Acupuncture Stimulation for Motor Cortex Activities: Evidence from 3T Functional MRI Study

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ABSTRACT

The purpose of this study was to investigate whether or not acupuncture of GB34 produces a significant response of the modulation of somatomotor areas by functional magnetic resonance imaging (fMRI) study. The acupoint, GB34, located in the back of the knee, is known to be effective in recovering motor function after stroke. Using 3T MRI scanner, functional MR imaging of the whole brain was performed in 12 normal healthy subjects during two stimulation paradigms; acupuncture manipulation on GB34 and sham points. This study investigates the activation of the mortor cortex elicited by a soft and an intensified stimulation of GB 34. Three different paradigms were carried out to detect any possible modulation of the Blood Oxygenation Level Dependent (BOLD) response in the somatomortor area to motor stimulation through acupuncture. Group analysis from seven 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. The present study shows that acupuncture fMRI study can be safely conducted in 3T MRI environment, and acupuncture stimulation in GB34 modulates the cortical activities of the somatomotor area in human. The present findings may shed light on the CNS mechanism of motor function by acupuncture and form a basis for future investigations of motor modulation circuits in the stroke patients.

Keywords: Acupuncture; functional magnetic resonance imaging

1. INTRODUCTION

Acupuncture is an ancient therapeutic modality originated in ancient China and has been used extensively in Oriental medicine. Acupuncture techniques are based on the theory of meridians and energy flow, which evolved after painstaking observation against a background of Chinese philosophy. However, acupuncture was not widely introduced as an alternative medicine in the West until the scientific basis of acupuncture analgesia began to be explored in the early 1980s.[1-4] In recent years, acupuncture has gained increasing popularity in modern health care and increasing support among scientific investigators. [5-6]

Acupuncture is emerging as important complementary and alternative medicine in the Western scientific and medical community.[7-9] 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 (CNS), and influence the designated treatment area.[10-11] 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.[12] In this present report, we studied the neural substrates targeting somatomotor 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 hemipleagia and rehabilitation for motor functional deficit/impairment after stroke.[13] Our experimental hypothesis is that acupuncture in GB34 directly modulates the activities in somatomotor 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.

2. MATERIALS AND METHODS

Subjects

The study was performed with informed consent on 12 right-handed normal, healthy volunteer adults (ten males and two females, age 27-33). None had a history of psychiatric or neurological disorders or head trauma with loss of consciousness, or intake of tranquilizing drugs in the last 3 days. Ten were naive to acupuncture, two had some knowledge of acupuncture by way of cultural exposure or learning but had never received treatment. No subject was in pain or distress at the time of the study. All subjects were briefed about the range of possible acupuncture sensations they might experience during needle manipulation before entering the magnet. There were no differences in the degree of acupuncture sensation experienced or in the fMRI results obtained due to differences in past acupuncture experience; thus the data were combined for analysis. The study was approved by Kangnam St. Mary's Hospital Subcommittee on Human Studies in College of Medicine, the Catholic University of Korea.

Functional MRI

The study was conducted using 3 Tesla whole body MRI (Medinus Co. LTD, Korea) system with a standard quadrature head coil for RF transmission and detection. 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 x 64 in-plane resolution).[14] Prior to functional scan, high-resolution T1 weighted anatomical data was acquired to provide anatomical reference.

Stainless steel used in the acupuncture needle did not raise any safety-related issues under 3T environment. 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 11th 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,[15] 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.

Data Analysis

After the off-line reconstruction, data was processed using SPM99 based on the Matlab computing environment.[16] 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 SPM's 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. Statistical analysis was performed using SPSS (SPSS for Windows, Version 6.0, SPSS Inc., Chicago, Illinois). The data were analyzed with paired-samples t tests, where $p<0.05$ was considered significant to account for multiple comparisons.

3. RESULTS

All subjects successfully underwent the designated acupuncture stimulation without any undesirable peripheral sensations that are known to be associated with high-field environment. Two subjects with significant motion (more than 2mm from the first image set) were excluded from further data analysis. All remaining 10 subjects 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 (Brodmann's 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.

