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Distinct brain networks for time-varied characteristics of acupuncture

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ABSTRACT

Clinical acupuncture typically involves an effective treatment phase several hours post-therapy. We previously identified regions that carry the time-varied signals based on the BLOCK experimental paradigm. Here we characterize the brain network by applying the graph theory analysis during the post-acupuncture resting state. Our results show gradually increasing connections in the brainstem during verum acupuncture (ACU). The anterior insula plays an important role in connecting the components of the brain networks following ACU. We suggest that acupuncture can induce significant complex response patterns with relatively more robust magnitudes. Our findings provide direct evidence that the post-needling resting state contains acupuncture-related effects that are due to the slow-acting nature of acupuncture.

Introduction

Spontaneous fluctuations in blood oxygenation level dependent (BOLD) functional magnetic resonance imaging (fMRI) signals have recently aroused a large amount of interest in fMRI studies [9]. Functional connectivity analysis can investigate these coherent signal fluctuations, and reveal coactivation in a distributed network of cortical regions that characterizes the resting state of the human brain [11]. Evidence from acupuncture analgesia studies suggested that a delayed response exists during resting state following acupuncture stimulation [16].

Our group has compared different modulatory effects on resting brain networks between verum and sham acupuncture. Numerous studies indicated the existence of different functional brain networks [2,3,15,18,21,22]. Bai found that the activity pattern during the post-acupuncture rest epoch was prominently associated with stimulus-related effects by using the multi-GLM paradigm; some of the brain regions showed higher BOLD signal intensity during rest rather than in the stimulation phases [4]. Such time-varied characteristics of acupuncture effects attract more interest for their importance in designing paradigms and statistical models involving acupuncture studies. However, for limitations of GLM in modeling such state-related activity, a flexible model was needed to investigate the dynamics underlying sustained effects of acupuncture.

In our current study, we revealed the functional connectivity of acupuncture-evoked regions in terms of the correlation structure of their BOLD activity. Considering that acupuncture can be long-lasting even beyond the needling being performed, we examined the post-acupuncture resting state (PARS) and post-sham resting state (PSRS) functional connectivities using MRI. Graph theory analysis (GTA) was used to characterize the functional integrated network of time-varied activities induced by acupuncture. GTA has the advantages of evaluating the strength as well as the temporal and spatial patterns of interactions in the human brain [19], and it defines a graph as a set of nodes (brain regions) and edges (functional connections). The visualization of graph provides strong hints for functional connections between brain regions. Topological properties of the network could characterize prominent status and contribution to the continuous basis related to acupuncture. This approach has successfully been applied in many previous brain network studies with convincing results [1,14,20]. We experienced the challenges of functional connectivity development at an acupoint versus those at a non-meridian point (NMP) similar to the network analysis described in Fair's study [8]. In addition, the non-repeated event-related fMRI (NRER-fMRI) design was employed for investigating sustained effects after acupuncture administration. This new experimental paradigm was first used in Qin's research [18].

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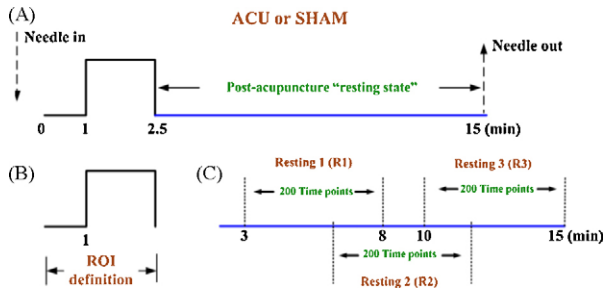

Fig. 1. Experimental paradigm. (A) The entire run lasted for 15 min. (B) Single BLOCK for ROIs definition. (C) PARS and PSRS for graph theory analysis.

Methods

All participants were recruited from a group of 28 right-handed college students (14 males and 14 females, 21.7 ± 1.9 (mean ± SD) years old). The subjects were acupuncture naïve and did not have a history of major medical illnesses, head trauma, neuropsychiatric disorders, had not used prescription medications within the last month, and had no contraindications for exposure to a high magnetic field. All subjects gave written, informed consent after the experimental procedures were fully explained, and all research procedures were approved by the West Chinese Hospital Subcommittee on Human Studies. The experiment was also conducted in accordance with the Declaration of Helsinki.

