Int J Clin Exp Med 2019;12(7):8950-8956
www.ijcem.com /ISSN:1940-5901/IJCEM0091689

Original Article

Amplitude changes in low frequency fluctuation in brains of primary dysmenorrheal treated by acupuncture: a resting-state fMRI study

Chengguo Su[1], Qunwen Lu[1], Huahui Liu[1], Caigui Luo[2*], Youlong Zhou[3*]

[1]Department of Acupuncture and Moxibustion, College of Acupuncture and Massage, Chengdu University of Traditional Chinese Medicine, Chengdu, Sichuan, China; [2]Department of Acupuncture and Moxibustion, Affiliated Hospital of Chengdu University of TCM, Chengdu, Sichuan, China; [3]Department of Acupuncture and Moxibustion, International College, Henan University of TCM, Zhengzhou, Henan, China. [*]Equal contributors and co-first authors.

Received January 23, 2019; Accepted March 11, 2019; Epub July 15, 2019; Published July 30, 2019

Abstract: Objective: The aim of this study was to observe changes in amplitude of low frequency fluctuation (ALFF), before and after acupuncture of the points of Sanyinjiao and Diji, with resting-state fMRI (rsfMRI) technology, investigating central analgesic mechanisms of acupuncture of the points of Sanyinjiao and Diji in patients with primary dysmenorrhea. Methods: A total of 16 primary dysmenorrhea-eligible patients underwent rsfMRI scanning with a feeling of pain on the first or second day of onset of the menstruation period. Anatomical images scanning, resting-state scanning (R1), stimulating-acupoints scanning (AP), and resting-state scanning (R2) after withdrawing the needles were used. Data were analyzed using ALFF. Moreover, pain scores, before, during, and after acupuncture, were evaluated according to VAS. Results: (1) After acupuncture treatment, the pain level decreased from 10 to 8. It further decreased to 4 after treatment; (2) Two-sample paired t-tests indicated brain regions with differences in ALFF between AP and R1. Increased ALFF (AP > R1) appeared in the bilateral medial frontal gyrus, bilateral superior frontal gyrus, bilateral anterior cingulate gyrus, and collosum; (3) Two-sample paired t-tests indicated brain regions with differences in ALFF between R2 and AP. Decreased ALFF (R2 < AP) appeared in the bilateral cingulate gyrus, bilateral anterior cingulate gyrus, insula, hippocampus, thalamus, lentiform nucleus, midbrain, pons, and cerebellum. Conclusion: Acupuncture points of Sanyinjiao and Diji play an important role in relieving pain and increasing or decreasing of ALFF in a series of pain-related encephalic regions. These encephalic regions may be a target of the analgesic effects of acupuncture. Moreover, these may be the conceivable central analgesic mechanisms of acupuncture of the points of Sanyinjiao and Diji for patients with primary dysmenorrhea.

Keywords: Primary dysmenorrhea, acupuncture, resting-state functional magnetic resonance imaging, amplitude of low frequency fluctuation (ALFF)

Introduction

Dysmenorrhea is a common and frequently-occurring disease in gynecology. Primary dysmenorrhea (PD) or functional dysmenorrhea are parts of this disease without reproductive organ lesions [1]. Primary dysmenorrhea is one of the most common menstrual disorders among female college students, affecting daily lives and study habits. In general, incidence of PD among college girls is on the rise [2]. PD has attracted much attention due to its high incidence.

Traditional Chinese Medicine-acupuncture and moxibustion have the advantages of simplicity, convenience, effectiveness, and low-priced, with non-toxic side effects. It is accepted by most patients. The clinical curative rate for primary dysmenorrhea is remarkable [3]. At present, research on acupuncture mechanisms using rsfMRI has become a hot topic at home and abroad, with achievements made [4, 5]. However, application of this technique in acupuncture treatment of primary dysmenorrhea is still rare. The current study aimed to observe changes in amplitude of low frequency fluctua-

tion (ALFF), before and after acupuncture of the points of Sanyinjiao and Diji, in patients with primary dysmenorrheal adopting resting-state fMRI technology, investigating the central analgesic mechanisms of acupuncture of the points of Sanyinjiao and Diji. All data were analyzed using ALFF.

