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An fMRI Investigation on Brain Activity in Response to Unilateral Acupuncture, Electroacupuncture and Electromyostimulation on ST36 and ST39

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1. Introduction

It is known that unilateral resistance exercise training may result in an increased muscular strength not only in the exercised muscle, but also in the unexercised homologous muscle in the contralateral limb. This phenomenon is termed cross education. Cross-education effect has been shown in hand, arm and leg muscles after various types of resistance training (Farthing, 2009; Hortobagyi, 2005; Lee & Carroll, 2007; Lee et al., 2010; Munn et al., 2004; Zhou, 2000). Furthermore, it has been reported that repeated unilateral transcutaneous electrical stimulation on a limb muscle or a nerve trunk may also cause cross-education effect (Bezerra et al., 2009; Cabric & Appell, 1987; Hortobagyi et al., 1999; Singer, 1986; Tachino et al., 1989; Zhou et al., 2002). Although the magnitude of strength gain in the contralateral limb is generally less than that in the exercised limb, this cross-over effect might have clinical values in neuromuscular rehabilitation (Farthing et al., 2009; Singer, 1986; Woo et al., 2006).

More interestingly, unilateral therapy for treatment of conditions on the contralateral side of the body has been used in traditional Chinese medicine for centuries (Kim et al., 2010; Woo et al., 2006). One particular type of treatment, *juci*, involves acupuncture on one side of the body to affect the function of the other side (Lin & Pan, 2004). This appears to be similar to the concept of cross education. A recent investigation in our laboratory has demonstrated that four weeks of electroacupuncture on tibialis anterior muscle (TA) of one limb can significantly increase dorsiflexion muscle strength in both the stimulated limb and the contralateral limb (Huang et al., 2007).

The exact mechanism of cross education is not clear. In principle, muscle strength can improve in adaptation to voluntary exercise training due to either or both an improved neural control and/or muscle hypertrophy. Because there has been little evidence of a significant muscle hypertrophy associated with improved strength in the contralateral limb,

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it is believed that cross education is primarily caused by adaptations in the central nervous system (Bezerra et al., 2009; Dragert & Zehr, 2011; Everaert et al., 2010). Several candidate mechanisms have been proposed in the literature, including ipsilateral innervation to the muscle due to a small proportion of uncrossed nerve fibres in the corticospinal pathway; bilateral activation of muscles for maintenance of posture during a unilateral exercise; and bilateral interaction between the two hemispheres of the brain (Carroll et al., 2006; Farthing, 2009; Hortobágyi et al., 2011; Zhou, 2000). However, the neural mechanisms for the cross education induced by electric stimulation or electroacupuncture may not be the same as that induced by voluntary exercise because the stimulation is applied to a peripheral nerve or muscle that by-passes the corticospinal pathway. It has been speculated that the sensory afferents may play an essential role in mediating cross-education effect induced by electric stimulation and electroacupuncture (Hortobagyi, 2005; Huang et al., 2007). Furthermore, whether the cross-education effect caused by electrical stimulation on surface or via needling at the acupoint involves similar or different neural mechanisms has not been examined.

The research presented in this Chapter utilised the functional magnetic resonance imaging (fMRI) technique to examine the brain activities during unilateral electric stimulation and acupuncture. The technique of fMRI is based on detection of blood oxygenation level dependent (BOLD) signals that provides a direct and precise indication of the regions in the brain involved in a given sensory-motor task.

The aim of the present study was to compare the areas of the brain that were activated, as indicated by fMRI, during unilateral transcutaneous electrostmulation, manual acupuncture and electroacupuncture on the acupoints of ST36 (*Zusanli*) and ST39 (*Xiajuxu*) in healthy young adults, in order to obtain a better understanding of the differences in the areas activated during these tasks and how these might contribute to the mechanisms of cross education or unilateral therapy. It was hypothesised that electroacupuncture on acupoints and transcutaneous electric stimulation on the same areas of the tibialis anterior muscle would induce similar level of activities in certain regions of the contralateral and ipsilateral side of the brain; and manual acupuncture at the same acupoints may also cause activation of the same regions in the brain, but to a less magnitude, as indicated by the BOLD signals.

2. Methods

Six healthy young men with a mean age of 23 years (range 21-26 years) volunteered for the study. All participants were right-foot dominant as identified using an established questionnaire (Li, 1983) and without current neuromuscular, orthopedic, diabetes mellitus and cardiovascular diseases or neuromuscular injuries. Participants were physically active, without a history of specific sport training, especially muscle strength training, during the six months prior to the study, and had no previous experience with acupuncture or electric stimulation. They did not show a fear to acupuncture and electric stimulation. All participants gave their consent to participation prior to the experiment. The experiment was carried out in accord with the Declaration of Helsinki, and the procedure obtained approval by the Human Research Ethics Committee of Southern Cross University, Australia.

One week prior to the formal experiment, each participant was given two familiarisation trials, one in the University's laboratory and the other in the MRI room at the hospital. During the familiarisation trials the detailed experimental procedure was explained to the participants. The participants were given transcutaneous electric stimulation, manual acupuncture and electroacupuncture at the acupoints ST36 and ST39 of the right leg, respectively. The stimulation intensity was increased gradually till the level that the participant could maximally tolerate. A post-hoc investigation (n=5) found that the electromyogram (EMG) activity of the left anterior tibialis muscle showed no significant changes ($P>0.05$ by ANOVA with repeated measures) between resting and when the right leg received electric stimulation (contraction intensity was up to 40% maximal voluntary contraction, MVC, at the maximum tolerance), electroacupuncture (up to 30%MVC) or manual acupuncture (up to 10%MVC). The EMG activity of the left anterior tibialis during the stimulation or acupuncture on the right leg was generally below 1.5% of that during a maximal voluntary contraction.

During the experimental trial for fMRI scanning, participant was in a supine position, relaxed and with eyes closed. The head position in the head coil was stabilised by foam padding. The right leg of the subject was strapped into a custom-built device at the thigh and foot with the knee joint angle at 0 degrees and the ankle joint at 15 degrees in plantar flexion. The left leg was in full extension and the participant was told to relax the muscles.

The experiment included three tasks with block-design to detect BOLD signals. The tasks were performed in the order of transcutaneous electric stimulation, manual acupuncture and electroacupuncture on the ST36 and ST39 of the right leg. In each task, there was three sets of 1 min rest (reference period) followed by 1 min stimulation or acupuncture. A minimum of 10 minutes rest was given between the tasks.

The location of the acupoints ST36 and ST39 were determined according to the description of traditional Chinese medicine (Beijing College of Traditional Chinese Medicine et al., 1980) by an accredited acupuncturist who had been practicing in hospital for 10 years. The ST36 is located at 3 *cun* distance (*cun* is a unit of length relative to patient's body size in traditional Chinese medicine. Three *cun* is the breadth of the patient's index, middle, ring, and little fingers at the level of proximal interphalangeal joint at the dorsum of the middle finger) from the depression below the patella and lateral to the patellar ligament, and one finger breadth lateral to the anterior crest of the tibia. The ST39 is located at 9 *cun* distance from the depression below the patella and lateral to the patellar ligament and one finger breadth lateral to the anterior crest of the tibia (Figure 1).

