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Clinical Application of Functional MRI : Motor Cortex Activities by Acupuncture

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Abstract

We report a preliminary fMRI evidence of modulation of somatomotor areas by acupuncture in GB34 acupoint. GB34, located in the back of the knee, is known to be effective in recovering motor function after stroke. Using 3T MR scanner, functional MR imaging was performed in five normal volunteers in two stimulation paradigms; acupuncture manipulation on GB34 and sham points. Group analysis from five individuals showed that bilateral sensorimotor areas (BA 3,4,6 and 7) showed stimulation related BOLD signal contrast of approximately 6% whereas very few areas were activated when sham stimulation is given. Our results suggest that acupuncture fMRI study can be safely conducted in 3T environment, and stimulation in GB34 modulate the cortical activities of the somatomotor area in human.

Introduction

Acupuncture, an ancient therapeutic modality, has been used extensively in Oriental medicine, and is emerging as important complementary and alternative medicine in the Western community [1,2]. Although the exact mechanism of acupuncture is still unknown and in need of further investigation, various animal data and clinical observations suggest that acupuncture modulates activities in the central nervous system, and influence the designated treatment area [3,4]. We postulate that widely connected neural networks that integrate multiple physiological and mental functions are modulated with the acupuncture stimulation. Therefore, demonstration of regionally specific characterization of activation in CNS by acupuncture would provide further knowledge and possible explanation for this hypothesized modulation.

We used Functional MRI (fMRI) to investigate the effect of acupuncture on the CNS by measuring changes in local blood oxygenation level associated with neuronal activities (*i.e.* BOLD effect) upon acupuncture on extremities [1,2]. In this present report, we studied the neural substrates targeting sensorimotor areas that are modulated by the stimulation of acupoint GB34 (*Yang-ling-quan*). GB34 is located in the lateral aspect of the posterior knee and is often used for the treatment of hemiplagia and rehabilitation for motor functional

deficit/impairment after stroke [5]. Our experimental hypothesis is that acupuncture in GB34 directly modulates the activities in sensorimotor areas, and assists in functional reorganization of the neural circuitry in motor areas to regain partial mobility after stroke-related CNS damage. Before we determine its efficacy on damaged brain, we performed function MR imaging on normal volunteers.

Methods

The study was conducted using 3 Tesla whole body MRI (Medinus, Korea) with standard quadrature head coil for RF transmission and detection. Seven right-handed subjects were initially recruited (one female and seven males, aged 27 ± 1.7) in the study. In each functional experiment, Gradient Echo EPI sequence with TR/TE=2500/35 msec was used for imaging 20 contiguous axial slices of 6mm thickness, covering the whole brain volume (240mm Field-of-view, 64×64 in-plane resolution). Prior to functional scan, high-resolution T1 weighted anatomical data was acquired to provide anatomical reference.

Two sets of conditions were used in the experiment. One with actual left GB 34 stimulation, and the other with sham stimulation adjacent to the designated acupuncture point (without known clinical effects). Sham condition was applied in order to examine the desired region-specific effects of acupuncture. The location of this sham point and real acupoint was not discernable by the subjects. After the five sets of dummy data are acquired to account for the T1 equilibration, each functional scan session was initiated without the needle insertion. At the 11^{th} scan, the needle was inserted and twisted for 25 seconds at a rate of approximately 120 times per minute. The needle manipulation was paused for the duration of 25 seconds as a control state. The process was repeated four times to have four epochs of stimulation interleaved by the five epochs of control states with equal length in time. Since the sensation of Deqi (tingling sensation near the site of acupuncture, different from pain or tactile sensation) is known to be important criteria in determining the efficacy of the acupuncture manipulation [1], subjects were interviewed about the possible pain and existence of Deqi after each functional session. Subjects were also questioned about the existence of motor imagery during the scan since imagery is known to elicit activations in the motor related areas. CCD camera and an observer confirmed the absence of actual movement during the session.

After the off-line reconstruction, data was processed using SPM99 based on the Matlab computing environment [6]. Data was realigned with respect to the first set of images, smoothed with 6mm FWHM Gaussian kernel to reduce the spatial noise, and normalized to Talairach-Tournoux space. For data analysis, we used SPMs general linear model to create a statistical map associated with the BOLD signal change associated with acupuncture

manipulation. A boxcar reference waveform, which conforms to the task paradigm, was used to calculate the T-values at each voxel to test for significance of measured BOLD signal correlated with stimulation paradigm. No temporal filtering, such as convolution with hemodynamic response function, was applied since the nature of hemodynamic response from the acupuncture stimulation is neither measured nor characterized.

Results and Discussion

All subjects successfully underwent the designated acupuncture stimulation without any undesirable peripheral sensations that are known to be associated with high-field environment. Stainless steel used in the acupuncture needle did not raise any safety-related issues under 3T environment. Two subjects with significant motion (more than 2mm from the first image set) were excluded from further data analysis. All five remaining subjects (all male, aged 281.6) reported the Deqi phenomenon present during the acupuncture stimulation but absent during the sham stimulation. Neither imagery nor pain was reported from any of the subjects.

