

Differential spectral power alteration following acupuncture at different designated places revealed by magnetoencephalography

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ABSTRACT

As an ancient therapeutic technique in Traditional Chinese Medicine, acupuncture has been used increasingly in modern society to treat a range of clinical conditions as an alternative and complementary therapy. However, acupoint specificity, lying at the core of acupuncture, still faces many controversies. Considering previous neuroimaging studies on acupuncture have mainly employed functional magnetic resonance imaging, which only measures the secondary effect of neural activity on cerebral metabolism and hemodynamics, in the current study, we adopted an electrophysiological measurement technique named magnetoencephalography (MEG) to measure the direct neural activity. 28 healthy college students were recruited in this study. We filtered MEG data into 5 consecutive frequency bands (delta, theta, alpha, beta and gamma band) and grouped 140 sensors into 10 main brain regions (left/right frontal, central, temporal, parietal and occipital regions). Fast Fourier Transformation (FFT) based spectral analysis approach was further performed to explore the differential band-limited power change patterns of acupuncture at Stomach Meridian 36 (ST36) using a nearby nonacupoint (NAP) as control condition. Significantly increased delta power and decreased alpha as well as beta power in bilateral frontal ROIs were observed following stimulation at ST36. Compared with ST36, decreased alpha power in left and right central, right parietal as well as right temporal ROIs were detected in NAP group. Our research results may provide additional evidence for acupoint specificity.

Keywords: magnetoencephalography, acupuncture, specificity, spectral power

1. INTRODUCTION

Acupuncture is an ancient East Asian healing technique that has been used to treat various illnesses for thousands of years. It has gained great popularity as an alternative and complementary therapeutic intervention in the western medicine. A promising efficacy of acupuncture has been shown in the treatments of postoperative and chemotherapy nausea and vomiting [1]. However, the scientific explanation regarding the physiological mechanisms of acupuncture stimulation has not been found out totally yet, hindering its better promotion in modern medicine practice.

The clinical effectiveness of acupuncture per se is said to depend on the specific placement of the needles at designated acupoint [2]. Although acupoint specificity lied at the core of traditional acupuncture theory, controversy regarding its representation still remains. To prove acupoint specificity, previous researches have focused on the relationship between acupuncture needle stimulations at vision-related acupoints and their corresponding cortical activation patterns. Cho was one of pioneers to find that the visual cortex can be induced by peripheral acupuncture at visual-associated acupoints, while such neural activities do not emerge after stimulation at a nearby nonacupoint [3]. Following investigation by others also supported that acupuncture given at traditional vision-related acupoints can elicit activity selectively within the visual cortex [4-6]. However, this conclusion is hard to be replicated by other researches [7]. One recent investigation has indicated that acupuncture stimulation at vision-related acupoints and non-acupoint can elicit similar signal changes

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in the visual cortex, which does not support the specificity of vision-related acupoints [8]. Some other researchers also report that stimulation at nonacupoints or treatment-irrelevant acupoints share the deactivated regions of the limbic system and subcortical structures, including the hippocampus, amygdala, parahippocampus and precuneus [9-11]. On the whole, the representations of acupoint specificity remain debatable and further work is awaited to test the neurological basis of acupoint specificity to promote its acceptance as a viable clinical treatment in the modern medicine practice.

In the last decades, the great advances in neuroimaging techniques have opened a window to the human brain, enabling us to study the anatomical and physiological responses associated with acupuncture. As one of the most frequently deployed techniques, functional Magnetic Resonance Imaging (fMRI) based on the blood oxygen level dependent (BOLD) has been the dominant imaging modality for exploring acupuncture mechanism [12-15]. Nevertheless, the measurement may be to some degree confounded since they are indirect assessments of brain activity. As fMRI only evaluates the secondary effect of neural activity on cerebral metabolism, it is limited by poor temporal resolution due to the protracted hemodynamic response [16]. Magnetoencephalography (MEG) is non-invasive technology to monitor the dynamic neural activity of the whole brain, through which the magnetic fields induced by neuronal current flow in the brain are directly measured above the scalp [17]. Since acupuncture can induce complex temporal neural responses in wide brain area, careful interpretations of interactions between acupuncture intervention and brain processing depend on how effectively we can characterize the nature of temporal variations underlying neural activities that give rise to hemodynamic responses.

