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Research Report

Tempo-spatial analysis of vision-related acupoint specificity in the occipital lobe using fMRI: An ICA study

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ARTICLE INFO

Article history:
Accepted 28 November 2011
Available online 4 December 2011

Keywords:
Temporal dynamic
Vision-related acupoint specificity
ICA
fMRI

ABSTRACT

Functional acupoint specificity is one of the most debated topics in acupuncture neuroimaging research. Conventional studies investigating vision-related acupoint specificity empirically assume that acupuncture-induced hemodynamic response can be defined a priori and thus concentrate on distinguishing the spatial variations of response patterns across acupoints in the occipital lobe. However, evidence suggests that acupuncture-invoked BOLD signal changes are independent of a priori time shape. Additionally, temporal profiles reflect how a stimulus corresponds with the brain, implying the hemodynamic coherence induced by stimulation. Therefore, temporal information carried in acupuncture-related neural activity may be more crucial to specificity issues. This paper initiates the detection into tempo-spatial dimension and the goal of this study is to detect functional acupoint specificity by uniquely comparing the temporal activities of the occipital lobe among vision-related acupoints (VRA) and a non-acupoint (NAP). We utilized the independent component analysis (ICA) to extract temporal patterns of occipital response by stimulating a VRA, i.e. GB37, and a NAP. As an improvement over previous ones, another VRA, i.e. BL60 was employed to consolidate our findings. Results showed that although all groups showed V1 activity in the occipital lobe, dissociable temporal activities in this region categorized GB37 and NAP ($r=0.05$, $p=0.64$). This finding was replicable with regard to BL60 and NAP ($r=-0.03$, $p=0.77$). Intriguingly, stimulation at two VRAs induced highly correlated temporal activities ($p<0.0001$). This study adds positive evidence to the issue of vision-related acupoint specificity. The utilization of ICA and consideration of temporal dynamics may shed light on future studies.

1. Introduction

Acupuncture, which originated 3000 years ago in China, has received prevailing acceptance and been applied in treating a wide range of human bodily disorders. Traditional Chinese Medicine (TCM) has established that acupuncture manipulation over certain acupoints elicits specific effects over target organ systems, which can be remote from the needling sites, and produces specific healing strength for various diseases (Beijing, 1980). However, whether acupuncture evoked brain responses are as specific as the purported indications of different acupoints remains to be verified.

Previous investigations regarding the vision-related acupoints (VRAs) specificity have established a converged

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doi:10.1016/j.brainres.2011.11.050

understanding that the cortical representations of acupuncture at VRAs are mainly characterized in the occipital lobe (Cho et al., 1998; Greicius et al., 2004; Kong et al., 2009; Li et al., 2003, 2010; Qin et al., 2011; Siedentopf et al., 2002). However, conventional understandings empirically implanted the hypothesis that the human brain responds to acupuncture stimulations in a predictable and fixed hemodynamic patterns, which can be reliably predefined by the experimental model (Friston, 1996), and this pattern is consistent across anatomical structures. As a logical consequence, most previous studies solely compared the spatial patterns of cerebral responses in the occipital lobe, drawing divergent conclusions (Cho et al., 1998; Gareus et al., 2002; Kong et al., 2009; Li et al., 2003). As a matter of fact, lines of evidence from both human behavior and animal studies have indicated that a striking feature of the acupuncture effect is its longevity—a delayed onset, gradual peaking and gradual returning to baseline (Pomeranz and Chiu, 1976; Price et al., 1984), implying that the kinetics of acupuncture are longer acting as a function of time (Bai et al., 2009b). Concomitantly, acupuncture induces long-lasting time-variant central effects (Dhond et al., 2008; Li et al., 2010; Napadow et al., 2009; Zhang et al., 2009b). More specifically, a study that precisely defined brain dynamic activities has concluded that acupuncture-invoked hemodynamic responses as reflected by blood oxygen level-dependent (BOLD) signal changes cannot be defined with a priori information and their temporal patterns also possess subtle dynamic variations across anatomical structures in temporal scales (Bai et al., 2010). In other words, temporal profiles of acupuncture-evoked BOLD signals cannot be empirically specified a priori. More recently, studies focusing on the unique temporal features of the acupuncture effect verify that functional acupoint specificity can be efficiently distinguished by categorizing temporal activities (Liu et al., 2009b; Zhang et al., 2009b). In this respect, we suggest that interpretations of acupoint specificity should depend on effectively characterizing the unique tempo-spatial variations underlying neural activities that give rise to hemodynamic responses.

