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Original Article

Effect of acupuncture at Zulinqi (GB41) on the amplitude of low frequency fluctuations in migraine without aura patients: a resting-state functional magnetic resonance imaging study

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Abstract: To study the modulatory effects of acupuncture on the amplitude of low frequency fluctuations (ALFF) in migraine without aura (MWoA) patients. 16 MWoA patients and 16 healthy controls were recruited to undergo resting-state fMRI scanning before and after needling at GB41. Voxel-based analysis to characterize the difference of amplitude of low frequency fluctuations was employed. Before needling, compared with healthy controls, the MWoA patients showed decreased ALFF values in the left calcarine, cuneus, parietal gyrus, and increased ALFF values in the right hippocampus, parahippocampal gyrus, insula, middle temporal gyrus and superior temporal gyrus. After acupuncture at GB41, decreased ALFF values in the bilateral precuneus, right middle frontal gyrus and right inferior parietal lobule, and increased ALFF values in the right precentral and postcentral gyri were observed in MWoA patients. Compared with healthy controls, the MWoA patients after needling showed mainly decreased ALFF values in the left precuneus, calcarine, cuneus, parietal gyrus, and increased ALFF values in the right precentral, postcentral gyri, hippocampus, middle temporal gyrus and superior temporal gyrus. Our findings provided further insight into possible mechanisms of the modulatory effects of acupuncture, which could be interpreted in terms of pain processing.

Keywords: Acupuncture, functional magnetic resonance imaging (fMRI), amplitude of low frequency fluctuations (ALFF), migraine without aura (MWoA) patients

Introduction

Migraine is a chronic neurological disorder with episodic attacks. The morbidity of migraine patients is about 12% in Western countries [1, 2]. The migraine has been ranked as the first disabling diseases among neurological disease by the Global Burden of Disease (GBD 2010) [3]. It has brought a large burden with personality, family and society [4]. Therefore, it is vital to explore effective intervention measures to treat migraine.

Acupuncture, as a main part of Traditional Chinese medicine, has gained popularity in China from ancient times. In recent years, it has became increasingly popular among patients and physicians across the world. In the United States, as many as 3.1 million Americans received acupuncture treatment per year [5]. Acupuncture could induce pain relief and prophylaxis of migraine, which had been confirmed by abundant randomized, controlled clinical trials [6-10]. Acupuncture is beneficial for migraine in the reduction of attack days and pain intensity of attacks. A recent review indicated that acupuncture is an effective, safe, long lasting, and cost-effective therapy for migraine [11]. However, the underlying neural mechanisms of acupuncture therapy for migraineare still not well interpreted.

Noninvasive Functional magnetic resonance imaging (fMRI) has been widely applied to measure intrinsic fluctuations, especially resting-state fMRI (rs-fMRI) which has attracted important attention in studies of various neurological diseases. As a main method of rs-fMRI, amplitude of low frequency fluctuations (ALFF) which is used to measure the total power of a given

Table 1. The demographic and clinical information of MWoA patients and healthy controls

Items	Healthy controls N = 16)	MWoA patients (N = 16)
Gender (male/female)	3/13	3/13
Age (years)	27.1 ± 4.8#	28.3 ± 6.0
Migraine history (months)	/	57.3 ± 42.3
Educational level (years)	14.6 ± 5.6#	15.1 ± 4.3
Frequency of migraine attacks (times/month)	/	4.1 ± 1.7
Duration of migraine attacks (days/month)	/	5.9 ± 3.1
VAS scores	/	5.4 ± 1.6

Note: #results from two-sample non-parametric test of the comparison between MWoA patients and healthy controls, z = -0.344, *P* = 0.731 (for age), z = -0.306, *P* = 0.759 (for educational level). VAS: Visual analogue scale.

Table 2. Comparison of ALFF between healthy controls and MWoA patients before acupuncture treatment

Cluster	Voxels of cluster	Brain region	Peak MNI coordinates			t-value	Voxels
			X	Y	Z		
Cluster 1	357	Temporal_Mid_R	39	-21	-18	5.5003	115
		Hippocampus_R					68
		Temporal_Sup_R					64
		ParaHippocampal_R					31
Cluster 2	131	Rolandic_Oper_R	39	-12	24	4.0941	34
		Insula _R					34
Cluster 3	97	Temporal_Inf_L	-66	-18	-12	3.7864	35
		Temporal_Mid_L					29
Cluster 4	97	Calcarine_L	-18	-54	6	-3.3768	46
		Cuneus_L					33
Cluster 5	94	Parietal_Sup_L	-30	-57	48	-3.867	48
		Parietal_Inf_L					40

Note: Results from two-sample t-test between healthy controls and MWoA patients before acupuncture (*P* < 0.05, corrected by Monte Carlo Simulations, iterated 1000 times, cluster size > 70 voxels). R: Right; L: Left; Mid: Middle.

time period, has been proved to be a useful parameter to reflect the intensity of regional spontaneous neural activity [12]. Hence, the ALFF has been used in studies of various brain diseases [12-16]. Previous studies had demonstrated that migraine without aura (MWoA) patients had the abnormalities in functional connectivity (FC) within the default mode network (DMN) [17], salience network (SN) [18], periaqueductal gray networks [19], and the right front oparietal networks (RFPN) [20]. Unfortunately, there are few studies focusing on the regional spontaneous neural activity of MWoA patients compared with healthy controls and MWoA patients after acupuncture treatment. Yu et al. and Zhao et al. applied the regional homogeneity method to investigate regional homogeneity abnormalities in migraine patients [21, 22]. Thus we hypothesized that the intensity of regional spontaneous neural activity of MWoA patients would be altered compared with healthy controls.