In the present paper, we applied spectral analysis methods based on Fast Fourier Transformation to compare the band-limited power of resting state under MEG circumstance before and after stimulation at ST36, using a nearby NAP as control condition. Paired t test was performed for each group to determine whether there exist differential power change patterns of ten main regions of interest induced by acupuncture between two groups. By comparing the differential oscillatory brain activity, we expected to provide further evidence to support acupoint specificity.

2. METHOD AND MATERIALS

2.1 Subjects

In order to reduce inter-subject difference, 28 Chinese right-handed healthy college students (14 males, aged 24.5 ± 1.8) from a homogeneous group were enrolled in this study. All of them were all acupuncture naïve. None of them have a history of major medical illness, head trauma, neuropsychiatric disorders, nor did they use any prescription medications within the last month according to a questionnaire they filled out. All subjects gave written, informed consent after the experimental procedures had been fully explained. The research procedures were approved by the Tiantan Hospital Subcommittee on Human Studies and conducted in accordance with the Declaration of Helsinki.

2.2 Experimental paradigm

All 28 participants were evenly divided into two groups, being matched by age and gender. Every subject received only once acupuncture stimulation. All participants were instructed to sit comfortably in a dark and magnetically shielded room with their eyes closed and asked to remain relaxed without engaging in any mental tasks. The precise locations of needling, the presumed acupuncture effects, and the stimulation paradigm were not divulged to all subjects.

The experiment consisted of two functional runs. Resting-state (RS) run lasted for 6 min. Acupuncture in both groups employed the single-block design paradigm, incorporating 2 min needle manipulation at a rate of 60 times per minute, preceded by 1 min rest epoch and followed by 6 min rest scanning (needle kept in place without manipulation). Acupuncture was performed at acupoint ST36 on the right leg, which has been proved to show various efficacies in pain-management in humans. It is located four finger breadths below the lower margin of the patella and one finger breadth laterally from the anterior crest of the tibia. Sham acupuncture was exerted with needling at non-meridian points as the control condition (NAP, 2-3 cm apart from ST36) with needle depth, stimulation intensity, and manipulation method all identical to those used in the verum acupuncture. Acupuncture stimulation was delivered using a sterile disposable 38 gauge stainless steel acupuncture needle, 0.2 mm in diameter and 40 mm in length, which was inserted perpendicularly to the skin surface to a depth of 1.5-2.5 cm. Administration was delivered by a balanced “tonifying and reducing” technique. The procedure was performed by the same experienced and licensed acupuncturist on all participants.

During the experiment, the subjects were told to keep their eyes closed and remain relaxed without engaging in any mental tasks. As a concurrent psychophysical analysis, we used a verbal analog scale to ask participants to quantify the

subjective sensations of acupuncture or *deqi* at the end of scanning. The sensation rates from 0 to 10 (0 = no sensation, 1-3 = mild, 4-6 = moderate, 7-8 = strong, 9 = severe and 10 = unbearable sensation). The *deqi* sensations consist of the aching, throbbing, soreness, heaviness, fullness, warmth, numbness, tingling, dull or sharp pain and any other sensations they felt during the scan.