Therefore, with particular interest in the tempo-spatial aspect of the occipital lobe, this paper issued the probe of vision-related acupoint specificity. We chose a most reported vision-related acupoint (VRA), i.e. GB37, which is stated to be useful in treating vision-related disorders, such as optic atrophy (Liu, 1997), and a nearby non-acupoint (NAP) and compare the corresponding temporal features of BOLD signal changes in the occipital lobe. We hope to find that the acupoint specificity between VRA and NAP could be distinguished by the temporal profiles embedded in the acupuncture-induced BOLD signal changes of the occipital lobe. To verify this observation, another VRA, i.e. BL60, was also adopted for cross-validation. We postulate that the findings regarding GB37 and NAP could be replicated in terms of BL60 and NAP. Furthermore, previous evidence has suggested that the temporal activity reflected by BOLD signals represents information (Buzsáki and Draguhn, 2004), which is indicative of the correspondence mechanisms through which large-scale organization of distributed neuroanatomical networks may be mediated by the stimuli (Bartels and Zeki, 2004; Fox et al., 2005). To a logical extent, temporal correlation implies functional preservation introduced by stimulation (Bartels and Zeki, 2005). With this consideration, we speculate that the time activity should show resemblance between the two VRAs due to similar underlying modulation mechanism which can be contributed to their parallel therapeutic functions and modalities.

To test the aforementioned hypotheses, approaches which are free of any a priori inferences for the temporal profile of the neural responses (Dhond et al., 2008) and are capable of distinguishing heterogeneous brain response patterns among delicate fMRI signal changes (Bai et al., 2010) should be introduced. Recently, independent component analysis (ICA), has shown considerable sensitivity for complicated tasks-associated fMRI datasets (Calhoun et al., 2002; McKeown et al., 1998a) and acupuncture datasets (Zhang et al., 2009a,b). It offers maximum flexibility exploring response dynamics in time without requiring any predefined time shape (Langers, 2010) and is also capable of identifying temporally coherent brain networks. In this paper, we applied ICA to delineate the subtle characteristics of neural responses following acupuncture stimulation.

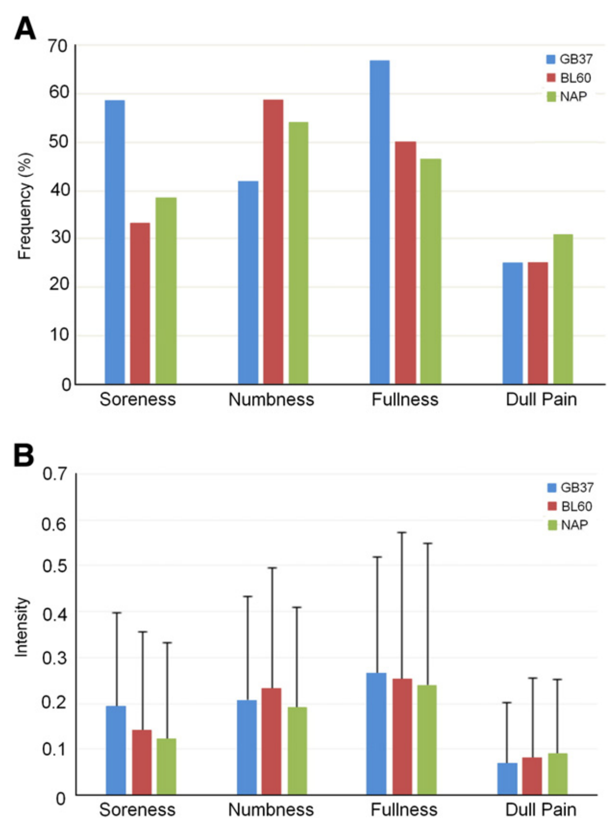

Fig. 1 – Result of psychophysical analysis. (A) Percentage of subjects who reported having experienced the given sensation. No statistical differences were found among groups with regard to each sensation ($p>0.05$). (B) The intensity of reported sensations measured by average scores (with standard error bars). There were no statistical differences among groups in each sensation ($p>0.05$).