Our previous studies supported that acupuncture could increase the FC of the frontal and temporal lobe [23], RFPN in MWoA patients [24]. A review also showed that acupuncture could lead to a stronger interplay between DMN in MWoA patients [25]. Accordingly, we also hypothesized that acupuncture could modulate the intensity of regional spontaneous neural activity and the modulated brain regions could be associated with pain processing, which would give more interpretation of the effect of acupuncture. To test our hypotheses, we collected the resting-state fMRI data of 16 MWoA patients before and after acupuncture therapy and 16 matched healthy controls. Based on traditional Chinese acupuncture theory and practice, acupoints on Gallbladder Meridian are the classical targets for migraine treatment. Hence, the acupoint Zulinqi (GB41), a frequently used acupoint belonging to the Gallbladder Meridian, was chosen to investigate the effect of acupuncture for MWoA patients.

Material and methods

Subjects

A total of 16 MWoA patients (13 females), were recruited from Dongzhimen Hospital Affiliated

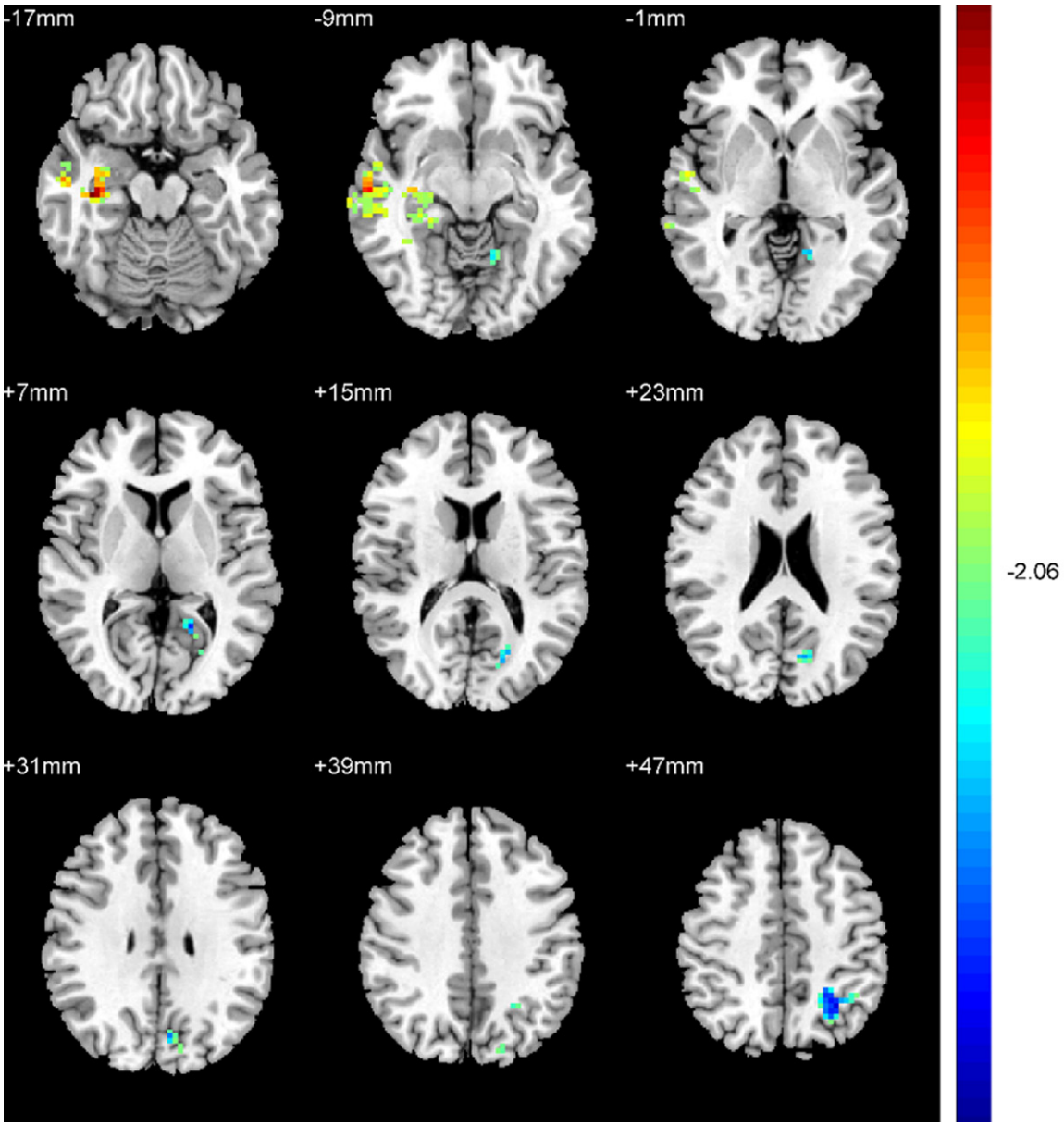

Figure 1. Differences in ALFF between MWoA patients and healthy controls. The warm color represents a higher ALFF value.