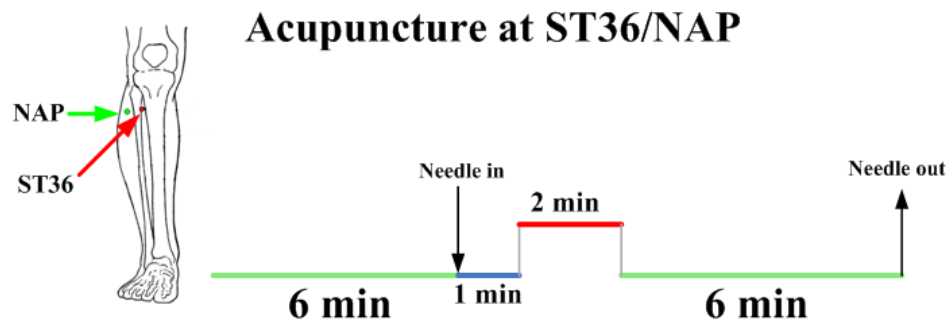


Figure 1: Experimental design. Illustration of anatomical locations of ST36 (Zusanli) and NAP (Non-acupoint).

2.3 Data acquisition and analysis

The MEG data were recorded while subjects were comfortably seated inside a magnetically shielded room using a 151-channel whole-head MEG system (CTF Systems Inc., Port Coquitlam, BC, Canada). Average distance between sensors in this system is 3.1 cm. The head position was monitored during the measurement using head position indicator coils. MEG data were recorded at the sample rate of 600 Hz. A third-order gradient noise reduction (computed with CTF software) was applied to all MEG signals to remove noise. During the recording, participants were instructed to close their eyes to reduce artifact signals due to eye movements, but remain awake as much as possible. Foam padding was used to immobilize the head with respect to the MEG sensors. The investigator and MEG technician checked the signal on-line for visual signs of drowsiness and observed the participants using a video monitor. At the beginning and end of each recording, the head position relative to the coordinate system of the helmet was recorded by leading small alternating currents through three head position coils attached to the left and right pre-auricular points and the nasion on the subject's head. If any subject's head moved more than 5 mm during the experiment, data from that subject would be discarded for further analysis. It turns out, for all participants, that the difference between the sensor locations evaluated before and after the experiment was insignificant, confirming a relatively stable head position.

The MEG data were further digitally filtered offline with a band pass of 0.5-48 Hz and down sampled to 300 Hz. Subsequently, the MEG data were band-passed into the following frequency ranges: delta (0.5-4Hz), theta (4-8Hz), alpha (8-13Hz), beta (13-30Hz) and gamma band (30-48Hz) [18]. The 6-min resting data before and after acupuncture were selected and split into 6 1-min-long epochs separately. The following processing was executed for the 6 epochs respectively and results were averaged for each subject. The MEG channels were grouped into regions of interest corresponding to the major cortical areas (frontal, central, temporal, parietal and occipital) on the left and right side of the brain. Two of the original 151 channels were not available due to technical problems during recording for all participants, and the 9 middle channels were left out of clustering, leaving a total of 140 channels divided over 10 ROIs for further analysis. Furthermore, relative spectral power for each ROI was computed for the 5 frequency bands by dividing the mean band power by the total power at 0.5-48 Hz [18-19]. Fast Fourier Transformation (FFT) was separately applied for every participant on the 6 epochs. Results of the 6 epochs were averaged for each subject and further used in statistical analysis. All analysis was conducted in Matlab R2008a and SPSS 17.0 software package.

3. RESULTS

3.1 Psychophysical responses

The prevalence of subjective “*deqi*” sensations was expressed as the percentage of the individuals in the group who reported the given sensations (Fig. 2A). The intensity was expressed as the average score \pm standard error (Fig. 2B). No subject opted to add an additional descriptor in the blank row provided. The occurrence frequency of all sensations

except coolness was found greater for the acupuncture at ST36 than NAP. The overall stimulus intensities (mean±SE) were greater for ST36, demonstrating a stronger deqi sensation in verum acupuncture than sham acupuncture.

