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Report

Expertise Modulates the Perception of Pain in Others

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Summary

Perceiving the pain of others activates a large part of the pain matrix in the observer [1]. Because this shared neural representation can lead to empathy or personal distress [2, 3], regulatory mechanisms must operate in people who inflict painful procedures in their practice with patient populations in order to prevent their distress from impairing their ability to be of assistance. In this functional magnetic resonance imaging MRI study, physicians who practice acupuncture were compared to naive participants while observing animated visual stimuli depicting needles being inserted into different body parts, including the mouth region, hands, and feet. Results indicate that the anterior insula somatosensory cortex, periaqueducal gray, and anterior cingulate cortex were significantly activated in the control group, but not in the expert group, who instead showed activation of the medial and superior prefrontal cortices and the temporoparietal junction, involved in emotion regulation and theory of mind.

Results

We investigated the difference in the neurohemodynamic response between two groups of participants (medical doctors with at least 2 years of practice in acupuncture, experts; and age and educational matched individuals, controls) who were scanned while watching dynamic visual stimuli depicting body parts in both nonpainful situations (being touched with a Q-tip) and (potentially painful) acupuncture (being pricked by needles) situations. We predicted that the pain matrix would be differentially activated in expert participants with experience in administering acupuncture as compared to control participants when watching acupuncture procedures. Indeed, although participants who have expertise in acupuncture procedures know that such situations can be painful for their patients, they have learned throughout their training and practice to keep a detached perspective; without such a mechanism, performing their clinical practice could be overwhelming or distressing. Therefore, we anticipated that the regions involved in the affective aspects of pain processing, namely the anterior insula and anterior cingulate cortex (ACC), would not show increased activation in the expert group. Instead, regions associated with emotion regulation and cognitive control, such as the medial and dorsolateral prefrontal cortices, were predicted to show selective activation in expert population. We further predicted an enhanced self-other distinction in the expert group, represented neurally as additional activation of the right temporoparietal junction, an area known to play a crucial role in self-other distinction processes and theory of mind [2, 4].

The analyses of the dispositional measures revealed no difference between the two groups [main effect of the group, $F(1, 13) = 1.273$, $p = 0.28$] (Table 1). However, the two one-way analyses of variance (ANOVAs) on the visual analog scale (VAS) ratings indicated significant differences between the two groups separately for pain intensity [$F(1, 26) = 18.887$, $p = 0.00019$] and unpleasantness [$F(1, 26) = 22.465$, $p = 0.00007$], such that control participants reported significantly higher pain intensity and unpleasantness ratings than did expert participants. Similar ratings from watching different body parts (mouth, hand, and foot) were also found [pain intensity: $F(2, 39) = 0.197$, $p = 0.912$; unpleasantness: $F(2, 39) = 0.67$, $p = 0.893$]. All participants correctly reported the number of stops on the continuous performance task when watching the visual stimuli in the scanning sessions.

The observation of body parts in painful situations (needle versus fixation) in the control participants resulted in the activation of a neural network similar to that observed in previous studies of pain empathy, including regions involved in the sensory and affective processing of pain (see Table S1 in the Supplemental Data available online). In contrast, the expert group showed no signal change in the insula and ACC (even when results were examined at the most liberal threshold). Instead, in the expert group, robust activation was detected in occipital, hippocampus, and precentral gyri, which indicates that participants had indeed attended to the stimuli. The observation of body parts in nonpainful situations (Q-tip versus fixation) elicited similar brain activity without involving the pain matrix in both the control and expert groups (see Table S2).

