

Acupuncture for gender differences and similarities in cerebral activity of health volunteers

A pilot fMRI study

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Abstract

This study aimed to explore the feasible gender differences and similarities in cerebral activity response to the acupuncture at local acupoints around knee.

Fifteen male and 15 female healthy adults were recruited and included in this study. Functional magnetic resonance imaging (fMRI) was applied to measure cerebral activity response to acupuncture at Liangqiu (ST34), Xuehai (SP-10), Neixiyan (EX-LE4), and Dubi (ST-35).

Acupuncture activated the postcentral gyrus, precuneus, temporal, posterior lobe, and occipital lobe in both males and females. When compared with females, males showed brain activation in the right middle frontal gyrus, inferior frontal gyrus, right precuneus, right superior parietal lobule, left cerebellum anterior lobe; and brain deactivation in the right frontal. When compared with males, females were observed brain activation in the right frontal lobe, right parietal lobe, and right middle temporal gyrus; and brain deactivation in the left and right medial frontal gyrus.

The results of this study demonstrated that the neural effects of local acupoints around knee might be different between male and female subjects. Further clinical trials should take this gender effect into account in their design of studies.

Abbreviations: EX-LE4 = Neixiyan, fMRI = Functional magnetic resonance imaging, MDD = major depressive disorder, SP-10 = Xuehai, ST34 = Liangqiu, ST-35 = Dubi.

Keywords: acupuncture, cerebral activity, fMRI, gender difference, knee

Editor: Muhammad Shahzad Aslam.

Ang Li and Yuan-hong Wang These authors contributed equally in this study.

The authors have no conflicts of interest to disclose.

Funding: This work was supported in part by the National Foundation of Natural Science of China (Grant nos. 81373714, 81172741, and 30972537), Natural Science of Heilongjiang Province (Grant No. D201214), Project of Young Innovative Talents of Heilongjiang Province Undergraduate College (UNPVSCT-2015119), and the "Chunhui Plan" of the Ministry of Education (No. Z2009-1-15030), and the Special Fund of Harbin Science and Technology Innovation Talents Research (No. 2016RAXYJ096).

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Medicine (2018) 97:50(e13655)

Received: 25 August 2018 / Accepted: 12 November 2018

<http://dx.doi.org/10.1097/MD.0000000000013655>

1. Introduction

Acupuncture therapy has been practiced in China for more than 2000 years. It consists of inserting thin, disposable needles into the skin with needles manipulation to achieve *deqi*. It has been reported to treat a variety of conditions, such as headache,^[1] chronic pain,^[2,3] stroke rehabilitation,^[4-6] tendonitis,^[7] arthritis,^[8] chronic fatigue syndrome,^[9,10] urinary incontinence,^[11,12] and so on. However, the mechanisms of the effects of acupuncture are still unclear, although some studies have explored the central mechanisms of acupuncture on the brain, especially functional magnetic resonance imaging (fMRI) was utilized to explore these kinds of studies.^[13-17]

Previous fMRI studies have provided evidence for the connections between acupuncture therapy and brain activation.^[18,19] It has been reported that specific brain areas are activated by the acupuncture stimulation, including limbic system,^[20] visual cortex,^[18] and areas processing language.^[21] Additionally, the neuronal specificity of acupoints has also been reported to support by the results of fMRI studies.^[16,17]

It has been reported that acupoints Liangqiu (ST34), Xuehai (SP-10), Neixiyan (EX-LE4), and Dubi (ST-35) have been utilized to treat knee pain.^[22,23] Therefore, in this study, we chose the right ST34, SP-10, EX-LE4, ST-35 acupoints to explore the feasible gender differences and similarities in cerebral activity response to the acupuncture at these acupoints. The results of this study may help to provide evidence for the further study of acupuncture for the treatment of knee pain.

