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Research Report

The effects of acupuncture on the brain networks for emotion and cognition: An observation of gender differences

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ABSTRACT

Acupuncture modulates brain activity at the limbic–paralimbic–neocortical network (LPNN) and the default mode network (DMN). Since these brain networks show gender differences when mediating emotional and cognitive tasks, we thus hypothesize that women and men may also respond differently to acupuncture procedure at these brain regions. In order to test this hypothesis, we retrieved the data of 38 subjects, 19 females and 19 males, who had brain fMRI during acupuncture from previous studies and reanalyzed them based on sex status. Deactivation at the LPNN/DMN during needle manipulation of acupuncture was more extensive in females than in males, particularly in the posterior cingulate (BA31), precuneus (BA7m) and angular gyrus (BA39). The functional correlations between the right BA31 and pregenual cingulate (BA32), hippocampus or contralateral BA31 were significantly stronger in females than in males. The angular gyrus (BA39) was functionally correlated with BA31 in females; in contrast, it was anticorrelated with BA31 in males. Soreness, a major component of the psychophysical responses to needle manipulation, *deqi*, was correlated in intensity with deactivation of the angular gyrus in females; no such relationships were observed in males. In contrast to lesser deactivation at the LPNN/DMN networks, needle manipulation during acupuncture induced greater activation at the secondary somatosensory cortex and stronger functional connectivity with the anterior-middle cingulate (BA32/24) in males than in females. Our study suggests that brains with sex dimorphism may process the acupuncture stimulation differently between women and men.

1. Introduction

Acupuncture, an ancient Chinese needle treatment, is used to relieve the clinical symptoms of pain, mood, and autonomic related disorders (Lundeberg et al., 2007). During the acupuncture procedure, needle is inserted at acupoints and then rotated manually. This manipulation of the needle after insertion induces *deqi*, a composite of unique sensations such as soreness, aching, pressure and heaviness, which is essential to the efficacy of acupuncture according to traditional Chinese medicine (Kong et al., 2007). It is proposed that pronounced action on the limbic system of the brain during the needle manipulation

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may underlie the beneficial effects of acupuncture on the clinical symptoms (Hui et al., 2007).

Using functional magnetic resonance imaging (fMRI), we and others have demonstrated that acupuncture produces deactivation of the limbic–paralimbic–neocortical network (LPNN) including the amygdala, hippocampus, septal nuclei, cingulate gyrus, precuneus and angular gyrus coupled with activation of the sensorimotor network (SMN) and a few paralimbic structures (Hui et al., 2005; Kong et al., 2007; Bai et al., 2007; Wang et al., 2007; Dhond et al., 2008; Fang et al., 2008; Qin et al., 2008). These limbic and limbic-associated structures have been shown to play a primary role in regulating emotion (Joseph, 1992; LeDoux, 1998). Furthermore, we have observed a marked similarity of the hemodynamic response to acupuncture with that of the default mode network (DMN) to attention tasks such as the cognitive examination (Buckner and Vincent, 2007; Raichle et al., 2001). The DMN structures modulated by acupuncture include 1) the frontal pole (FP) and the anterior cingulate in the medial prefrontal cortex (mPFC); 2) the hippocampus in the medial temporal lobe (MTL) and 3) the posterior cingulate (BA31), retrosplenial cortex (RSC) and precuneus (PCN) in the medial parietal cortex (MPC) (Bai et al., 2007; Dhond et al., 2008; Fang et al., 2008; Hui et al., 2005; Qin et al., 2008; Wang et al., 2007).