to Beijing University of Chinese Medicine. All 16 patients were diagnosed as MWoA according to the classification criteria of the International Headache Society and met the criteria below: Right-handed; From 18 to 60 years old; At least 2 migraine attacks every month in the past 3 months; With a more than one-year history of migraine; With no history of prophylactic or therapeutic medicine in the past 3 months; With no history of drug or alcohol abuse; With no history of long-term use of analgesics; With no history of dysmenorrhea or other chronic paining disease; Without any MRI contraindications. The exclusion criteria were as follows: Other types of migraine; With history of other neurological disease; With history of chronic medical diseases; The first attack occurred after 50 years old. Another 16 right-handed normal subjects (13 females) matched in age and education levels were recruited to serve as healthy controls. All 16 healthy subjects underwent normal neurological test and had no history of migraine or other neurological disease or any MRI contraindications. The clinical and

Table 3. Comparison of ALFF in MWoA patients after and before acupuncture treatment

Cluster	Voxels of cluster	Brain region	Peak MNI coordinates			t-value	Voxels
			X	Y	Z		
Cluster 1	74	Precuneus_R	15	-51	24	-4.418	66
Cluster 2	185	Precuneus_L	0	-57	42	-4.9094	98
Cluster 3	111	Frontal_Mid_R	39	15	60	-5.1039	96
		Angular_R					36
Cluster 4	96	Parietal_Inf_R	42	-54	36	-5.3583	36
		SupraMarginal_R					21
Cluster 5	149	Precentral_R	27	-30	57	5.4424	80
		Postcentral_R					64

Note: Results from paired t-test ($P < 0.05$, corrected by Monte Carlo Simulations, iterated 1000 times, cluster size > 70 voxels). R: Right; L: Left; Mid: Middle; Inf: Inferior.

demographic information of patients and controls was showed in **Table 1**.

The Ethical committee of Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine approved the research. All procedures were conducted in accordance with the Declaration of Helsinki and the data was analyzed anonymously.

Experimental paradigm

In the current research, we employed then on-repeated event-related-fMRI (NRER-fMRI) design to investigate the prolonged effects after needling, which was used in our previous study [26]. Following the design paradigm of our previous study, we employed 1-minute needle manipulation before 1-minute resting epoch and followed by 8-minute resting scan (without acupuncture manipulation). Acupuncture was performed at Zulinqi (GB41, located in the depression between the fourth and fifth metatarsal bones on the dorsum of the foot). Acupuncture was performed by inserting a sterile, single-use silver needle (25 mm in length and 0.30 mm in diameter) vertically into GB41 to a depth of 2-3 cm, and the stimulation included rotating the needle clockwise and counterclockwise at 1 Hz with even reinforcing and reducing manipulation for 60 s. All acupuncture procedures were performed by one licensed and skilled acupuncturist. Another 8-minute resting scan was performed before the acupuncture procedure as the baseline.

De-qi is believed to be crucial to the therapeutic effectiveness of acupuncture [27]. After each fMRI scanning, subjects were asked to fill questionnaires to record their experience of De-qi. Since the sharp pain was thought to be an inadvertent noxious stimulation, we would rule out the subjects if they reported the sharp pain. Among all the subjects, none reported the sharp pain.

Data acquisition and processing

A 3.0T MRI scanner (Siemens, Sonata, Germany) was used to acquire fMRI images. During the scanning, foam cushions were used to reduce head translation movement and rotation. The fMRI data was collected using an echo-planar imaging sequence with the scan parameters as follows: Repetition time = 2000 ms, echo time = 30 ms, field of view = 225 mm × 225 mm, matrix = 64 × 64, thickness = 3.5 mm flip angle = 90°). All subjects were required to keep their eyes closed and to remain conscious.

The structural and functional images were preprocessed by using Data Processing Assistant for Resting-State fMRI (DPARSF, http://www.restfmri.net) and SPM8 (http://www.fil.ion.ucl.ac.uk/spm). The first 10 time points of the functional images were discarded to ensure subjects adapted the scanning circumstance. Then, slicing time, spatial realignment, normalization into the Montreal Neurological Institute (MNI) space, and smoothing were performed. Finally, we removed the linear trends. Two patients and one healthy control were ruled out, for exhibiting head motion > 1.5° rotation maximum translation and/or 1.5 mm during the course of scans.

ALFF analysis

The ALFF was performed using REST software (http://restfmri.net) [12]. First, the time series were transformed into a frequency domain with a fast Fourier transform and the power spectrum was then obtained. The power spectrum, crossing 0.01-0.08 Hz at each voxel, was square-rooted and averaged, and the result was taken as the ALFF. The ALFF value, which implied the sum of amplitudes within the low-frequency range (0.01-0.08 Hz), was extracted from voxels in whole brain [28]. The ALFF maps