During the surface electric stimulation task, the stimulation was applied to the tibialis anterior muscle via a Trio300 stimulator (ITO, Japan). Two 5 cm x 5 cm self-adhesive MRI-compatible electrodes (ITO, Japan) were placed over the muscle with the cathode on ST36 and the anode on ST39. The stimulator was located outside of the MRI room and linked to the electrodes via MRI-compatible wires. The stimulation was delivered at a duty cycle of 5 s rest followed by 5 s stimulation, 6 cycles per set (a total of 1 minute). The electrical pulses were square waves at 50 Hz, with the pulse width of 200 μs and intensity of 48-55 mA according to the level that the participant could maximally tolerate in the familiarisation trials.

During the manual acupuncture task, a pure silver acupuncture needle with diameter of 0.3 mm and length of 50 mm (GB2024-94, Suzhou Medical Appliance Company, Ltd., China) was inserted vertically into the muscle at each acupoint to a depth of 20 to 30 mm by the accredited acupuncturist. The needles were manually twirled at 1 Hz to induce a feeling of *de qi*. The *de qi* sensation is a combination of aching, pressure, soreness, heaviness, fullness, warmth, cooling, numbness, tingling, and dull pain, but not a sharp pain (Hui et al., 2007). The acupuncture was applied for 60 s after 60 s rest in each set. Three sets were performed.

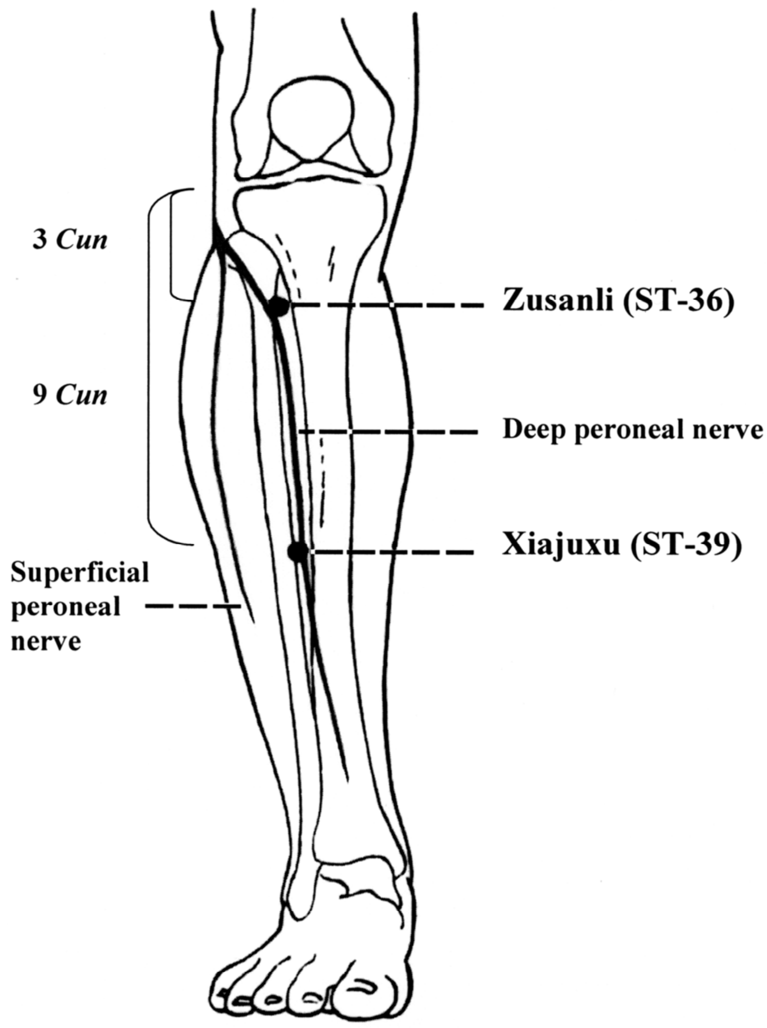


Fig. 1. Location of the acupoints ST36 and ST39 [Figure from Huang et al. (2007). Journal of Alternative and Complementary Medicine, 13(5), 539-546, with permission].

The protocol of electroacupuncture task was similar to that of electric stimulation, with the surface electrodes replaced by acupuncture needles inserted into the muscle at the acupoints. The electrical pulses were delivered to the needles by using an electroacupuncture apparatus (SDZ-II, Suzhou Medical Appliance Company, Ltd., China), with square waves at 50 Hz, pulse width of 200 μs and intensity of 8 to 11 mA which was the maximal level that the participant could tolerate in the familiarisation trials.

A 1.5 T whole body MRI scanner (GE, 1.5 T twin speed infinity with Excite II, USA) was used for fluid attenuation inverse recovery T1-weighted imaging (FLAIR T1WI) and gradient echo-echo planar imaging (GRE-EPI) fMRI scanning. Anatomical images were acquired with a repetition time (TR) of 2250 ms, a time for echo (TE) of 11.6 ms, a time for inversion of 760 ms, bandwidth (BH) 19.32 KHz, field of vision (FOV) 24 cm x 18 cm, data matrix 320 x 224, slice thickness 6 mm with 1 mm gap, for 20 slices that covered the distance from the apex of the scull to the lower edge of the cerebellum. The fMRI used the GRE-EPI technique with parameters of TR 3000 ms, TE 40 ms, flip angle 90 degrees, BH 62.50 KHz, FOV 24 cm x 24 cm, data matrix 128 x 128 for an in-plane resolution of 1.875 mm x 1.875

