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Brain activation and inhibition after acupuncture at *Taichong* and *Taixi*: resting-state functional magnetic resonance imaging

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Abstract

Acupuncture can induce changes in the brain. However, the majority of studies to date have focused on a single acupoint at a time. In the present study, we observed activity changes in the brains of healthy volunteers before and after acupuncture at *Taichong* (LR3) and *Taixi* (KI3) using resting-state functional magnetic resonance imaging. Fifteen healthy volunteers underwent resting-state functional magnetic resonance imaging of the brain 15 minutes before acupuncture, then received acupuncture at *Taichong* and *Taixi* using the nail-pressing needle insertion method, after which the needle was retained in place for 30 minutes. Fifteen minutes after withdrawal of the needle, the volunteers underwent a further session of resting-state functional magnetic resonance imaging, which revealed that the amplitude of low-frequency fluctuation, a measure of spontaneous neuronal activity, increased mainly in the cerebral occipital lobe and middle occipital gyrus (Brodmann area 18/19), inferior occipital gyrus (Brodmann area 18) and cuneus (Brodmann area 18), but decreased mainly in the gyrus rectus of the frontal lobe (Brodmann area 11), inferior frontal gyrus (Brodmann area 44) and the center of the posterior lobe of the cerebellum. The present findings indicate that acupuncture at *Taichong* and *Taixi* specifically promote blood flow and activation in the brain areas related to vision, emotion and cognition, and inhibit brain areas related to emotion, attention, phonological and semantic processing, and memory.

Key Words: *nerve regeneration; acupuncture; neuroimaging; resting-state functional magnetic resonance imaging; Taichong (LR3); Taixi (KI3); amplitude of low-frequency fluctuation; Brodmann area 11; Brodmann area 18; Brodmann area 19; Brodmann area 44; posterior lobe of the cerebellum; neural regeneration*

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Introduction

Imaging studies of cerebral function have shown that acupuncture can induce changes in specific brain regions, providing a non-invasive quantitative method for studying the central mechanisms underlying the clinical effects of acupuncture. To date, the majority of acupuncture studies using functional magnetic resonance imaging (fMRI) have examined single acupoints, commonly PC6, ST36 or LI4 (Wang et al., 2006; Liu et al., 2012; Zhang et al., 2012; You et al., 2013; Chen et al., 2014; Yeo et al., 2014), comparing true and sham acupuncture (Wang et al., 2009; Wu et al., 2014) and different acupuncture methods (Litscher, 2009). Physiological functions and pathological states have been widely examined using fMRI (Cole et al., 2006; Liang et al., 2014). Furthermore, numerous studies have provided evidence for the functional specificity of meridians and acupoints in humans (Wu et al., 2002; Zhang et al., 2004; Chang et al., 2013; Rong et al., 2013; Xing et al., 2013; Li et al., 2014), and the acupoints-brain relation hypothesis (Lai et al., 2007) has now been suggested as a likely mechanism underlying the therapeutic effects of acupuncture.

However, previous studies using fMRI with acupuncture have a number of limitations. Most studies have focused on a single acupoint at a time (Liu et al., 2011; Zhang et al., 2012) and have confirmed that acupuncture at a specific acupoint can activate certain brain areas. However, there are discrepancies between studies as to which brain areas are activated by stimulation of the same acupoint (Yan et al., 2005; Liu et al., 2011; Zhang et al., 2012). In the clinic, acupuncture treatment commonly involves the selection of combined acupoints, as this produces better therapeutic effects than using a single acupoint (Ji et al., 2008). The fewest points used in clinical acupuncture is two (paired combination) (Zheng et al., 2012); however, very few imaging studies have examined cerebral function with stimulation at more than one acupoint. In addition, the majority of studies use a block design (Wu et al., 2002; Kong et al., 2007; Xu et al., 2007; Xiao et al., 2008) involving the needle being rotated, retained, rotated, and retained within each treatment block, and then observing the changes of functional brain imaging under the state of needle rotation and needle retention. This method only observed the effect of needle rotation and needle retention, and ignored the post-acupuncture effect. In other words, it failed to observe the change of functional brain imaging after withdrawing the needle, and thus is not truly representative of clinical acupuncture. Moreover, after needle rotation, the brain does not return to the same steady state as pre-acupuncture, but remains active during the period in which the needle is retained in place. Thus, the data calculated by subtracting the effects of the retained needle from those of the rotated needle may include false positives (Zheng et al., 2012).