Table 1**Brain area response to the acupuncture stimulation at acupoints around knee.**

Regions	Side (R/L)	Male participants (n=15)							Female participants (n=15)						
		BA	No. of voxels	T values	Z values	MNI coordinate system (mm)			BA	No. of voxels	T values	Z values	MNI coordinate system (mm)		
						X	Y	Z					X	Y	Z
Activation															
Frontal lobe															
Middle frontal gyrus	R	-	218	6.43	4.32	42	6	42							
Inferior frontal gyrus	L	46	58	3.43	2.87	-42	27	15							
Frontal lobe	L								47	40	4.60	3.53	-42	42	0
Parietal lobe															
Postcentral gyrus	R	40	476	9.14	5.13	57	-30	18	40	56	3.97	3.20	63	-24	21
Precuneus	R	39	30	3.26	2.77	18	-72	33							
Insula	L	13	671	9.65	5.26	-39	0	-3							
	R								13	10	3.77	3.08	51	-30	18
Parietal lobe	R								19	77	3.52	2.93	30	-54	33
Superior parietal lobule	R	7	11	3.44	2.88	27	-66	51							
Temporal lobe															
Middle temporal gyrus	R	-							37	15	3.55	2.95	57	-63	-3
Temporal lobe	L								19	94	5.18	3.81	-45	-51	-9
	R	-	35	3.24	2.75	24	-66	24							
Cerebellum															
Cerebellum posterior lobe	L	-	230	5.51	3.95	-27	-57	-45							
	R	-	369	4.72	3.59	18	-69	-45	-	308	5.77	4.06	-12	-78	-27
Cerebellum anterior lobe	L	-	15	3.34	2.82	-12	-42	-21							
Occipital lobe															
Occipital lobe	L	-							19	135	5.46	3.93	-30	-69	-6
	R	-	39	4.69	3.57	30	-75	27							
Cuneus	L	18	42	4.34	3.40	-12	-81	15							
limbic lobe															
Cingulate gyrus	L								31	25	3.63	2.99	-12	-27	45
Midbrain	R								-	13	3.65	3.01	15	-21	-12
Deactivation															
Frontal lobe	L	-	20	5.10	3.77	-24	21	24							
Medial frontal gyrus	L								10	22	4.40	3.43	-9	57	0
	R								10	60	5.74	4.05	9	57	6

Voxels with $P < .01$, $t > 2.62$ and clustered with 10 as threshold.

2. Methods and materials

2.1. Ethical approval

This study was approved by the Ethics Review Board of the First Affiliated Hospital of the Heilongjiang University of Chinese Medicine.

2.2. Study design

This study was designed as a non-randomized case controlled pilot study. It was conducted at First Affiliated Hospital of Heilongjiang University of Chinese Medicine according to the Declaration of Helsinki. All Participants provided informed consents before the study. A total of 30 healthy subjects were recruited, including 15 females and 15 males in 2 different groups. The investigators and participants were not blinded to the study, except the data analysts.

2.3. Participants

Thirty healthy right-handed volunteers (15 males [range: 22–26 years; mean: 24.3 years] and 15 female [range: 23–26 years; mean: 24.6 years]), were recruited in this study. The inclusion

criteria including participants with regular diet; normal sleeping patterns; and normal body mass index. Additionally, all participants had no history of chronic disease, neurological or psychiatric diseases, and minimal consumption of alcohol, tobacco, tea, and coffee. Furthermore, the participants were excluded if they had history of head trauma; and acupuncture therapy within 1 month before the study.

2.4. Intervention schedule

The acupoints of acupoints ST34 (located with knee flexed, 2 cun above the superior lateral border of the patella), SP-10 (located with knee flexed, 2 cun above the superior medial border of the patella), EX-LE4 (located flex the knee joints; on the lower border of patella, in the depression of the medial side of patellar ligament), and ST-35 (located with knee flexed, below the patella in a depression lateral to the patellar ligament) were used in this pilot study.

Acupuncture was operated by a single experienced acupuncturist with sterilized, disposable, stainless steel needles (0.25 × 40mm; Suzhou Medical Supplies Factory Co. Ltd, Suzhou, China). The specific operations and manipulations were the same as our previous study.^[16,17] The entire process still lasted

