

Power estimation predicts specific function action of acupuncture: an fMRI study

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Abstract

Purpose: The purpose was to investigate the distinct pattern of brain response induced by electroacupuncture stimulation (EAS) related to sustained acupuncture effects.

Material and Methods: Twenty-eight healthy volunteers were enrolled and randomized into two groups. According to grouping, volunteers were separately treated by EAS at GB37 (Guangming) or KI8 (Jiaoxin) during functional magnetic resonance imaging. Differences in acupuncture effects between the groups were tested by the power estimation approach.

Results: Spatial patterns of the whole brain power were different in the periaqueductal gray, occipital cortex (OC) and temporal cortex when induced by EAS at GB37 and KI8. Moreover, the differences in the sustained effects between these two acupoints were also identified and associated with the OC, dorsolateral prefrontal cortex, medial prefrontal cortex, anterior cingulate cortex and insula.

Conclusion: Electroacupuncture stimulation induced different power fluctuation patterns related to GB37 and KI8. We suggest that these findings might be attributed to the specific function action of these acupoints.

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Keywords: fMRI; Power estimation; Acupuncture

1. Introduction

Acupuncture, originating in the East, has been popularly accepted as an alternative or complementary medicine in the West and is proven to effectively treat a variety of disorders. Nevertheless, the underlying mechanism of acupuncture remains elusive. With the development of noninvasive functional magnetic resonance imaging (fMRI) brain imaging technique, it opens up opportunities for more direct information about the mechanism of acupuncture.

In the acupuncture field, functional specificity of an acupoint is a hot topic under current discussion. A large number of neuroimaging studies have provided further evidence to support the possibility of the existence of acupoint specificity. Cho et al. found that acupuncture stimuli at the vision-related acupoints (BL67–BL60) induced specific fMRI signal changes at the occipital cortices, while nonacupoints and

sham did not induce the similar results [1]. They demonstrated relationships between activation of specific areas of brain cortices and corresponding acupoint stimulation. It was later reported that the visual cortex was activated by the laser- or electroacupuncture at eye-related acupoints [2–4]. Moreover, acupuncture stimuli at the auditory-related acupoint K3 (Taixi) attained auditory cortex activation [5]. However, several other fMRI studies have not replicated the same results as described above, especially regarding the specificity of vision. Gareus et al. reported that the significant blood oxygenation level-dependent (BOLD) signal changes were not detected in the visual cortex induced by acupuncture at GB37 (Guangming) [6]. Kong et al. indicated that electroacupuncture stimulation (EAS) produced no significant differences in the occipital cortex (OC) among UB60 and GB37, as compared to a nonacupoint [7]. Recently, Cho et al. have retracted their early research in the PNAS article, and they have not agreed on the specificity of any acupoint [8]. Therefore, controversial results still remain, which further promote the investigation of neural substrates in acupoint specificity.

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The human brain accounts for 2% of total body weight but merely 20% of the whole energy consumption. Currently, in the fMRI field, the level of spontaneous low-frequency (0.01–0.1 Hz) fluctuations of BOLD signals is of more interest. The spontaneous fluctuations of brain activity at rest are associated with the ongoing cerebral energy consumption. When performing cognitive or other tasks, the spontaneous-related power will transiently change. And it is likely seen as a competition for processing resources [9,10]. Furthermore, Jiao et al. reported the BOLD activity levels in the default mode network (DMN) by power spectral and Granger causal approaches [11]. These suggest the importance of studying power consumption of spontaneous brain activity. However, few acupuncture–fMRI studies examined the relationships between the variation of brain resources and acupoint specificity at spontaneous low-frequency fluctuations. Thus, this raised the question of how brain resources were modulated by stimulation at an acupoint.

Additionally, evidence from an acupuncture analgesia study suggested that the analgesic effects of acupuncture actually peaked long after acupuncture stimulation [12]. Our further data analysis stated that the sustained acupuncture effects modulated DMN [13]. Therefore, the sustained effects are seemed as critical roles in acupuncture studies.