Materials and methods

Subjects

There were 16 PD patients, studying at Henan University of TCM, included in the current study. All patients were in accordance with the following inclusion criteria: (1) In accord with diagnostic criteria (refers to the 1993 edition *the Guiding Principles of Clinical Research in the Treatment of Chinese New Medicine in Dysmenorrhea* by the Bureau of Drug Administration of the Ministry of Public Health of PRC and *Gynecology* in college teaching material); (2) Between 19 and 30 years old without bearing a baby; (3) Regular menstruation (28 ± 7 d); (4) No acupuncture treatment in the previous 3 months and no paregoric, sedatives, or hormones within 2 weeks of this trial; (5) Total points of CMSS ≥10; (6) VAS score ≥4; (7) Dextro-manual; and (8) Provided informed consent. Exclusion criteria: (1) Patients combined with severe life-threatening diseases and mental illness; (2) Pregnant or preparing for pregnancy; and (3) Patients contraindicated with acupuncture or MRI scanning.

Methods

Acupuncture method: Researchers located the bilateral sanyinjiao in the spleen meridian of foot-taiyin (SP6) and acupunctured the points when patients felt pain (sensations of tingling and throbbing). The professional acupuncturist used a 0.30 mm*40.00 mm needle (special and nonmagnetic; Great Wall of China Medical Supplies Factory (Jiangsu), batch number: 20010168). The needle was inserted vertically at sanyinjiao (SP6) about 1-1.5 cun, with the same operation to diji (SP8). After getting a Qi sensation, the needle was manipulated at each acupoint for about 0.5 minutes, with the method of twisting 60 times per minute and a range of about 180-360 degrees. Needles were then withdrawn without lifting, thrusting, or retaining. In the whole trail, all manipulations were done by one experienced acupuncturist. Pain scores were assessed according to visual analogue scores (VAS), using a 10-cm line with the description of “no pain” at one extreme (representing zero) and “intolerable pain” at the other extreme (representing ten). Participants were asked to rate the degree of pain by making a mark on the line. Pain scores were calculated by measuring the distance from zero to that mark using a ruler with a minimum measurement of one mm [6].

Scanning methods and data acquisition of rsfMRI: Structural and functional data of all subjects were collected by PHILIPS Achieva 1.5T MRI scanner of the First affiliated Hospital of Henan University of TCM. When the subjects achieved menstruation and felt pain, they followed these instructions: 1) Stick 1 grain of oleum morrhuae on the tip of the left ear to get the location to process data; 2) Plug the ear with a rubber plug to reduce the distraction of noise; 3) Lie flat on the scanning table, fixing the head after the subject feels at ease; and 4) Turn off the lights and tell the subject to be relaxed and clear-minded, with eyes closed and still. The trial was conducted under the conditions of audio-visual closed without lights. After scanning, subjects were asked about the acupuncture sensation and if there was head-movement, body-movement, or thinking activities, getting the picture of the scanning process. Each of the 16 subjects had obvious needle sensations, with no obvious head or body movements. Thus, all data was adopted for subsequent analysis.

Spin-echo sequence was adopted as the scanning parameter of anatomical imaging, while fast-card gradient echo train was adopted for functional imaging. For T1W anatomical images, the SE sequence was chosen with an axial view, flip angle 90-degree, TR 7.1 s, TE 3.2 s, and Matris 256*256. For functional images, EPI-BOLD sequence was used, with an axial view, flip angle 90-degree, TR 2000 ms, TE 50 ms, Matris 64*64, depth 5.0 mm, and gap 1 mm. Procedures included: Rest 1 (R1), acupuncture at bilateral sanyinjiao (SP6) and diji (SP8), Acupuncture (AP), and structural scan after withdrawing the needles (T) and Rest (R2).

Data processing and statistical analysis

Differences in pain scores were evaluated using Student’s *t*-test with two-tailed 95% confi-

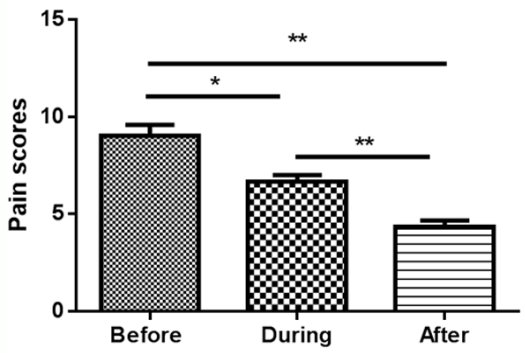

Figure 1. Changes in pain scores before, during, and after acupuncture. (*represents P < 0.05 and **represents P < 0.01).

dence intervals. Results with *P* values less than 0.05 are considered statistically significant.