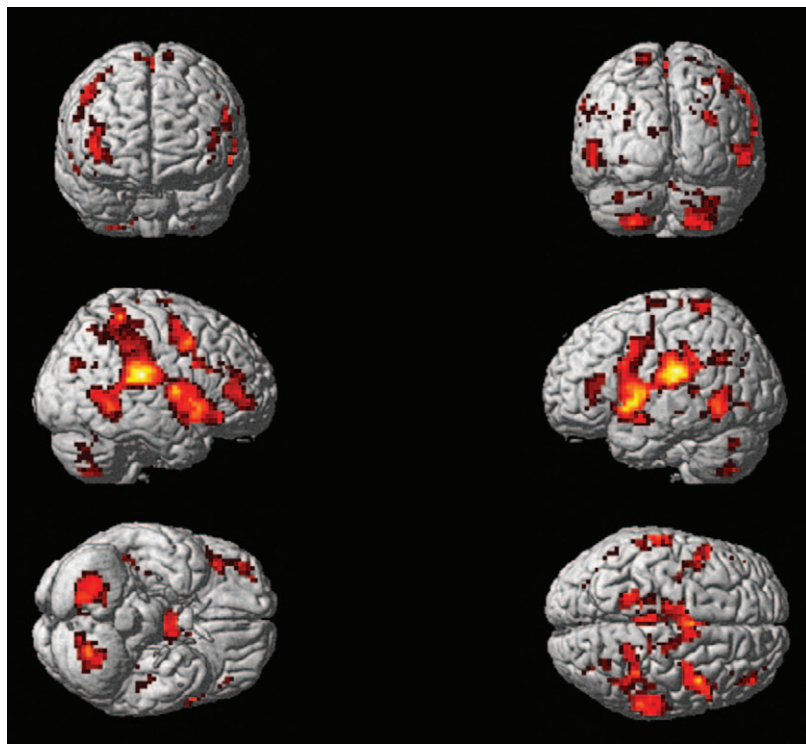


Figure 1. : 3D results showed activated brain areas by acupuncture stimulation in male participants.

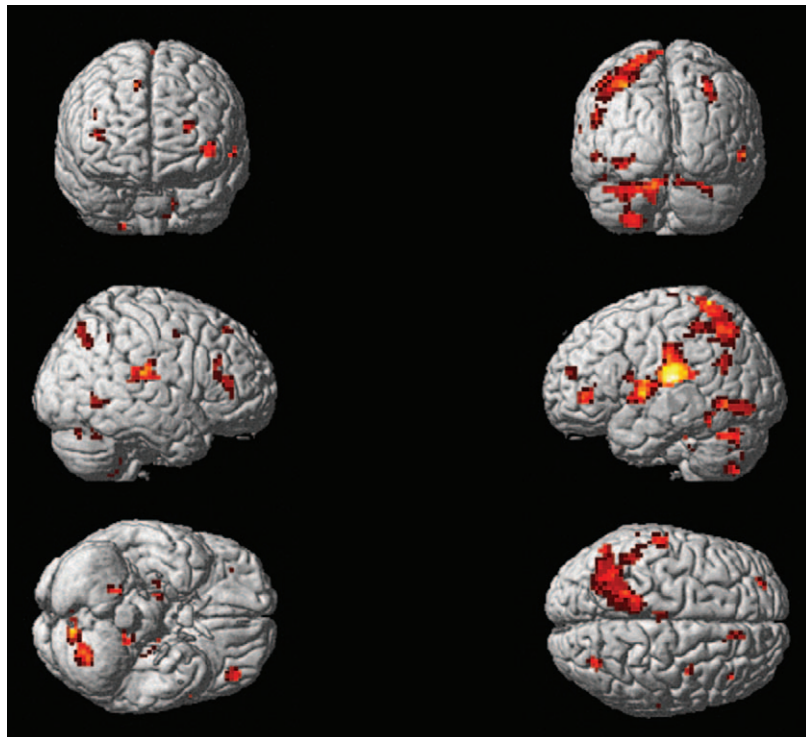


Figure 2. : 3D results showed activated brain areas by acupuncture stimulation in female participants.