2. Results

2.1. Results of psychophysical responses

The prevalence of acupuncture sensations was expressed as the percentage of individuals reporting the given sensations in each group (Fig. 1A). Soreness and numbness were more frequent for GB 37 than BL 60 and NAP (58% vs. 33% and 38% for soreness; 65% vs. 43% and 35% for numbness). Although differences did exist with respect to the type of sensations, no statistical differences were found regarding the prevalence of the listed sensations elicited by acupuncture stimulation compared across all acupoints (ANOVA, $p>0.05$). The level of sensations was kept low (mild to moderate), and no significant differences were identified in the average sensation intensity across groups (ANOVA, $p>0.05$) (Fig. 1B).

2.2. ICA results

The components estimation produced 37 ICs for each group. ICA transforms the observed fMRI data into a number of component maps, each with a unique representative time course. A 'best-fit' IC corresponding to the occipital lobe was identified for each group. For each group, each subject's chosen component was utilized to conduct one-sample *t* analysis, determining the group mapping of homogeneous activity in the occipital lobe. The results of one-sample *t* analysis ($p<0.01$, False Discovery Rate (FDR) corrected, with 10 contiguous voxels) showed that all points induced V1 activity, although these regions differ in response multitude and patterns of distribution. In detail, GB37 and BL60 induced similar homogenous distribution in the V1 area, whereas the counterpart of NAP spared less distribution in this area (Fig. 2B). Specific information is shown in Table 1.

2.3. Temporal dynamic correlation analysis

The time waveform of the NAP group was dissociable from those of the VRA group, with a correlation coefficient of −0.03, $p=0.77$ (BL60 vs. NAP) and a correlation coefficient of 0.05, $p=0.64$ (GB37 vs. NAP) (Fig. 2A, Table 2). Provokingly, the time courses extracted from the two VRA groups were highly correlated, with a correlation coefficient of 0.38 ($p<0.0001$). Further analysis showed that, time activities evoked by acupuncture at two VRAs disobeyed the periodically changing pattern which is calculated by convolving the task paradigm and a canonical hemodynamic response function, with $r=-0.04$ ($p=0.67$) and $r=-0.13$ ($p=0.40$) for GB37 vs. task paradigm and BL60 vs. task paradigm respectively. As a contrast, the counterparts for NAP and task paradigm are $r=0.25$ ($p=0.01$).

3. Discussion

Previous conclusions have come to a realigned understanding that vision-related acupoint specificity is mostly characterized by cerebral BOLD signal changes in the occipital lobe (Cho et al., 1998; Kong et al., 2009; Li et al., 2003, 2010; Qin et al., 2011; Siedentopf et al., 2002). This paper advances the detection of functional acupoint specificity into the tempo-spatial domain, with more focus on the temporal dimension. We utilized a novel method, ICA, which identifies distinct groups of brain regions with the same temporal pattern of hemodynamic signal change (Calhoun et al., 2001b; McKeown et al., 1998b; Quigley et al., 2002), to accurately decouple the time activity embedded in the fMRI BOLD signals evoked by stimulation over two TCM vision-related acupoints and a non-acupoint.

