of precentral (Waberski et al. 1999) or postcentral (Valeriani et al. 1998) cortical regions. The P45 component showed a radial distribution with its positive peak over centroparietal electrodes (CP3) at about 43 ms. It has been suggested that this component originates from the crown of S1, probably by the activity of area 1 or area 2 (Allison et al. 1992). The small counterparts of tangential components (P20, P24), visible in grand-averaged traces, were impossible in identify in many subjects and therefore were not included in statistical analysis. Given the frequency of electrical stimulation, waveforms over 60 ms latency were difficult to characterize (Huttunen and Homberg 1991). Despite this difficulty, a negative component was identified at centrofrontal scalp sites and labeled N60. This component is supposed to arise from supplementary motor area and from S1 (Barba et al. 2002).

For each component, normalized peak amplitude values were analyzed by means of repeated measure 1-way ANOVAs with condition as main within-subject effect (3 levels: Pain, Touch, Hand). The only significant main effect of condition was found for peak amplitude values of P45 ($F_{2,32} = 8.86$, $P = 0.001$, see Table 1).

The amplitudes and topographic distributions of the P45 in the 3 hand observation conditions (Pain, Touch, Hand) are illustrated in Figure 3.

Post hoc analysis indicated that P45 amplitude was significantly enhanced in the Pain with respect to Hand ($P = 0.03$) and Touch ($P = 0.001$) conditions. Moreover, P45 amplitude in the Touch condition was significantly smaller than in the Hand condition ($P = 0.05$) (Fig. 4).

The analysis conducted on the peak amplitude ratio values for the other components did not show any significance. For each component, peak latency did not differ in any conditions (Table 2).

Subjective Reports and Correlation Analysis

In the post-test session, 3 subjective measures were collected. We asked subjects to rate on a 10-cm VAS: 1) Intensity and Unpleasantness of the sensations supposedly felt by the model during Pain and Touch conditions (other-oriented measures) and 2) Aversion experienced during observation of each movie (self-oriented measure). The bodily sensation ascribed to the model in the Pain condition was considered as more intense ($t_{17} = 7.95$, $P < 0.0001$) and unpleasant ($t_{17} = 13.37$, $P < 0.0001$) than in the Touch condition. Moreover, the high significance ($F_{2,34} = 105.66$, $P < 0.0001$) of the aversion personally experienced by the subjects is accounted for by higher values in the Pain than the Touch ($P < 0.0001$) and Hand conditions ($P < 0.0001$). Mean and SDs of the different subjective ratings are reported in Table 3.

To assess whether the pain-related modulation of P45 was linked to the resonant mapping of sensory or affective qualities of the pain ascribed to the model or to general self-oriented emotional reactions induced by the movies, we performed a correlation analysis between neurophysiological and subjective measures in the Pain conditions.

Simple correlations indicated that P45 modulation was significantly related to VAS Intensity ($r = 0.52$, $P = 0.03$) but not to VAS Unpleasantness ($r = 0.23$, $P = 0.37$) or VAS Aversion ($r = 0.30$, $P = 0.24$) (Fig. 5). Importantly, the partial correlation between P45 and VAS Intensity while controlling for VAS Unpleasantness and VAS Aversion resulted significant ($r = 0.63$, $P = 0.01$). Thus, the largest increase of P45 amplitude was found in the subjects who rated the model's pain sensation as most intense independently of emotional other- or self-related judgments (Fig. 5, right column).

In a similar vein, we tested the relation between the P45 amplitude during the observation of touch and the subjective reports concerning the touch movies. Simple correlations showed that P45 modulation was significantly related to VAS Intensity ($r = -0.56$, $P = 0.02$) but not to VAS Unpleasantness