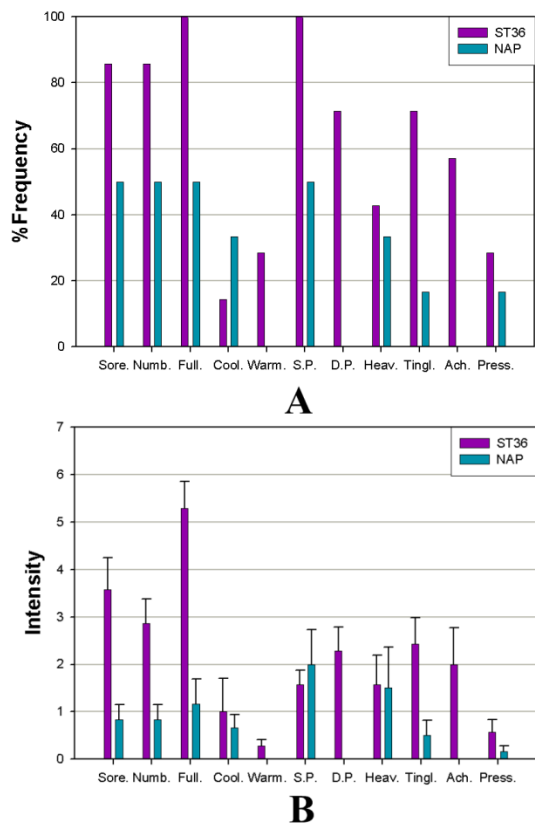


Figure 2: Results of psychophysical analysis: A. Percentage of subjects who reported having experienced the given sensations; B. The intensity of the reported sensations measured by an averaged score (with standard error bars) on a scale from 0 to 10. Sore, soreness; Numb, numbness; Full, fullness; Cool, coolness; Warm, warmth; SP, sharp pain; DP, dull pain; Heav, heaviness; Tinkl, tingling; Ach, aching; Press, pressure.

3.2 Relative power alterations

Spectral and statistical analysis revealed prominently differential power change between two groups. Following acupuncture at ST36, the delta-band power of resting state in both left and right frontal regions was significant higher than that of before acupuncture ($P=0.006$ and $P=0.001$ respectively), while alpha-band and beta-band power in frontal regions significantly decreased after acupuncture ($P<0.05$). On the contrary, there is no significant power change referring to frontal regions of all five frequency bands after acupuncture at NAP. Besides, a loss of alpha power in bilateral central, right parietal as well as right temporal ROIs was detected after acupuncture in the NAP group (See Table 1 and Figure 3 for details).

Table 1: Relative spectral power values and statistical results in the five frequency bands for ST36 and NAP group. Significant differences are indicated in bold ($P<0.05$). L=left, R=right. B_rest, resting data before acupuncture. P_rest, resting data after acupuncture.