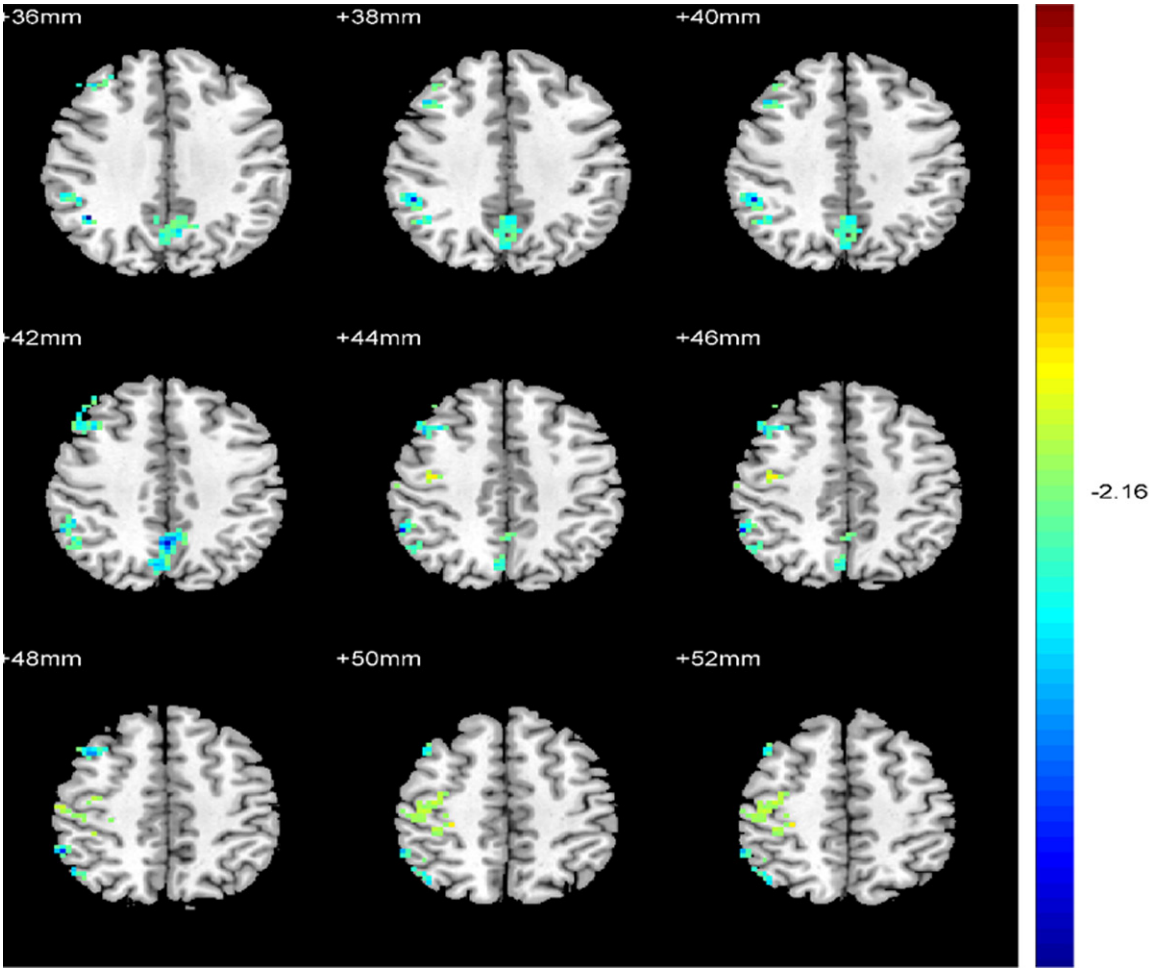

Figure 2. Differences in ALFF between after and before acupuncture treatment for MWoA patients. The warm color represents a higher ALFF value.

were divided by mean ALFF value of the whole brain to ensure the data to coincide with normal distribution.

Data analyses

For the group-level analyses, the mean ALFF values were conducted by two-sample t-test between MWoA patients and healthy controls before needling. The paired t-test was applied in MWoA patients before and after needling. The two-sample t-test was also applied between healthy controls and MWoA patients after needling. Differences between any two groups were considered significant if $P < 0.05$, corrected by Monte Carlo Simulations, iterated 1000 times, and cluster size > 70 voxels in the AAL (Anatomical Automatic Labeling) brain mask without cerebellum. The reported statistics were normalized to MNI space based on AAL and mapped by REST software.

Results

Before acupuncture treatment, compared with the controls, the MWoA patients showed significantly decreased ALFF values in the left calcarine, cuneus, superior parietal gyrus, inferior parietal but supramarginal and angular gyri. Besides, increased ALFF values in the right hippocampus, superior temporal gyrus, parahippocampalgyrus, rolandic operculumandinsular lobe, bilateral middle temporal gyrus and left inferiortemporal gyrus were observed (shown in **Table 2**). Specific cluster locations are shown in **Figure 1**.

After acupuncture treatment, the MWoA patients showed decreased ALFF values in the bilateral precuneus, right inferior parietal lobule and middle frontal gyrus. The right precentral and postcentral gyri of ALFF values

Table 4. Comparison of ALFF between after acupuncture treatment for MWoA patients and healthy controls

Cluster	Voxels of cluster	Brain region	Peak MNI coordinates			t-value	Voxels
			X	Y	Z		
Cluster 1	170	Temporal_Inf_L	-27	-42	-30	3.5865	71
Cluster 2	621	Temporal_Mid_R	39	-24	-18	4.7507	106
		Temporal_Sup_R					80
		Rolandic_Oper_R					77
		Hippocampus_R					47
Cluster 3	378	Precentral_R	0	-24	51	4.6739	124
		Postcentral_R					71
Cluster 4	300	Precuneus_R	9	-69	39	-3.9041	77
		Precuneus_L					50
		Calcarine_L					49
		Cuneus_L					46
Cluster 5	88	Frontal_Sup_Medial_L	-3	36	45	-4.5611	50
Cluster 6	101	Parietal_Sup_L	-27	-60	45	-3.9902	48
		Parietal_Inf_L					43

Note: Results from paired t-test ($P < 0.05$, corrected by Monte Carlo Simulations, iterated 1000 times, cluster size > 70 voxels). R: Right; L: Left; Mid: Middle; Sup: Superior; Inf: Inferior.

increased (shown in **Table 3**). Specific cluster locations are shown in **Figure 2**.