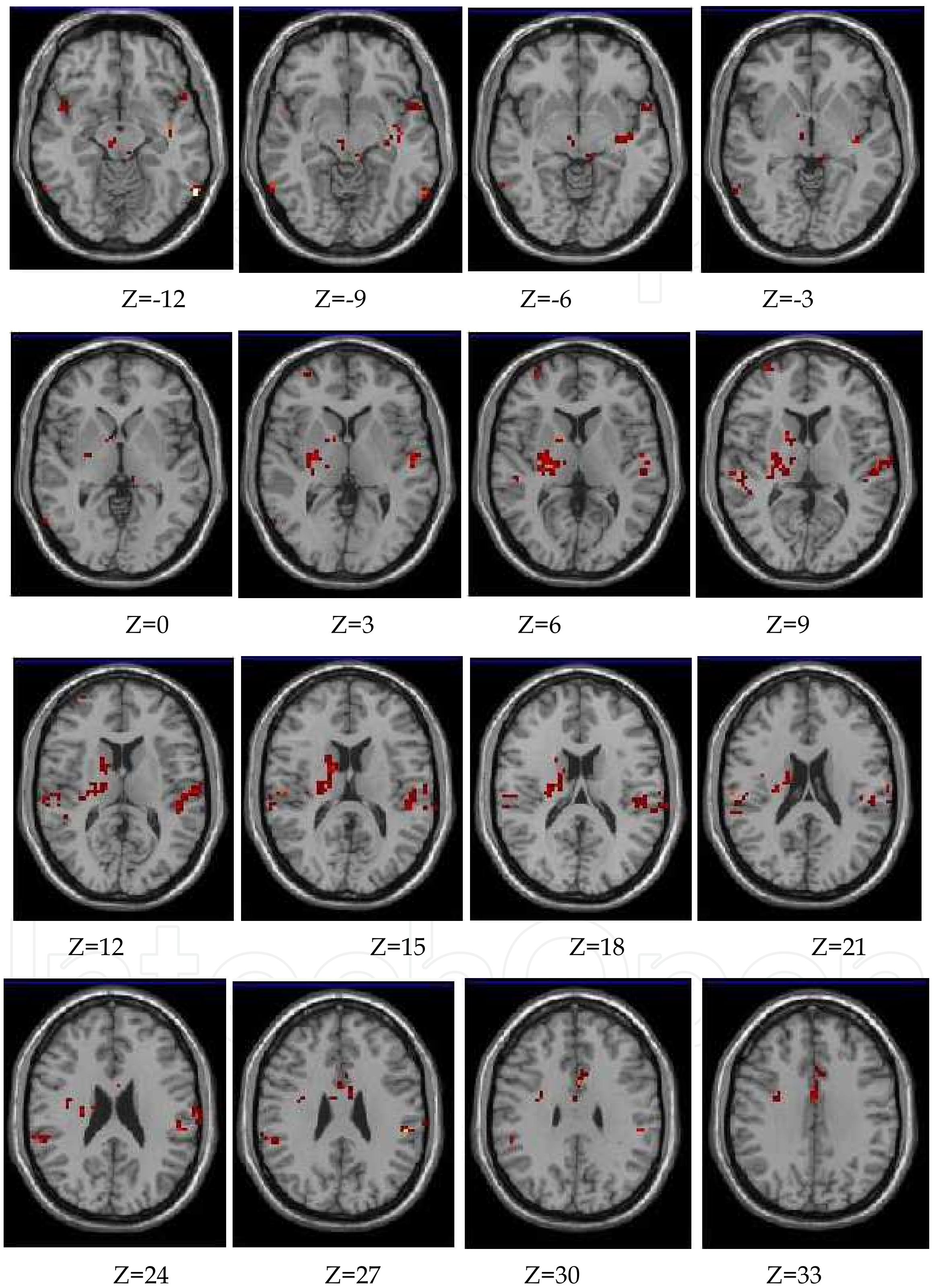
mm. Slice thickness 6 mm, gap 1 mm, with 20 slices that corresponded to the T1WI. Three scans with a total scanning time of 7 minutes were performed for each task.
The fMRI signals were monitored by a real time imaging processor. If participant's head position moved for more than 5 mm, the scan would stop automatically. The participants in this study cooperated well and there was no case of significant head movement that required repositioning. The original fMRI data in DICOM format was transferred to a computer where the statistics parameter mapping software was used for analysis (SPM99, Wellcome Department of Imaging Neuroscience, University College London, UK). Conjunction analysis was performed to compare the fMRI signals among the three tasks. The activation of the areas in the brain was estimated by correlative analysis for temporal-signal intensity curve with stimulation. The threshold for identifying an active area was set as 10 voxels. The fMRI image analysis was performed by a medical imaging specialist. Paired *t*-test was used to identify task-related activities as compared to the resting period, with the Alpha level of 0.005 was used for significant differences (uncorrected) (Bai et al., 2009).

3. Results

All fMRI trials were completed successfully. During the transcutaneous electric stimulation task, significant activation ($p<0.005$) was detected in the areas of bilateral gyrus postcentralis (GOPC, Brodmann area [BA]43), lobulus parietalis inferior (LPi, BA40), gyrus frontalis medius (GFm, BA8,10), inferior temporal gyrus (GTi, BA37), gyrus temporalis superior (GTs, BA38,42) and brain stem; ipsilateral gyrus frontalis superior (GFs, BA6), insula (INS) and hippocampus (HI); and contralateral gyrus frontalis medialis (GFd, BA6), gyrus cinguli (GC, BA24), nucleus lentiformis (NL), lobulus paracentralis (LPC, BA5,7), gyrus precentralis (GPRC, BA4), cerebellum (Cb) and internal capsule (IC) (Table 1, Figure 2).

Activated Area	Brodmann	Contralateral (mm) x	y	z	T value	Ipsilateral (mm) x	y	z	T value
GPOC	43	-57	-21	15	14.63	45	-39	63	22.38
LPi	40	-60	-39	24	9.4	51	-30	27	21.70
GTi	37	-63	-54	-9	13.17	60	-60	-12	31.78
GTs	38, 42	-66	-24	12	8.12	63	-12	9	14.07
GFm	8, 10	-36	60	12	9.00	39	12	48	14.14
Brainstem	/	-6	-21	-9	9.61	15	-30	-39	11.59
INS	/	/	/	/	/	39	-9	-12	15.09
HI	/	/	/	/	/	30	-18	-9	8.13
GFS	6	/	/	/	/	9	9	63	10.82
GFd	6	-3	-21	63	12.47	/	/	/	/
GC	24	-3	-6	33	10.10	/	/	/	/
NL	/	-18	6	6	15.70	/	/	/	/
LPC	5, 7	-6	-33	63	16.86	/	/	/	/
GPRC	4	-33	-6	36	9.73	/	/	/	/
Cb	/	-15	-66	-33	9.58	/	/	/	/
IC	/	-15	0	15	12.54	/	/	/	/

Table 1. Montreal Neurology Institute (MNI) coordinates of local maxima of cortical clusters showing significant ($P<0.005$) activity associated with transcutaneous electric stimulation at the acupoints of ST36 and ST39 in the right leg.



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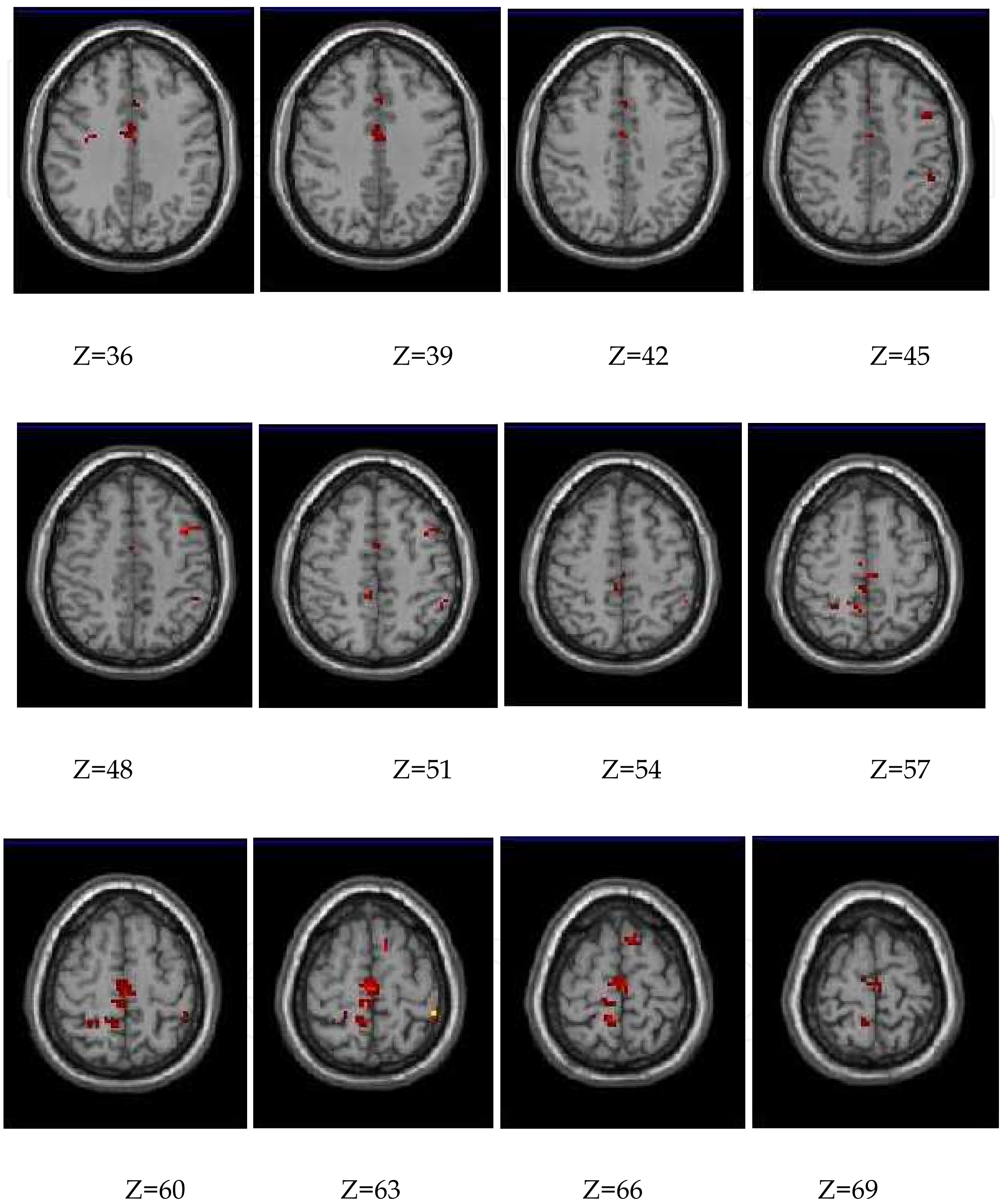