Frequency band	ROIs	Group ST36 (N=14)				Group NAP (N=14)			
		B_rest	P_rest	t value	P value	B_rest	P_rest	t value	P value
Delta (0.5-4Hz)	L Central	0.234±0.086	0.256±0.070	1.591	0.136	0.327±0.127	0.352±0.129	1.327	0.207
	L Frontal	0.370±0.142	0.418±0.120	3.257	0.006	0.528±0.175	0.560±0.182	1.185	0.257
	L Occipital	0.139±0.051	0.154±0.060	0.918	0.375	0.223±0.174	0.226±0.150	0.262	0.797
	L Parietal	0.163±0.060	0.173±0.056	0.686	0.505	0.261±0.146	0.276±0.129	1.019	0.327
	L Temporal	0.302±0.137	0.342±0.119	1.875	0.083	0.442±0.143	0.468±0.155	1.018	0.327
	R Central	0.227±0.083	0.246±0.061	1.366	0.195	0.317±0.111	0.343±0.114	1.357	0.198
	R Frontal	0.384±0.148	0.442±0.125	4.148	0.001	0.506±0.151	0.544±0.164	1.171	0.262
	R Occipital	0.146±0.056	0.159±0.064	0.756	0.463	0.244±0.201	0.243±0.179	-0.083	0.935
	R Parietal	0.163±0.055	0.174±0.053	0.715	0.487	0.249±0.117	0.265±0.103	1.129	0.279
	R Temporal	0.302±0.166	0.333±0.128	1.277	0.224	0.381±0.107	0.424±0.145	1.765	0.101
Theta (4-8Hz)	L Central	0.145±0.030	0.142±0.033	-0.293	0.774	0.169±0.059	0.153±0.056	-1.149	0.271
	L Frontal	0.130±0.028	0.123±0.028	-1.162	0.266	0.129±0.057	0.117±0.053	-1.294	0.218
	L Occipital	0.124±0.033	0.128±0.045	0.431	0.673	0.129±0.066	0.116±0.052	-0.721	0.484
	L Parietal	0.127±0.029	0.124±0.037	-0.342	0.738	0.154±0.061	0.138±0.051	-0.900	0.384
	L Temporal	0.129±0.026	0.128±0.036	-0.121	0.905	0.128±0.046	0.119±0.052	-0.675	0.512
	R Central	0.143±0.025	0.139±0.031	-0.386	0.706	0.169±0.056	0.149±0.050	-1.173	0.262
	R Frontal	0.138±0.030	0.127±0.028	-1.534	0.149	0.138±0.054	0.123±0.055	-1.143	0.274
	R Occipital	0.130±0.035	0.131±0.045	0.127	0.901	0.126±0.068	0.113±0.053	-0.760	0.461
	R Parietal	0.126±0.030	0.124±0.036	-0.199	0.845	0.156±0.065	0.138±0.047	-0.936	0.366
	R Temporal	0.130±0.029	0.128±0.036	-0.280	0.784	0.136±0.041	0.122±0.045	-1.084	0.298
Alpha (8-13Hz)	L Central	0.280±0.088	0.258±0.072	-1.386	0.189	0.228±0.108	0.209±0.093	-2.510	0.026
	L Frontal	0.189±0.065	0.165±0.046	-2.637	0.020	0.134±0.067	0.118±0.054	-1.780	0.098
	L Occipital	0.457±0.094	0.441±0.112	-0.734	0.476	0.393±0.157	0.381±0.150	-1.524	0.151
	L Parietal	0.388±0.098	0.371±0.112	-0.878	0.396	0.309±0.137	0.291±0.130	-2.122	0.054