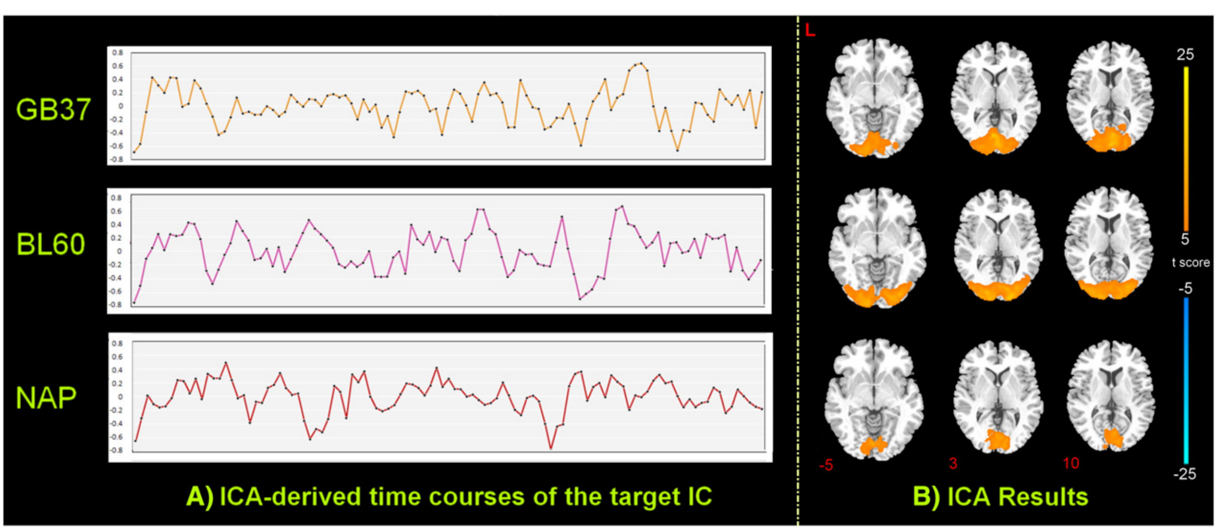

Fig. 2 – ICA results showing the temporal features and spatial distributions of the most relevant IC for each task. (A) The time course of the visual cortex for each group. (B) The random effect one-sample *t*-test group-level activation in the occipital lobe ($p<0.01$, FDR corrected, with 10 contiguous voxels). The time activity characterizing response patterns in GB37 and BL60 are highly correlated, with a correlation coefficient of 0.38 ($p<0.0001$); as a contrast, NAP has a dissociable relationship with both of them (BL60 vs. NAP, $r=-0.03$, $p=0.77$; GB37 vs. NAP, $r=0.05$, $p=0.64$).

Table 1 – Coordination and *t* scores of significant responses in the occipital lobe estimated by ICA following acupuncture at GB 37, BL60 and NAP ($p<0.01$, FDR corrected).

Regions	GB37					BL60					NAP				
	Hem	Talairach			t value	Hem	Talairach			t value	Hem	Talairach			t value
		x	y	z			x	y	z			x	y	z	
Lingual gyrus	L	−3	−76	4	19.46	L	−12	−93	0	15.31	L	−3	−79	−1	13.51
	R	3	−76	4	15.94	R	15	−84	4	17.04	R	3	−81	4	13.13
Cuneus	L	−3	−75	7	16.38	L	−12	−102	3	24.27	L	−3	−93	5	13.24
	R	3	−90	16	18.91	R	21	−99	2	20.52	R	15	−81	7	13.02
Inferior occipital gyrus	L	−21	−94	−8	6.05	L	−24	−88	−8	15.27					
						R	33	−82	−6	16.31					
Middle occipital gyrus	L	−12	−95	16	9.53	L	−15	−98	16	17.85					
	R	12	−92	16	10.07	R	21	−99	8	20.81					
Fusiform gyrus	L	−45	−68	−12	8.62	L	−21	−88	−11	8.18					
	R	36	−71	−12	7.60										

The Talairach coordination of voxel for peak activation voxel in each brain region was listed (*t*-score from random effects analysis).