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Table 1. Dispositional Measures of Empathy and Ratings of Pain Intensity and Unpleasantness in the Expert and Control Groups

	Experts (n = 14)		Controls (n = 14)	
Task	Mean	SD	Mean	SD
EQ	30.7	14.3	24.6	19.4
EC	25.8	2.9	25.7	5.5
IRI (PT)	17.8	4.4	16.9	3.8
IRI (EC)	21.8	3.6	20.1	3.5
IRI (PD)	13.1	4.4	13.7	5.0
IRI (FS)	17.6	3.8	15.6	7.8
SPQ	5.5	0.7	5.5	1.2
PAIN	4.1	1.7	6.5	1.2
UNPL	3.5	1.9	6.5	1.4

The following abbreviations are used: empathy quotient (EQ), emotional contagion scale (EC), interpersonal reaction index (IRI), perspective taking (PT), empathic concern (EC), personal distress (PD), fantasy (FS), situational pain questionnaire (SPQ), pain intensity ratings (PAIN), and unpleasantness ratings (UNPL). Ratings of pain intensity ($p = 0.00019$) and unpleasantness ($p = 0.00007$); underlined rows report significant difference between the expert and control groups.

The differential activation of watching the painful (needle) and nonpainful (Q-tip) situations within each group confirmed that the control participants but not the expert participants activated the pain matrix when watching body parts being pricked by a needle relative to being touched by a Q-tip (see Table S3). Specifically, a significant signal increase was detected in the anterior medial cingulate cortex (aMCC) (x 4, y 18, z 45) and bilateral anterior insula (x 40, y 20, z −10; x −36, y 16, z −2), as well as the periaqueducal gray (PAG). Direct comparison between the controls and experts revealed that the activity in the ACC and bilateral insula was reliably greater in the controls when watching the acupuncture procedures. In contrast, the activity in the parahippocampal gyrus, medial prefrontal cortex (mPFC) (x 4, y 62,z 6), superior frontal gyrus (x 14, y 42, z 50), and right temporoparietal junction (x 36, y −54, z 40) was stronger in the experts while performing the same task (see Table S4) (Figure 1). Besides, the left postcentral gyrus (x −60, y −26, z 20) was activated in the controls, a finding consistent with the automatic mapping of seen pain onto the (contralateral) sensorimotor cortex [5, 6]; whereas the right postcentral gyrus (x 50, y −14, z 28) was activated in the experts. For the Q-tip stimuli, however, no such double dissociation was observed (see Table S5).

So that the differential activity related to the effect of expertise could be uncovered, an interaction analysis was calculated for the two contrasts (controls watching needles versus Q-tips and experts watching needles versus Q-tips). This interaction demonstrates that the controls had stronger bilateral activation in the insula (x 40, y 22, z −14; x −38, y 16, z −8) and ACC (x 0, y 24, z 30) than did the experts. The reverse comparison, however, shows that the experts had stronger activation in the superior frontal gyrus (x 14, y 34, z 48; x −12, y 24, z 52) and mPFC (x −14, y 58, z 8; x 10, y 60, z 14) than did the controls (see Table S6). This suggests that the significance of the interaction was mainly driven from the