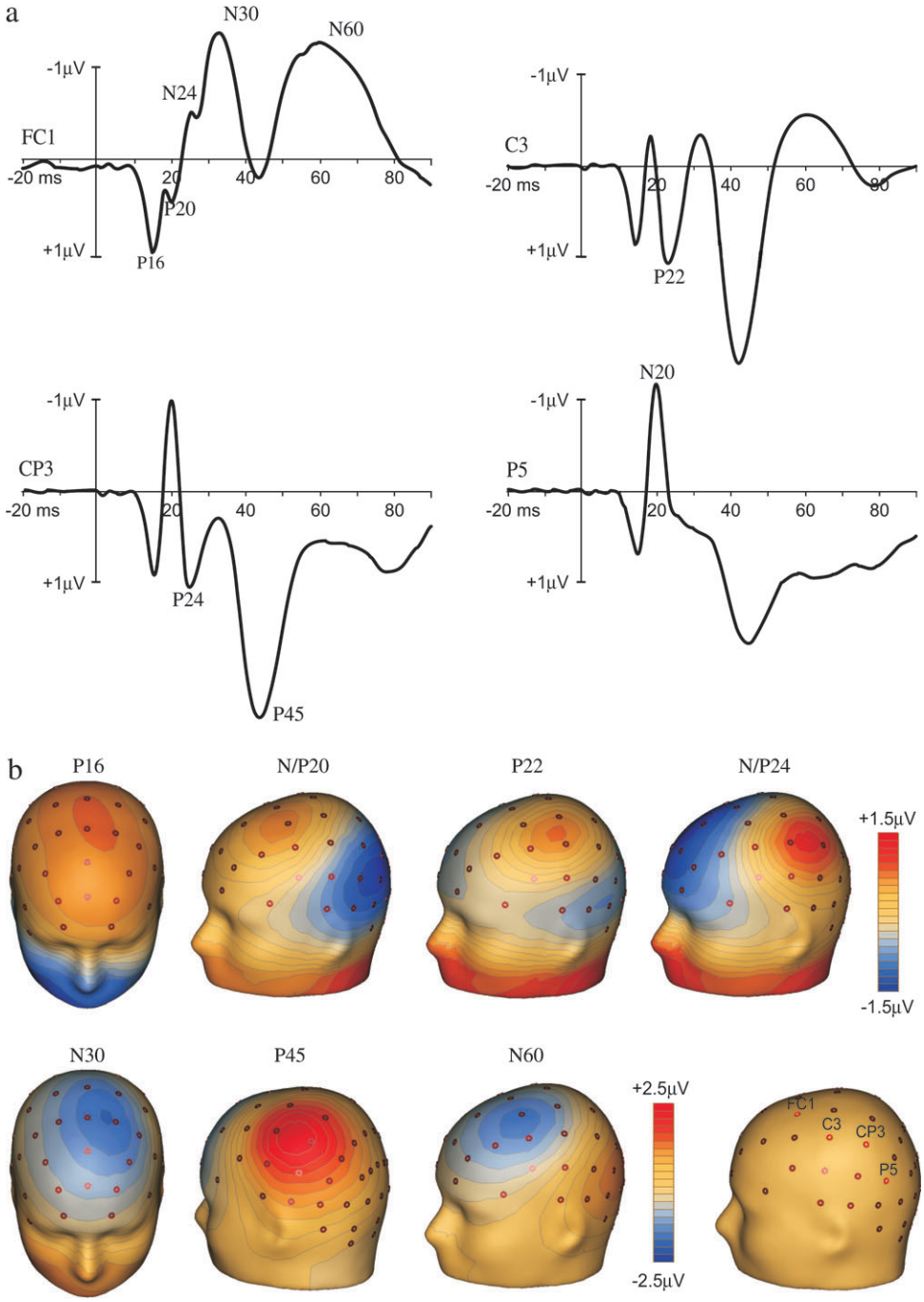

Figure 2. Grand average median nerve SEP in the Baseline condition. (*a*) Waveforms recorded at 4 most representative electrodes (FC1, C3, CP3, and P5) of the identified components. (*b*) 3-dimensional voltage topography of the identified components.

($r = -0.20$, $P = 0.44$) or VAS aversion ($r = 0.27$, $P = 0.29$). Partial correlation between P45 and VAS Intensity remained significant after controlling for VAS Unpleasantness and VAS Aversion ($r = -0.52$, $P = 0.049$). Thus, the largest decrease of P45 amplitude was found in the subjects who rated the model's tactile sensation as most intense independently of other- or self-related emotional judgments (Fig. 5, left column).

After the SEP recording sessions, all the participants reported that they were able to ignore the nonpainful electric stimulation of the median nerve used for eliciting somatosensory potentials.

Discussion

This study represents the first report of modulations of EEG somatosensory activity specifically triggered by observation of pain and touch in others. We show that viewing "flesh and bone" painful stimuli delivered to the hand of a human model unknown to the observer causes an increase in the amplitude of the P45 component of the SEPs induced by median nerve stimulation. The P45 amplitude during observation of pain positively correlated with the intensity of the pain ascribed to the model. Moreover, the P45 amplitude was reduced by the