To more accurately determine the complex brain activities that occur during acupuncture, the technique of resting-state fMRI is gaining attention in acupuncture studies (Bai et al., 2009; Zhong et al., 2011). Unlike the block design, resting-state fMRI compares the state without a needle before and after acupuncture, thus avoiding imaging during the manipulation but focusing on the effects ultimately produced. Additionally, resting-state fMRI separates the conventional acupuncture–response signal processing mode. The different signal linearity provides information about actual cerebral functional responses to various physiological states, thus being a more accurate reflection of complex human brain activities compared with more traditional methods.

In the present study, we measured the amplitude of low-frequency fluctuations using resting-state fMRI and performed acupuncture at *Taichong* (LR3) and *Taixi* (KI3). Our results provide further evidence for the acupoints–brain relation hypothesis that pointed out that the regulating action of acupuncture should be adjusted and integrated through the brain, and then acted on the target organ. Brain response to this stimulus is the key to recognition of acupoints and non-acupoints. We also explore the functional characterization of specific brain areas activated by combined acupoint stimulation, to guide acupuncture treatment in the clinic.

Subjects and Methods

Subjects

Fifteen healthy volunteers (8 males and 7 females), aged 21–23 (21.8 ± 0.6) years were included in this study. Subjects weighed 46–72 (55.40 ± 8.35) kg and were 160–180 (168.6 ± 6.81) cm tall. All subjects gave full informed consent before the experiment. This study was approved by the Chinese Ethics Committee of Registering Clinical Trials (ChiECRCT-2012011) and registered in the Chinese Clinical Trial Register (ChiCTR-TRC-12002427).

Inclusion criteria

(1) Undergraduates in the city of Guangzhou and aged 21–28 years, who had not undergone acupuncture more recently than 1 month prior to volunteering for our study. (2) Good previous and present physical and mental health. (3) Right-handed. (4) Acupoint site without skin damage or disease.

Exclusion criteria

(1) Left handedness. (2) Metal in the body, such as a pacemaker or metal dentures. (3) Acupuncture hypersensitivity during a preliminary test of acupuncture response 1 month prior to the experiment. (4) Previous recent (within 1 month) acupuncture treatment. (5) Fear of confined spaces or strong reactions to noise and hypothermia.

Procedure outline

Subjects were asked to pass urine and stool prior to treatment. After resting in the supine position for 15 minutes, scanning was performed for 8 minutes, comprising a 2-minute transverse scan and a 6-minute resting-state blood oxygenation level dependent sequence scan. Acupuncture was then conducted, and the needle was maintained in place for 30 minutes. Fifteen minutes after the needle was withdrawn, a further 8-minute scan was performed. The volunteers' eyes were masked (Hanjiang Xinhua Tourist Supplies Factory, Yangzhou, Jiangsu Province, China), and earplugs (Aearo, Indianapolis, IN, USA) were worn, to avoid audio-visual stimulation during the experiment. The volunteers were unaware which acupoints were used. All procedures (including initial screening) were performed by a chief physician. The experimental design chart is shown in **Figure 1**.

Acupuncture methods

Acupuncture was performed in all subjects by the same experienced physician. *Taichong* and *Taixi* were identified in accordance with Name and Location of Acupoints: Chinese National Standards GB12346-90 (2006) (**Figure 2**). Disposable stainless steel acupuncture needles (25.0 mm × 0.3 mm; Huatuo; Suzhou Medical Supplies Co., Suzhou, Jiangsu Province, China) were used throughout the study. Each needle was inserted using the nail-pressing method, first at *Taichong*, bilaterally, and once the subject indicated that he or she could feel each needle, the remaining two needles were inserted at *Taixi*, bilaterally. All needling was performed from the patient's left to right sides. Once sensation of all needles occurred, we rotated them at an angle of 90°–180° and frequency of 60–90 times/min, with lifting and thrusting at 0.3–0.5 cm and at a frequency of 60–90 times/minute. After manipulating the needle for 1 minute, it was retained for 30 minutes. The needle was manipulated for 1 minute with an interval of 10 minutes.