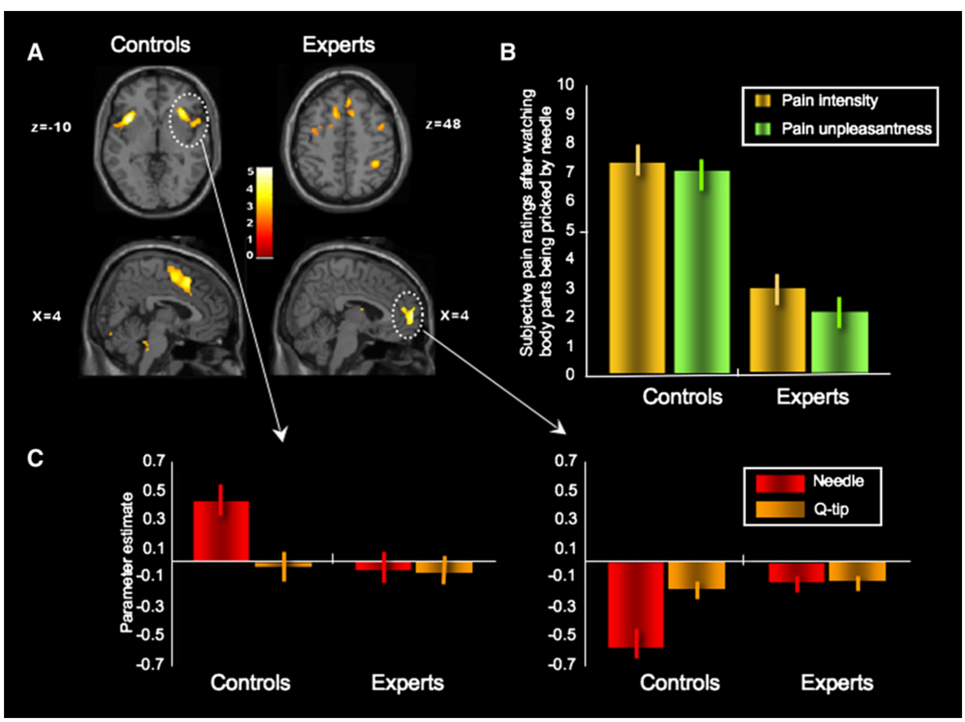

Figure 1. Differential Neural Activations between the Experts and Controls When Watching Body Parts Being Pricked by an Acupuncture Needle

(A) Participants from the control group activated bilateral insula, PAG, ACC, and SMA, whereas participants from the expert group activated right inferior parietal lobule and medial prefrontal gyrus.

(B) Compared to the expert group, participants from the control group scored significantly higher on pain intensity and unpleasantness ratings.

(C) Parameter estimate graphs show signal change in the insula and medial prefrontal cortex for each condition in each group. When watching acupuncture procedures, stronger activation was detected in the anterior insula in the control group, whereas the experts showed stronger activation in the medial prefrontal cortex. When watching a Q-tip, there is no such double dissociation.

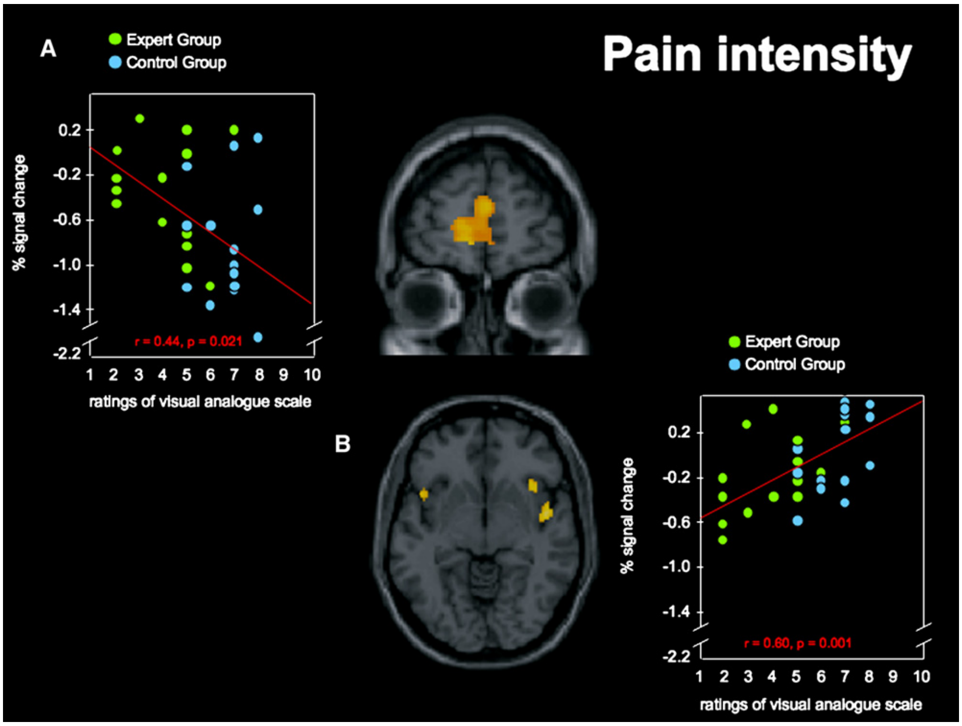

Figure 2. Correlations between Pain Intensity Ratings and the Hemodynamic Responses of All Participants When Watching the Mouth Region Being Pricked by an Acupuncture Needle

(A) The activation in the medial prefrontal cortex is negatively correlated with ratings of pain intensity.