	L Temporal	0.328±0.114	0.294±0.089	-1.575	0.139	0.244±0.133	0.222±0.117	-1.722	0.109
	R Central	0.279±0.087	0.256±0.071	-1.237	0.238	0.224±0.099	0.204±0.084	-2.605	0.022
	R Frontal	0.186±0.064	0.158±0.042	-2.697	0.018	0.148±0.070	0.129±0.052	-1.804	0.095
	R Occipital	0.442±0.084	0.429±0.104	-0.591	0.564	0.378±0.157	0.369±0.154	-0.978	0.346
	R Parietal	0.388±0.097	0.372±0.108	-0.719	0.485	0.307±0.114	0.287±0.111	-2.282	0.040
	R Temporal	0.324±0.117	0.298±0.095	-1.117	0.284	0.267±0.126	0.240±0.120	-2.433	0.030
Beta (13-30Hz)	L Central	0.267±0.059	0.265±0.057	-0.164	0.872	0.219±0.050	0.213±0.049	-0.659	0.521
	L Frontal	0.223±0.062	0.211±0.059	-2.459	0.029	0.149±0.059	0.140±0.063	-1.017	0.328
	L Occipital	0.243±0.062	0.241±0.059	-0.274	0.788	0.233±0.069	0.239±0.067	1.215	0.246
	L Parietal	0.276±0.057	0.281±0.054	0.616	0.549	0.241±0.064	0.240±0.057	-0.237	0.816
	L Temporal	0.203±0.062	0.199±0.061	-0.707	0.492	0.161±0.039	0.155±0.048	-0.700	0.496
	R Central	0.271±0.050	0.270±0.051	-0.044	0.966	0.229±0.055	0.223±0.047	-0.638	0.535
	R Frontal	0.219±0.065	0.202±0.062	-4.234	0.001	0.158±0.056	0.147±0.059	-1.022	0.325
	R Occipital	0.243±0.055	0.240±0.055	-0.423	0.679	0.231±0.081	0.236±0.076	1.451	0.171
	R Parietal	0.279±0.051	0.280±0.051	0.133	0.896	0.254±0.069	0.254±0.056	0.006	0.996
	R Temporal	0.208±0.071	0.204±0.069	-0.664	0.519	0.187±0.041	0.175±0.050	-1.255	0.232
Gamma (30-48Hz)	L Central	0.074±0.034	0.079±0.042	1.111	0.287	0.070±0.035	0.073±0.039	0.850	0.411
	L Frontal	0.087±0.034	0.083±0.033	-1.331	0.206	0.065±0.035	0.065±0.041	-0.076	0.940
	L Occipital	0.037±0.024	0.036±0.021	-0.326	0.750	0.037±0.025	0.038±0.025	0.667	0.516
	L Parietal	0.045±0.023	0.051±0.033	1.316	0.211	0.051±0.030	0.055±0.035	1.672	0.118
	L Temporal	0.038±0.020	0.038±0.020	-0.131	0.898	0.036±0.019	0.036±0.022	0.001	0.999
	R Central	0.080±0.035	0.089±0.045	1.306	0.214	0.077±0.035	0.081±0.044	0.786	0.446
	R Frontal	0.072±0.029	0.070±0.030	-1.151	0.270	0.058±0.030	0.057±0.037	-0.222	0.828
	R Occipital	0.038±0.019	0.040±0.024	0.334	0.744	0.036±0.025	0.038±0.026	1.466	0.166
	R Parietal	0.044±0.021	0.050±0.030	1.263	0.229	0.052±0.029	0.056±0.034	1.451	0.170
	R Temporal	0.036±0.018	0.037±0.020	0.737	0.474	0.040±0.022	0.039±0.026	-0.257	0.801

