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Cerebral activation effects of acupuncture at Yanglinquan(GB34) point acquired using resting-state fMRI

Liansheng Liu[a], Shuqi Chen[a], Daohui Zeng[a], Hengguo Li[b], Changzheng Shi[b], Lihong Zhang[c,*]

[a] Medical Imaging Department, First Affiliated Hospital of Guangzhou University of Traditional Chinese Medicine, Guangzhou 510405, Guangdong, China
[b] Medical Imaging Center, First Affiliated Hospital of Jinan University, Guangzhou 510632, Guangdong, China
[c] Department of Radiology, Jining No.1 People's Hospital, Jining 272011, Shandong, China

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ABSTRACT

Objective: To explore the central mechanism of acupuncture points for regional homogeneity(ReHo) of resting state in brain function after acupuncture at GB34.
Methods: Ten healthy volunteers were enrolled, which included 4 males and 6 females, aged 20–34 years old with median age of 23. The GE Signa HDxt 3.0 T magnetic resonance imaging were performed before (control group) and after acupuncture at GB34, and differences of different brain ReHo of 2 groups by statistical parametric mapping (SPM8) software and ReHo data processing methods were analyzed. The statistically different brain regions were obtained by false discovery rate corrected (FDR-Corrected).
Results: Compared with control group, the anterior cingulated gyrus, left temporal gyrus, right inferior parietal lobule, right frontal gyrus were enhanced ReHo after acupuncture at GB34. The left thalamus, right insular cortex, left inferior frontal gyrus, right anterior cingulate were decreased ReHo after acupuncture at GB34.
Conclusion: It is demonstrated that the signal synchronization change ReHo in different brain regions including cognitive, motor, default network, limbic system and other parts of encephalic region after acupuncture at GB34, suggesting that the central mechanism of acupuncture at GB34 is the result of all levels of the combined effects of brain networks.

1. Introduction

As a unique therapy of Chinese medicine, Acupuncture and moxibustion's clinical effect is exact, but its mechanism has not been fully expounded, especially lacking the objective and visual evidence. Specific activation of cerebral certain regions caused by acupuncture has been found by scholars using functional magnetic resonance (fMRI) task-state design pattern, which verifies the functional specificity of acupuncture theory exists, but the difference of the results is inconstant because the repeatability of the research model is poor (Wong et al., 2013). GB34 has become a common point to explore the mechanism of meridians and acupoints in clinical and basic researches due to its wide range of clinical effect (Yeo et al., 2014; Ning et al., 2017). The method of ReHo will be used in this paper to compare and analyse the difference of ReHo value in cerebral areas before and after puncture on GB34. The resting-state cerebral activity after puncture on GB34 will be studied and the central mechanism of acupuncture will be explored.

2. Materials and methods

2.1. Clinical datas

This study was approved by the Medical Research Ethics Committee of Guangzhou University of Traditional Chinese Medicine, China.This study included 10 healthy volunteers consisting of 4 males and 6 females, aged 20–34 years, with a median age of 23 years. All of the volunteers, healthy previously, had not taken drugs or undergone acupuncture within the last month. The inclusion criteria included: (1) right-handedness and (2) age > 19 years. The exclusion criteria included: (1) any history of psychiatric or neurologic diseases, and (2) identifiable MRI abnormalities, such as vascular malformations or tumors. They had signed informed consent forms.

2.2. Methods

Apparatus, equipments and venues: 0.32 mm × 40.00 mm disposable sterile acupuncture needles (*Tianxie* Acupuncture Instruments corporation in Suzhou); Signa HDxt 3.0 T MRI scanner produced by GE

* Corresponding author.
E-mail address: zhanglh968968@sina.com (L. Zhang).

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company; MRI chamber in the First Affiliated Hospital of Guangzhou University of Traditional Chinese Medicine.

2.3. Experimental design and data collection

2.3.1. Acupuncture methods

The puncture is performed by one highly qualified acupuncture doctor. Acupoints are the left GB34. Manipulation: Puncture for 15 min after getting the needle reaction, and twist the needle once every 2 min (10 s for once).

2.3.2. Imaging design for resting-state cerebral function

Collection for the resting-state fMRI data including pre and post puncture, as well as two-dimensional (two-dimensional, 2D) and three-dimensional (three-dimensional, 3D) anatomical image data.