Resting-state fMRI scanning

Subjects remained conscious throughout. They were placed

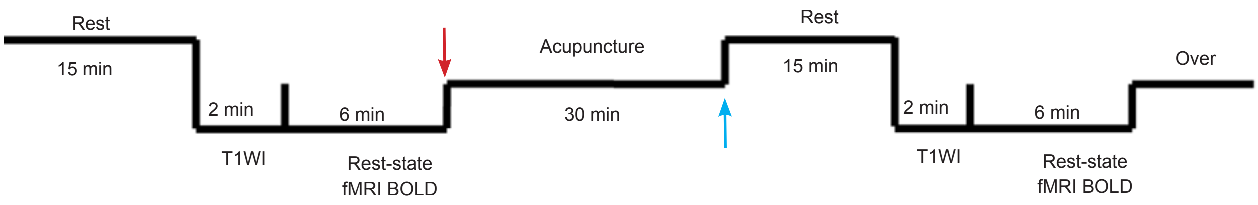

Figure 1 Flow chart of the experimental procedure.
Red arrow represents needle insertion; blue arrow represents needle withdrawal. T1WI: T1-weighted image; fMRI: functional magnetic resonance imaging; BOLD: blood-oxygen-level dependent contrast; min: minutes.

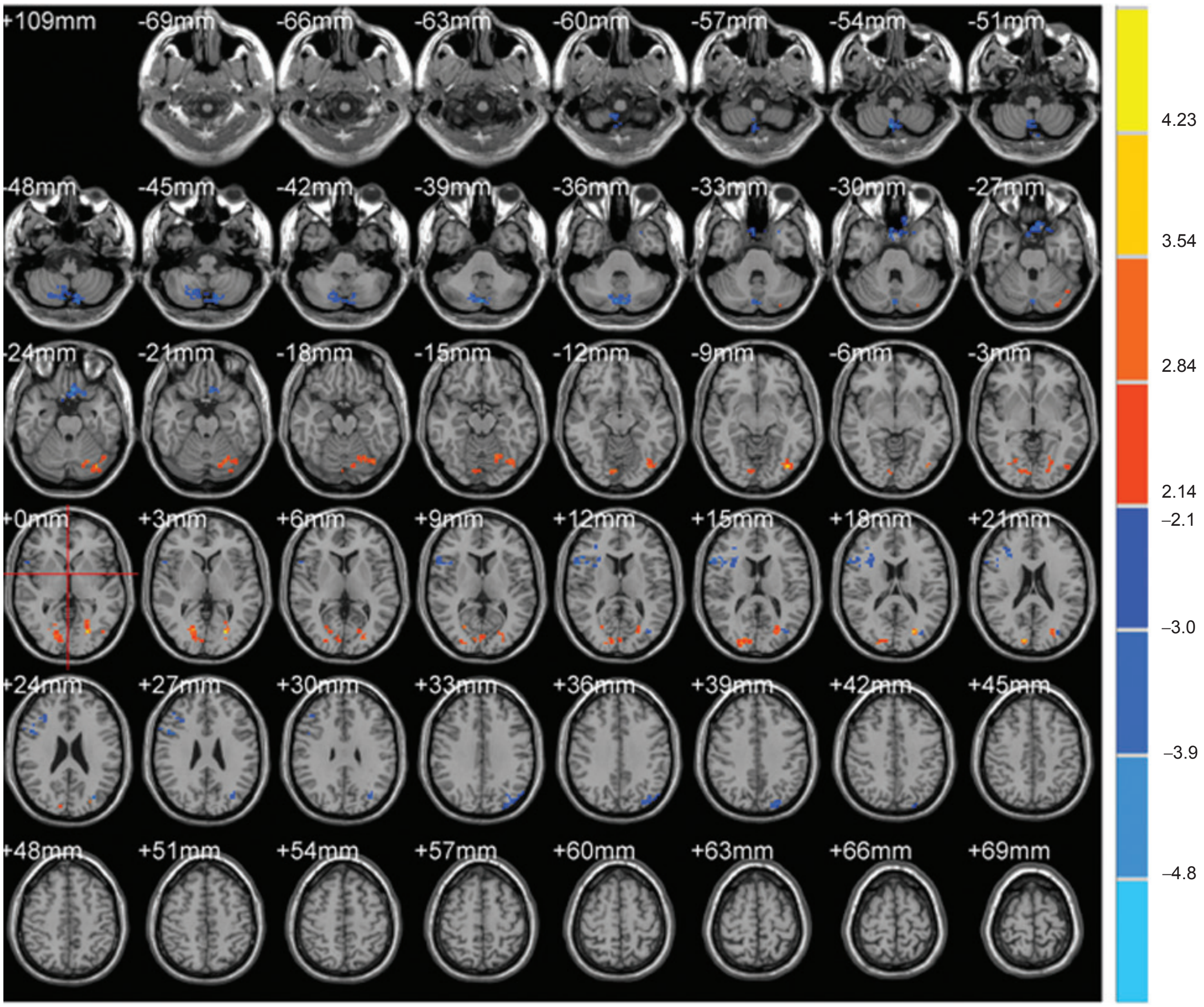

Figure 3 Brain areas with altered amplitude of low-frequency fluctuation 15 minutes after acupuncture at *Taichong* (LR3) and *Taixi* (KI3).
Blue areas represent decreases in the amplitude of low-frequency fluctuation; red areas represent increases in the amplitude of low-frequency fluctuation; grey areas represent no difference in activation.