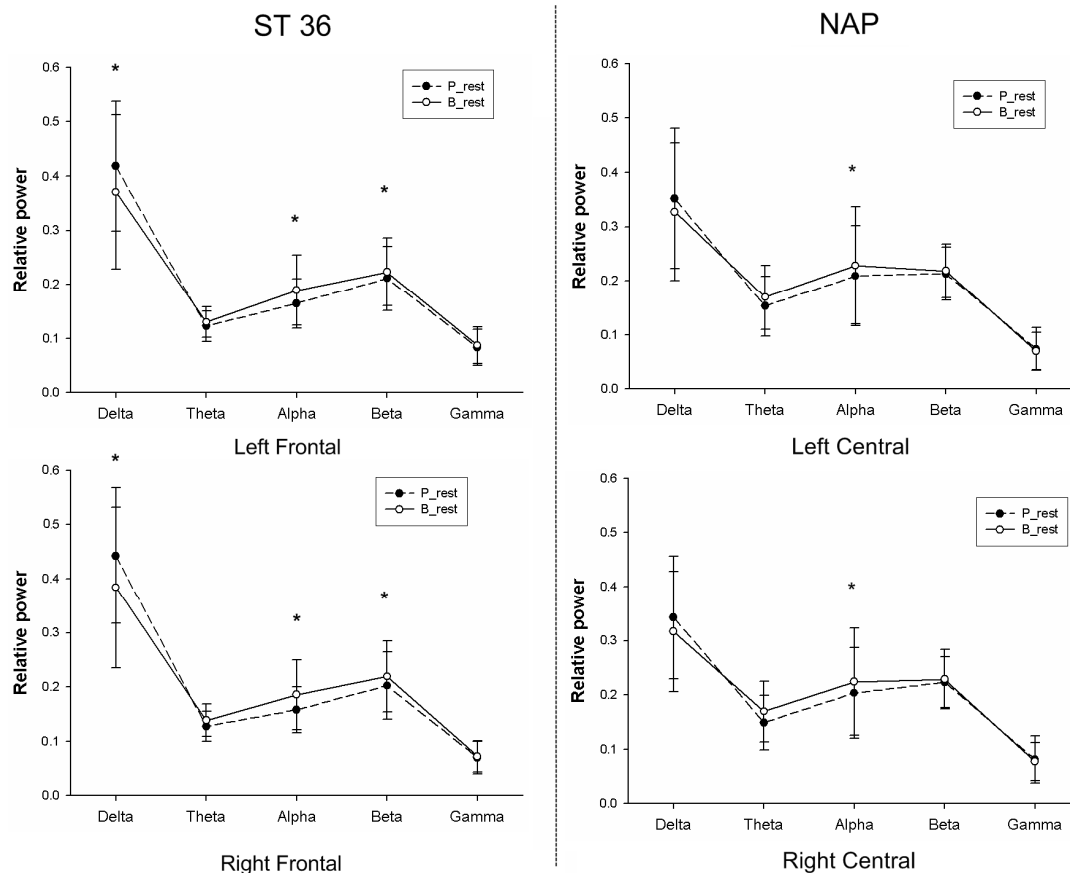


Figure 3: Mean relative power and standard errors in the five frequency bands of main ROIs which showed significant difference after acupuncture for ST36 and NAP group.* $P < 0.05$.

4. DISCUSSIONS

To our knowledge, this is the first magnetoencephalographic study exploring the resting band-limited power change of main brain regions induced by acupuncture at ST36 using a nearby nonacupoint as control condition on healthy subjects. The current research demonstrated the significantly differential spectral power changes in oscillatory brain activity following acupuncture at ST36, using a nearby nonacupoint as control condition. It is worth noting, following acupuncture at ST36, that relative spectral power alterations of delta, alpha and beta bands were observed conspicuously, comparing with the exclusively detection of alpha band in NAP group. Furthermore, in the ST36 group, we observed an increase in delta power and decrease in alpha and beta power restricted to bilateral frontal ROIs. Regarding the NAP group, more widespread decreases in alpha power in bilateral central, right parietal and right temporal ROIs were illustrated.

The increase power of delta band together with decrease of alpha and beta band may indicate an energy flow of brain oscillatory activity from high frequency to low frequency underlying acupuncture at ST36. Moreover, as ST36 is a clinically frequently used acupoint for analgesia [20], it could be inferred that bilateral frontal ROIs may play a key role in mediating the influence of human expectation on the perception of pain, considering that these regions in three bands showed conspicuous alterations following stimulation at ST36 rather than NAP. Note that the present work was performed on MEG data at the level of sensor space, limiting anatomical inferences drawn from the data. Given the sparsity of work on acupuncture together with MEG, it is difficult to generate clear hypotheses about oscillatory neuronal dynamics of power changes induced by acupuncture. Future work will include a source reconstruction of the activity in the brain, which will allow improved extrapolation to anatomical locations.

5. CONCLUSIONS

In the current study, we applied FFT based approach to elucidate the discordance of power change between acupuncture at ST36 and NAP. Group results showed the significant delta-band power increased as well as alpha- and beta-band power decreased in frontal regions following acupuncture at ST36, while decreased power of alpha band mainly focused in bilateral central, right parietal and temporal regions were detected after acupuncture at NAP. From these observations, we proposed that specific neural substrates might underlie the differential acupuncture actions and may provide additional evidence for acupoint specificity.

6. ACKNOWLEDGMENTS

This paper is supported by the knowledge innovation program of the Chinese academy of sciences under grant No.KGCX2-YW-129, the Project for the National Key Basic Research and Development Program (973) under Grant No. 2011CB707700, 2007CB512500, 2007CB512503, 2009CB521905, the National Natural Science Foundation of China under Grant No. 30873462, 30970774, 60901064, 81071137, 81071217.

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