Processing of fMRI data: Preprocessed statistical analysis of data was conducted on the LINUX system platform. First, MRI Convert 2.0 Software (http://lcni.uoregon.edu/~jolinda/MRIConvert) transformed data into the NIFTI format. Second, BASH script was used, published on 1000 Functional Connectomes Project (http://www.nitrc.org/projects/fcon_1000), to preprocess the ALFF of all subjects. Next, it was normalized to standard MN152 space and statistical analysis was performed. There was a sample t-test of R1, AP, R2, respectively, choosing activated brain regions with significant differences (clumps were not less than 100 voxel, voxel t > 2.262 (uncorrected p < 0.05), Z > 2.3, clumps corrected p < 0.05) in ALFF. Next, results of the variety of ALFF of R1, AP, and R2 in each brain region were obtained. Afterward, paired t-test intergroup analysis was conducted between AP and R1 and AP and R2 of ALFF, choosing activated brain regions with significant differences (clumps were not less than 100 voxel, voxel t > 2.262 (uncorrected p < 0.05), Z > 2.3, clumps corrected p < 0.05) in ALFF. Results of the variety of ALFF of AP relative to R1 and R2 were obtained, respectively. Coordinates were conducted in MNI space and volume of the activated brain functional regions, locating them with Broadmann Area (BA).

The current study was approved by the Medical Ethics Committee of Henan University of TCM, Third Affiliated Hospital. All subjects participated in this study willingly, getting detailed explanations about the study before and providing informed consent.

Results

Changes in pain scores before, during, and after acupuncture

After each acupuncture treatment, patients felt relaxed and reported less stiffness in general, as well as noticeable pain improvement in primary dysmenorrheal. As shown in **Figure 1**, compared with before treatment, pain scores during acupuncture treatment significantly decreased, further decreasing after treatment.

Variation conditions of brain regions according to comparison of AP with R1

Two-sample paired t-tests indicated brain regions with differences in ALFF between AP and R1. Increased ALFF (AP > R1) appeared in the bilateral medial frontal gyrus, bilateral superior frontal gyrus, bilateral anterior cingulate gyrus, and collosum (see **Figure 2**, **Table 1**).

Variation conditions of brain regions according to comparison of R2 with AP

Results of R2 and AP paired t-tests indicated that decreased ALFF (R2 < AP) appeared in the bilateral cingulate cortex, bilateral anterior cingulate cortex, insula, hippocampus, thalamus, lenticular nucleus, midbrain, pons, and cerebellum (see **Figure 3**, **Table 2**).

Discussion

Dysmenorrhea is a common and frequently-occurring diseases in gynecology, seriously impacting the daily lives of women. The clinical curative of acupuncture and moxibustion for primary dysmenorrhea is remarkable. At present, research on acupuncture mechanisms using rsfMRI has become a hot topic at home and abroad, with some achievements made. However, application of this technique in acupuncture treatment of primary dysmenorrhea is still rare.

The current study aimed to observe changes in amplitude of low frequency fluctuation (ALFF), before and after acupuncture of the points of Sanyinjiao and Diji in patients with primary dysmenorrheal, adopting resting-state fMRI tech-