in a supine position and asked to breathe calmly. Their heads were fixed with a foam mat to minimize voluntary and involuntary movements. Earplugs were used to reduce hearing, and eye masks were used to avoid visual stimulation. The scan began after the volunteers had rested for 15 minutes. Experiments were conducted on a GE 3.0T MRI scanner (Signa Excite System, General Electric Medical Systems, Milwaukee, WI, USA) with an 8-channel head coil. MRI data were collected 15 minutes before needle insertion and 15 minutes after needle withdrawal, as follows:

(1) Transverse T1-weighted image (T1WI) sequence: 2 minutes, fast spin echo sequence; OAx T1 FLAIR, repetition time = 1,750 ms, echo time = 24 ms, inversion time = 960 ms, field of view = 24 × 24 cm^2, matrix = 320 × 224, number of excitations = 1, thickness = 5.0 mm; interval = 1.0 mm; slice layers = 30; echo train length = 8; bandwidth = 31.25.

(2) Resting-state fMRI blood-oxygen-level dependent data collection: gradient echo-echo-planar imaging sequence scanning was used for 6 minutes, with the following scan parameters: repetition time = 3,000 ms/minimum, echo time = min-

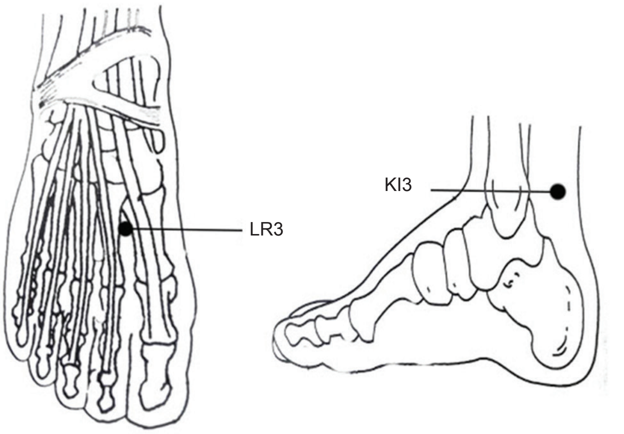

Figure 2 Localization of *Taichong* (LR3) and *Taixi* (KI3).

imum; flip angle = 90°; field of view = 240 mm × 240 mm; thickness = 5.0 mm; interval = 1.0 mm; slice layer = 30 slices per acquisition; matrix = 96 × 96; number of excitations = 1.

Image processing

Preprocessing was conducted using Data Processing Assistant for resting-state fMRI (Yan and Zang, 2010, http://www.restfmri.net), which is based on Statistical Parametric Mapping (SPM8; http://www.fil.ion.ucl.ac.uk/spm) and the resting-state fMRI Data Analysis Toolkit (REST, Song et al., 2011; http://www.restfmri.net) (Chao-Gan et al., 2010; Song et al., 2011). This contains DICOM format conversion, removal of 10 time points prior to image scanning, time correction, correction of head movement, space standardization, and space smoothing. Correction of head movement was used to calculate the head movement value during panning and rotation in the *X*, *Y*, and *Z* planes. The data of subjects with three-dimensional panning > 1.5 mm and (or) rotating > 1.5° were excluded. Space standardization used the MNI template developed by the Montreal Neurological Institute, Canada. A 3 mm^3 sample was fitted to the MNI template. After assessing the degree of standardization, subjects with poorly fitted data were excluded. Gaussian smoothing was applied with a full width at half maximum of 4 mm^3. After image preprocessing, all 15 subjects were included in the statistical analysis, with no exclusions.

REST1.8 software (http://www.restfmri.net/forum/REST_V1.8) was used for the amplitude of low-frequency fluctuations analysis. After preprocessing, the linear tendency of the data was removed by linear regression. Time and curve were convolved using Hamming bandpass filtering. The amplitude of low-frequency fluctuations was obtained (0.01–0.08 Hz), and obtained data from each subject were computed to obtain a map of the amplitude of low-frequency fluctuations. The values of the amplitude of low-frequency fluctuations were divided by the mean of the whole brain, and standardized amplitude of low-frequency fluctuations was obtained (Zang et al., 2007).