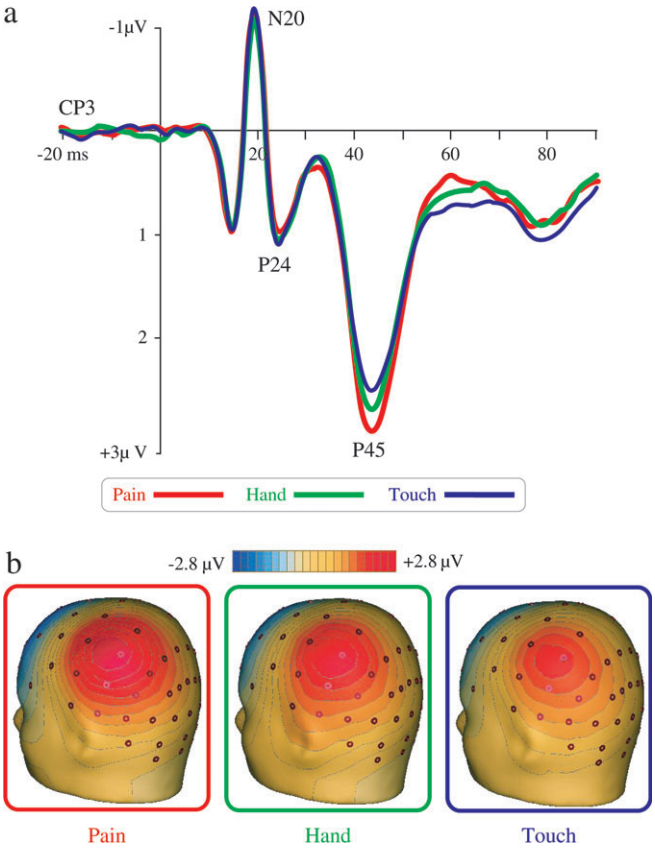

Figure 3. Effect on P45 component. (*a*) Superimposed waveforms in the 3 hand observation conditions (Pain, Touch, Hand; red, blue, and green traces, respectively) recorded at the CP3 peak electrode. (*b*) P45 topographic distribution in the same conditions.

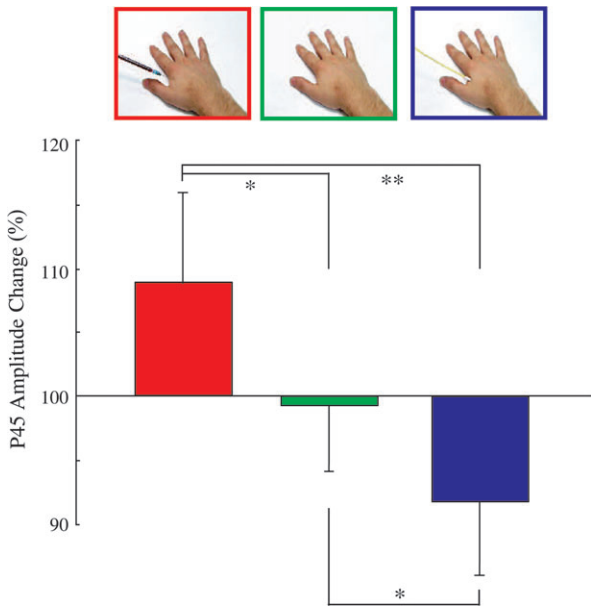

Figure 4. P45 percent changes (with respect to the baseline) in the 3 hand observation conditions (Pain, Touch, Hand; red, blue, and green columns). Asterisks indicate significant comparisons.* P values ≤ 0.05, ** for P values ≤ 0.001.

Table 3
Means and standard deviations of VAS Intensity, Unpleasantness and Aversion subjective ratings

	VAS intensity		VAS unpleasantness		VAS aversion		
	Touch	Pain	Touch	Pain	Touch	Pain	Hand
Mean	2.21	7.38	0.80	7.75	0.80	7.14	0.51
SD	0.94	2.29	0.86	2.15	0.72	2.65	1.35

observation of harmless tactile stimuli and was negatively correlated with the intensity of the tactile sensation ascribed to the model. We found no correlation between the P45 amplitude in Touch and Pain observation conditions and subjective emotional ratings, whether other-oriented (unpleasantness of the sensation supposedly felt by the model) or self-oriented (aversion felt by the onlooker). These findings indicate a specific relationship between encoding the sensory qualities of others' painful and nonpainful bodily sensations and modulations of the P45 component. These results also suggest that observing others' bodily sensations may influence the way we process our own somatic sensations; furthermore, the results indicate that different processes are involved in mapping others' noxious and non-noxious bodily experiences and that both processes may be mapped onto the somatosensory cortex.