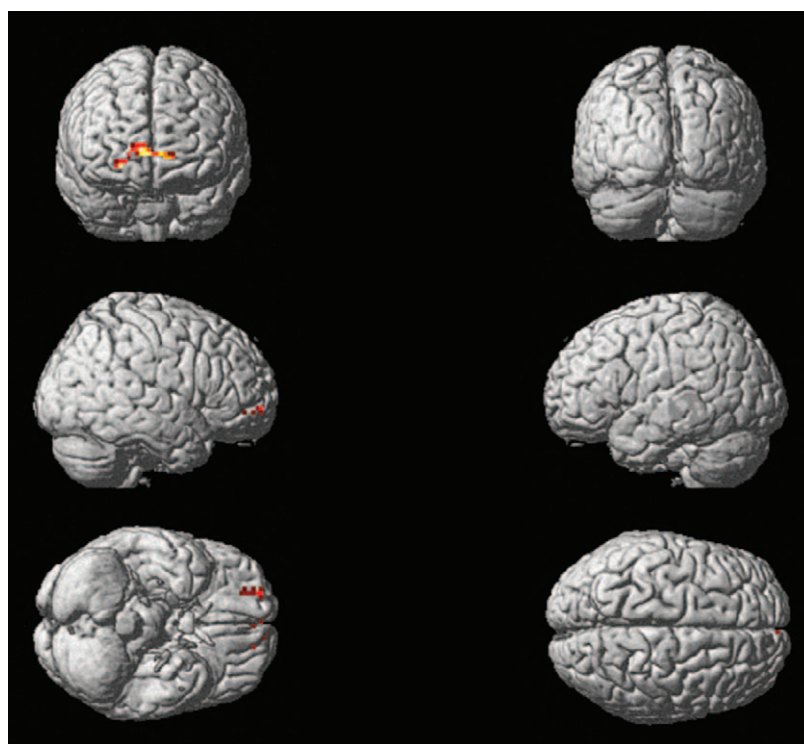


Figure 3. : 3D results showed deactivated brain areas by acupuncture stimulation in female participants.

8 min, which including 2 stages (manipulation and retention).^[16] All participants and data analyst were masked in this study.

A 3.0 T MRI system (Achieva 3.0T TX; Philips, Eindhoven, the Netherlands) was used for data acquisition. Duration the scan process, all participants were conscious and were required to be placed in a supine position and not to move. Their eyes were masked with eyeshades, and ears wore earplugs. The specific scan process was the same as our previous studies.^[16,17]

2.5. Sample size

No clinical trial has been conducted to address the feasible gender differences and similarities in cerebral activity response to the acupuncture at local acupoints around knee. Thus, in this pilot study, we will be adopted the minimum number of patients recommended for a preliminary study in clinical trial.^[24] The desired sample size for this pilot study is 30 participants, 15 subjects in each group, and assuming a dropout rate of 20%.

2.6. Statistical analysis

In this study, we used SPM 12 software (Statistical Parametric Mapping, <http://www.fil.ion.ucl.ac.uk/spm/>) to analyze all the data. We assessed the voxel-based individual task-related activation. For all data analyses, significance was designated at $P < .05$. In addition, a cluster size of >10 voxels was considered significantly different.

3. Results

Data from all 30 participants (15 males, 15 females) were analyzed. All included subjects are Chinese. The results of fMRI from both male and female subjects showed an increased signal in the postcentral gyrus (both at right side), precuneus (male at right side, female at left side), temporal lobe (male at right side, female at left side), posterior lobe (male at both sides, female at right side), and occipital lobe (male at right side, female at left side) (Table 1, Figs. 1–3).

When compared with females, a significant increase fMRI signal was observed in males in the right middle frontal gyrus, inferior frontal gyrus, right precuneus, right superior parietal lobule, left cerebellum anterior lobe (Table 1, Fig. 4). Additionally, a significant decrease signal was found in the right frontal lobe (Table 1, Fig. 5).

When compared with males, a significant increase fMRI signal was showed in females in the right frontal lobe, right parietal lobe, and right middle temporal gyrus (Table 1, Fig. 6); and signal decreased in the left and right medial frontal gyrus (Table 1, Fig. 7).

4. Discussion

Previous studies also explored the gender differences in cerebral activity by using fMRI. Dr Qiu and colleagues included 38 participants, 19 males and 19 females.^[24] They all received brain fMRI scale during the acupuncture intervention, and then analyzed the data based on the sex status.^[25] The results found that acupuncture stimulation works differently between males and females in brain with sex dimorphism.^[25] Dr Yeo and colleagues explored the gender differences and similarities of