Statistical analysis

The data were analyzed using REST 1.8 software (Song et al., 2011). Intragroup standardized values of the amplitude of low-frequency fluctuations were evaluated using a two-sample *t*-test (α = 0.05, AlphaSim correction $P < 0.05$, continuous voxel > 85). Differences between pre- and post-acupuncture amplitude of low-frequency fluctuations were obtained in all subjects. The precise anatomical position in the brain corresponding to the MNI coordinate was identified using Rest1.8 software Viewer.

Table 1 Brain areas with increased amplitude of low-frequency fluctuation 15 minutes after acupuncture at *Taichong* and *Taixi*

Brain region	Side	Brodmann area	Voxels	Talairach (mm)			*T* value
				X	*Y*	*Z*	
Middle occipital gyrus	Left	18/19	136	−24	−75	3	4.27
Inferior occipital gyrus	Left	18	120	−42	−75	−9	3.97
Occipital lobe, cuneus	Right	18	132	12	−87	21	4.05

Intragroup standardized values of the amplitude of low-frequency fluctuation were analyzed using a two-sample *t*-test.

Table 2 Brain areas with decreased amplitude of low-frequency fluctuation 15 minutes after acupuncture at *Taichong* and *Taixi*

Brain region	Side	Brodmann area	Voxels	Talairach (mm)			*T* value
				X	*Y*	*Z*	
Frontal lobe, rectal gyrus	Left	11	87	−3	27	−24	−4.53
Cerebellum posterior lobe, pyramis	Left	–	187	−3	−78	−36	−4.58
Inferior frontal gyrus	Right	44	120	57	15	12	−4.31

Intragroup standardized values of the amplitude of low-frequency fluctuation were analyzed using a two-sample *t*-test.

Results

Changes in amplitude of low-frequency fluctuations after acupuncture at *Taichong* and *Taixi*

Fifteen minutes after needle withdrawal, the middle occipital gyrus and inferior occipital gyrus [Brodmann area (BA) 18] of the left occipital lobe, and the cuneus (BA18) of the right occipital lobe showed increases in amplitude of low-frequency fluctuations compared with pre-acupuncture values, whereas decreases from pre-acupuncture values were observed in the gyrus rectus (BA11) of the left frontal lobe, the center of the posterior lobe of the left cerebellum, and the inferior frontal gyrus (BA44) of the right frontal lobe (**Figure 3; Tables 1, 2**).

Discussion

We examined alterations in the amplitude of low-frequency fluctuations in different brain areas before and after acupuncture at *Taichong* and *Taixi*. The largest increases in the amplitude of low-frequency fluctuations were found in the cerebral occipital lobe, including the middle occipital gyrus (BA18/19), inferior occipital gyrus (BA18) and cuneus (BA18), and the largest decreases occurred in the frontal lobe, including the gyrus rectus (BA11) and inferior frontal gyrus (BA44), and the center of the posterior lobe of the left cerebellum.

The observed increased amplitude of low-frequency fluctuations in the occipital lobe, mainly in BA18, was consistent with a previous study by Yan et al. (2005) where the occipital lobe was specifically activated during acupuncture at *Taichong*. BA18 belongs to the high-level visual cortex, and is also associated with regulation of emotional activity (Vogt et al., 1996; Lang et al., 1998). As *Taichong* belongs to the Liver Channel of Foot *Jueyin*, activation of BA18 by acupuncture at *Taichong* supports the traditional Chinese theory that regulation of the liver can influence human affection. Similarly, the middle occipital gyrus belongs to the visual cortex, and acupuncture at *Taichong* and *Taixi* is traditionally thought to promote blood flow in brain areas related to vision and affection, activating these brain regions.