Comparisons of intracranial and scalp-evoked potential recordings indicate that SEP components elicited up to 60 ms after stimulus onset originate in the S1, whereas later activity originates in higher order somatosensory cortices (Allison et al. 1991, 1992; Frot and Mauguière 1999). More specifically, the radial distribution of P45 component, which turned out to be modulated by the observation of pain and touch stimuli delivered to others, likely reflects neural activity of the crown of S1, including areas 1 and 2 (Allison et al. 1991, 1992).

The S1 has classically been considered as specifically involved in the personal experience of somatic sensations. Although the role of S1 in pain processing has been intensely debated (for a review, see Bushnell et al. 1999), studies in animal and human subjects converge to suggest a prominent role of this area in sensory discriminative aspects of both pain and touch perception. For example, single-neuron recordings in monkeys demonstrate that S1 contains neurons coding spatial and temporal properties and intensity of noxious and non-noxious stimuli (Kenshalo and Isensee 1983). Moreover, neuroimaging and neurophysiological studies indicate that the human S1 is involved in encoding the sensory qualities of pain and touch (Porro et al. 1998; Ploner et al. 2000; Timmermann et al. 2001; Bingel et al. 2004). EEG studies also suggest that whereas tactile stimuli activate 2 sequentially peaking sources in area 3b and 1, nociceptive stimuli activate a single source localized in area 1 (Kanda et al. 2000; Ploner et al. 2000; Inui et al. 2003). In line with these findings, intracranial recording studies reported that laser nociceptive stimulation activates area 1 (Kanda et al. 2000) but not area 3b (Valeriani et al. 2004).

Evoked potentials arise from membrane processes such as excitatory and inhibitory postsynaptic potentials (Li 1961). Because the polarity of the evoked potentials is determined by the direction of the current flow, positivity on the surface can be due to soma excitation or to hyperpolarization of the apical dendrites. Similarly, soma inhibition and depolarization of the apical dendrites can both lead to surface negativity (Humphrey 1968a, 1968b). In view of this, we cannot tell whether the changes in the amplitude of the P45 component during the observation of others' pain and touch feelings reflect an increase

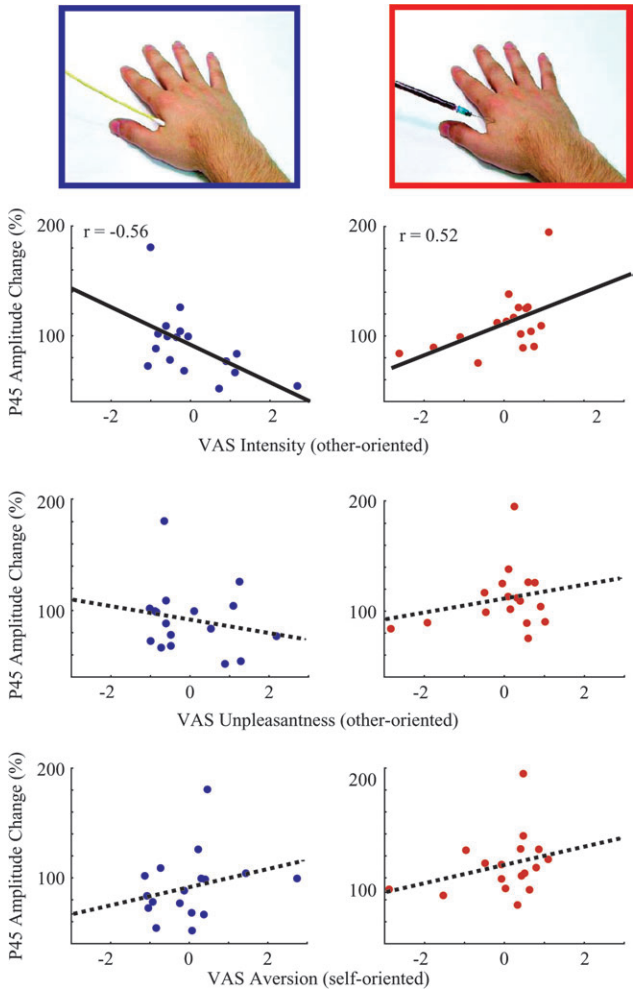

Figure 5. Scatterplots of P45 amplitude changes and VAS subjective ratings of Intensity (upper row) and Unpleasantness (middle row) attributed to the model and of Aversion (bottom row) in Touch (left column) and Pain (right column) observation conditions. To make *x* axes scales comparable for the different ratings, the raw subjective VAS measures used in the correlation analysis were plotted as standardized *z* scores. Continuous lines indicate significant correlations.

in underlying neuronal excitatory or inhibitory activity. However, the modulation of neural activity in S1 during the mere viewing of pain and touch stimuli delivered to others indicates that S1 is involved not only in the personal experience of pain and touch but also in resonant mapping of others' pain and touch.