Compared with healthy controls, the MWoA patients after needling showed mainly decreased ALFF values in the left precuneus, calcarine, cuneus, superior parietal gyrus, inferior parietal but supramarginal and angular gyri, and increased ALFF values in the right precentral, postcentral gyri, hippocampus, middle temporal gyrus and superior temporal gyrus (shown in **Table 4**). Specific cluster locations are shown in **Figure 3**.

Discussion

In this study, we found differences in ALFF between MWoA patients and healthy controls, which suggested abnormalities in pain processing. Furthermore, the results, that the participants showed deactivation of important components in DMN and increased regional activity in right precentral and postcentral gyri, may provide possible interpretations for the central neural mechanisms of acupuncture for pain modulation.

Differences in ALFF between MWoA patients and healthy controls

In this study, we observed significant differences in ALFF between MWoA patients and HC. Brain regions with lower ALFF mainly located in occipital lobe, superior parietal lobule and inferior parietal lobule within the main regions of the DMN. Xue et al. also applied the same way to explore differences in ALFF between MWoA patients and HC, and found increased ALFF values in the right thalamus as well as decreased ALFF values in the bilateral prefrontal cortex (PFC) [29]. Obviously, our results matched those observed in this study. As we know, the DMN is considered to be related with adaptive behavior, cognitive, emotional and attention processing [30]. Important components of DMN are involved in the "medial pain system", which are considered to respond to pain stimulus [31]. The disruption of the DMN caused by pain will affect the individual's ability to properly regulate internal experiences. A prior study had showed decreased FC within DMN for MWoA patients [17]. The occipital lobe is closely associated with visual sense and motion perception. Numerous studies had revealed abnormalities of function in the occipital lobe during attacks of migraine with aura, based on the cortical spreading depression [32]. An fMRI study also found that the occipital cortex showed structural deficits in MWoA patients [33].

We also found that MWoA patients showed increased ALFF values in the right hippocampus (Hip) and parahippocampal gyrus (PHG). The PHG is the main part of the cortico-basal ganglia-thalamic-cortical loop, which is known to be critical in pain processing [34]. The Hip is involved in memory consolidation and very often found in investigating pain anxiety [35], which is also known to have an inhibitory effect on the hypothalamic-pituitary-adrenal axis [36]. Maleki et al. studied the hippocampal structure and function in migraine, and found the voxels of Hip negatively correlated with the number of migraine attacks. Meanwhile the functional neuroimaging study demonstrated that the Hip dysfunction occurs with increasing frequency of migraine attacks [37]. Furthermore, the insu-