Of the brain areas that exhibited decreased amplitude of low-frequency fluctuations in the present study, namely BA11, BA44 and the center of the posterior lobe of the cerebellum, BA11 is associated with human social behavior, emotion and decision-making. Emotional changes can affect blood pressure (Rutledge et al., 2002), consistent with the blood pressure regulating effect of *Taichong* (Yang et al., 2008). Furthermore, human social behavior and decision-making relate to a promising effect of acupuncture at *Taixi* and *Taichong* recently observed on mild cognitive impairment (Chen et al., 2014). Previous studies (Gabrieli et al., 1998; Etard et al., 2000; Saur et al., 2006) also confirmed that BA44 (Broca's area) was involved in phonological and semantic processing, as well as cue precision and memory behavior detection (McDermott et al., 1999). With respect to the deactivated cerebellar posterior lobe observed in our study, the cerebellum is known to be strongly involved in sensation, movement and attention, as well as other cognitive and non-cognitive systems (Randich et al., 1992). The cerebellum is responsible for the body adapting to known stimuli or new environments (Randich et al., 1992). Acupuncture at *Taichong* and *Taixi* induced a decrease in amplitude of low-frequency fluctuations in the posterior lobe of the cerebellum, which may reflect the regulatory action of the cerebellum on various behaviors. Recently, Moulton et al. (2010) showed that the cerebellum plays a central role in sensation, as well as in movement and attention; this is supported by our present results. Acupuncture at *Taichong* and *Taixi* is also effective against headache, dizziness, insomnia, and excessive dreaming, which may be correlated with the regulatory effects of the cerebellum on high-level cognitive function and sleep (Dharani, 2005). Together, our data indicate that acupuncture at *Taichong* and *Taixi* specifically suppresses blood flow and causes deactivation in brain areas related to emotion, decision making, semantic handling, memory, attention, and sensation.

Our study has a number of limitations. First, MRI had been performed in some, but not all, volunteers, prior to our study. It is therefore possible that the volunteers with no prior experience of MRI may have had heightened anxiety during pre-acupuncture MRI, which may have affected MRI results, such as the activation of BA11, associated with emotional responses. In future studies, the relevant history of the subjects (*i.e.*, whether the volunteers had received MRI) should be taken into account. Second, the volunteers in this study were healthy subjects. Brain fMRI images are different between healthy subjects and patients with cardiovascular or visual diseases. Therefore, to confirm the therapeutic value of activation of the observed brain areas by acupuncture at *Taichong* and *Taixi*, we will perform resting-state fMRI in hypertensive patients undergoing stimulation at these acupoints in future studies.

In summary, our study provides evidence for the functional specificity of meridians and acupoints, further supporting the acupoints-brain relation hypothesis (Wu et al., 2002; Zhang et al., 2004). Acupuncture at *Taichong* and *Taixi* also deactivated brain areas related to emotion, attention, and phonological and semantic processing, but activated brain areas related to vision. We therefore suggest that the activated brain regions represent the target brain areas in people undergoing acupuncture at *Taichong* and *Taixi*. The activation of these target brain areas is associated with the functions of *Taichong*, such as decreasing blood pressure (Yang et al., 2010) and improving vision, and the functions of *Taixi*, such as improving memory loss and inattention. Importantly, we used resting-state fMRI to observe functional measures before and after acupuncture, allowing us to examine the effects of acupuncture more accurately than with the commonly used block design. Moreover, we used a combined acupuncture treatment, a more clinically relevant approach than the majority of experimental studies using a single acupoint.

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Author contributions: *CZT was responsible for the funds. YH and CZT participated in the study concept and design, and manuscript authorization. JPZ, CXW and SQZ recruited volunteers and wrote the manuscript. HLO performed the acupuncture. ZPL and JRC ensured the integrity of the data. All authors approved the final version of the manuscript.*
Conflicts of interest: *None declared.*

References

Bai L, Qin W, Tian J, Dong M, Pan X, Chen P, Dai J, Yang W, Liu Y (2009) Acupuncture modulates spontaneous activities in the anticorrelated resting brain networks. Brain Res 1279:37-49.

Chang XB, Fan XN, Wang S, Meng ZH, Yang X, Shi XM (2013) Cluster analysis for acupoint specificity of acupuncture effect based on cerebral infarction rat model. Chin J Integr Med 19:853-858.

Chao-Gan Y, Yu-Feng Z (2010) DPARSF: a MATLAB toolbox for "pipeline" data analysis of resting-state fMRI. Front Syst Neurosci 4:13.

Chen S, Xu M, Li H, Liang J, Yin L, Liu X, Jia X, Zhu F, Wang D, Shi X, Zhao L (2014) Acupuncture at the Taixi (KI3) acupoint activates cerebral neurons in elderly patients with mild cognitive impairment. Neural Regen Res 9:1163-1168.

Cole LJ, Farrell MJ, Duff EP, Barber JB, Egan GF, Gibson SJ (2006) Pain sensitivity and fMRI pain-related brain activity in Alzheimer's disease. Brain 129:2957-2965.