Pain studies demonstrate that the responses evoked by electrical stimulation of the forearm in the 45- to 55-ms latency range are selectively increased by the application of tonic pain (injection of capsaicin) to surrounding regions (Baron et al. 2000). Similarly, experimental pain studies (Maihofner et al. 2004) and studies on chronic pain patients (Peyron et al. 2004) show that tactile stimuli delivered to an aching body part induce an increase of S1 activity.

The increase of P45 amplitude during the observation of others' pain found in the present study hints, for the first time, at a role in S1 in processing others' pain. It is worth noting that our subjects scored higher on self-oriented emotional reactions in the Pain condition than in the Hand and Touch conditions. Thus, it is possible that P45 modulation is linked to increased attention to the stimulated hand induced by painful stimuli. Indeed, previous studies demonstrate that different attentional variables may modulate SEP components in the 40-ms latency range (Desmedt and Tomberg 1989; Garcia-Larrea et al. 1991; Forster and Eimer 2005). However, if our experimental effects were due to a nonspecific increase of pain-related attention, they should have systematically influenced different SEP components (Desmedt and Tomberg 1989; Garcia-Larrea et al. 1991; Forster and Eimer 2005), instead of being selective for the P45. Moreover, nonspecific attentional effects can hardly explain the pattern of correlations between neurophysiological and subjective measures found in the present study.

Neuroimaging and neurophysiological studies indicate that S1 plays a crucial role in encoding the sensory qualities of ones' own pain (Porro et al. 1998; Timmermann et al. 2001). That modulation of P45 correlated with sensory but not with affective aspects of the pain attributed to others greatly extends the above studies by indicating that specific aspects of the pain observed in others are mapped in S1. Thus, the results indicate that the modulation of P45 during observation of others' pain may more directly reflect the activity of a mirror "sensory" mechanism that extracts basic sensory features of others' pain (intensity, localization) and maps them onto the primary somatic cortex.

The reduction of P45 amplitude found in our study during observation of touch expands EEG studies in which amplitude of short-latency (30–50 ms) SEP components induced by electrical stimulation of the right median nerve was reduced by concomitant tactile stimuli to the right hand (Gandevia et al. 1983; Jones and Power 1984; Burke and Gandevia 1988). Indeed, the gating effect found in the above studies and attributed to the interference of 2 physical inputs to S1 may be at work in our study where, however, the interference effect is cross-modally (visuotactile) derived by observation of the touch experience in others. The reduction of P45 amplitude indicates that S1 is an important node in the simulative mirror network for mapping touch in others. This is in keeping with fMRI studies on empathy for touch, which show a somatotopic activation of S1 during observation of tactile stimuli delivered to other individuals (Blakemore et al. 2005).

Conclusions

The S1, classically considered as almost exclusively involved in somatic processing (Penfield and Boldrey 1937), seems to play an important role in complex cognitive functions, including some aspects of social cognition. Indeed, in keeping with simulation theories, previous studies suggest that activity in somatosensory structures during observation of others' emotional facial expressions (Adolphs et al. 2000; Pourtois et al. 2004) or others' bodily sensations (Keysers et al. 2004; Blakemore et al. 2005) could provide a somatic description of what the emotional expression or the sensation would feel like if it were produced or experienced by the observer. We expand current evidence on shared neural modulations elicited by personally experiencing pain or touch and perceiving the same feelings in others. In keeping with previous studies, we show that empathic neural responses to others' bodily sensations may be related to simulation of somatomotor (Keyser et al. 2004; Avenanti et al. 2005, 2006; Blakemore et al. 2005; Minio-Paluello et al. 2006; Saarela et al. 2007), and not just emotional, aspects of others' experience (Morrison et al. 2004; Singer et al. 2004, 2006; Botvinick et al. 2005; Jackson et al. 2005). Our SEP study indicates that neural activity in S1 is modulated by observing

others' painful and nonpainful bodily stimulations. This is similar to the S1 modulation that occurs during real perception of pain and touch stimuli. Naturally, our results do not imply that resonance with pain or touch stimuli occurs in the primary somatic cortex and not in neural structures commonly associated with different forms of empathy such as SII, anterior cingulated, and insular cortices. Indeed the SEP technique, particularly when using the 3-Hz stimulation, is particularly adept to explore neural activity in S1. All in all, the modulation of activity in the S1 found in the present study may reflect the activation of pain and touch resonant systems similar to those called into play during the sharing of motor (Rizzolatti et al. 2001), emotional (Carr et al. 2003; Wicker et al. 2003), and somatic representations (Keysers et al. 2004; Avenanti et al. 2005, 2006; Blakemore et al. 2005; Avenanti and Aglioti 2006; Minio-Paluello et al. 2006). Thus, the somatosensory system may play a crucial role in providing detailed information about one's own and others' sensory states.