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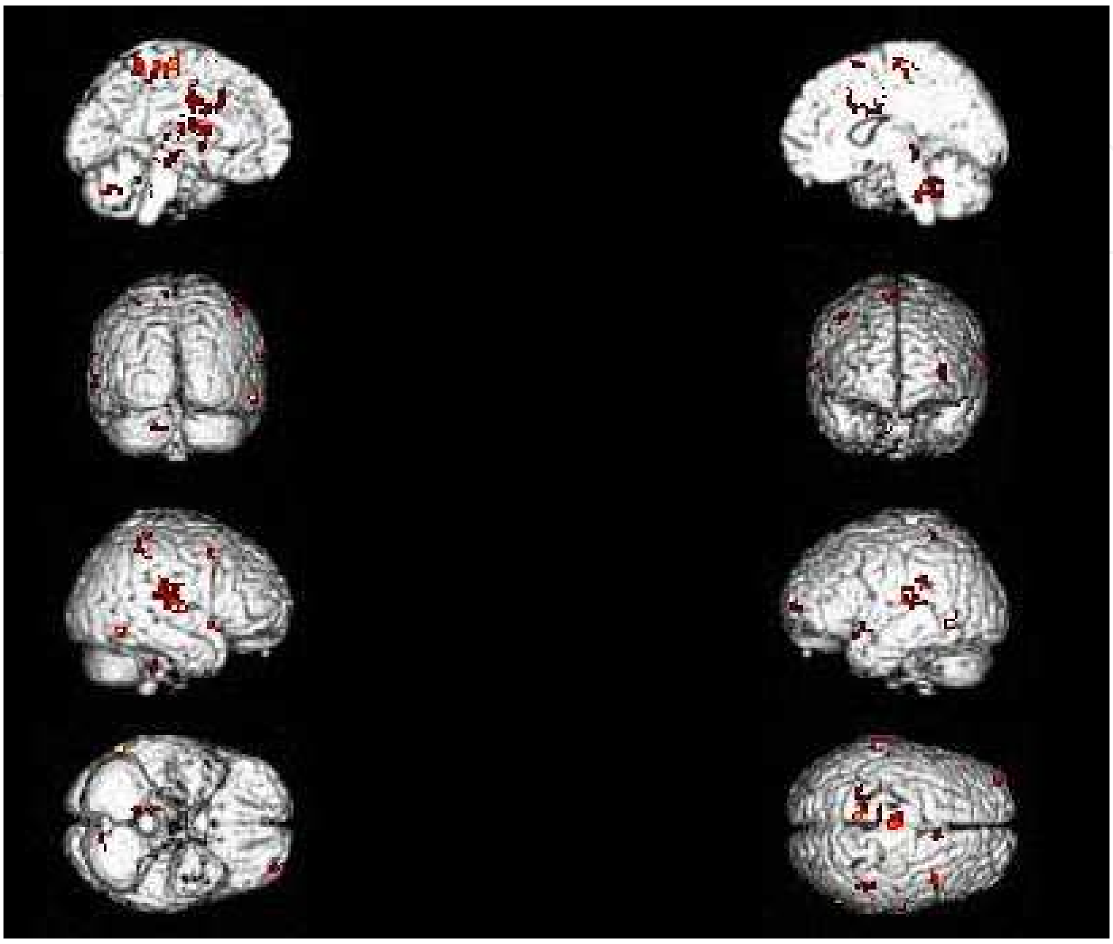
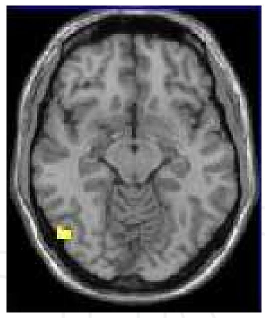


Fig. 2. Brain areas activated (coloured areas) during transcutaneous electric stimulation on the acupoints of ST36 and ST39 in the right leg (P<0.005).

During the manual acupuncture task, significant activation was detected only in the area of the contralateral gyrus occipitalis medius (Gom, BA19) (Table 2 and Figure 3).

Activated Area	Brodmann	Contralateral (mm) x	y	z	T value	Ipsilateral (mm) x	y	z	T value
Gom	19	-51	-69	-12	5.55	/	/	/	/

Table 2. Montreal Neurology Institute (MNI) coordinates of local maxima of cortical clusters showing significant (P<0.005) activity associated with manual acupuncture at the acupoints of ST36 and ST39 in the right leg.