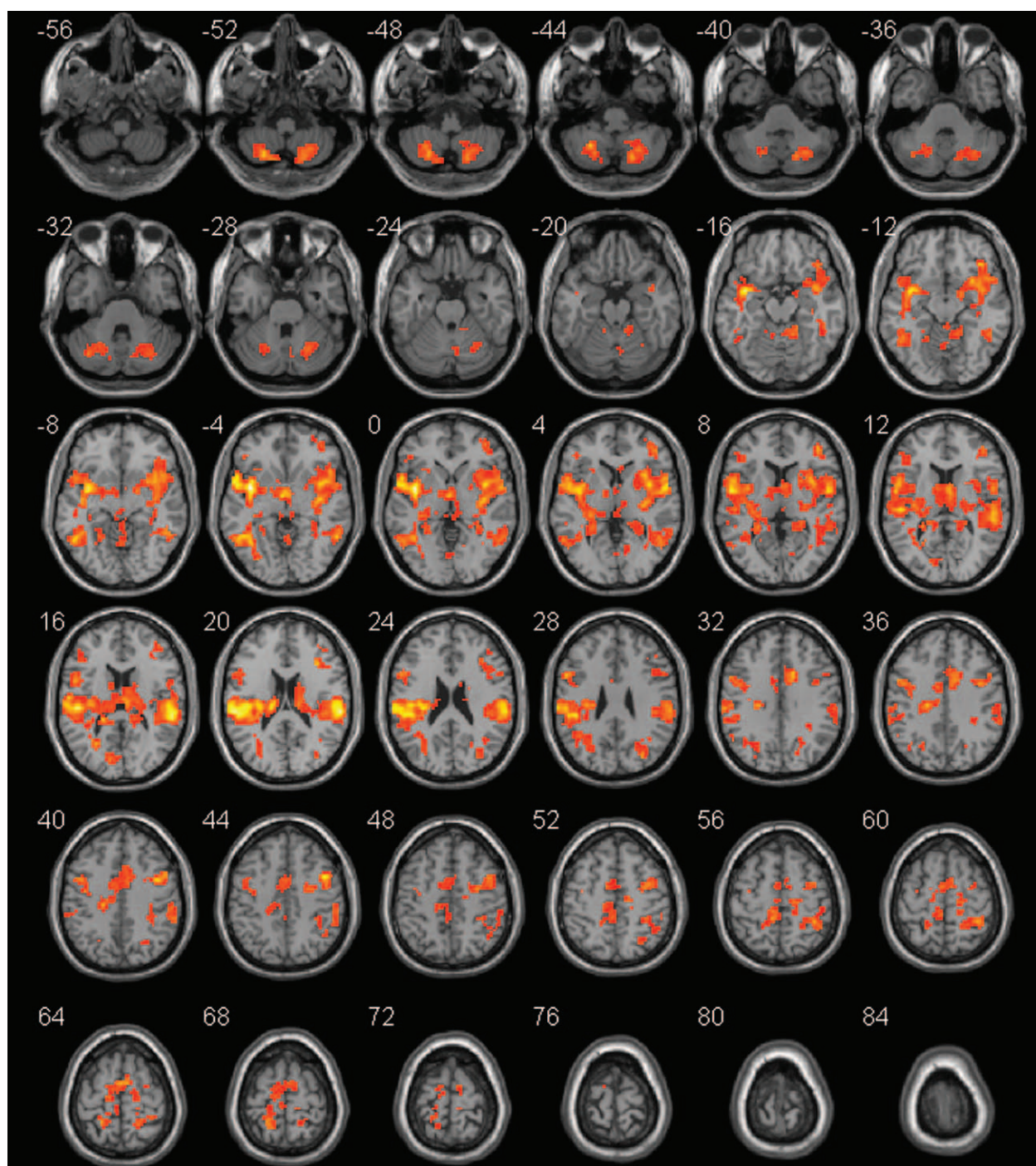


Figure 4. : Activated brain areas by acupuncture stimulation in male participants.

acupuncture at GB34 in order to examine their psychophysical and brain responses.^[26] Their results showed that the neural effects of acupuncture stimulation at acupoint GB34 might differ between males and females, because of different modulated brain structures between them.^[26] Dr Qiu and colleagues examined the effect of resting-state fMRI on the gender-difference in brain activity between male and female patients with major depressive disorder (MDD).^[27] The results demonstrated that gender

differences widely distributed abnormal brain activity between male and female patients with MDD.^[27] In addition, such abnormal brain activity is often associated with different somatic symptoms between different genders in patients with MDD.^[27] Dr Qiu and colleagues investigated the effect of fMRI on the gender differences of spontaneous brain activity in young adult healthy volunteers.^[28] The results of their study found that males and females had regional specific differences during the resting