Notes

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References

Adolphs R, Damasio H, Tranel D, Cooper G, Damasio AR. 2000. A role for somatosensory cortices in the visual recognition of emotions as revealed by three-dimensional lesion mapping. J Neurosci. 20:2683–2690.

Allison T, McCarthy G, Wood CC. 1992. The relationship between human long-latency somatosensory evoked potentials recorded from the cortical surface and from the scalp. Electroencephalogr Clin Neurophysiol. 84:301–314.

Allison T, McCarthy G, Wood CC, Jones SJ. 1991. Potentials evoked in human and monkey cerebral cortex by stimulation of the median nerve: a review of scalp and intracranial recordings. Brain. 114:2465–2503.

Avenanti A, Aglioti SM. 2006. The sensorimotor side of empathy for pain. In: Mancia M, editor. Psychoanalysis and neuroscience. Milan (Italy): Springer-Verlag. p. 235–256.

Avenanti A, Bueti D, Galati G, Aglioti SM. 2005. Transcranial magnetic stimulation highlights the sensorimotor side of empathy for pain. Nat Neurosci. 8:955–960.

Avenanti A, Paluello IM, Bufalari I, Aglioti SM. 2006. Stimulus-driven modulation of motor evoked potentials during observation of others' pain. Neuroimage. 32:316–324.

Avikainen S, Forss N, Hari R. 2002. Modulated activation of the human SI and SII cortices during observation of hand actions. Neuroimage. 15:640–646.

Barba C, Frot M, Valeriani M, Tonali P, Mauguiere F. 2002. Distinct fronto-central N60 and supra-sylvian N70 middle-latency components of the median nerve SEPs as assessed by scalp topographic analysis, dipolar source modeling and depth recordings. Clin Neurophysiol. 113:981–992.

Baron R, Baron Y, Disbrow E, Roberts TP. 2000. Activation of the somatosensory cortex during Abeta-fiber mediated hyperalgesia. A MSI study. Brain Res. 871:75–82.

Bingel U, Lorenz J, Glauche V, Knab R, Glascher J, Weiller C, Buchel C. 2004. Somatotopic organization of human somatosensory cortices for pain: a single trial fMRI study. Neuroimage. 23:224–232.

Blakemore SJ, Bristow D, Bird G, Frith C, Ward J. 2005. Somatosensory activations during the observation of touch and a case of vision–touch synaesthesia. Brain. 128:1571–1583.

Botvinick M, Jha AP, Bylsma LM, Fabian SA, Solomon PE, Prkachin KM. 2005. Viewing facial expressions of pain engages cortical areas involved in the direct experience of pain. Neuroimage. 25:312–319.

Buchner H, Waberski TD, Fuchs M, Wischmann HA, Beckmann R, Rienacker A. 1995. Origin of P16 median nerve SEP component identified by dipole source analysis—subthalamic or within the thalamo-cortical radiation? Exp Brain Res. 104:511–518.

Burke D, Gandevia SC. 1988. Interfering cutaneous stimulation and muscle afferent contribution to cortical potentials. Electroencephalogr Clin Neurophysiol. 70:118–125.

Bushnell MC, Duncan GH, Hofbauer RK, Ha B, Chen JI, Carrier B. 1999. Pain perception: is there a role for primary somatosensory cortex? Proc Natl Acad Sci USA. 96:7705–7709.

Carr L, Iacoboni M, Dubeau MC, Mazziotta JC, Lenzi GL. 2003. Neural mechanisms of empathy in humans: a relay from neural systems for imitation to limbic areas. Proc Natl Acad Sci USA. 100:5497–5502.

Davis H. 1996. Empathy: a social psychological approach. Madison (WI): Westview Press.

Decety J, Grezes J. 2006. The power of simulation: imagining one's own and other's behavior. Brain Res. 1079:4–14.

Decety J, Jackson PL. 2004. The functional architecture of human empathy. Behav Cogn Neurosci Rev. 3:71–100.

Desmedt JE, Nguyen TH, Bourguet M. 1987. Bit-mapped color imaging of human evoked potentials with reference to the N20, P22, P27 and N30 somatosensory responses. Electroencephalogr Clin Neurophysiol. 68:1–19.

Desmedt JE, Tomberg C. 1989. Mapping early somatosensory evoked potentials in selective attention: critical evaluation of control conditions used for titrating by difference the cognitive P30, P40, P100 and N140. Electroencephalogr Clin Neurophysiol. 74:321–346.