Dharani NE (2000) The role of vestibular system and the cerebellum in apapting to gravitoinertial, spatial orientation and postural challenges of REM sleep. Med Hypotheses 65:83-89.
Etard O, Mellet E, Papathanassiou D, Benali K, Houdé O, Mazoyer B, Tzourio-Mazoyer N (2000) Picture naming without Broca's and Wernicke's area. Neuroreport 11:617-622.
Gabrieli JD, Poldrack RA, Desmond JE (1998) The role of left prefrontal cortex in language and memory. Proc Natl Acad Sci U S A 95:906-913.
General Administration of Quality Supervision, Inspection and Quarantine, the Standardization Administration, People's Republic of China. Name and location of Acupoints: Chinese National Standards. GB/T12346, 2006.
Ji LX, Yan LP, Wang HJ, Wang B, Zhang XY, Zhang TS, Jin XF (2008) Selection of basic acupoints for composing gastric-disorder-formulao for electroacupuncture prevention of acute gastric mucosal lesion in rats. Zhen Ci Yan Jiu 33:296-300, 325.
Kong J, Gollub RL, Webb JM, Kong JT, Vangel MG, Kwong K (2007) Test-retest study of fMRI signal change evoked by electro acupuncture stimulation. Neuroimage 34:1171-1181.
Lai XS, Huang Y (2007) A cerebral functional definition on the specificity of acupoints, needling sensation and association of acupoints based on the "acupoints-brain relation hypothesis". Zhongguo Zhen Jiu 27:777-780.
Lang PJ, Bradley MM, Fitzsimmons JR, Cuthbert BN, Scott JD, Moulder B, Nangia V (1998) Emotional arousal and activation of the visual cortex: an fMRI analysis. Psychophysiology 35:199-210.
Li D, Yang M, Zhao L, Zheng H, Li Y, Chang X, Cui J, Wang R, Shi J, Lv J, Leng J, Li J, Liang F (2014) Acupuncture for chronic, stable angina pectoris and an investigation of the characteristics of acupoint specificity: study protocol for a multicenter randomized controlled. Trial 15:50.
Liang P, Wang Z, Qian T, Li K (2014) Acupuncture stimulation of taichong (Liv3) and Hegu (LI4) modulates the default mode network activity in Alzheimer's disease. Am J Alzheimers Dis Other Demen 6:1-10.
Litscher G (2009) Ten years evidence-based high-tech acupuncture-a short review of centrally measured effects (Part II). Evid Based Complement Alternat Med 6:305-314.
Liu B, Chen J, Wang J, Liu X, Duan X, Shang X, Long Y, Chen Z, Li X, Huang Y, He Y (2012) Altered small-world efficiency of brain functional networks in acupuncture at st36: a functional MRI study. PLoS One 7:e39342.
Liu J, Qin W, Guo Q, Sun J, Yuan K, Dong M, Liu P, Zhang Y, von Deneen KM, Liu Y, Tian J (2011) Divergent neural processes specificto the acute and sustained phases of verum and sham acupuncture. J Magn Reson Imaging 33:33-40.
McDermott KB, Buckner RL, Petersen SE, Kelley WM, Sanders AL (1999) Set and code specific activation in the frontal cortex: an fMRI study of encoding and retrieval of faces and words. J Cogn Neurosci 11:631-640.
Moulton EA, Schmahmann JD, Becerra L, Borsook D (2010) The cerebellum and pain: passive integrator or active participator? Brain Res Rev 65:14-27.
Randich A, Gebhart GF (1992) Vagal afferent modulation of nociception. Brain Res Rev 17:77-99.
Rong PJ, Zhao JJ, Gao JH, Li X, Li SY, Ben H, Pearson B (2013) Progress of research on specificity of meridian acupoint efficacy. Chin J Integr Med 19:889-893.
Rutledge T, Hogan BE (2002) A quantitative review of prospective evidence linking psychological factors with hypertension development. Psychosomatic Med 64:758-766.
Saur D, Lange R, Baumgaertner A, Schraknepper V, Willmes K, Rijntjes M, Weiller C (2006) Dynamics of language reorganization after stroke. Brain 129:1371-1384.
Song XW, Dong ZY, Long XY, Li SF, Zuo XN, Zhu CZ, He Y, Yan CG, Zang YF (2011) REST: a toolkit for resting-state functional magnetic resonance imaging data processing. PLoS One 6:e25031.