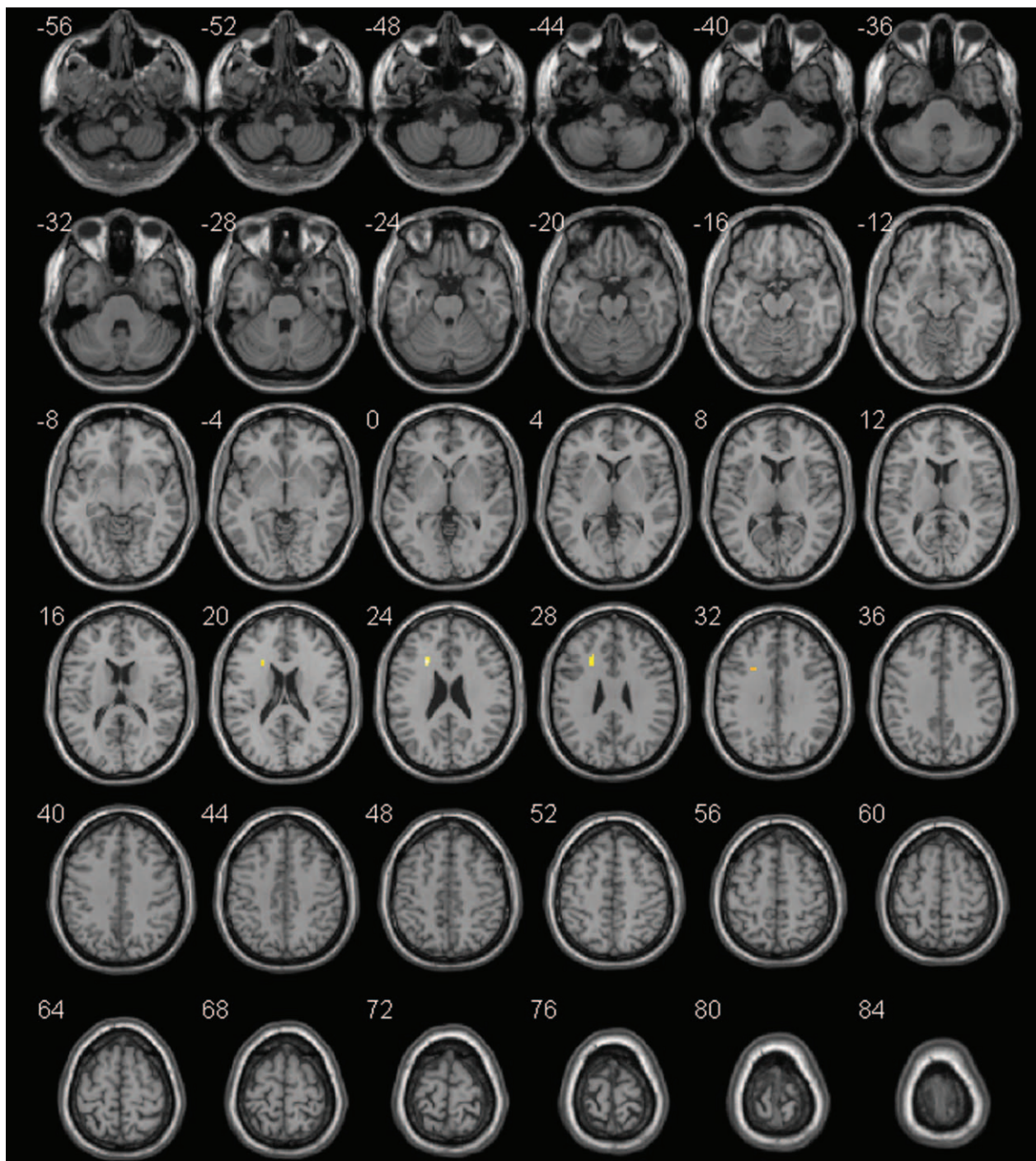


Figure 5. : Deactivated brain areas by acupuncture stimulation in male participants.

state.^[28] Additionally, such findings may help to understand gender differences in behavior and cognition.^[28]

The present study showed brain activation by acupuncture stimulation in both male and female subjects in the postcentral gyrus, precuneus, temporal lobe, posterior lobe, and occipital lobe. However, when analyzed male subjects only, the brain activation was found in the areas of middle frontal gyrus, inferior frontal gyrus, precuneus, right superior parietal lobule,

and cerebellum anterior lobe; and brain deactivation was observed in the areas frontal lobe. Moreover, the results of female subjects demonstrated that brain activation in the frontal lobe, parietal lobe, and middle temporal gyrus; and brain deactivation in the bilateral medial frontal gyrus. The results of the present study indicate that acupuncture stimulation at local acupoints around knee had either common brain activity signals in both males and females, and also showed