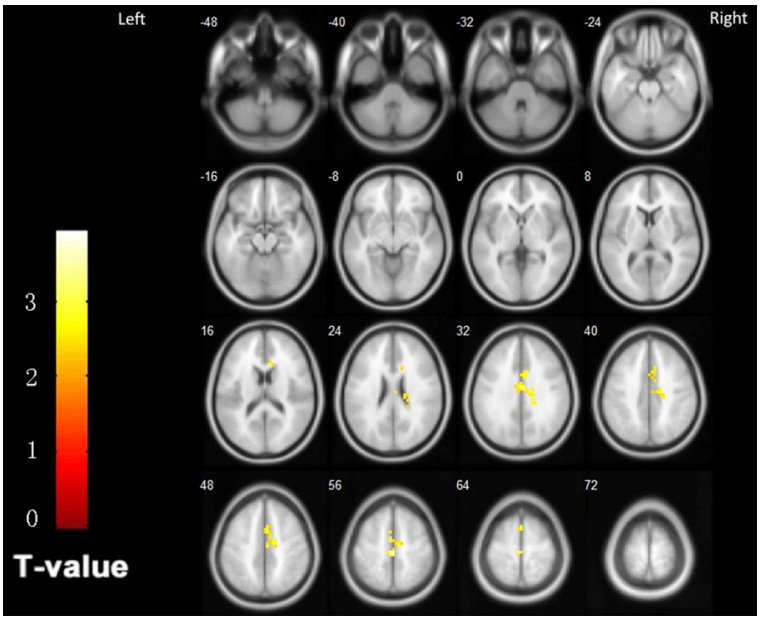

Figure 2. Comparing AP and R1 in brain regions with obvious differences in ALFF (note: the left brain in this figure corresponds to subject's right side, while the left in this figure corresponds to the right side; the clumps in this figure are not less than 10 voxel, voxel $t > 2.262$, uncorrected $p < 0.05$).

nology, investigating the central analgesic mechanisms of acupuncture of the points of Sanyinjiao and Diji.

The ALFF algorithm obtains the power spectrum of the time series of each voxel signal in the brain from data processed by Fourier transform, calculating the ALFF of each voxel. ALFF has been considered to reflect spontaneous neural synchronization directly [7, 8], while spontaneous neural synchronization can reflect the interaction and neural network connection of each related brain region, to some extent. Therefore, the fMRI based ALFF algorithm can reflect a variety of neural activity and network connections of related brain regions in a resting state. This algorithm has been verified in studies concerning attention deficit hyperactivity disorder (ADHD) and differences of visual stimulation between eyes opening and closing [9-13], proving to be a credible algorithm [14].

Acupuncturing at points could make some brain regions activated or inhibited, reflecting the immediate effects of acupuncture. It also has after effects [15].

In the current study, results of the paired t-test of AP and R1 showed that brain regions with increased ALFF (reflecting the brain functional regions of immediate effect of acupuncture) were the bilateral medial frontal gyrus, bilateral superior frontal gyrus, bilateral anterior cingulate gyrus, and collosum. After withdrawing the needles, results of the paired t-test of R2 and AP showed that brain regions with decreased ALFF (reflecting the brain functional regions of after effect of acupuncture) were the bilateral anterior cingulate cortex, insula, hippocampus, thalamus, lenticular nucleus, midbrain, pons, and cerebellum. Xu Jianyang [16] adopted modified temporal clustering analysis to do the fMRI study concerning the after effects of acupuncturing at Hegu (LI4). It was found that, after 14 minutes, brain activity was still in a state of activating or inhibiting, which nearly matched the effects in the science of acupuncture and moxibustion. These activated brain regions also fit the phenomenon of after effects of acupuncture.

Acupuncture analgesia is related to the function of every part of the nerve system. Spinal marrow is the first step, dealing with and translating the information of acupuncture analgesia. The brainstem is the relay station, collating, analyzing, activating, synthesizing, and connecting the information. This has a significant effect in acupuncture analgesia [17]. In this study, considering the activating of midbrain and pons, it was speculated that acupuncture activates the thalamus, which is the element exchange station of pain and reaction due to the nociceptive information comes into cerebral cortex. Therefore, the para-fascicular nucleus and centro-median nucleus of intralaminar thalamic nuclei are very important centers of feeling and regulating pain. Results indicate that activating the centro-median nucleus could inhibit para-fascicular nucleus firing. When the centro-median nucleus is activated, it inhibits para-fascicular nucleus firing through 3 ways, cutting off the delivery of nociceptive information to the cerebral cortex [17]. The current study discovered that the bilateral thala-

Table 1. Comparing AP and R1 in brain regions with significant differences in ALFF, peak coordinates, and cluster size

Location	BA	Peak coordinates (mm)			Peak Z-value	Cluster size (mm^3)
		x	y	z		
L. medial frontal gyrus	6, 24, 32	0	-24	62	3.93	191