Vogt BA, Debyshire S, Jones AK (1996) Pain Processing in four regions of human cingulated cortex localized with co-registered PET and MR imaging. Eur J Neurosci 8:1461-1473.
Wang WD, Kong KM, Xiao YY, Wang XJ, Liang B, Qi WL, Wu RH (2006) Functional MR imaging of the cervical spinal cord by use of electrical stimulation at LI4 (Hegu). Conf Proc IEEE Eng Med Biol Soc 1:1029-1031.
Wang WD, Kong KM, Xiao YY, Wang XJ, Liang B, Qi WL, Wu RH (2009) An fMRI study of neuronal specificity of an acupoint: electro acupuncture stimulation of Yanglingquan (GB34) and its sham point. Neurosci Lett 464:1-5.
Wu C, Qu S, Zhang J, Chen J, Zhang S, Li Z, Chen J, Ouyang H, Huang Y, Tang C (2014) Correlation between the effects of acupuncture at taichong (LR3) and functional brain areas: a resting-state functional magnetic resonance imaging study using true versus sham acupuncture. Evid Based Complement Alternat Med 2014:729091.
Wu MT, Sheen JM, Chuang KH, Yang P, Chin SL, Tsai CY, Chen CJ, Liao JR, Lai PH, Chu KA, Pan HB, Yang CF (2002) Neuronal specificity of acupuncture response: a fMRI study with electro acupuncture. Neuroimage 16:1028-1037.
Xiao YY, Du L, Hong BK (2008) Study on fMRI brain map in patients undergoing needling at Zusanli (ST 36) by reinforcing method. Zhonggou Zhong Xi Yi Jie He Za Zhi 28:122-125.
Xing JJ, Zeng BY, Li J, Zhuang Y, Liang FR (2013) Acupuncture point specificity. Int Rev Neurobiol 111:49-65.
Xu FM, Xie P, Lü FJ, Mou J, Li YM, Zhao JN, Chen WJ, Gong QY, Zhao LB, Liu QJ, Shen L, Zhai H, Yan B, Li K, Xu J, Wang W, Li K, Liu H, Shan B, Tang X (2005) Acupoint-specific fMRI patterns in human brain. Neurosci Lett 383:236-240.
Yang DH (2010) Effect of electro acupuncture on Quchi (LI 11) and Taichong (LR 3) on blood pressure variability in young patient swith hypertension. Zhongguo Zhen Jiu 30:547-550.
Yang DY (2007) Study on corresponding areas the liver and lung channels in brain with fMRI. Zhongguo Zhen Jiu 27:749-752.
Yang HY, Zhong XH, Liu TY, Kuai L, Gao M (2008) Impact of different emulated acupuncture-needle manipulations on blood pressure and myocardial angiotensin II content in spontaneous hypertension rats. Zhen Ci Yan Jiu 33:186-190.
Yeo S, Choe IH, van den Noort M, Bosch P, Jahng GH, Rosen B, Kim SH, Lim S (2014) Acupuncture on GB34 activates the precentral gyrus and prefrontal cortex in Parkinson's disease. BMC Complement Altern Med 14:336.
You Y, Bai L, Dai R, Cheng H, Liu Z, Wei W, Tian J (2013) Altered hub configurations within default mode network following acupuncture at st36: a multimodal investigation combining fMRI and MEG. PLoS One 8:e64509.
Zang YF, He Y, Zhu CZ, Cao QJ, Sui MQ, Liang M, Tian LX, Jiang TZ, Wang YF (2007) Altered baseline brain activity in children with ADHD revealed by resting-state functional MRI. Brain Dev 29:83-91.
Zhang G, Yin H, Zhou YL, Han HY, Wu YH, Xing W, Xu HZ, Zuo XN (2012) Capturing amplitude changes of low-frequency fluctuations in functional magnetic resonance imaging signal: a pilot acupuncture study on NeiGuan (PC6). J Altern Complement Med 18:387-393.
Zhang WT, Jin Z, Luo F, Zhang L, Zeng YW, Han JS (2004) Evidence from brain imaging with fMRI supporting functional specificity of acupoints in humans. Neurosci Lett 354:50-53.
Zheng Y, Qu S, Wang N, Liu L, Zhang G, Jiang X, Chen J, Huang Y, Zhang Z (2012) Post-stimulation effect of electroacupuncture at Yintang (EX-HN3) and GV20 on cerebral functional regions in healthy volunteers: a resting functional MRI study. Acupunct Med 30:307-315.
Zhong ZP, Wu SS, Chen ZG, Bo L (2011) Study on response of resting-state functional magnetic resonance imaging induced by abdominal acupuncture with invigorating the kidney and nourishing marrow method. Zhongguo Zhen Jiu 31:139-143.

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