(B) The activation in the insula shows a significant positive correlation with ratings of pain intensity.

needle stimuli between two groups instead of the Q-tip. Here, we also plotted the parameter estimate graphs to illustrate the interaction between the two groups and stimulus category (Figure 1).

The random-effect correlation analysis between the brain BOLD response and VAS ratings in the two groups disclosed that ratings of pain intensity correlated positively with anterior insula (x −38, y 10, z −4; t = 3.23) and anterior cingulate cortex (x 4, y 8, z 44; t = 4.94) but negatively with mPFC (x 0, y 62, z 4; t = 4.31) and superior frontal gyrus (x 26, y 22, z 56; t = 3.23) (Figure 2). For unpleasantness ratings, there was also positive correlation in the activity of insula and ACC but negative correlation in the superior frontal gyrus and mPFC (see Table S7). Besides, the analysis separately conducted within each group (experts and controls) also showed similar correlations (see Table S8). Thus, higher pain intensity and unpleasantness ratings, which the controls were more likely to give, were associated with stronger activation in the anterior insula and ACC but weaker activation in the mPFC.

The psychophysiological interaction (PPI) analysis indicated that the experts differed from the controls in how activity in the mPFC covaried with the insula. The experts revealed negative covariation of mPFC with anterior insula (centered at −40, 14, −8; $p < 0.01$). Instead, the controls showed neither negative nor positive covariation with mPFC ($p < 0.01$, $k \geq 50$). This suggests that the experts had stronger functional connectivity between mPFC and insula than did the controls.

Watching different body parts (mouth, hand, and foot) being pricked by a needle and touched by a Q-tip was associated with signal increase in the somatosensory cortex. A region of interest (ROI) analysis performed at the postcentral gyrus (x −40, y −44, z 60) showed that watching painful situations resulted in a stronger signal increase than did watching nonpainful situations [$F(1, 13) = 18.971$, $p = 0.001$]. The controls displayed a stronger signal increase than did the experts [$F(1, 13) = 5.097$, $p = 0.041$] (see Figure 3). The interaction of the body part and stimulus type reached significance [$F(2, 26) = 6.159$, $p = 0.014$], but the interaction of the group and stimulus type tended to significance [$F(1, 13) = 3.124$, $p = 0.052$]. Notably, watching the mouth and hand regions being pricked by a needle was associated with stronger signal than was watching a Q-tip in the controls (mouth: $p = 0.0002$; hand: $p = 0.0483$), whereas the Q-tip and needle resulted in similar signal changes of the postcentral gyrus in the experts (mouth: $p = 0.3151$; hand: $p = 0.1030$).

Discussion

In recent years, a number of functional neuroimaging studies have shown striking similarities in the neural circuits involved in the processing of both the first-hand experience of pain and by the sight of other individuals in pain [1]. These studies have consistently shown that the perception of pain in others elicits the activation of the neural circuit subserving the processing of the affective and motivational dimensions of pain [3, 7–18]. This neural circuit includes the anterior cingulate cortex (ACC) and anterior insula [19]. In addition, transcranial magnetic resonance [5], somatosensory-evoked potentials [20], and magnetoencephalography (MEG) studies