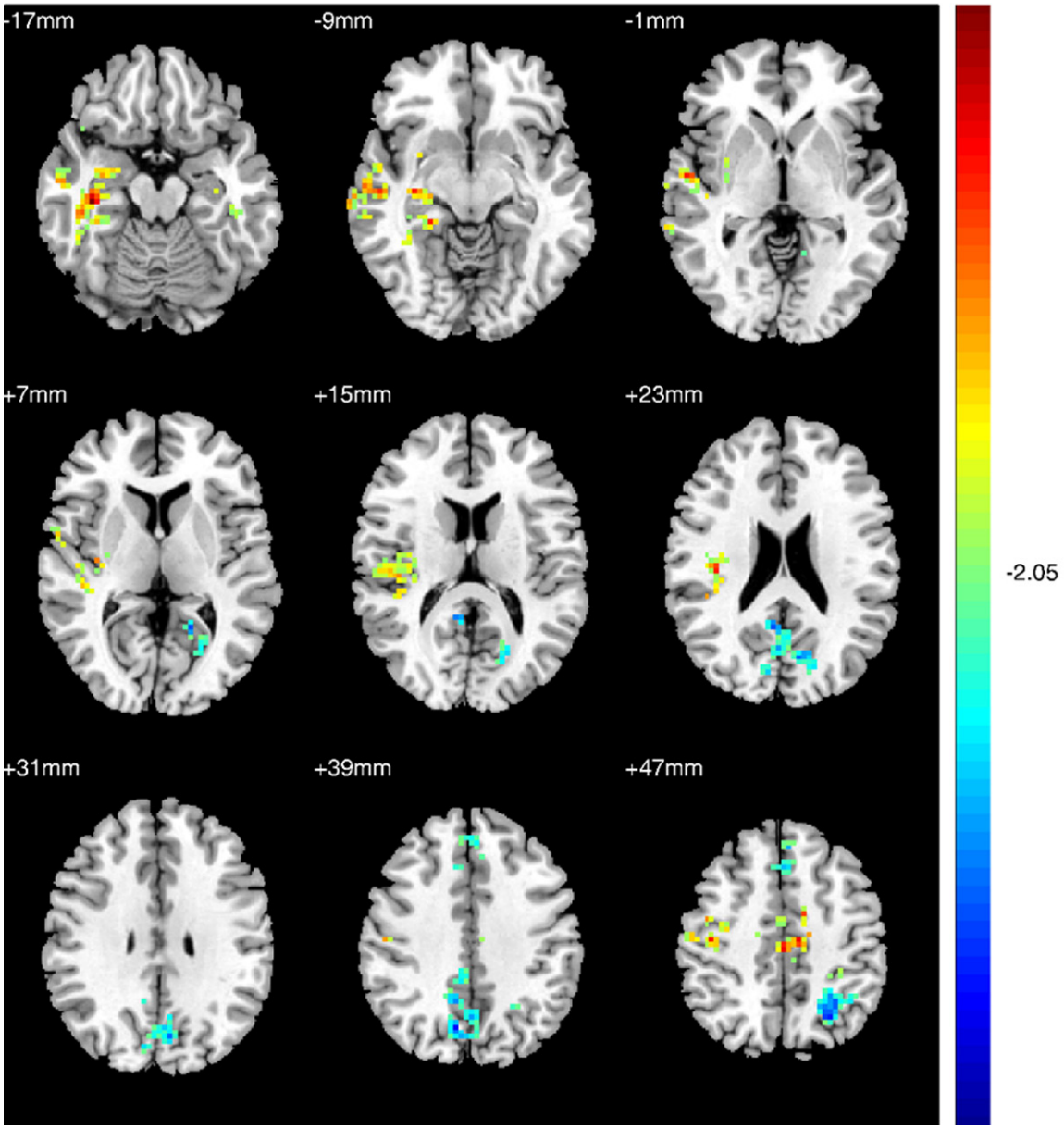

Figure 3. Differences in ALFF between after acupuncture treatment for MWoA patients and healthy controls. The warm color represents a higher ALFF value.

la, which had been proved to play a vital role in pain processing [18, 38], was also observed with increased ALFF. Previous functional neuroimaging studies had also found insula hyperactivations in migraine patients [39, 40]. It seems possible that these results are due to the impairment in pain processing.

Taken together, our findings improved the understanding of intrinsic functional architecture of baseline brain activity in MwoA.

Differences in ALFF between before and after acupuncture treatment for MWoA patients

In the present study, we found decreased ALFF values in the bilateral precuneus, right inferior parietal lobule and middle frontal gyrus after needling. The precuneus and inferior parietal lobule are included in the main distribution of DMN. The results were consistent with previous studies that DMN activity was diminished during needling [37, 41]. Previous studies had con-

firmed that acupuncture treatment could help to establish psychophysical pain homeostasis by enhancing the FC of the DMN in MWoA patients [23, 25]. Consequently, the intensity of regional spontaneous neural activity belonging to DMN would probably be stronger after needling, if attention to the stimulus solely accounted for the neural response. However, our study applied a temporary acupuncture treatment rather than a long-term treatment, which might lead to the decreased ALFF values. As it had been revealed, the DMN is activated during the resting state. Conversely, the DMN is inhibited during the task state [30]. Furthermore, a previous study showed the genuine acupuncture led to the decreased DMN deactivation in comparison with the sham acupuncture, which indicated that attentional processes could not fully explain the DMN deactivation evoked by acupuncture [41]. Thus, we speculated that the DMN deactivation elicited by acupuncture probably reflected the central neural mechanism of acupuncture analgesia.

Right middle frontal gyrus (MFG) locates in the prefrontal cortex (PFC). The PFC, which also belongs to the DMN, is considered to be critical to process the painful stimuli [42]. A previous study revealed that the PFC was a hub of the descending pain modulatory system [43]. Moreover, several studies revealed that the abnormalities in MFG were correlated with the pain intensity of migraine attacks [20, 22]. Hence, the decreased ALFF value in the MFG after needling may reflect the neural mechanism of acupuncture for pain modulation.

In this study, we also found increased ALFF values in the right precentral gyrus and postcentral gyrus after needling. The postcentral gyrus, referred as the primary somatosensory cortex (S1), is the main part of the pain matrix and accepts pain signals directly [44]. A precious study had found its cortex got thicken in migraine patients [45]. The precentral gyrus, called primary sensorimotor cortex (M1), is thought to be an abnormal hub related to pain processing [46]. The results of this study showed increased regional activity in both S1 and M1, which suggested that the S1 was closely associated with the M1 in pain processing. Taken together, our result might provide further evidence that the two brain regions were associated with pain modulation. Meanwhile, we also speculated that the increased activity reflected the neural mechanism of acupuncture for pain modulation.

Differences in ALFF between after acupuncture treatment for MWoA patients and healthy controls

Compared with healthy controls, the MWoA patients after needling showed not only most of the same changes of ALFF values in the comparison of MWoA patients and healthy controls before needling, but also part of the same changes with the comparison in MWoA Patients after and before needling. It could be easily understood that the changes of ALFF values could not be entirely reserved by the temporary acupuncture treatment. In hence, compared with healthy controls, the MWoA patients after needling showed some unchanged ALFF values in comparison of the MWoA patients and healthy controls before needling.

The increased ALFF values in the right precentral gyrus and postcentral gyrus are included in the main distribution of RFPN. The RFPN is recognized as an important brain network that corresponds to perception, somesthesis, and pain [47]. Our previous study had confirmed that the decreased FC in the RFPN could be reversed by acupuncture treatment [24]. Accordingly, we speculate that the increased ALFF values are possibly related with the recovery of MWoA.

Limitations of this study

This study might have some limitations. First, as a preliminary study, the sample size was small. This could be the reason that there was no finding in some regions related to pain processing, such as the thalamus which was thought to be the hub for pain processing [29]. Second, it would be better to set up a sham acupuncture group for proving specificity of acupuncture effect. In the future, these findings need to be further confirmed by enlarging sample size, including a placebogroup for the acupuncture.

Conclusions

In the current study, we demonstrated that widespread ALFF abnormalities in MWoA patients, and that needling GB41 could change the amplitude of the intrinsic cortical activity of the brain. Taken together, this study provided

further insights into the complex scenario of migraine mechanisms, and indicated that mechanisms of the effect of acupuncture could be interpreted in terms of pain processing.

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Disclosure of conflict of interest

None.

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References

[1] Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF; AMPP Advisory Group. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology 2007; 68: 343-349.