Our results revealed that the VRA's shape of time course in the occipital lobe is disobedient with the timing sequence of experimental paradigm (Table 2, see Experimental procedures for details). We would like to note that the current results confirm and expand observations from previous acupuncture fMRI studies (Bai et al., 2009a,b, 2010; Liu et al., 2009b, 2010). Evidence has shown that acupuncture is a slow act of time (Bai et al., 2009b) and its striking feature lies in the sustained influence over both humans and animals (Pomeranz and Chiu, 1976; Price et al., 1984). Furthermore, the long lasting acupuncture effect exerts the sustained influence over central representations and reveals itself as time-variant features (Bai et al., 2010; Li et al., 2010; Qin et al., 2011). Similarly, this paper confirms this notion. Temporal dynamic analysis showed that unique temporal activities in the occipital lobe induced by acupuncture at two VRAs (Fig. 2A,Table 2) disobeyed the precise rhythmically changing patterns as predicted by the convolution of experimental paradigm and the presumed hemodynamic response (HR) template (Fox et al., 2005; McKeown et al., 1998a). As noted, it should also be emphasized that acupuncture induces heterogeneous HR across brain regions (Bai et al., 2010). Together with the aforementioned acupuncture's sustained effect, we propose that conventional ideas which empirically regard brain hemodynamic response to acupuncture stimulation as a homogenous entity may be inappropriate to comprehensively reveal the purported specific acupuncture effect per se. To a certain extent, such hypothesis would introduce biased results (Bai et al., 2009b). As an alternative solution, ICA provides a way to extract the neural correlates without having an a priori hemodynamic model (Calhoun et al., 2002). Therefore, when applied to our datasets, it may produce more accurate results than convention analytic approach which constrains the shape of the HR (Calhoun et al., 2001a). In addition, instead of presuming the homogeneity of HR in the brain, ICA focuses on the inherent structure of fMRI data (McKeown et al., 1998a) and is more compatible with the well-established principle of functional brain modularity (different parts of the brain do different things) (Svensén et al., 2002). Also, other studies which employed ICA delineating acupoint specificity has as well shown the strength of ICA in acupuncture fMRI studies (Zhang et al., 2009a,b). Thus, we believe that ICA is an appropriate choice. Yet, there is an important difference between the previous acupuncture ICA study and the present work (Zhang et al., 2009a). The former study used a vision-related acupoint and non-vision related acupoint. Although their results demonstrated that the temporal activities in the occipital lobe were distinguished between the two conditions, there was no further proof or discussion showing that the features were consistent and robust. However, in the current study, we utilized two vision-related acupoints, with one serving as a cross validation for the other. We argue that our work is an improvement.

Table 2 – Results of temporal dynamic correlation analysis.

	GB37	BL60	NAP	PTC
GB37				
BL60	0.38(1E–04)			
NAP	0.05(0.64)	−0.03(0.77)		
PTC	−0.04(0.67)	−0.13(0.40)	0.25(0.01)	

Correlation coefficients (*r*) and corresponding statistical threshold (*p*) between representative ICs of each group (GB37, BL60 and NAP) as well as presumed time course (PTC). PTC was obtained by convolving the experimental design and standard hemodynamic function. The information are shown in lower diagonal indicates in the form of *r* (*p*).

Based on the methodological rationale, our current findings show that GB37 and NAP possess distinct temporal features in the occipital lobe (Fig. 2A, Table 2). Considering the established notion that the characteristics in temporal dynamics are as effective as an indicator to categorize functional acupoint specificity (Liu et al., 2009b; Zhang et al., 2009a,b), this is an expected finding because VRA and NAP possess potentially different functions (Kong et al., 2009). Also, the results drawn from another VRA group, i.e. BL60, replicated this finding (Fig. 2A, Table 2). The temporal dynamic could represent information (Buzsáki and Draguhn, 2004) which is suggestive of the manner on how brain operations are to be carried out (Buzsáki, 2004). Combing these results, we suggest that the dissociation in temporal patterns may imply that stimulations over NAP and VRAs modulate the activity in the occipital cortex in differentiated manners, which may be due to their distinction in functions. Our interesting finding is that stimulation at two VRAs induced similar temporal activities in the occipital lobe (Fig. 2A), as evidenced by a high degree in temporal correlation (see Results for details). A former conclusion states that the highly correlated temporal relations provide information about their functional preservation (Bartels and Zeki, 2004). Given that these two VRAs possess shared nature of being effective in treating ophthalmic disorders (Beijing, 1980; Stux and Pomeranz, 1997), we suggest that the high level of resemblance in the temporal dynamics between two VRAs is likely to explicate that needling at two acupoints exerts similar modulating mechanism over this area. On the other hand, the temporal activity in the occipital lobe induced by NAP is dissociable with those of VRAs, while obeying the experimental design. An additional line of evidence notes that manipulation at NAP produces little or no acupuncture effect (Beijing, 1980; Wong et al., 2009), thus we suggest that the needling over NAP may be caused by different 'origin' compared to VRAs. In our experiment, the subjects kept their eyes closed throughout the whole procedure. Under such circumstance, the unique sensation acupuncture brings along could draw subjects' attention. One area that has often been shown to be involved in attention changes in sensory task is the visual cortex (Kastner et al., 1999; Pessoa et al., 2003; Zangaladze et al., 1999). Therefore, we speculate that the activities identified in the NAP group may basically serve as a sensory input. By this means, it is quite probable that acupuncture over NAP produced distinct modulation over the occipital lobe which differentiated from acupuncture effect produced by stimulating at acupoints, although this task conceives common essence of being acupuncture stimulation.