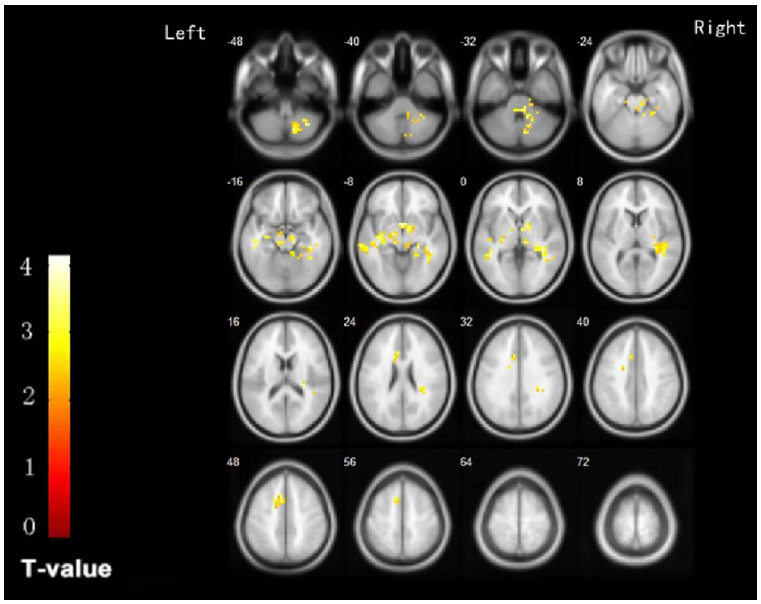

Figure 3. Comparing AP and R2 in brain regions with obvious differences in ALFF (note: the left brain in this figure corresponds to subject's right side, while the left in this figure corresponds to the right side; the clumps in this figure are not less than 10 voxel, voxel $t > 2.262$, uncorrected $p < 0.05$).

mus had been activated after acupuncture. It was hypothesized that acupuncture information and nociceptive information interacts with each other in the thalamus, producing analgesic effects by cutting off the pathway of nociceptive information delivery to the cerebral cortex.

The frontal lobe is the largest lobe in the hemisphere. The superior frontal gyrus and middle frontal gyrus are located in the prefrontal area mainly related to mental and emotional activities (such as thinking, emotion, judgment, intelligence, memory, etc.) and muscle synergistic movement [18]. The central prefrontal lobe is involved in the integration of internal and external environmental information, emotional integration, and other functions of the human brain [19]. Perception is the unique function of the most advanced central cortex of sensory integration. A kind of stimulation, the afferent impulse of acupuncture will in-evitably reach the cerebral cortex for information processing, eventually transforming into consciousness. The cerebral cortex is the highest center, which not only feels the information of pain but also participates in the modulation of pain. The cerebral cortex is not only a process of excitement and inhibition of acupuncture analgesia, but also a complex adjustment and command center. It can not only strengthen analgesia but also inhibit it. It plays the role of maintaining dynamic balance. Previous studies have found many connections between the prefrontal lobe and limbic system, playing an important role in regulating the expectation of pain. In this study, acupuncture at bilateral sanyinjiao (SP6) and diji (SP8) points activated both the superior bilateral frontal gyrus and medial frontal gyrus. The primary somatosensory cortex was activated during acupuncture, supporting regulation of acupuncture on the cortex and subcortical brain region. Therefore, these brain regions may be involved in theanalgesic effects of acupuncture on dysmenorrhea.

Multiple studies have found that pain stimulation could cause functional activity in the anterior cingulate area, which is associated with pain-induced emotional activity [20-22]. Pain leads to an increase of blood flow of the anterior cingulate cortex, increasing the fMRI signal of this area. However, results of acupuncturing at sanyinjiao (SP6) and diji (SP8) are different. It decreases the signal, indicating that acupuncture analgesia may be related to the regulating effects of the anterior cingulate cortex. Some studies have suggested that basal ganglia (including lenticular nucleus, caudate nucleus, amygdaloid body, and etc.) are involved in deal-

Table 2. Comparing AP and R2 in brain regions with significant differences in ALFF, peak coordinates, and cluster size

Location	BA	Peak coordinates (mm)			Peak Z-value	Cluster size (mm^3)
		x	y	z		
L.extra-nuclear.white matter		0	4	-4	3.34	330
R.temporal lobe.caudate.gray matter	40	35	-37	2	4.5	135
L. cingulate gyrus	33	-8	20	50	4.4	60

ing with nociceptive and non-nociceptive information, playing a very important role in regulating pain [23]. Insula has the ability to differentiate painful sensation of internal organs, showing the big influence in regulating pain [24]. The hippocampus belongs to the limbic system, controlling emotional activities [25]. This study discovered that, after acupuncturing at sanyinjiao (SP6) and diji (SP8), pain-related brain regions of the limbic system, like the anterior cingulate cortex, lenticular nucleus, insula, and hippocampus, were obviously activated. This implies that, in the process of acupuncture analgesia, psychological activities have significant effects. Maybe this is one way to influence the analgesic effects.