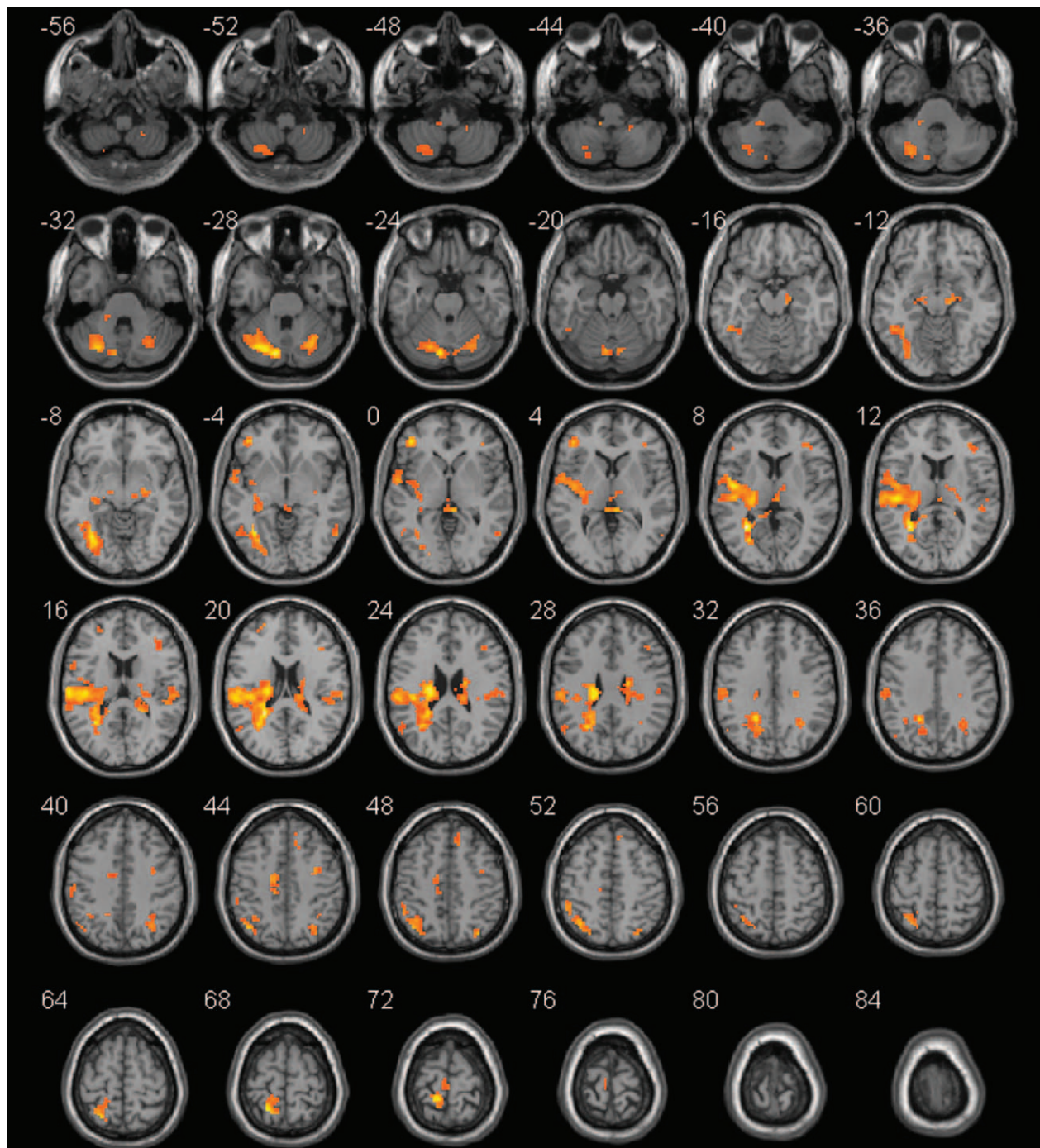


Figure 6. : Activated brain areas by acupuncture stimulation in female participants.

different signals between both genders. It may provide neurological evidence to explore the mechanism of gender differences.