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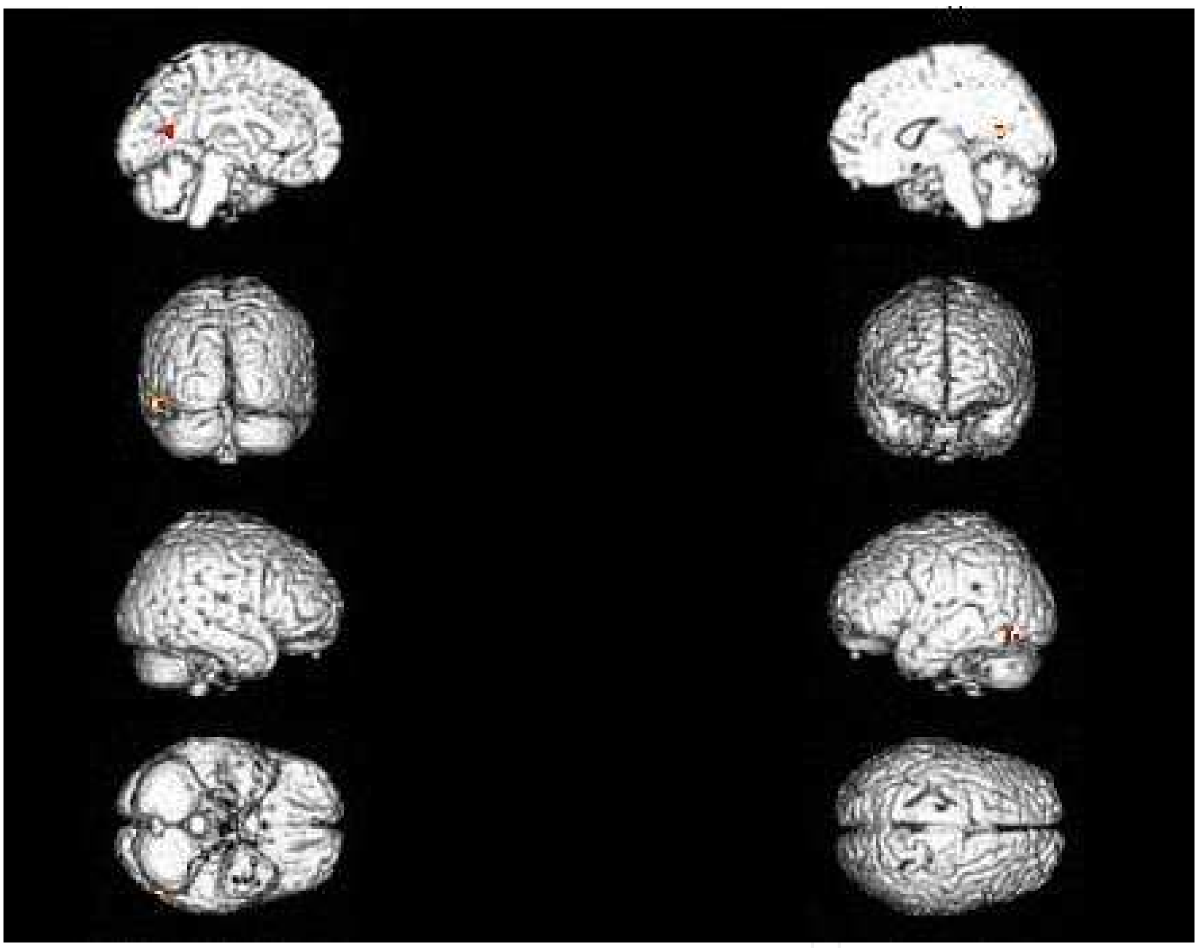
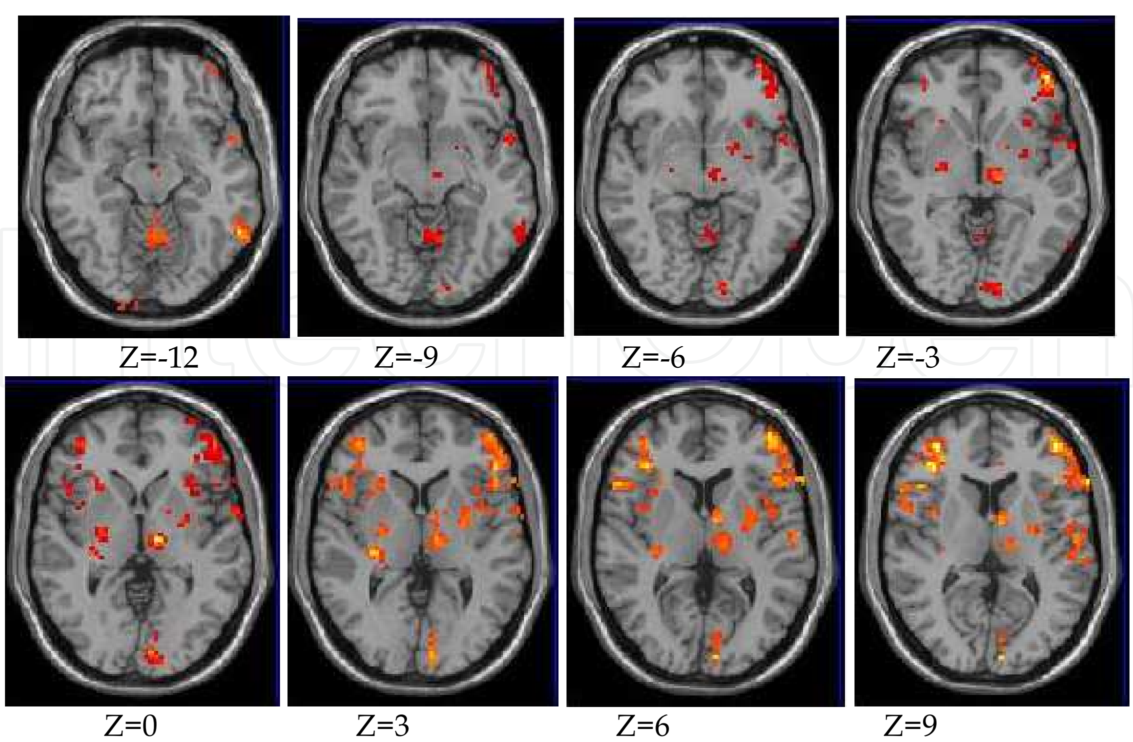


Fig. 3. Brain areas activated (coloured areas) during manual acupuncture on the acupoints ST36 and ST39 in the right leg (P<0.005).

During the electroacupuncture task, significant activation was identified in the areas of bilateral gyrus frontalis superior (GFs, BA6), gyrus frontalis medius (GFm, BA6,10,46), gyrus frontalis inferior (GFi, BA44-47), gyrus frontalis medialis (GFd, BA6,8), gyrus postcentralis (GPOC, BA40), lobulus parietalis inferior (LPi, BA40), precuneus (PCU, BA7), nucleus lentiformis (NL), insula (INS, BA13), gyrus cinguli (GC, BA 24,32), cerebellum (Cb) and brain stem; ipsilateral thalamus (TH) and cuneus (CU, BA18); and contralateral gyrus parahippocampalis (GH, BA35) and gyrus precentralis (GPRC, BA4) (Table 3, Figure 4).

Activated Area	Brodmann	Contralateral(mm) x	y	z	T value	Ipsilateral(mm) x	y	z	T value
GPOC	40	-66	-24	21	6.69	60	-24	21	11.52
GFd	6, 8	-3	-21	57	9.17	6	27	51	5.80
GFm	6, 10, 46	-36	48	9	10.87	45	39	24	13.27
GFi	44,45,46,47	-39	33	9	12.40	33	24	0	4.69
GC	24, 32	-3	0	39	9.67	6	39	12	6.54
Brainstem	/	-3	-24	-30	5.52	3	-18	-27	6.56
GTS	22, 42	-60	-21	12	6.12	66	-27	15	9.69
GL	18	-18	-102	-15	6.00	9	-93	-9	6.58
PCU	7	-18	-54	57	3.91	18	-54	54	6.85
LPi	40	-57	-39	45	5.85	48	-45	54	7.79
NL	/	-24	-12	0	5.96	15	3	-3	7.09
INS	13	-39	9	0	3.83	39	9	6	4.56
U	28, 36	-27	-3	-39	4.91	33	6	-24	5.64
GFs	6, 8	-12	24	57	5.38	6	21	57	7.20
Cb	/	-9	-72	-33	7.52	6	-60	-9	5.85
TH	/	/	/	/	/	9	-15	0	11.83
GTm	21	/	/	/	/	57	-54	-12	9.14
CU	18	/	/	/	/	6	-93	6	8.54
GPRC	4	-39	-3	39	5.87	/	/	/	/
GH	35	-27	0	-30	7.11	/	/	/	/
IC	/	-33	-24	3	7.97	/	/	/	/

Table 3. Montreal Neurology Institute (MNI) coordinates of local maxima of cortical clusters showing significant (P<0.005) activity associated with electroacupuncture at the acupoints of ST36 and ST39 in the right leg.