The cerebellum has been widely associated with the brain, brain stem, and spinal cord, which not only receive sensory information associated with motion, but also nociceptive afferent information [26]. Some animal experiments have reported that the C fibers convey nociceptive information to the cerebellum through the ipsilateral dorsal cord [27] and that antagonistic information of the cerebellum may be transmitted through the downlink inhibitory conduction pathway of the brain stem [28]. Activation of the cerebellum in this study suggests that the cerebellum is also involved in pain modulation.

Acupuncture of the points of Sanyinjiao and Diji plays an important role in the increasing or decreasing of ALFF in a series of brain regions (such as thalamus, midbrain, pons, bilateral anterior cingulate, bilateral medial frontal gyrus, bilateral superior frontal gyrus, insula, hippocampus, corpus callosum, legume nucleus, cerebellum). These regions are related with pain regulation and mood. These brain regions may be targets of the analgesic effects of acupuncture. These may be the conceivable central analgesic mechanisms of acupuncture of the points of Sanyinjiao and Diji for patients with primary dysmenorrhea.

Disclosure of conflict of interest

None.

Address correspondence to: Caigui Luo, Department of Moxibustion, Affiliated Hospital of Chengdu University of TCM, No. 39, Shierqiao Road, Chengdu 610075, Sichuan, China. Tel: +86-13541278288; E-mail: caigui288@163.com; Youlong Zhou, International College, Henan University of TCM, No. 156, Jinshui Road, Zhengzhou 450046, Henan, China. Tel: +86-0371-65676793/+86-13592688883; E-mail: youlong6666@163.com

References

[1] De Sanctis V, Soliman A, Bernasconi S, Bianchin L, Bona G, Bozzola M, Buzi F, De Sanctis C, Tonini G, Rigon F, Perissinotto E. Primary dysmenorrhea in adolescents: prevalence, impact and recent knowledge. Pediatr Endocrinol Rev 2015; 13: 512-520.

[2] Polat A, Celik H, Gurates B, Kaya D, Nalbant M, Kavak E and Hanay F. Prevalence of primary dysmenorrhea in young adult female university students. Arch Gynecol Obstet 2009; 279: 527-532.

[3] Yu SY, Lv ZT, Zhang Q, Yang S, Wu X, Hu YP, Zeng F, Liang FR and Yang J. Electroacupuncture is beneficial for primary dysmenorrhea: the evidence from meta-analysis of randomized controlled trials. Evid Based Complement Alternat Med 2017; 2017: 1791258.

[4] Wang Y, Zheng Y, Qu S, Zhang J, Zhong Z, Zhang J, Huang H, Li M, Xu Y and Chen J, Wang Steiner GZ, Tang C, Huang Y. Cerebral targeting of acupuncture at combined acupoints in treating essential hypertension: an Rs-fMRI study and curative effect evidence. Evid Based Complement Alternat Med 2016; 2016: 5392954.

[5] Shi Y, Zhang S, Li Q, Liu Z, Guo S, Yang J and Wu W. A study of the brain functional network of Deqi via acupuncturing stimulation at BL40 by rs-fMRI. Complement Ther Med.2016; 25: 71-77.

[6] Tanmahasamut P, Chawengsettakul S. Dysmenorrhea in Siriraj medical students; prevalence, quality of life, and knowledge of man-