In this study, we mainly focused on the sustained acupuncture effects and tried to investigate the specific function action of acupoints by examining the different power intensity patterns of low-frequency signal fluctuations in the whole brain induced by acupuncture. Meanwhile, we hypothesized that stimulation at different acupoints induced distinct patterns of power modulation, which could attribute to the function of different acupoints.

2. Materials and methods

2.1. Subjects and experimental paradigm

Twenty-eight healthy, right-handed volunteers participated in the present study (14 males, 14 females; 20–26 years old). Volunteers were all acupuncture naïve and had no history of neurological or psychiatric disorder; they also refrained from alcohol or drug consumption in the previous 48 h. Every volunteer was given informed consent approved by the local review board for human studies.

The nonrepeated event-related paradigm was adopted in this study [14]. The entire scanning run lasted 18 min, including a 6-min resting scan, a 6-min resting scan, followed by another 6-min EAS, and the needle was inserted into acupoints at GB37 or KI8 (Jiaoxin). The needling depth ranged from 1 to 1.5 cm, using a pure stainless steel disposable needle 0.18 mm in diameter and 40 mm in length. The EAS was operated by a professional acupuncturist, with a modified current-constant HANS (Han's Acupoint Nerve Stimulator) LH202 (Neuroscience Research Center, Peking University, Beijing, China) at 2-Hz pulses and 2–3 mA. Two electrodes were separately attached to the acupuncture needle and to a shallowly inserted point 1 cm nearby, as similarly described by Liu et al. [15].

During scanning, volunteers were asked to relax and stay awake. At the end of scanning, volunteers were then asked about the sensations they felt during scanning: aching, soreness, numbness, fullness, sharp or dull pain, pressure, heaviness, warmth, coolness, tingling, itching and any other sensations. The intensity of each sensation was measured using a 10-point visual analogue scale, similarly to the other studies [16]. And they were also asked whether they stayed awake during the whole scanning. If someone fell asleep, the related data would be removed without further analysis.

2.2. fMRI imaging

The fMRI experiment was performed using a 3.0-T Signa (GE) MR with a standard head coil. Functional images were acquired with a single-shot gradient-recalled echo planar imaging sequence (TR/TE=2000 ms/30 ms, FOV=240 mm×240 mm, matrix size=64×64, flip angle=90°, slice thickness=5 mm thick with no gaps, 32 sagittal slices). A set of T1-weighted high-resolution structural images was also collected (TR/TE=5.7 ms/2.2 ms, FOV=256 mm×256 mm, matrix size=256×256, flip angle=12°, slice thickness=1 mm with no gaps).

2.3. Image processing

The first five time points were discarded to avoid the instability of the initial MRI signal. Data sets were preprocessed using SPM5 (www.fil.ion.ucl.ac.uk/spm). The images first underwent slice-timing correction and realignment for head motion correction. The images were then normalized to a Montreal Neurological Institute template and resampled to 3 mm×3 mm×3 mm. The before-stimulation state (BSS) contained the images from 0.5 to 5.5 min, and the poststimulation state (PSS) contained the images from 12.5 to 17.5 min. BSS and PSS were then processed with a band-pass filter of 0.009–0.08 Hz. Finally, the filtered images were smoothed using a Gaussian kernel of full width at half maximum 6 mm.

On the first-level analysis, the power of the BOLD signal of each voxel was obtained at each BSS and PSS of volunteers by integrating the power spectral density over the frequency band of 0.009–0.08 Hz [9]. On the second-level analysis, a paired *t* test was used to compare the whole brain power before and after the EAS under the threshold $P<.005$ [false discovery rate (FDR) corrected] and cluster size >3 voxels. A two-sample *t* test was applied for differences in the whole brain power between the different acupoint groups during PSS. The contrast was thresholded at $P<.005$ (FDR corrected) with a cluster size >3 voxels.

3. Results

3.1. Behavior results

All volunteers stayed awake according to their reports after scanning. The prevalence of Deqi sensations was expressed as the intensity of sensations with mean score±S.D.