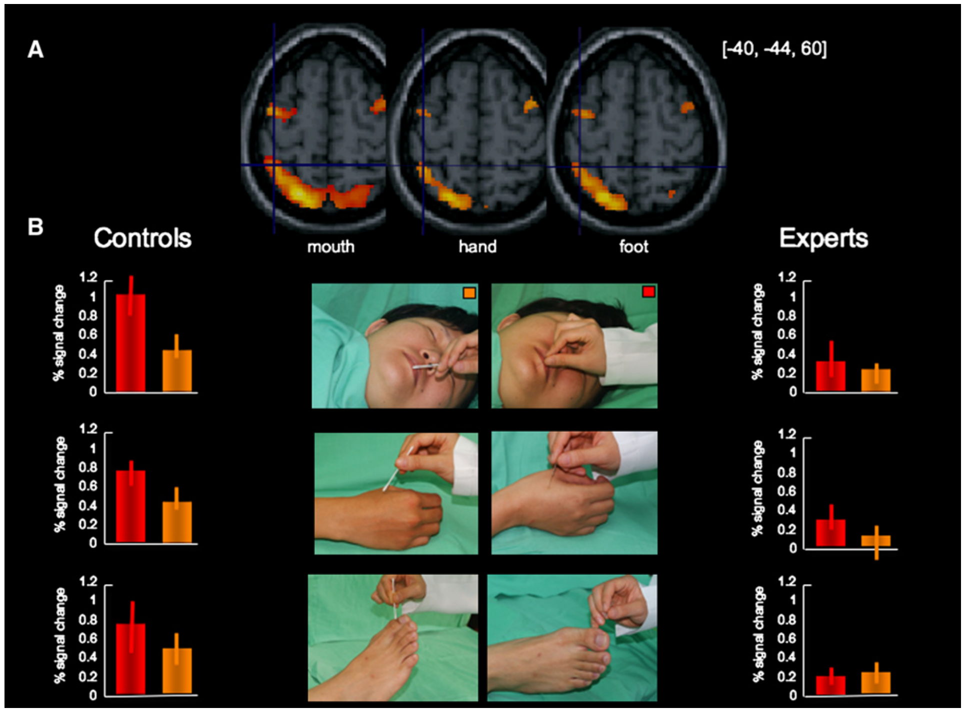

Figure 3. Region of Interest Activity within the Somatosensory Cortex When Watching Different Body Parts Being Pricked by a Needle and Touched by a Q-Tip in the Expert and Control Groups

(A) Watching different body parts (from left to right: mouth region, hand, foot) elicited the differential activations around the somatosensory cortex (−40, −44, 60).

(B) The somatosensory activations are modulated by the expertise of the participants and the level pain inferred. Watching the painful situations (needle) induced apparently stronger response than did the nonpainful situations (Q-tip) [$F(1, 13) = 18.971$, $p = 0.001$]. The activation was greater in the control group than it was in the expert group [$F(1, 13) = 5.097$, $p = 0.041$]. The interaction of the body part and stimulus type reached significance [$F(2, 26) = 6.159$, $p = 0.014$], but the interaction of the group and stimulus type tended to significance [$F(1, 13) = 3.124$, $p = 0.052$]. Notably, watching the mouth and hand regions pricked by a needle was associated with stronger signal than was watching a Q-tip in the controls (mouth: $p = 0.0002$; hand: $p = 0.0483$), whereas the Q-tip and needle resulted in similarly signal changes in the postcentral gyrus in the experts (mouth: $p = 0.3151$; hand: $p = 0.1030$).

[6] have demonstrated that areas processing the sensory dimension of pain processing can also be elicited by the mere visual perception of pain in others. Altogether, there is strong evidence to suggest that the perception of the pain of others triggers an automatic resonance mechanism between other and self, emulating almost the entire neural pain matrix. Such a mechanism provides a functional bridge between first-person and third-person information on which the experience of empathy develops.

Yet the significant overlap in neural circuits between self and other has the potential to instigate personal distress, i.e., a self-oriented aversive emotional response [2, 3]. However, it would not be adaptive if this automatic sharing mechanism for pain was not modulated by cognitive control and metacognition. Think, for instance, of situations that surgeons, dentists, and nurses face in their everyday professional practices. Without some regulatory mechanism, it is very likely that medical practitioners would experience personal distress and anxiety that would interfere with their ability to heal.