Prominent attention of our work has been uniquely given to tempo-spatial dynamics as consequences of acupoints' distinctive modulations over the brain. We suggest that the present findings should be considered in the context of rich neurophysiological literature on acupoint functions and coherent synchronization of brain activities. We urge that acupoint functions are worth of being appreciated, since randomized controlled clinical reports verified that distinctive acupoints are optimal for different pathological conditions (Cao et al., 2010; Kwon et al., 2006; Meng et al., 2003) or have different modulation over healthy subjects (Shiotani et al., 2003), whereas NAP or disease-irrelevant acupoints produce little healing outcomes (Wong et al., 2009), despite of the fact what exact neurobiological and cognitive procedures are mapped onto this neural activity and what biological basis subserves the functionality differences is a matter for further investigation. Moreover, several neuroimaging studies also support differentiated central response patterns in response to acupoints, proving acupuncture's role more than a simple painful stimulus (Li et al., 2010; Lijun et al., 2010; Liu et al., 2009a; Yoo et al., 2004). A proposed theoretical models of acupuncture central effect states that acupuncture is a complex computational process of sensory coding and encoding, which is concomitant with brain source reorganization and redistribution (Liu et al., 2009b; Wei et al., 2011), explicated as an acupuncture-induced regional synchronous brain activity. ICA, as applied to fMRI, assumes a set of spatially independent brain networks (Gu et al., 2001) and constrains the fluctuations of each voxel in a given component to have the same time course, thus the resulting components are appropriately defined as synchronous hemodynamic independent maps (Bartels and Zeki, 2004; Calhoun et al., 2001b, 2004). The synchronous activities can be considered as a trace of the underlying neuronal activity (Laufs et al., 2003; Shmuel and Leopold, 2008). Specifically, neuronal synchrony may serve to facilitate the coordination and organization of information processing in the brain across spatial and temporal ranges (Buzsáki and Chrobak, 1995). Consequently, we propose that the activity in the occipital lobe, including V1 activity, is the consequence of brain resource reorganization and redistribution induced by acupuncture stimulation rather than vision-related acupoints' 'directly projecting' into the area. Additional evidence illustrates that the patterns throughout time may reflect functional differences as well (Bartels and Zeki, 2004), thus we explicit that our results add positive evidence to functional vision-related acupoint specificity. More prominently, detection in the tempo-spatial domain is especially enlightening.

Last but not least, we have to point out that this study is only a preliminary step in a long March. We identified the commonality and differentiation in temporal scales, which is informative of how the brain responds to the stimulus in a designed sequence. This study focuses locally on the occipital lobe which is believed to be a characteristic region to vision-related acupoints. In the next investigation, we further probe how acupuncture influences other brain subdivisions on tempo-spatial scales and this is to be reported in our next study (in preparation).