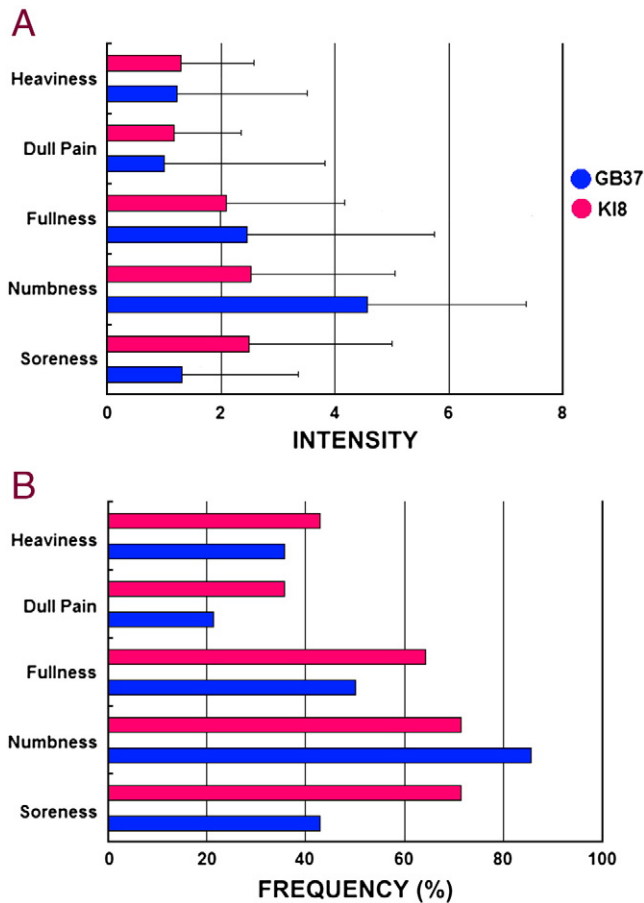


Fig. 1. Results of psychophysical analysis.

(Fig. 1A). The main sensations included fullness (4.58 ± 2.78 at GB37 and 2.53 ± 3.07 at KI8), numbness (4.46 ± 3.28 at GB37 and 2.09 ± 2.26 at KI8) and soreness (1.31 ± 3.20 at GB37 and 2.50 ± 2.86 at KI8). The percentages of individuals

in the group that reported the given sensations are reported in Fig. 1B, mainly consisting of fullness (50.00% at GB37 and 64.29% at KI8), numbness (85.43% at GB37 and 71.43% at KI8) and soreness (42.86% at GB37 and 71.43% at KI8). The comparisons did not reach statistical significance for Deqi scores between GB37 and KI8 (two-sample *t* test, $P < .05$).

3.2. fMRI results

It was first indicated that the power intensity patterns of the whole brain during BSS in the two acupoint groups were not significantly different ($P < .005$, FDR corrected). On the second-level analysis, differences of power distribution were represented by modulation of distinct acupoints compared to the power patterns before EAS. Statistically significant increases in the GB37 group were observed in the periaqueductal gray (PAG) and OC. The decreases were observed in the temporal cortex (TC). However, statistically significant increases in the KI8 group were observed in the TC, and the decreases were observed in the PAG and OC (Fig. 2 and Table 1). Results from the two-sample *t* test of the two acupoints during PSS are shown in Fig. 3 and Table 2. The most important and obvious differences were observed in the OC, the left insula, anterior cingulate cortex (ACC) and medial prefrontal cortex (MPFC).

4. Discussion

The present study employed a power estimation of the whole brain to investigate the sustained effects of different acupoints. Firstly, it was significantly found that the changes of the whole brain power distribution were distinctly induced by GB37 and KI8. Furthermore, the more significant differences were observed in the PAG, OC and TC, which presented an opposite direction in power modulation. Secondly, it was found that the statistically significant