Here, we investigated how the neural circuits associated with the perception of pain in others are modulated by the expertise of observer and found a clear effect of expertise in trials involving watching body parts being pricked by a needle. In participants from the control group, the perception of painful situations was associated with a signal increase in areas underlying the neural processing of the affective dimension of pain, including the anterior insula, aMCC, supplementary motor area, and also the somatosensory cortex and the PAG. This is in line with previous studies on pain empathy that have reliably detected the activation in these regions [7–17]. Notably, the PAG is part of a circuit that controls nociceptive neurons in the dorsal horn of the spinal cord and is considered to be an important site for the integration of homeostatic control and limbic motor output in response to threats [21]. It has been argued that the PAG serves as the coordinator of the panic response and is thus at the base of the hierarchically organized neuroanatomical threat-defense system [22]. However, these regions (i.e., the ACC, insula, and PAG) were not activated in the expert group. Instead, when expert participants watched painful situations, activation was found in the parahippocampal gyrus, middle frontal gyrus, medial prefrontal cortex, and right inferior parietal lobule. Interestingly, experts rated these situations as significantly less unpleasant and painful that did the control participants. These differences cannot be attributed to dispositional variables such as sensitivity to pain, empathy disposition, or emotion contagion because the two groups did not differ on these personality traits (see Table 1). It is also unlikely that this difference was due to attentional demands because both groups performed similarly on the continuous performance task.

We argue that the difference in activated neural networks between the two groups reflects top-down processes, induced by one's degree of knowledge about acupuncture. The parahippocampal gyrus is known to play a key role in memory retrieval. This, in conjunction with areas implicated in executive control, theory of mind, and emotion regulation, such as the dorsolateral and medial prefrontal cortex, contribute in the regulation of how these individuals attend and appraise a painful situation [2, 3]. The fact that the temporoparietal region was selectively activated in the expert group provides additional support for the role of this region in self-other distinction and metacognition [4], and support the notion that a complete self-other overlap would be detrimental to expert practice. Rather than suggesting that humans respond on the basis of automatically activated stimulus-response linkages, the present findings support the notion that humans regulate their emotions by relying on higher cognitive processes involving knowledge in working memory, long-term memory, and metacognition [23].

Additionally, the differential behavioral VAS ratings observed between the experts and controls, their correlation with the hemodynamic response, and the PPI analysis support our claim that expertise modulates the pain matrix. This is illustrated by the fact that the insula activation in the expert group did not reach the statistical threshold, even though that of the control group did. Participants from the expert group also displayed significantly lower VAS ratings, even when they had similar dispositional empathy measures, reflecting a relative insensitivity to the acupuncture observations. These results match those of a previous study by Jackson, Meltzoff, and Decety [8] that found a positive correlation between the activity of the ACC and insula and subjective pain ratings. Besides, the medial prefrontal cortex cognitively controlling the pain matrix correlated negatively with the pain ratings. In other words, lower VAS ratings, which the participants from the expert group are more likely to give, correlated with weaker activation of insula but with stronger activation of mPFC (see Figure 2). Importantly, the PPI analysis further revealed that the experts, not the controls, have a significant negative functional connectivity between mPFC and insula. We therefore argue from the present findings that the experts' insensitivity to the acupuncture procedures might result from the cognitive inhibition of the affective processing in the pain matrix.