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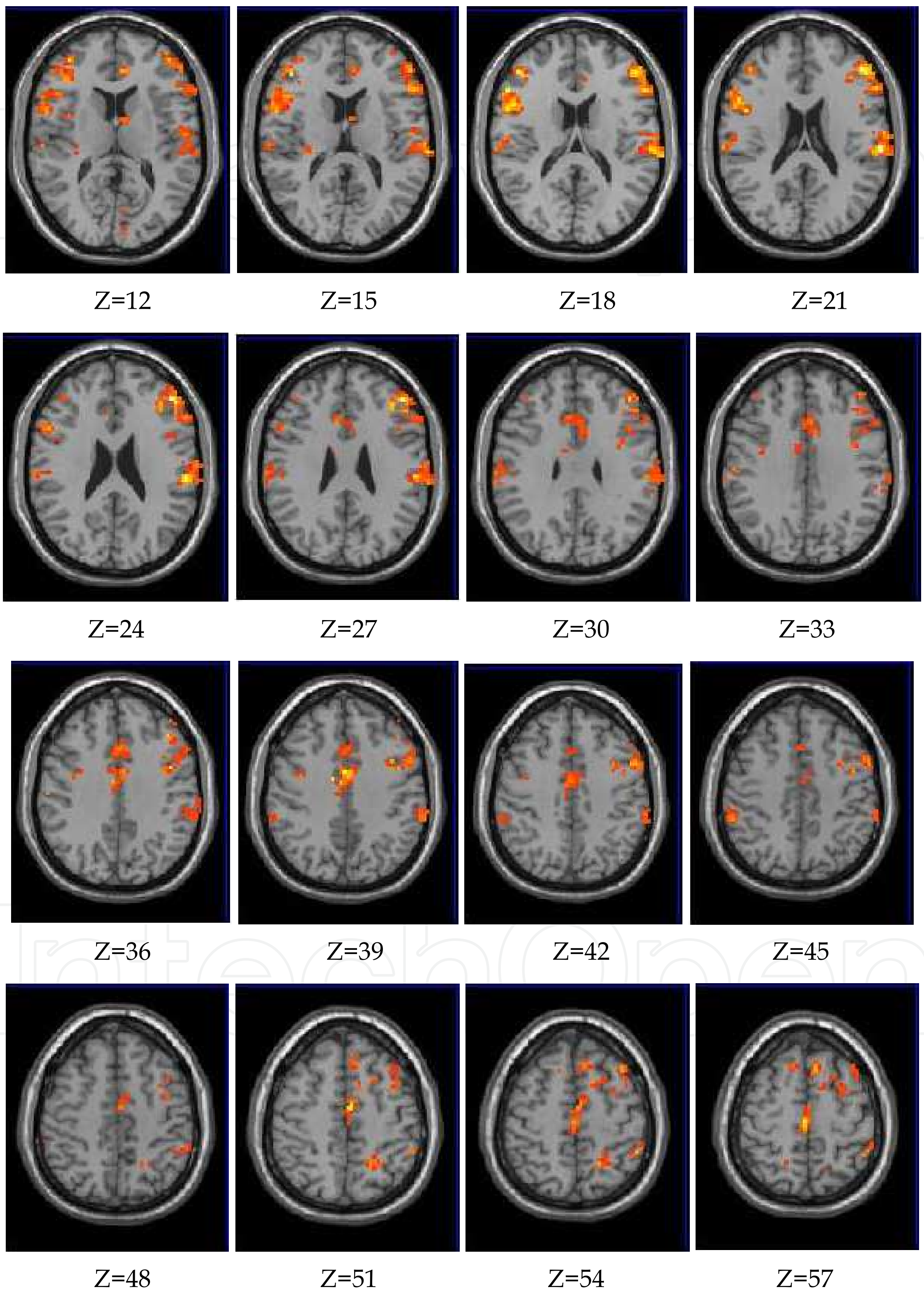

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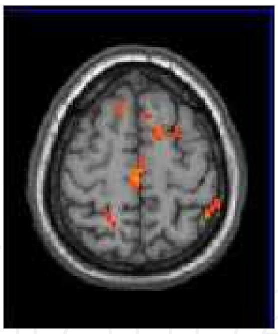
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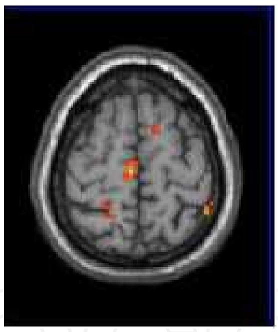
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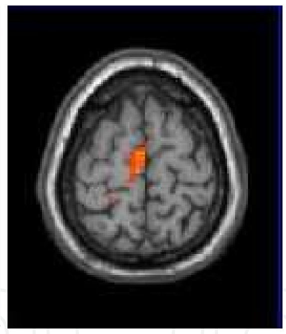
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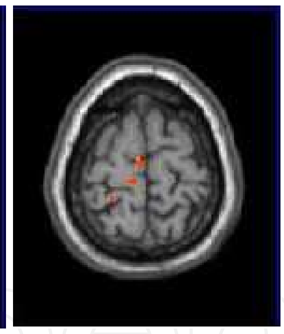
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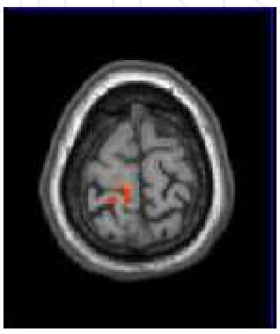
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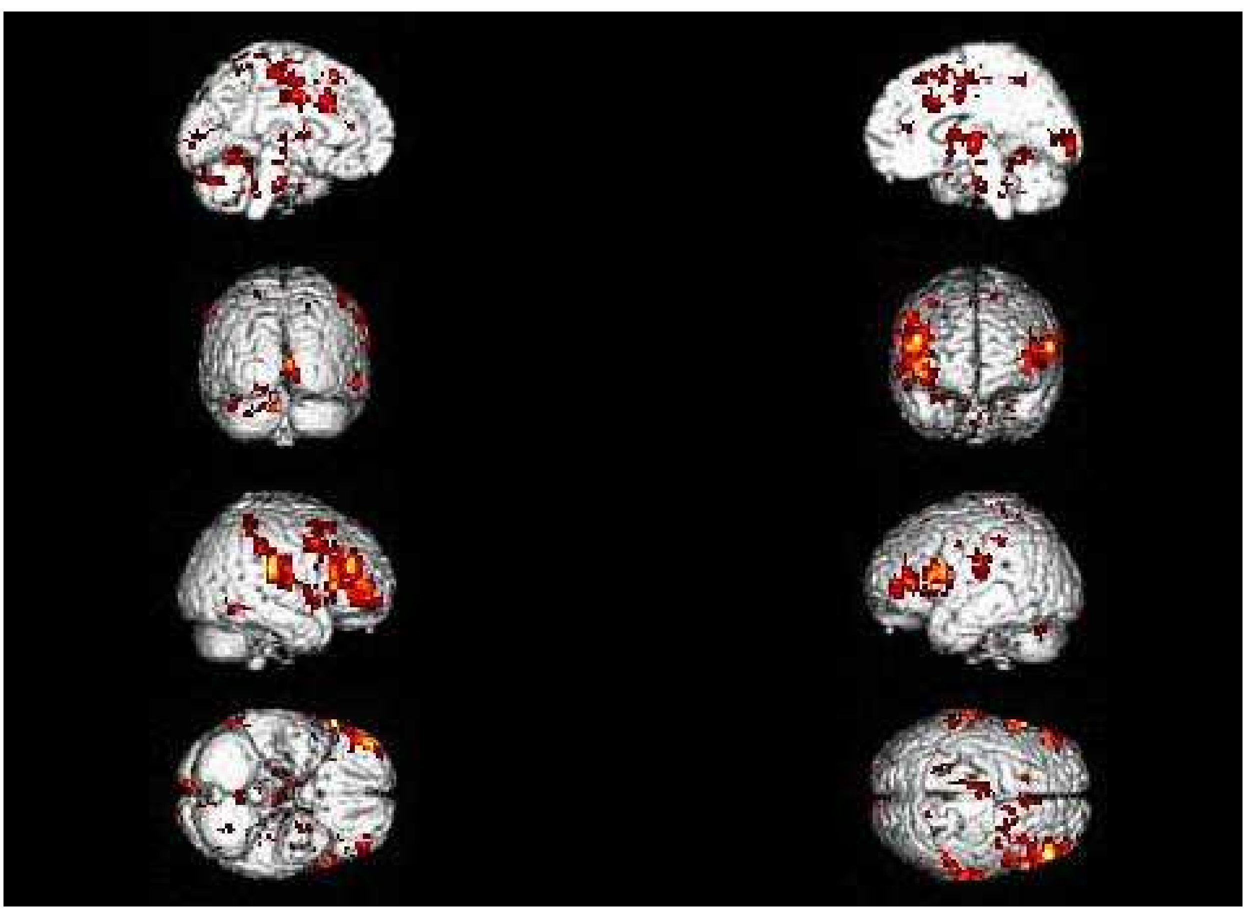