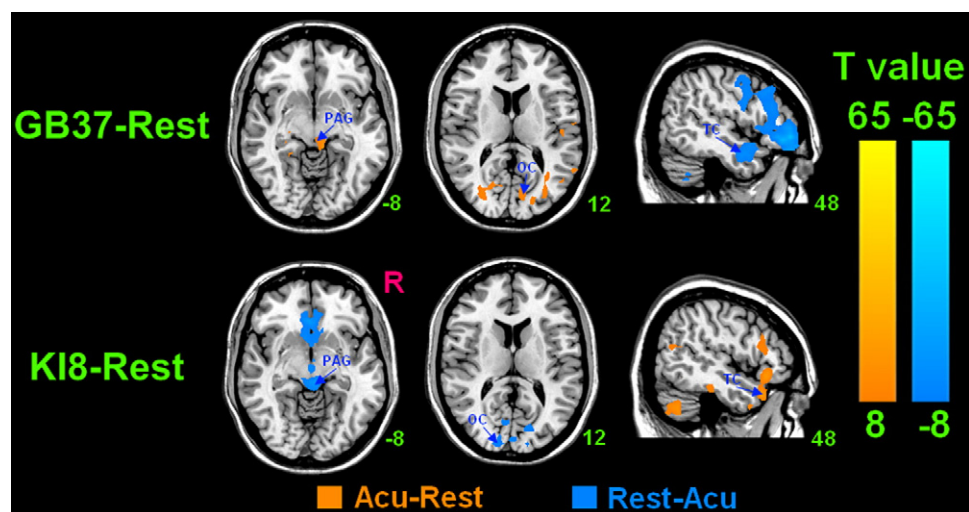


Fig. 2. Brain regions showing the significant differences of power intensity patterns during PSS compared to those during BSS.

Table 1

Brain regions activated significantly compared to the power intensity pattern during PSS and those during BSS at GB37 and KI8

Regions	GB37 (Guangming)-rest						KI8 (Jiaoxin)-rest					
	Hem	BA	Talairach			<i>t</i> value	BA	Talairach			<i>t</i> value	
			<i>x</i>	<i>y</i>	<i>z</i>			<i>x</i>	<i>y</i>	<i>z</i>		
OC	L	17/18/19	−3	−89	29	16.79	9/10	0	−89	18	−13.03	
	R	17/18/19	9	−78	15	17.80	9/10	6	56	19	−17.60	
TC	L	20/21/38	−50	11	−3	−9.22	22	−45	−57	17	9.24	
	R	20/21/38					22	56	−57	17	9.99	
PAG			6	−28	−8	11.72		−6	−29	−6	−14.93	

Abbreviations: BA, Brodmann area; Hem, hemisphere; L, left; R, right.

increases of power were located in different brain regions, which could feature the specific function of acupoints including the OC at the vision-related acupoint GB37, and the insula, ACC, dorsolateral prefrontal cortex (DLPFC) and MPFC at the non-vision-related acupoint KI8.

Spontaneous neuronal activity represents neuronal activity that is intrinsically generated by the brain [17]. During an EAS-sustained state, the acupuncture effects might stem solely from intrinsic brain modulation. We first found that significant power fluctuation in the PAG was induced by the two acupoints. Furthermore, the modulation patterns of acupoints were distinct. PAG plays a crucial role in ascending nociceptive transmission. It transmits afferents from nociceptive neurons in the spinal cord to thalamic nuclei. On the other hand, PAG is part of an opioid-related circuit, which contains many of the brain's opioid-containing neurons. An analgesic effect is produced with opioid agonist being injected into PAG and rostroventromedial medulla [18,19]. Certain human literature also indicates that opioid activity in the PAG is associated with human therapeutic treatments for chronic pain [20,21]. We suggested that these power fluctuations reflected the general effect of acupoint needling, which was likely to indicate that acupuncture

might have similar analgesic properties. Other similarities were observed in the OC and TC. We therefore speculated that acupuncture sustained effects, appearing after EAS, might induce such resource redistributions.