Fogassi L, Ferrari PF, Gesierich B, Rozzi S, Chersi F, Rizzolatti G. 2005. Parietal lobe: from action organization to intention understanding. Science. 308:662–667.

Forster B, Eimer M. 2005. Vision and gaze direction modulates tactile processing in somatosensory cortex: evidence from event-related brain potentials. Exp Brain Res. 165:8–18.

Frot M, Mauguière F. 1999. Timing and spatial distribution of somatosensory responses recorded in the upper bank of the sylvian fissure (SII area) in humans. Cereb Cortex. 9:854–863.

Gallese V. 2003. The manifold nature of interpersonal relations: the quest for a common mechanism. Philos Trans R Soc Lond B Biol Sci. 358:517–528.

Gallese V, Fadiga L, Fogassi L, Rizzolatti G. 1996. Action recognition in the premotor cortex. Brain. 119:593–609.

Gandevia SC, Burke P, McKeon B. 1983. Convergence in the somatosensory pathway between cutaneous afferents from index and middle finger in man. Exp Brain Res. 50:415–425.

Garcia-Larrea L, Bastuji H, Mauguiere F. 1991. Mapping study of somatosensory evoked potentials during selective spatial attention. Electroencephalogr Clin Neurophysiol. 80:201–214.

Garcia-Larrea L, Bastuji H, Mauguiére F. 1992. Unmasking of cortical SEP components by change in stimulus rate: a topographic study. Electroencephalogr Clin Neurophysiol. 84:71–83.

Humphrey DR. 1968a. Re-analysis of the antidromic cortical response. I. Potentials evoked by stimulation of the isolated pyramidal tract. Electroencephalogr Clin Neurophysiol. 24:116–129.

Humphrey DR. 1968b. Re-analysis of the antidromic cortical response. II. On the contribution of cell discharge and PSPs to evoked potentials. Electroencephalogr Clin Neurophysiol. 24:421–442.

Huttunen J, Homberg V. 1991. Influence of stimulus repetition rate on cortical somatosensory potentials evoked by median nerve stimulation: implications for generation mechanisms. J Neurol Sci. 105:37–43.

Inui K, Wang X, Qiu Y, Nguyen YT, Ojima S, Tamura Y, Nakata H, Wasaka T, Tran TD, Kakigi R. 2003. Pain processing within the primary somatosensory cortex in humans. Eur J Neurosci. 18:2859–2866.

Jackson PL, Brunet E, Meltzoff AN, Decety J. 2006. Empathy examined through the neural mechanisms involved in imagining how I feel versus how you feel pain. Neuropsychologia. 44:752–761.

Jackson PL, Meltzoff AN, Decety J. 2005. How do we perceive the pain of others? A window into the neural processes involved in empathy. Neuroimage. 24:771–779.