2.3.3. MRI scan

The volunteers were in a supine position on the examination bed, were awake with calm breathing, and had no proactive thinking movement but were informed of the scanning environment in advance. A foam pad was used to fix the head, and rubber earplugs were used to reduce the noise. Scanning steps: Structural positioning imaging, fast spin echo sequence (FSE) and axial T1-weighted fluid-attenuated inversion recovery (T1-FLAIR) were used to perform the scan, with the baseline parallel to the anterior and posterior combine-line (AC-PC) of the corpus callosum. A total of 28 slices covering the entire brain were acquired. Resting-state blood oxygenation level dependent (BOLD) imaging, echo planar imaging (EPI) sequence and T1-FLAIR image positioning were used with the same number of scanning layers to structurally position the image, and 8400 images were obtained. A high-resolution image of the entire brain scan, including a three-dimensional structure used for brain volume imaging (BRAVO) sequences, was constructed and used to obtain 136 images. The parameters of each sequence scan are listed in Table 1. During fMRI scans, all subjects were instructed to keep their eyes closed, relax, do not move, think of nothing in particular, and stay awake. After the scan, the MRI images and subjects' conditions should be checked instantly in order to make sure whether they satisfied the requirements; if not, the MRI data were abandoned and scanned again.

2.4. Data processed and statistic of fMRI

2.4.1. Data preprocessing

The original images were input to the offline workstation. The package for statistical parametric mapping software (SPM8, http://www.fil.ion.ucl.ac.uk/spm/) which is run using MATLAB2009b, and a software package based on SPM8 and DPARSF of REST 1.2 were used. Main steps: The first 10 images were removed to exclude the effects by the time for magnetic fields to the steady-state, and the volunteers adaption to the environment. Time correction: Aimed at reducing the differences of the moment to get each picture. Head movement correction: This step aimed to reduce the effect of signals due to the noise generated by movement of the head. Data corresponding to the three-dimensional translation of head moving > 1 mm and three-dimensional rotation > 1° were removed. Spatial normalization: The functional sequence of images of all volunteers was spatially normalized to the Montreal Neurological Institute (MNI) template to locate the active region of the brain. Low-pass filtering: The obtained signal was subjected to low-pass filtering by 0.01–0.08 Hz to remove the interference generated by high- and low-frequency signals. Finally, the obtained frequency wave signals were analyzed using ReHo.

Table 1
MRI scan parameters for each sequence.

Sequence	TE/ms	TR/ms	Layer thickness/mm	Layer spacing/mm	Vision/cm^2	Matrix
BOLD	40	2000	3.8	0	24 × 24	64 × 64
T_1-FLAIR	24	1500	4	0.5	24 × 24	320 × 256
3D-BRAVO	3.0	7.8	1.2	0	24 × 24	256 × 256

2.4.2. ReHo analyzation

Resting state fMRI data analysis toolkit (REST), which is a software developed by the National Key Laboratory of Cognitive Neuroscience and Study of Beijing Normal University (more information at http://sourceforge.net/projects/resting-fmri), was adopted for ReHo analysis. Consistency in the time series of every voxel with its adjacent voxel in the brain was calculated to obtain the Kendall's coefficient of concordance (KCC). The KCC was the ReHo of the voxel, and the ReHo of every voxel constituted the subjects' ReHo brain. The following Eq. (1) for the KCC for a fixed point was used:

$$W = \frac{\sum (R_i)^2 - n(\overline{R})^2}{\frac{1}{12}K^2(n^3 - n)} \tag{1}$$

where W is the KCC of a fixed point with the range 0–1; n is the time point and n = 250 in the study; K is the total number of the given voxels with their adjacent voxel point and $K = 27$ in the study, i.e., the given point itself and its 26 adjacent points comprise a voxel clusters; R_i is the total level of 27 points voxel values of 27 points at the ith time point; and $\overline{R}$ is the meaning of R_i (Qin et al., 2011).

2.4.3. Image viewing

Brain images that were statistically significant after the above processing were superimposed on standard brain images to obtain images that displayed anatomical and statistical information, including image information for the sagittal, coronal, horizontal position or 3D mode images. Figure plugins such as Slice Viewer and Xjview were used to read the coordinates of the activated brain areas, the anatomical location and the T values in the MNI template.

2.5. Statistical methods

Standardized ReHo brain diagrams of GB34 group and the control group are performed with two-sample paired t-test by SPM8 software, undergone with two one-sample t-test results and been set as a mask, in this context the results are false discovery rate (FDR) corrected, $P < 0.05$, $T = 2.262$, $K > 405$, then regions of no significance which the voxel values are less than 10 are removed to obtain the difference of ReHo value in cerebral areas pre and post puncture on GB34.

3. Results

Cerebral areas of increased ReHo values in GB34 group compared to the group before puncture (control group) (Table 2): The anterior cingulate gyrus, the left superior temporal gyrus, right inferior parietal lobule and right middle frontal gyrus; Cerebral areas of reduced ReHo

Table 2
Cerebral areas of increased ReHo values in GB34 group compared to the control group.

Location	Brodman Partition	Voxel	T vavle	MNI Coordinate		
				X	Y	Z
anterior cingulate	BA24	96	10.35	15	36	9
left superior temporal gyrus	BA22	32	4.36	−45	0	−9
right inferior parietal lobule	BA40	76	6.46	51	−54	48
right middle frontal gyrus	BA8、9	96	6.23	21	21	54