To investigate the special differences of the two acupoints, their power distribution patterns were then investigated. It was found that activations in the OC were related to GB37 in comparison with KI8, which might correctly reflect the evidence that GB37 is one of the important acupoints used to treat eye diseases based on Traditional Chinese Medicine. On the contrary, the activations in the insula, ACC, DLPFC and MPFC may more reflect the specific treatment of KI8. Insula is widely connected with the cortex, subcortex and brainstem structures, and the function of insula is involved in pain-related modulation, behavior, emotion and cognitive control [22–25]. ACC is associated with information processing and regulation in the brain including attention, emotion, visuospatial functions and nociception. Moreover, ACC is deemed to be the key structure involved in regulation of nociceptive processes [26]. In addition, the significant activation was also observed in the DLPFC and MPFC. Human neuroimaging studies have shown that these areas

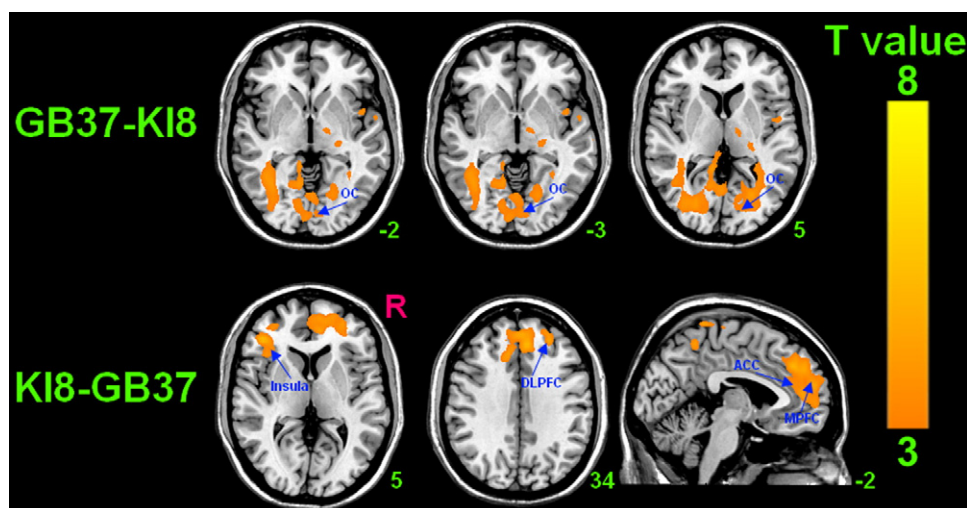


Fig. 3. Brain regions showing the specificity of GB37 and KI8 compared with the power intensity patterns of each other during PSS.

Table 2

Brain regions activated significantly for specific effects of GB37 and KI8

Regions	GB37-KI8						KI8-GB37				
	Hem	BA	Talairach			<i>t</i> value	BA	Talairach			<i>t</i> value
			<i>x</i>	<i>y</i>	<i>z</i>			<i>x</i>	<i>y</i>	<i>z</i>	
OC (BA17)	L	17	−18	−78	7	3.04					
	R	17	21	−81	10	3.17					
OC (BA18)	L	18	−18	−73	1	3.53					
	R	18	27	−93	−3	3.51					
OC (BA19)	L	19	−36	−83	32	4.01					
	R	19	42	−80	34	5.42					
DLPFC	L						46/9/10	−24	62	16	3.76
	R						46/9/10	42	−14	12	4.23
MPFC	L						9/10	−3	39	31	3.91
	R						9/10	9	53	11	3.75
ACC	L						32	−12	36	23	3.24
	R						32	9	44	1	3.33
Insula	L						13	−36	23	2	3.49
	R						13	−12	36	23	3.24

are implicated in pain suppression and are associated with top-down pain [27,28]. It is well known that KI8 is generally used to treat menstrual pain, irregular menstruation and gonalgia. Thus, the current results suggested that the specificity of KI8 pertains to analgesia.

To our knowledge, this was the first fMRI neuroimaging study to show the spatial power intensity patterns induced by the different effects of acupoints. The current results might provide neuroimaging evidence in support of the specific action of certain acupoints. However, the fundamental mechanisms underlying acupuncture processes await further investigation. Additionally, it is necessary to apply certain approaches for acupuncture studies because of the complexity of mechanism underlying the acupuncture. And the current results reflected the significant methodological contribution of this study.

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