Jones SJ, Power C. 1984. Scalp topography of human SEPs: the effect of interfering tactile stimuli applied to the hand. Electroencephalogr Clin Neurophysiol. 58:25–36.
Kanda M, Nagamine T, Ikeda A, Ohara S, Kunieda T, Fujiwara N, Yazawa S, Sawamoto N, Matsumoto R, Taki W, Shibasaki H. 2000. Primary somatosensory cortex is actively involved in pain processing in human. Brain Res. 853:282–289.
Kenshalo DR Jr, Isensee O. 1983. Responses of primate S1 cortical neurons to noxious stimuli. J Neurophysiol. 50:1479–1496.
Keysers C, Wicker B, Gazzola V, Anton JL, Fogassi L, Gallese V. 2004. A touching sight: SII/PV activation during the observation and experience of touch. Neuron. 42:335–346.
Li CL. 1961. Cortical intracellular synaptic potentials. J Cell Comp Physiol. 58:153–167.
Maihofner C, Schmelz M, Forster C, Neundorfer B, Handwerker HO. 2004. Neural activation during experimental allodynia: a functional magnetic resonance imaging study. Eur J Neurosci. 19:3211–3218.
McCarthy G, Wood CC. 1985. Scalp distributions of event-related potentials: an ambiguity associated with analysis of variance models. Electroencephalogr Clin Neurophysiol. 62:203–208.
Melzack R. 1999. From the gate to the neuromatrix. Pain. 6(Suppl): 121–126.
Minio-Paluello I, Avenanti A, Aglioti SM. Forthcoming 2006. Left hemisphere dominance in reading the sensory qualities of others' pain? Soc Neurosci.1:320–333.
Morrison I, Lloyd D, di Pellegrino G, Roberts N. 2004. Vicarious responses to pain in anterior cingulate cortex: is empathy a multisensory issue? Cogn Affect Behav Neurosci. 4:270–278.
Ogino Y, Nemoto H, Inui K, Saito S, Kakigi R, Goto F. July 19, 2006. Inner experience of pain: imagination of pain while viewing images showing painful events forms subjective pain representation in human brain. Cereb Cortex. 10.1093/cercor/bhl023.
Oldfield RC. 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia. 9:97–113.
Penfield W, Boldrey E. 1937. Somatic motor and sensory representation of man as studied by electrical stimulation. Brain. 60:389–443.
Peyron R, Laurent B, Garcia-Larrea L. 2000. Functional imaging of brain responses to pain. A review and meta-analysis. Clin Neurophysiol. 30:263–288.
Peyron R, Schneider F, Faillenot I, Convers P, Barral FG, Garcia-Larrea L, Laurent B. 2004. An fMRI study of cortical representation of mechanical allodynia in patients with neuropathic pain. Neurology. 63:1838–1846.
Ploner M, Schmitz F, Freund HJ, Schnitzler A. 2000. Differential organization of touch and pain in human primary somatosensory cortex. J Neurophysiol. 83:1770–1776.
Porro CA, Cettolo V, Francescato MP, Baraldi P. 1998. Temporal and intensity coding of pain in human cortex. J Neurophysiol. 80:3312–3320.
Pourtois G, Sander D, Andres M, Grandjean D, Reveret L, Olivier E, Vuilleumier P. 2004. Dissociable roles of the human somatosensory and superior temporal cortices for processing social face signals. Eur J Neurosci. 20:3507–3515.
Preston SD, de Waal FBM. 2002. Empathy: its ultimate and proximate bases. Behav Brain Sci. 25:1–71.
Rizzolatti G, Fogassi L, Gallese V. 2001. Neurophysiologic mechanisms underlying the understanding and imitation of action. Nat Rev Neurosci. 2:661–670.
Rossi S, Tecchio F, Pasqualetti P, Ulivelli M, Pizzella V, Romani GL, Passero S, Battistini N, Rossini PM. 2002. Somatosensory processing during movement observation in humans. Clin Neurophysiol. 113:16–24.
Saarela MV, Hlushchuk Y, Williams AC, Schurmann M, Kalso E, Hari R. 2007. The compassionate brain: humans detect intensity of pain from another's face. Cereb Cortex. 17:230–237.
Schaefer M, Flor H, Heinze HJ, Rotte M. 2006. Dynamic modulation of the primary somatosensory cortex during seeing and feeling a touched hand. Neuroimage. 29:587–592.
Singer T, Seymour B, O'Doherty J, Kaube H, Dolan RJ, Frith CD. 2004. Empathy for pain involves the affective but not sensory components of pain. Science. 303:1157–1162.
Singer T, Seymour B, O'Doherty JP, Stephan KE, Dolan RJ, Frith CD. 2006. Empathic neural responses are modulated by the perceived fairness of others. Nature. 439:466–469.
Timmermann L, Ploner M, Haucke K, Schmitz F, Baltissen R, Schnitzler A. 2001. Differential coding of pain intensity in the human primary and secondary somatosensory cortex. J Neurophysiol. 86:1499–1503.
Valeriani M, Barba C, Le Pera D, Restuccia D, Colicchio G, Tonali P, Gagliardo O, Treede RD. 2004. Different neuronal contribution to N20 somatosensory evoked potential and to CO2 laser evoked potentials: an intracerebral recording study. Clin Neurophysiol. 115:211–216.
Valeriani M, Le Pera D, Tonali P. 2001. Characterizing somatosensory evoked potential sources with dipole models: advantages and limitations. Muscle Nerve. 24:325–339.
Valeriani M, Restuccia D, Di Lazzaro V, Le Pera D, Barba C, Tonali P, Mauguiere F. 1998. Dipolar source of the early scalp somatosensory evoked potentials to upper limb stimulation. Effect of increasing stimulus rates. Exp Brain Res. 120:306–315.
Waberski TD, Buchner H, Perkuhn M, Gobbele R, Wagner M, Kucker W, Silny J. 1999. N30 and the effect of explorative finger movements: a model of the contribution of the motor cortex to early somatosensory potentials. Clin Neurophysiol. 110:1589–1600.
Wicker B, Keysers C, Plailly J, Royet JP, Gallese V, Rizzolatti G. 2003. Both of us disgusted in my insula: the common neural basis of seeing and feeling disgust. Neuron. 40:655–664.