4. Conclusion

In conclusion, the current study redirects the detection of vision-related acupoint specificity from solely spatial domain into the tempo-spatial domain. The findings provide positive evidence for the notion that acupuncture-induced activity is time-variant. Our study shows that functional acupoint specificity can be distinguished on temporal scales. Also, the application of ICA provides an alternative solution to address the methodological problem existing in the investigation of neural mechanisms of acupuncture. Furthermore, we suggest that distinct time courses are probably characteristic to intermediating processes which are initiated by stimulation over different acupoints and the specific tempo-spatial patterns may serve sufficiently as a 'fingerprint' or an indicator to chart the acupoint-specified intermediating processes.

5. Experimental procedures

5.1. *Subjects*

To reduce inter-subject variability, participants were recruited from a homogeneous group of 39 college students (21 males, age 20–25 years) who had no previous history of neurological illness, substance abuse or smoking. All were free from taking any medication at the time of testing. Subjects were all acupuncture naïve and right-handed. Subjects gave written informed consent approved by the local Ethics Committee and the whole experiment was conducted in accordance with the Declaration of Helsinki.

5.2. *Experimental paradigm*

An envelope method was used to allocate subjects to one of three groups respectively in a semi-random sequence. Acupuncture was performed at two Traditional Chinese Medicine (TCM) acupoints: Guangming (GB37), Kunlun (BL60) and a non-acupoint (NAP). Both GB37 and BL60 are commonly used to treat vision-related disorders and also have been previously studied with fMRI (Cho et al., 1998; Kong et al., 2009; Stux and Pomeranz, 1997). We located NAP 1.5 cm near GB37 where there is neither an acupoint nor a meridian crossing this area according to TCM theory. Stimulation was delivered by the same acupuncturist with a balanced 'tonifying and reducing' technique and rotated manually in a clockwise and counterclockwise direction at 1 Hz. The detailed procedures are shown in Fig. 3.

5.3. *fMRI scanning protocol*

Functional images were acquired on a 3.0-T GE Signa scanner using a standard whole head coil (LX platform, gradients 40 mT/m, 150 T/m/s, GE Medical Systems, Milwaukee, WI). A custom-built head holder was used to prevent head movements. Functional images were collected in a sagittal orientation parallel to the AC–PC plane using a single shot gradient-recalled echo planar imaging (EPI) sequence. The EPI pulse sequence had the following parameters: TE=30 ms, TR=2000 ms, flip angle=90°; matrix size=64×64, field of view 240×240 mm^2, in-plane resolution=3.75×3.75 mm, thickness=5 mm. The scan covered the entire brain including the cerebellum and brainstem. At the end of each run, the participant was questioned about *De-qi* sensations (i.e., soreness, numbness, dull pain and fullness). The sensations were rated from 0 to 10 (0 denoting no sensation to 10 denoting an unbearable sensation).

5.4. *Data preprocessing*

For each subject, 110 functional volumes were acquired in each run and the first 5 volumes of each run were removed to eliminate non-equilibrium effects of magnetization and allow subjects to return to baseline after the needle was inserted into the body. The remaining scans were realigned to the first image to correct inter-scan head motion and subjects with movement in any direction of greater than 1 mm or head rotation greater than 1° were excluded. The realigned images were spatially normalized in MNI space, then resampled at 3×3×3 mm and finally smoothed with a Gaussian kernel of 6×6×6 mm FWHM to decrease spatial noises. Data preprocessing and analysis were implemented using various routines from the Statistical Parametric Mapping 5 software package (SPM5, http://www.fil.ion.uclac.uk/spm). Both GLM and ICA were operated on the same set of preprocessed images. Since we are primarily interested in occipital cortex brain activity, in this article we will only present fMRI signal changes observed in occipital regions evoked by acupuncture stimulation at three different acupoints.

5.5. *Group ICA analysis and component identification*

To reveal spatio-temporal associations, we conducted Group spatial ICA (Calhoun et al., 2001b) for all three groups using the GIFT software (GIFT, http://icatb.sourceforge.net, version 1.3h). The preprocessed datasets were pooled into GIFT fMRI Toolbox. The processing in GIFT included initialization, principle component analysis (PCA) reduction and ICA extraction. The mutually independent components were estimated by ICA using the infomax approach (Bell and Sejnowski, 1995; McKeown et al., 1998c), and the number of components was determined using the minimum length description (MDL) criteria adjusted to account for correlated samples (Li et al., 2007). Time courses and spatial maps were then reconstructed for each subject. Procedurally, single subject time courses and spatial maps were computed, during which the aggregate components and the results from data reduction were used to compute the individual subject components (i.e. back-reconstruction; Assaf et al., 2010; Calhoun et al., 2001b).