Fig. 4. Brain areas activated (coloured areas) during electroacupuncture on the acupoints of ST36 and ST39 in the right leg ($P<0.005$).

4. Discussion

The results of present study demonstrated significant changes of BOLD signals in multiple brain areas during the tasks of unilateral transcutaneous electric stimulation and electroacupuncture on the acupoints of ST36 and ST39 (Table 1 and 3, Figure 2 and 4). In contrast, significantly activity was observed only in one area during the manual acupuncture task (Table 2 and Figure 3).

The present findings on the fMRI changes in response to electric stimulation appear to be in line with the information obtained from other studies. There have been reports that unilateral electric stimulation to upper limb muscles (wrist extensors and flexors) caused increased BOLD signals in the bilateral secondary somatosensory cortex, the supplementary motor area and anterior cingulate cortex; contralateral primary motor cortex, primary somatosensory cortex and premotor cortex; and the ipsilateral cerebellum (Blickenstorfer et al., 2009; Han et al., 2003). In respect of lower limb muscles, Francis and associates compared BOLD signals during unilateral active and passive dorsiflexion movement, and electric stimulation-induced dorsiflexion, and reported that the electric stimulation induced greater brain activities than passive movement, but lower activities than that induced by active movement (Francis et al., 2009). The major brain areas that showed significant activities during the electric stimulation task included bilateral dorsal and ventral premotor areas and cerebellum; and contralateral primary motor, primary sensory, secondary somatosensory areas, as well as in supplementary motor area and cingulate motor areas (Francis et al., 2009). The present results showed a similar pattern with significant activities found in the contralateral (BA4, 6, 8, 10) and bilateral (BA8, 10) motor-related areas and somatosensory areas (BA40) (Table 4).

Brain area	Electric stimulation		Electroacupuncture	
(Abbreviation, Brodmann area)	Contralat.	Ipsilat.	Contralat.	Ipsilat.
Gyrus presentralis (GPRC, BA4)	+		+	
Gyrus frontalis medius (GFm, BA8,10)	+	+	+	+
Gyrus frontalis medialis (GFd, BA6)	+		+	+
Gyrus frontalis superior (GFs, BA6,8)		+	+	+
Gyrus frontalis inferior (GFi, BA44-47)			+	+
Brain stem	+	+	+	+
Cerebellum (Cb)	+		+	+
Gyrus postcentralis (GOPC, BA40)	+	+	+	+
Lobulus parietalis inferior (LPi, BA40)	+	+	+	+
Precuneus (PCU, BA7)			+	+
Nucleus lentiformis (NL)	+		+	+
Gyrus cinguli (GC, BA24)	+		+	+
Uncus (U, BA28,36)			+	+
Insula (INS, BA13)		+	+	+

Table 4. Comparison of brain areas that showed significant changes in fMRI signals during transcutaneous electric stimulation and electroacupuncture on acupoints of ST36 and ST39. "+" indicates a significant change in BOLD signals at P<0.005 level.

A number of studies have also reported the effects of acupuncture and electroacupuncture on brain activities as indicated by BOLD signal changes. For example, Bai and colleagues reported fMRI signal changes in response to manual acupuncture at ST36 in sensorimotor cortices, bilaterally in BA9, 10, 11, 40, 44 and 45, brainstem and cerebellum; ipsilaterally in BA6; and contralaterally in BA3, etc. (Bai et al., 2009). Zhang and associates investigated the effects of electroacupuncture on acupoints of *Yanglingquan* (GB34) and *Xuanzhong* (GB39) on the left leg, and reported significantly increased brain activities bilaterally in BA4, 6, 10, 11, 18, 23 and 24, insula and cerebellum; and contralaterally in BA44 and 45, caudate, putamen and midbrain (Zhang et al., 2007). The present study also found significantly increased activities in bilateral BA6, 7, 8, 10, 13, 28, 26, 40 and 44-47, brainstem and cerebellum; and contralaterally in BA4 (Table 3 and 4). However, the manual acupuncture induced significant activity only in BA19 of the contralateral side (Table 2). The lack of significant changes in BOLD signals compared with other reports might be related to the higher threshold (10 voxels vs 3 voxels used in Bai et al., 2009) and alpha level (0.005 vs 0.05 or 0.01 used in Zhang et al., 2007) used in this study. Another possible reason could be that only the twirling manipulation of the needles was used during the experiment without the use of lifting and thrusting techniques. Therefore, the stimulation might not be strong enough to produce wider activations in the brain.

Electric stimulation has been widely used as a supplementary training method for improving muscular strength and fitness as well as a means of rehabilitation (Maffiuletti, 2010; Paillard, 2008). Electroacupuncture has recently been shown to be able to improve muscle strength as well (Huang et al., 2007). Although the electric stimulation and electroacupuncture can directly activate peripheral nerve and muscle fibres and by-pass the central nervous system, recent evidence has suggested that the training/therapeutic effects of electric stimulation may also include neural plasticity (Chae et al., 2008; Maffiuletti, 2010; Wolpaw, 2007). The current results provide new evidence about the cortical responses by comparison of the BOLD signal changes during electroacupuncture and electric stimulation.

It was interesting to find that there were common bilateral activations during electric stimulation and electroacupuncture tasks in the somatosensory areas (GPOC and LPi) and secondary motor areas (GFm) that are known to be associated with somatosensory inputs processing and motor preparation, motor program encoding and sensorimotor integration (Table 4). Furthermore, electroacupuncture induced much wider bilateral brain activation than surface electric stimulation and manual acupuncture.