In the acupuncture experiment, all subjects were blinded to the type and order of stimulations. During the procedure, subjects were instructed to keep their eyes closed in order to prevent them from actually observing the procedures. The presentation sequence of the acupuncture and NMP protocols was randomized for all fMRI runs, and the order of presentation was counterbalanced across subjects. Acupuncture was performed at acupoint ST36 (Zusanli) on the right leg. The needles used in the acupuncture protocol were sterile disposable 38 gauge stainless steel acupuncture needle 0.2 mm in diameter and 40 mm in length. The needle was inserted perpendicularly to a depth of 2–3 cm. Stimulation consisted of rotating the needle clockwise and counterclockwise for 1 min at a rate of 60 times per min. The procedure was performed by the same experienced and licensed acupuncturist on all subjects. We employed the new NRER-fMRI design consisting of two functional runs: verum acupuncture (ACU) and sham acupuncture (SHAM). Only a single stimulation period was performed during each of these two runs (Fig. 1A). This NRER-fMRI design has the advantage of evaluating potential long-lasting effects following acupuncture administration. In ACU, an acupuncture needle was inserted at ST 36 for 1 min without manipulation and then the needle was manipulated for 1.5 min (Fig. 1B); the needle remained inserted in the acupoint for another 12.5 min. In SHAM, the procedure was the same as in ACU except that the stimula-

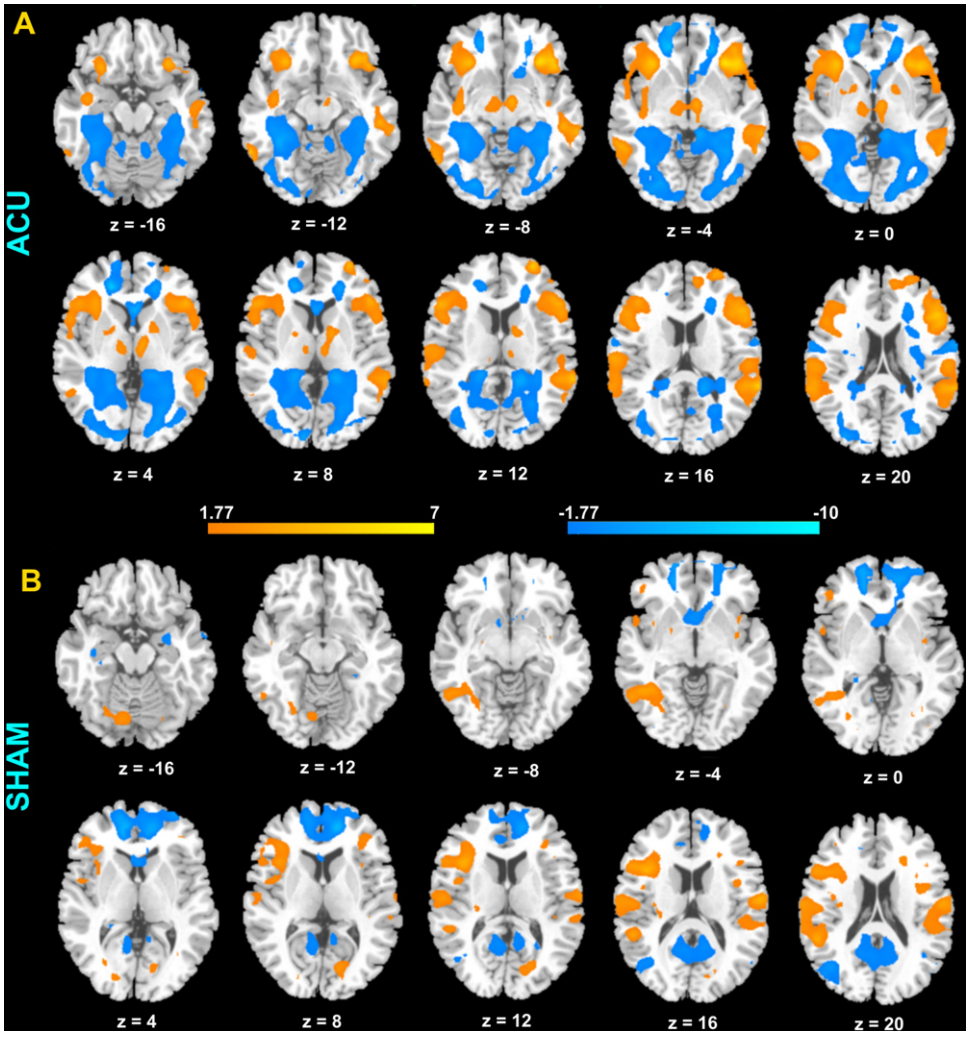

Fig. 2. Group results of brain activation for a single BLOCK.