The activation map from group analysis across the five individuals (Random Effect Analysis, thresholded at $p<0.01$ d.f.=4) from Fig 1 and 2 showed that there were several motor related regions that showed BOLD signal change during GB34 stimulation. The areas include bilateral premotor (Brodmanns Area (BA) 6), superior parietal lobule (BA7) and left primary motor areas (BA4). During the sham stimulation near GB34, majority of these areas except premotor areas (BA6) did not show eloquent activation, suggesting the spatially-dependent selective efficacy of the acupuncture. A small activation locus of the right middle frontal lobe (BA8) was observed during the sham stimulation. In the examination of the time course of signal changes during the primary motor area from subjects, signal contrast of ~6% (compared to 2-3% in 1.5T environment) with respect to the baseline signal level was observed. The Talairach coordinate of the activation in BA4 was x-y-z = -37; -22; 62, that was very close to the hand motor area observed from brain mapping via electro cortical stimulation and PET study (x-y-z = -37; -23; 57) [7].

The imagery of hand movement is known to elicit activations in the sensorimotor areas in the absence of overt hand movement; however, the possibility of occurrences of motor imagery during the stimulation was unlikely since the subjects did not report any imagery events during the acupuncture manipulation. Hypothesized activation in the somatosensory areas (BA 3,1,2 and 5) was not evident in our group analysis. The sensation of 'Deqi' may not elicit significant activation in somatosensory areas to pass the p-threshold condition for display. It is interesting to find that both right and left motor areas were activated, but more dominantly in the left hemisphere where it is ipsilateral to the site of the acupuncture application.

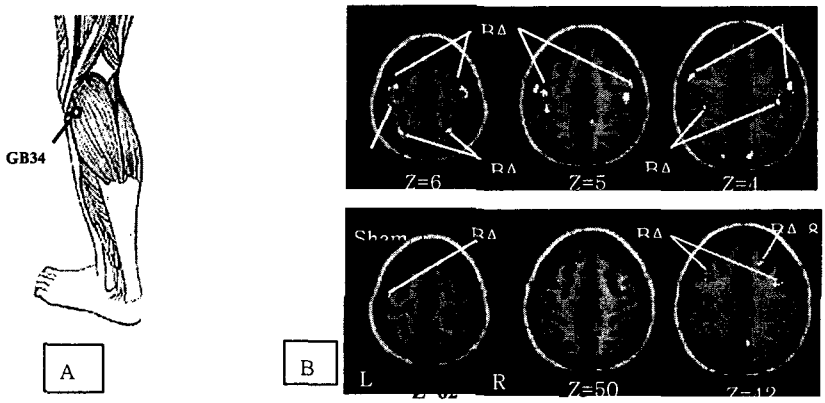

Fig. 1. (A) The illustration of GB34 in the left leg. (B) Averaged group activation map (thresholded in $p<0.01$) from five subjects using random effect analysis employing two stages of hierarchical process. Axial slices at three different Talairach coordinate levels in superior-inferior directions (z=62, 50 and 42) were shown for both GB34 stimulation (upper row) and for sham stimulation (lower row).

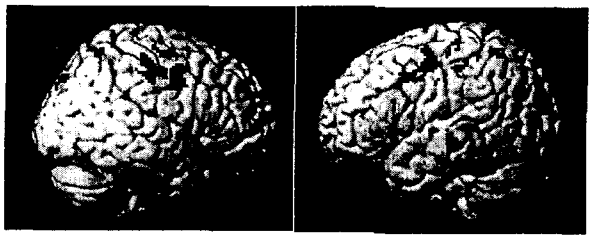

Fig. 2. Averaged group activation map (thresholded in $p<0.01$) from five subjects overlaid on surface- rendered brain model normalized to the Talairach space.

Conclusion

All fMRI sessions were safely administered for all volunteers in the absence of pain or without engaging motor imagery during acupuncture in 3T environment. Although preliminary, we have demonstrated that several cortical areas, especially motor functional areas, manifested quantifiable BOLD signal changes associated with the acupuncture stimulation. Based on the comparison with fMRI data from sham stimulation, modulation of neural sustrates was spatially specific to the acupoints. It is possible, as hypothesized [1-3], that the activation in these somatomotor areas were mediated by activations in subcortical areas including limbic and paralimbic systems. An investigation of fMRI targeting subcortical areas is, therefore, urgently needed. Since the consistency and reproducibility of the acupuncture vary significantly depending on subjects, choice of acupoints and imaging parameters, further studies are directed to examine the reproducibility among subjects for the stimulation of GB34 and other relevant acupoints to wider subject population including both normal and patients.

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