[2] Olesen J, Gustavsson A, Svensson M, Wittchen HU, Jonsson B; CDBE2010 study group; European Brain Council. The economic cost of brain disorders in Europe. Eur J Neurol 2012; 19: 155-162.

[3] Leonardi M and Raggi A. Burden of migraine: international perspectives. Neurol Sci 2013; 34 Suppl 1: S117-118.

[4] Buse DC and Lipton RB. Global perspectives on the burden of episodic and chronic migraine. Cephalalgia 2013; 33: 885-890.

[5] Barnes PM, Bloom B and Nahin RL. Complementary and alternative medicine use among adults and children: United States, 2007. Natl Health Stat Report 2008; 1-23.

[6] Diener HC, Kronfeld K, Boewing G, Lungenhausen M, Maier C, Molsberger A, Tegenth off M, Trampisch HJ, Zenz M and Meinert R. Efficacy of acupuncture for the prophylaxis of migraine: a multicentre randomised controlled clinical trial. Lancet Neurol 2006; 5: 310-316.

[7] Yang CP, Chang MH, Liu PE, Li TC, Hsieh CL, Hwang KL and Chang HH. Acupuncture versus topiramate in chronic migraine prophylaxis: a randomized clinical trial. Cephalalgia 2011; 31: 1510-1521.

[8] Streng A, Linde K, Hoppe A, Pfaffenrath V, Hammes M, Wagenpfeil S, Weidenhammer W and Melchart D. Effectiveness and tolerability of acupuncture compared with metoprolol in migraine prophylaxis. Headache 2006; 46: 1492-1502.

[9] Li Y, Zheng H, Witt CM, Roll S, Yu SG, Yan J, Sun GJ, Zhao L, Huang WJ, Chang XR, Zhang HX, Wang DJ, Lan L, Zou R and Liang FR. Acupuncture for migraine prophylaxis: a randomized controlled trial. CMAJ 2012; 184: 401-410.

[10] Wang Y, Xue CC, Helme R, Da Costa C, Zheng Z. Acupuncture for frequent migraine: a randomized, patient/assessor blinded, controlled trial with one-year follow-up. Evid Based Complement Alternat Med 2015; 2015: 920353.

[11] Da Silva AN. Acupuncture for migraine prevention. Headache 2015; 55: 470-473.

[12] Zang YF, He Y, Zhu CZ, Cao QJ, Sui MQ, Liang M, Tian LX, Jiang TZ and Wang YF. Altered baseline brain activity in children with ADHD revealed by resting-state functional MRI. Brain Dev 2007; 29: 83-91.

[13] Guo WB, Liu F, Xue ZM, Xu XJ, Wu RR, Ma CQ, Wooderson SC, Tan CL, Sun XL, Chen JD, Liu ZN, Xiao CQ, Chen HF and Zhao JP. Alterations of the amplitude of low-frequency fluctuations in treatment-resistant and treatment-response depression: a resting-state fMRI study. Prog Neuropsychopharmacol Biol Psychiatry 2012; 37: 153-160.

[14] Liu X, Wang S, Zhang X, Wang Z, Tian X and He Y. Abnormal amplitude of low-frequency fluctuations of intrinsic brain activity in Alzheimer's disease. J Alzheimers Dis 2014; 40: 387-397.

[15] McHugo M, Rogers BP, Talati P, Woodward ND and Heckers S. Increased amplitude of low frequency fluctuations but normal hippocampal-default mode network connectivity in schizophrenia. Front Psychiatry 2015; 6: 92.

[16] Xu K, Liu H, Li H, Tang Y, Womer F, Jiang X, Chen K, Zhou Y, Jiang W, Luo X, Fan G and Wang F. Amplitude of low-frequency fluctuations in bipolar disorder: a resting state fMRI study. J Affect Disord 2014; 152-154: 237-242.

[17] Tessitore A, Russo A, Giordano A, Conte F, Corbo D, De Stefano M, Cirillo S, Cirillo M, Esposito F and Tedeschi G. Disrupted default mode network connectivity in migraine without aura. J Headache Pain 2013; 14: 89.

[18] Xue T, Yuan K, Zhao L, Yu D, Zhao L, Dong T, Cheng P, von Deneen KM, Qin W and Tian J. Intrinsic brain network abnormalities in migraines without aura revealed in resting-state fMRI. PLoS One 2012; 7: e52927.