This study also had several limitations. First, the sample size is relatively small, because this pilot study tries to explore the feasible mechanism of acupuncture at local acupoints around knee. Second, this study was conducted just based on healthy participants. Patients with knee disease will be included in our

following study. Third, this study did not apply randomization, blinding procedure, which may result in high risk of subject selection.

5. Conclusions

The results of this study found that the neural effects differ between healthy male and female adults by stimulation acupoints

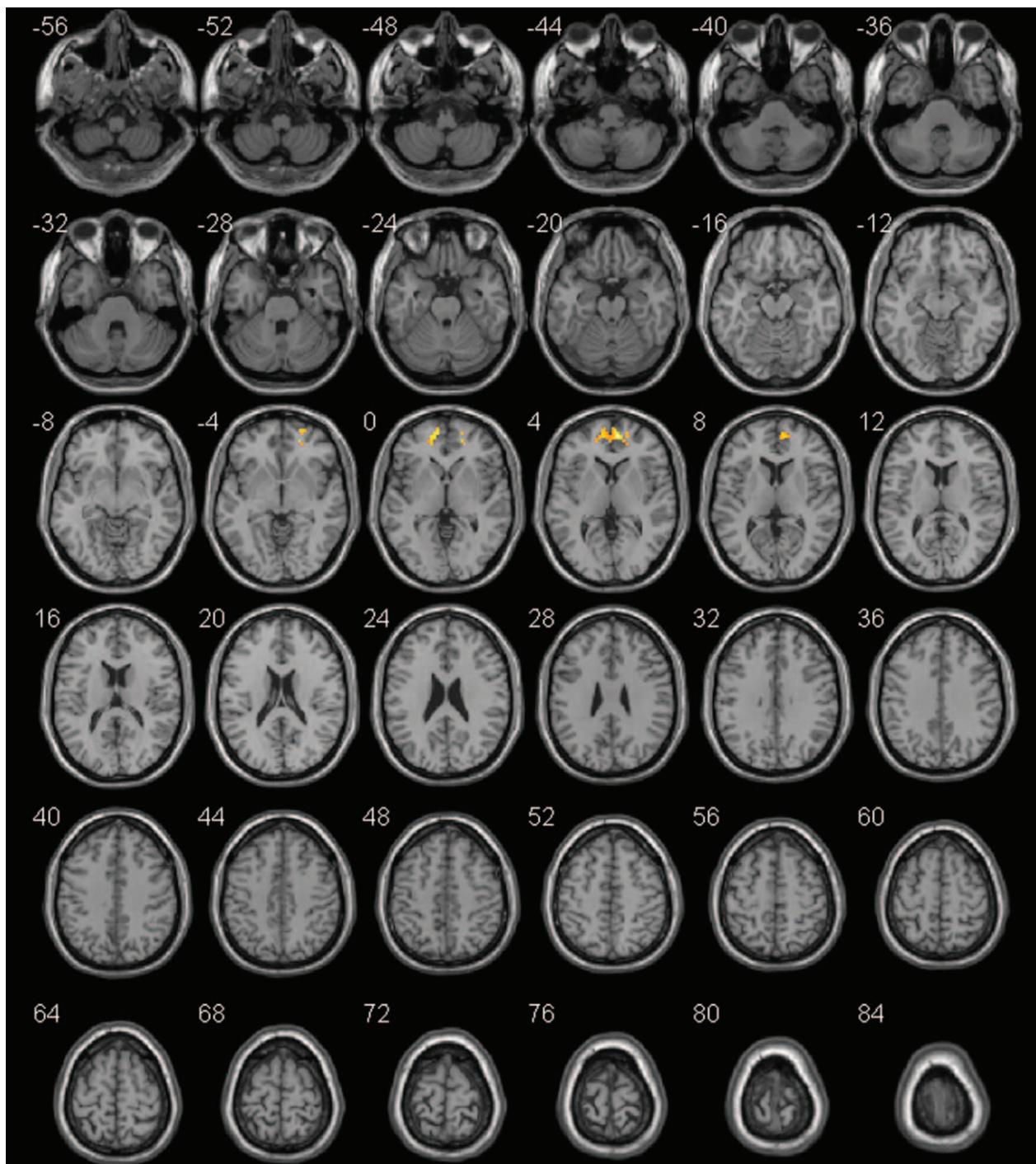


Figure 7. : Deactivated brain areas by acupuncture stimulation in female participants.

around the knees. The present results may provide helpful evidence for the further study.

Acknowledgments

Thank you.

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