agement. J Med Assoc Thai 2012; 95: 1115-1121.
[7] Zang YF, He Y, Zhu CZ, Cao QJ, Sui MQ, Liang M, Tian LX, Jiang TZ, Wang YF. Altered baseline brain activity in children with ADHD revealed by resting-state functional MRI. Brain Dev 2007; 29: 83-91.
[8] Leopold DA, Murayama Y and Logothetis NK. Very slow activity fluctuations in monkey visual cortex: implications for functional brain imaging. Cereb Cortex 2003; 13: 422-433.
[9] Yang H, Long XY, Yang Y, Yan H, Zhu CZ, Zhou XP, Zang YF and Gong QY. Amplitude of low frequency fluctuation within visual areas revealed by resting-state functional MRI. Neuroimage 2007; 36: 144-152.
[10] Hoptman MJ, Zuo XN, Butler PD, Javitt DC, D'Angelo D, Mauro CJ and Milham MP. Amplitude of low-frequency oscillations in schizophrenia: a resting state fMRI study. Schizophr Res 2010; 117: 13-20.
[11] Huang XQ, Lui S, Deng W, Chan RC, Wu QZ, Jiang LJ, Zhang JR, Jia ZY, Li XL and Li F. Localization of cerebral functional deficits in treatment-naive, first-episode schizophrenia using resting-state fMRI. Neuroimage 2010; 49: 2901-2906.
[12] Yang H, Wu QZ, Guo LT, Li QQ, Long XY, Huang XQ, Chan RC, Gong QY. Abnormal spontaneous brain activity in medication-naive ADHD children: a resting state fMRI study. Neurosci Lett 2011; 502: 89-93.
[13] Zhang Z, Lu G, Zhong Y, Tan Q, Chen H, Liao W, Tian L, Li Z, Shi J and Liu Y. fMRI study of mesial temporal lobe epilepsy using amplitude of low < frequency fluctuation analysis. Hum Brain Map 2010; 31: 1851-1861.
[14] Zuo XN, Di Martino A, Kelly C, Shehzad ZE, Gee DG, Klein DF, Castellanos FX, Biswal BB and Milham MP. The oscillating brain: complex and reliable. Neuroimage 2010; 49: 1432-1445.
[15] Long Y, Liu B, Liu X, Yan C, Chen Z, Chen J, Shang XJ and Mo WZ. Resting-state functional MRI evaluation of after-effect of acupuncture at Zusanli point. Chin J Med Imaging Technol 2009; 25: 373-376.
[16] Xu J, Yan B, Wang W, Hao J, Lu N, Li K and Shan B. Cerebral function imaging re-search on the after-effect of point Hegu acupuncture. Shanghai Zhen Jiu Za Zhi (Shanghai J Acu-moxi, Chin) 2005; 24: 33-35.
[17] Zhang J and Zhang N. Study on mechanisms of acupuncture analgesia. Zhongguo Zhen Jiu 2007; 27: 72-75.
[18] Snell RS. Clinical neuroanatomy. Lippincott Williams & Wilkins, 2010.
[19] D'Argembeau A, Ruby P, Collette F, Degueldre C, Balteau E, Luxen A, Maquet P and Salmon E. Distinct regions of the medial prefrontal cortex are associated with self-referential processing and perspective taking. J Cogn Neurosci 2007; 19: 935-944.
[20] Mandeville JB, Marota JJ, Kosofsky BE, Keltner JR, Weissleder R, Rosen BR and Weisskoff RM. Dynamic functional imaging of relative cerebral blood volume during rat forepaw stimulation. Magn Reson Med 1998; 39: 615-624.
[21] Baciu MV, Bonaz BL, Papillon E, Bost RA, Le Bas JF, Fournet J and Segebarth CM. Central processing of rectal pain: a functional MR imaging study. AJNR Am J Neuroradiol 1999; 20: 1920-1924.
[22] Davis KD, Taylor SJ, Crawley AP, Wood ML and Mikulis DJ. Functional MRI of pain-and attention-related activations in the human cingulate cortex. J Neurophysiol 1997; 77: 3370-3380.
[23] Chudler EH and Dong WK. The role of the basal ganglia in nociception and pain. Pain 1995; 60: 3-38.
[24] Pariente J, White P, Frackowiak RS and Lewith G. Expectancy and belief modulate the neuronal substrates of pain treated by acupuncture. Neuroimage 2005; 25: 1161-1167.
[25] Li J, Zhang J and Dong J. Influence of acupuncture analgesia on cerebral function imaging in sciatica patients. Shanghai J Acu-mox 2007; 26: 3-6.
[26] Gong P, Zhang M, Wang Q, Wu Z, Huang X, Wang W and Huang G. Effect of acupuncture at Sanyinjiao (SP6) on glucose metabolism in the patient of dysmenorrhea. Zhongguo Zhen Jiu 2006; 26: 51-55.
[27] Ekerot C, Garwicz M and Schouenborg J. The postsynaptic dorsal column pathway mediates cutaneous nociceptive information to cerebellar climbing fibres in the cat. J Physiol 1991; 441: 275-284.
[28] Saab CY, Willis WD. Cerebellar stimulation modulates the intensity of a visceral nociceptive reflex in the rat. Exp Brain Res 2002; 146: 117-121.