In the present study, the stimulation intensity utilised in the electric stimulation and electroacupuncture task was limited by participants' tolerance to the discomfort and pain. Obviously, a common factor in these two treatments was the nociceptive afferents. Pain (from nociceptors) has been shown to elicit activation of the sensorimotor cortices, rostral anterior cingulate cortex, insula, cerebellum, hippocampus and brain stem (Hui et al., 2005; Hui et al., 2009; Kong et al., 2007; Lewith et al., 2005; Seidler et al., 2004) through spinothalamus bundle. A number of cortical areas have been shown to be involved in pain processing, including the primary somatosensory cortex, the secondary somatosensory cortex, the insula, the anterior cingulate, the prefrontal cortex, the hypothalamus and periaqueductal gray (PAG) (Kong et al., 2009; Zhang et al., 2004). The primary and secondary somatosensory cortices are involved in the sensory discriminative aspect of pain processing (Liu et al., 2010), such as intensity determination and location of nociceptive stimulation (Tracey, 2005), as components of the sensory (pain) network (Wager, 2005). Afferent inputs have shown to alter the excitability of motoneurons and interneurons that affects the contralateral limb at the spinal (Robinson et al., 1979) or higher levels in the central nervous system (Hortobagyi et al., 2003; Kaelin-Lang et al., 2002). Therefore, it is speculated that the nociceptive inputs, together with other somatosensory afferents, may play an important role in mediating neural plasticity in adaptation to unilateral electric stimulation training and electroacupuncture. However, changes in fMRI signals observed in this study can only provide neuroanatomical evidence for the brain areas involved in the prescribed tasks and cannot provide direct evidence for the functional links between these cortical areas. How the sensory afferents affect motor function that results in improved expression of muscular strength requires further investigations.

An interesting finding of the present study is that the electroacupuncture induced a much wider cortical activation than the surface electric stimulation at the two acupoints. One possible explanation is that acupuncture required insertion of a needle into the muscle and manipulation of the needle to induce the sensation of *de qi*. The *de qi* sensation reported by the participants included aching, soreness and pressure, tingling, numbness, dull pain, heaviness, warmth, fullness and coolness without sharp pain. The complex sensations in *de qi* suggest involvement of a wide spectrum of myelinated and unmyelinated nerve fibers, particularly the slower conducting fibers in the tendinomuscular layers (Hui et al., 2007). In addition of *de qi*, electric pulses were delivered to the needle.

Whether the wider cortical responses observed in the electroacupuncture task compared with the surface electric stimulation task indicates the unique treatment effect of inserting needle at the acupoint would be an interesting question. There has been a study on rats that compared the effects of acupuncture or electroacupunture at different depth (sham acupuncture), and with (true electroacupuncture) or without electric current (sham electroacupuncture) (Chiu et al., 2003). The results of the study showed that there was no neural activation caused by the sham acupuncture. The sham electroacupuncture only induced a slight increase in brain activity in the hypothalamus; however, true electroacupuncture elicited enhanced hypothalamus response (Chiu et al., 2003). The results suggested that electroacupuncture at the acupoint produce greater activation of the central nervous system. However, one limitation of using animal models to investigate the effects of acupuncture is that no *de qi* sensation can be substantiated as that observed in humans. It has been suggested that transcutaneous electric stimulation should make no difference as compared with electroacupuncture on the identified points in respect of pain control (Han, 1997). However, the present results indicate there are differences between the cortical responses to the surface and needle stimulation at the given acupoints.

It has been reported that the increases of BOLD signal in secondary somatosensory area and insula were the most consistently observed regardless of acupoints or acupuncture modes (Kong et al., 2007). The insula is purported to process sensory/discriminative, rather than affective information (Craig et al., 2000; Napadow et al., 2005). Recent studies showed that insula is widely connected with cortex, subcortex and brainstem structures and is involved in decision making and subsequent behavior emotional experience and pain-related modulation. The fMRI imaging data also indicated that insula played an important role in a dynamic switching between the central-executive network and the default mode network (Liu et al., 2010; Sridharan et al., 2008). The posterior middle cingulate cortex, receiving information from insula, appeared to be important in coding acupuncture sensation intensity, then interacting with the posterolateral parietal cortex in orienting the body in response to somatosensory stimuli (Vogt, 2005). Recently, a functional imaging study also suggested a central role for the precuneus in a wide spectrum of highly integrated tasks (Hsieh et al., 2010). Based on these reports and present findings, we speculate that these

structures may be responsible for integration of the sensory inputs associated with pain and proprioceptors, and the motor cortices for manifestation of cross education.
In summary, the present results showed that the electroacupuncture induced a much wider activation of brain areas bilaterally than that induced by the transcutaneous electric stimulation over the same acupoints, as indicated by the BOLD signal changes. Therefore the outcomes of the study did not fully support the hypotheses that electroacupuncture and surface electric stimulation at the same areas would induce similar level of activities in the brain; and that manual acupuncture at the same acupoints may also cause activation of the same regions in the brain.

5. Conclusion

The results of this study indicated that the unilateral electroacupunture task induced a wider bilateral activation in the brain than that induced by the unilateral transcutaneous electric stimulation at the acupoints of ST36 and ST39, although the electrical current utilised in the electroacupuncture was lower. The manual acupuncture did not induce a sufficient level of activation in the brain, as indicated by the BOLD signals, possibly due to the high threshold for identifying activation and the needle handling technique used in the study. Although the bilateral brain activities as indicated by the BOLD signals cannot directly explain the functional changes in adaptation to unilateral interventions, this study has provided new evidence for the differences between the effects of the three treatments.

6. Acknowledgment

This project was supported by Tianjin Scientific Research Foundation (No. 05YFGDSF02100). The researchers appreciate the guidance on acupuncture given by Dr Qing-Wen Li, and the contributions from Jian-Zhong Yin and Li-Hua Liu from the Medical Imaging Department of the Tianjin First Central Hospital to fMRI data collection. We also would like to express our thanks to Professor Yu-Feng Zang from the Cognitive Institute of Beijing Normal University for his advice on data analysis.

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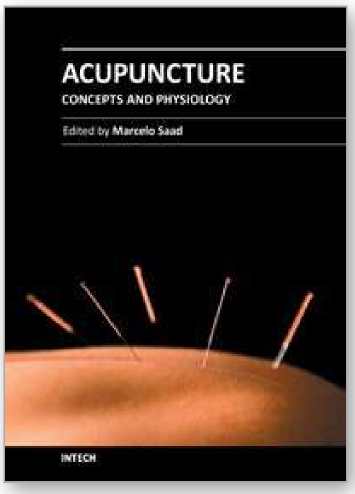

Acupuncture - Concepts and Physiology
Edited by Prof. Marcelo Saad

ISBN 978-953-307-410-8
Hard cover, 222 pages
Publisher InTech
Published online 10, October, 2011
Published in print edition October, 2011

Acupuncture and related techniques are useful tools for treating a spectrum of diseases. However, there are still many areas of controversy surrounding it. We hope this book can contribute to guide the advance of this ancient medical art. In the present work, the reader will find texts written by authors from different parts of the world. The chapters cover strategic areas to collaborate with the consolidation of the knowledge in acupuncture. The book doesnâ€™t intend to solve all the questions regarding this issue but the main objective is to share elements to make acupuncture more and better understood at health systems worldwide.

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