While sex is a biological term used to describe female vs. male, gender is a social term used to describe the identification of female vs. male. Although the majority of the studies do not measure sex hormones, except in some unusual situations, gender and sex are identical for the human subjects in the research studies. Studies have shown that the LPNN and DMN are sexually differentiated (Joseph, 2000), and sex dimorphisms exhibit significantly at the amygdala, hippocampus and neocortex (Juraska, 1991; Cahill, 2006). Functionally, gender differences in the brain are observed in the limbic system or the DMN when conducting emotional or cognitive tasks (Gur et al., 2000; Cahill et al., 2004; Goldstein et al., 2005). Though women seek complementary treatment modalities including acupuncture more frequently than men (Ben-Arye et al., 2009), the majority of studies evaluating acupuncture effects combine genders. Lund and Lundeberg (2008) have noticed that pain shows gender variations that might influence acupuncture treatment (Lund and Lundeberg, 2008)";. Brain fMRI shows the gender differences when experiencing calibrated pain (Kong et al., 2010a,b) or during resting state (Kong et al., 2010a,b). Because gender differences are shown in the LPNN and the DMN to mediate the tasks of emotion, cognition and pain and that these neural networks are also affected by acupuncture, we hypothesize that women and men may have different brain activation/deactivation patterns at the LPNN and the DMN in response to acupuncture procedure. In this study, using fMRI, we compared neural responses of the task-negative LPNN/DMN as well as the task-positive SMN in response to needle manipulation of acupuncture between two genders.

2. Results

2.1. Subjects

Data on 38 subjects (19 females and 19 males) who had brain fMRI during acupuncture at matched acupoints were used for this study. All the subjects reported *deqi* sensations with a minimum total score of 3, and none reported sharp pain during needle manipulation. Females were comparable with males in age (Mean ± SE: 28.7 ± 1.8 vs. 29.4 ± 2.0) and ethnicity (percentage of Caucasian: 68% *vs.* 74%) (Table 1). There was no statistical difference in the total score of *deqi* between two genders (Table 1). The status of feeling anxious during the procedure between the two sex groups was also similar.

2.2. The BOLD deactivation/activation patterns induced by acupuncture needle manipulation between females and males

Consistent with our previous study (Hui et al., 2005; Napadow et al., 2007), needle manipulation during acupuncture induced clusters of the deactivated regions, especially at the pregenual cingulate (BA32/24), subgenual area (SG25), temporal pole, medial temporal lobe, posterior cingulate (BA31), precuneus and the visual cortex (BA18/19), in both females and males (Fig. 1). However, the procedure induced more extensive decreases in signal intensity in the regions that are known to be core regions of the DMN, especially marked in the posterior cingulate (BA31) and precuneus, in females than in males ($P < 0.0001$) (Fig. 2A). Using peak signal changes, the left angular gyrus (BA39) showed deactivation in females but activation in males during acupuncture needle manipulation (Fig. 1). The differences in signal intensities at the area of the angular gyrus on both left and right sides were more deactivated in females than in males ($P < 0.0001$) (Fig. 2B).

Activation of the brain during acupuncture procedure was more limited in distribution, occurring primarily in the somatosensory and association cortices, the insula and the anterior middle cingulate in both genders (Fig. 1). In contrast to having weaker deactivation of the task-positive LPNN/DMN networks, males had stronger activation at the sensorimotor brain regions during acupuncture than females, as shown by the peak signal changes in the supplementary motor area (SMA), contralateral secondary somatosensory cortex (SII), posterior cingulate (BA23 dorsal), posterior middle cingulate (BA24 dorsal) and middle temporal gyrus (BA22) (Fig. 1). For differences of regional signal change, females had less activation at left contralateral SII and deactivation at right SII as opposed to male subjects who had activation at both sides ($P < 0.0001$) (Fig. 2C); no significant difference was observed between genders in other sensorimotor, insula and cerebellar vermis regions (data not shown).

Table 1 – Sample characteristics by subjects' sex.

	Female n = 19	Male n = 19	P value
Age, year, mean ± SE	28.7 ± 1.8	29.4 ± 2.0	0.79
Caucasians, n/total (%)	13/19 (68%)	14/19 (74%)	0.59
Total *deqi* score, mean ± SE	10.0 ± 1.4	8.0 ± 1.1	0.27
Aching score, mean ± SE	1.9 ± 0.4	1.6 ± 0.3	0.55
Dull pain score, mean ± SE	1.0 ± 0.3	0.8 ± 0.2	0.50
Soreness score, mean ± SE	1.2 ± 0.2	0.7 ± 0.2	0.10
Feeling anxious, n/total (%)	5/16 (31%)	4/16 (25%)	0.69

Deqi is the unique sensation of acupuncture which includes aching, dull pain and soreness. Mean ± SE with T-test or n/total (%) with Chi Square test are presented. P values for statistical significance are shown.