The identification of component corresponding to the occipital lobe was conducted in 2 steps. First, for each group, each of the components was manually inspected to make sure components whose patterns of correlated signal change were largely constrained to gray matter from the 28 estimated components (Stevens et al., 2007). To do so, the correlations of each component's spatial map with a priori mask maps of gray matter, white matter, and cerebral spinal fluid (CSF) within standardized brain space provided in WFU Pickatlas (http://www.fmri.wfubmc.edu/) (Tzourio-Mazoyer et al., 2002) were computed (Maldjian et al., 2003). Components with

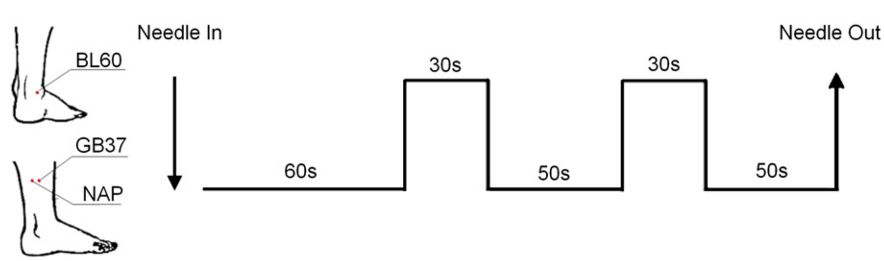

Fig. 3 – Experimental design. During scanning, a conventional ON/OFF block design of acupuncture stimulation was delivered. Each run consisted of a 60 s baseline scan at the beginning; two 30 s stimulation epochs were separated by a 50 s interval period, followed by a 50 s resting period.

high correlation to a priori localized CSF or white matter, or with low correlation to gray matter, were inferred to be likely artifactual. Visual inspection of discarded components suggested that the discarded IC patterns were attributed to two major forms of artifacts: IC patterns representing tissue border artifacts near the ventricular system, the skull, and cerebrospinal fluid space or IC patterns representing head motion and related susceptibility artifact at the frontal sinus, eye movements, or cardiac-induced pulsatile artifact at the base of the brain. Next, a spatial correlation analysis between the remaining components and an a priori binary mask of the occipital lobe generated by WFU Pickatlas was performed. The component that (spatially) correlated most significantly with the template was selected as the target component (Garrity et al., 2007). Visual inspection and systematic evaluation confirmed that components which included all or part of the occipital region ranked highest in this analysis.

For the group-level analysis, individual maps of the selected IC were entered into random effect one-sample t-tests in SPM5 and thresholded at $p_{FDR}<0.01$ with 10 contiguous voxels, to create a sample-specific component map.

Identical procedures were performed to choose the target IC for each group.

5.6. *Examination of component temporal dynamics*

Since this paper set out to explore the acupoint specificity in terms of temporal aspects, the first priority was to define the relationship between the time waveforms of each group. Therefore, the Pearson Correlation analysis was conducted between either of the two groups comparing time courses of the selected IC. Additionally, to identify whether the temporal dynamics follow the periodically changing patterns, we built a canonical model by convolving the experimental design and standard HRF (Cohen, 1997). Then, the Pearson Correlation analysis was conducted between each representative time course of the selected ICs and this model.

Acknowledgments

This paper is supported by the Project for the National Key Basic Research and Development Program (973) under Grant Nos. 2011CB707702, 2012CB518501, the National Natural Science Foundation of China under Grant Nos. 30930112, 30970774, 60901064, 30873462, 81000640, 81000641, 81071217, 81101036, 81101108, 31150110171, the Fundamental Research Funds for the Central Universities and the Knowledge Innovation Program of the Chinese Academy of Sciences under Grant No. KGCX2-YW-129.

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