In both groups, observing body parts being touched by a Q-tip was associated with activation of the somatosensory cortex. This is in accordance with previous neuroimaging studies reporting similar results in individuals watching [20, 24, 25] or even imagining [26] different body parts being touched. However, because no clear somatotopic organization was detected that could distinguish which body part was being touched, general interindividual variability in somatotopic maps might play a role. Indeed, one functional MRI (fMRI) study investigated the response of the somatosensory cortex to different somatic stimuli applied to the lips, face, trunk, and foot [27]; the authors found that the pattern of activation generated by the same stimulus was highly variable across subjects. In addition, large overlaps between the representations of the different body parts in second the somatosensory cortex (SII) were found, and these overlaps are thought to serve the purpose of integrating information across body parts. Interestingly, activation in the somatosensory cortex was present during the observation of needle insertions, and significantly stronger than it was during the observation of Q-tips. In line with this finding, transcranial magnetic stimulation experiments and electroencephalographic studies demonstrated that somatic resonance occurs during the perception of pain in others [5, 6, 20]. By contrast, this effect was not seen in the expert group: The activity level did not change between the two conditions (Q-tip and needle).

Overall, our study clearly demonstrates that learned experience and metacognition play a role in the way we perceive other people in pain (reflecting a difference between theory of mind in experts and empathy in controls). Activation in the regions underpinning the affective-motivational aspects of pain processing, as detected in the control group, was suppressed in the expert group. People who practice acupuncture know that such situations can be painful for their patients and have learned throughout their training to inhibit the empathy-pain response. This knowledge is important for them to regulate their feelings of unpleasantness generated by the perception of pain in others, and is therefore necessary for successful professional practice. Our results add to the recent findings that the perception of pain can be modulated by attentional demands [18], as well as by social relations between individuals [17]. However, it should be acknowledged that, because of the low temporal resolution of fMRI-BOLD responses, it is not possible to tell when the top-down modulation occurs in the pain matrix. To address this issue, we are replicating this experiment by using event-related potential measures with a similar paradigm.

Experimental Procedures

Participants

Twenty-eight (14 females) right-handed participants were enrolled in the study (Mean age 35; standard deviation [SD] 8 years) after providing written informed consent approved by the local ethics committee. One group (n = 14; seven females) was composed of physicians with experience in acupuncture for at least 2 years (expert group). The other group, matched for age and educational level (n = 14; seven females) was composed of participants with no acupuncture experience (control group). All participants had no history of neurological or psychiatric disorders and were free of medication at the time of the testing. Participants received monetary compensation for their participation. Prescreening interviews were conducted so that the level of expertise in acupuncture could be determined.

Dynamic Visual Stimuli

Participants were shown 120 3 s dynamic visual stimuli (120 GIF files). These stimuli consisted of pictures of different body parts (40 for mouth region, 40 for hand, and 40 for foot). All body parts were chosen with the assistance of an acupuncture physician with over ten years of practice to be appropriate acupuncture sites. In half of the stimuli, the body parts were touched by a Q-tip (nonpainful situations), and in the other half they were pricked by an acupuncture needle (painful situations).

General Procedures

One week before the scanning session, participants filled out a series of self-report dispositional measures, including the situational pain questionnaire (SPQ) that assess sensitivity to pain [28], the emotional contagion scale (ECS) [29], the interpersonal reactivity index (IRI) [30], and the empathy quotient (EQ) [31].

Functional MRI scanning consisted of three runs (one with the mouth region, one with the foot region, and one with the hand region) in a block design. The visual stimuli were shown in 30 s blocks, with 30 s fixation periods between blocks. Each run included three repetitions of the situations with body parts being either touched by Q-tip or pricked by a needle. The order of the blocks was randomized in each run. The order of the runs was randomized and counterbalanced across participants. A continuous performance task was used in order to make sure that participants attended to the stimuli presentation. Specifically, the stimuli presentation was interrupted by a brief pause at random intervals, and participants were requested to report at the end of each run how many stops they had seen in the stimuli.

After being scanned, participants were asked to rate pain intensity and pain unpleasantness with the same visual dynamic situations that they had seen in the scanner by using a computerized visual-analogical scale (VAS) with no pain to extreme pain and no effect to extreme unpleasantness as target words.

Supplemental Data

Experimental Procedures and eight tables are available at http://www.current-biology.com/cgi/content/full/17/19/1708/DC1/.

Acknowledgments

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