[19] Mainero C, Boshyan J and Hadjikhani N. Altered functional magnetic resonance imaging resting-state connectivity in periaqueductal gray networks in migraine. Ann Neurol 2011; 70: 838-845.
[20] Russo A, Tessitore A, Giordano A, Corbo D, Marcuccio L, De Stefano M, Salemi F, Conforti R, Esposito F and Tedeschi G. Executive resting-state network connectivity in migraine without aura. Cephalalgia 2012; 32: 1041-1048.
[21] Yu D, Yuan K, Zhao L, Zhao L, Dong M, Liu P, Wang G, Liu J, Sun J, Zhou G, von Deneen KM, Liang F, Qin W and Tian J. Regional homogeneity abnormalities in patients with interictal migraine without aura: a resting-state study. NMR Biomed 2012; 25: 806-812.
[22] Zhao L, Liu J, Dong X, Peng Y, Yuan K, Wu F, Sun J, Gong Q, Qin W and Liang F. Alterations in regional homogeneity assessed by fMRI in patients with migraine without aura stratified by disease duration. J Headache Pain 2013; 14: 85.
[23] Zhang Y, Li KS, Liu HW, Fu CH, Chen S, Tan ZJ and Ren Y. Acupuncture treatment modulates the resting-state functional connectivity of brain regions in migraine patients without aura. Chin J Integr Med 2016; 22: 293-301.
[24] Li K, Zhang Y, Ning Y, Zhang H, Liu H, Fu C, Ren Y and Zou Y. The effects of acupuncture treatment on the right frontoparietal network in migraine without aura patients. J Headache Pain 2015; 16: 518.
[25] Otti A and Noll-Hussong M. Acupuncture-induced pain relief and the human brain's default mode network-an extended view of central effects of acupuncture analgesia. Forsch Komplementmed 2012; 19: 197-201.
[26] Zhang Y, Li KS, Ren Y, Cui FY, Xie ZJ, Shin JY, Tan ZJ, Tang LX, Bai LJ and Zou YH. Acupuncture modulates the functional connectivity of the default mode network in stroke patients. Evid Based Complement Alternat Med 2014; 2014: 765413.
[27] Bai LJ, Cui FY, Zou YH and Lao LX. Acupuncture de qi in stable somatosensory stroke patients: relations with effective brain network for motor recovery. Evid Based Complement Alternat Med 2013; 2013: 197238.
[28] Wang X, Han Z, He Y, Caramazza A, Song L and Bi Y. Where color rests: spontaneous brain activity of bilateral fusiform and lingual regions predicts object color knowledge performance. Neuroimage 2013; 76: 252-263.
[29] Xue T, Yuan K, Cheng P, Zhao L, Zhao L, Yu D, Dong T, von Deneen KM, Gong Q, Qin W and Tian J. Alterations of regional spontaneous neuronal activity and corresponding brain circuit changes during resting state in migraine without aura. NMR Biomed 2013; 26: 1051-1058.
[30] Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA and Shulman GL. A default mode of brain function. Proc Natl Acad Sci U S A 2001; 98: 676-682.
[31] Zhuo M. Cortical excitation and chronic pain. Trends Neurosci 2008; 31: 199-207.
[32] Hadjikhani N, Sanchez Del Rio M, Wu O, Schwartz D, Bakker D, Fischl B, Kwong KK, Cutrer FM, Rosen BR, Tootell RB, Sorensen AG and Moskowitz MA. Mechanisms of migraine aura revealed by functional MRI in human visual cortex. Proc Natl Acad Sci U S A 2001; 98: 4687-4692.
[33] Jin C, Yuan K, Zhao L, Zhao L, Yu D, von Deneen KM, Zhang M, Qin W, Sun W and Tian J. Structural and functional abnormalities in migraine patients without aura. NMR Biomed 2013; 26: 58-64.
[34] Borsook D, Upadhyay J, Chudler EH and Becerra L. A key role of the basal ganglia in pain and analgesia-insights gained through human functional imaging. Mol Pain 2010; 6: 27.
[35] Ellerbrock I, Engel AK and May A. Microstructural and network abnormalities in headache. Curr Opin Neurol 2013; 26: 353-359.
[36] McEwen BS and Gianaros PJ. Central role of the brain in stress and adaptation: links to socioeconomic status, health, and disease. Ann N Y Acad Sci 2010; 1186: 190-222.
[37] Maleki N, Becerra L, Brawn J, McEwen B, Burstein R and Borsook D. Common hippocampal structural and functional changes in migraine. Brain Struct Funct 2013; 218: 903-912.
[38] Peyron R, Laurent B and Garcia-Larrea L. Functional imaging of brain responses to pain. a review and meta-analysis (2000). Neurophysiol Clin 2000; 30: 263-288.
[39] Tso AR, Trujillo A, Guo CC, Goadsby PJ and Seeley WW. The anterior insula shows heightened interictal intrinsic connectivity in migraine without aura. Neurology 2015; 84: 1043-1050.
[40] Apkarian AV, Bushnell MC, Treede RD and Zubieta JK. Human brain mechanisms of pain perception and regulation in health and disease. Eur J Pain 2005; 9: 463-484.
[41] Hui KK, Marina O, Claunch JD, Nixon EE, Fang JL, Liu J, Li M, Napadow V, Vangel M, Makris N, Chan ST, Kwong KK and Rosen BR. Acupuncture mobilizes the brain's default mode and its anti-correlated network in healthy subjects. Brain Res 2009; 1287: 84-103.
[42] Casey KL. Forebrain mechanisms of nociception and pain: analysis through imaging. Proc Natl Acad Sci U S A 1999; 96: 7668-7674.

[43] Lorenz J, Minoshima S and Casey KL. Keeping pain out of mind: The role of the dorsolateral prefrontal cortex in pain modulation. Brain 2003; 126: 1079-1091.
[44] May A. A review of diagnostic and functional imaging in headache. J Headache Pain 2006; 7: 174-184.
[45] Kim JH, Kim JB, Suh SI, Seo WK, Oh K and Koh SB. Thickening of the somatosensory cortex in migraine without aura. Cephalalgia 2014; 34: 1125-1133.
[46] Liu J, Zhao L, Li G, Xiong S, Nan J, Li J, Yuan K, von Deneen KM, Liang F, Qin W and Tian J. Hierarchical alteration of brain structural and functional networks in female migraine sufferers. PLoS One 2012; 7: e51250.
[47] Smith SM, Fox PT, Miller KL, Glahn DC, Fox PM, Mackay CE, Filippini N, Watkins KE, Toro R, Laird AR and Beckmann CF. Correspondence of the brain's functional architecture during activation and rest. Proc Natl Acad Sci U S A 2009; 106: 13040-13045.