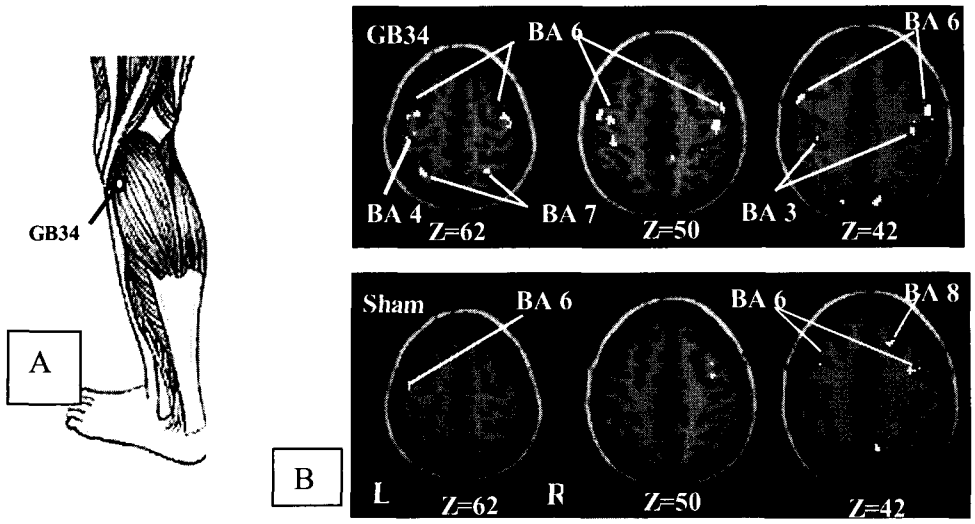

Fig 1. (A) The illustration of GB34 in the left leg. (B) Averaged group activation map (thresholded in $p<0.01$) from five subjects using random effect analysis employing two stages of hierarchical process. Axial slices at three different Talairach coordinate levels in superior-inferior directions (z=62,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

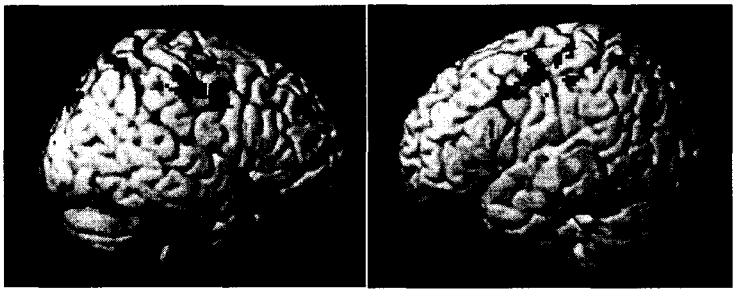

Fig 2. Averaged group activation map (thresholded in $p<0.01$) from five subjects overlaid on surface- rendered brain model normalized to the Talairach space.

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).[17]

4. DISCUSSION

The imagery of hand movement is known to elicit activations in the somatomotor 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.

In oriental medicine, acupuncture stimulation is usually applied at the contralateral part of lesions, when acupuncture is clinically needed. This acupuncture treatment based on the theory that, when patients complain hemiplegia, acupuncture is applied at the contralateral part of lesion (i.e., when patients complain right hemiplegia, acupuncture is applied at the acupoint (GB34) of left leg. Our results might be correspond with the theory of oriental medicine. The

stimulation of acupuncture evoked ipsilateral activation of brain. This activation signal might be transduced to hemiplegic lesions through crossed corticospinal tract.

All fMRI sessions were safely administered for all volunteers in the absence of pain or without engaging motor imagery during acupuncture in 3T environment. The preliminary results suggest that functional MR imaging is useful for demonstrating brain activation associated with acupuncture stimulation. Thus, 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 substrates 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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REFERENCES

1. Han JS. Neurochemical basis of acupuncture. Annu Rev Pharmacol Toxicol 1982;22:193-220.
2. Melzack R. Folk medicine and the sensory modulation of pain. In: Wall PD, Melzack R, eds. The textbook of pain. 3rd ed. London, England: Churchill Livingstone, 1994;1209-1218.
3. Pomeranz B. Scientific basis of acupuncture. In: Stux G, Pomeranz B, eds. Basics of acupuncture. 3rd ed. New York, NY: Springer-Verlag, 1995; 4-60.
4. Filshie J, White A. Medical acupuncture: a Western scientific approach London, England: Churchill Livingstone, 1998.
5. Eisenberg DM, Kesseler RC, Foster C, Norlock FE, Calkins DR, Delbanco TL. Unconventional medicine in the United States: prevalence, costs and patterns of use. N Engl J Med 1993;328:246-252.
6. Fisher P, Ward A. Complementary medicine in Europe. Br Med J 1994; 309:107-111.
7. Diehl D, Kaplan G, Coulter I, Glik D, Hurwitz EL. Use of acupuncture by American physicians. J Alternative Complementary Med 1997:119-126.
8. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, Kessler RC. Trends in alternative medicine use in the United Sates, 1990-1997. JAMA 1998;280: 1569-1575.
9. Eisenberg DM, Kessler RC, Foster C. Unconventional medicine in the United Sates N Engl J Med 1993;328:246-252.
10. Wu, MT, Xiong C, Yang PC et al Central nervous pathway for acupuncture stimulation: localization of processing with functional MRI of the brain– Preliminary experience. Radiology 1999;212:133-141.
11. Cho ZH, Chung SC, Jones JP, Park JB, Park HJ, Lee HJ, Wong EK, Min BI. New findings of the correlation between acupoints and corresponding brain cortices using functional MRI. Proc Natl Acad Sci USA. 1998;95:2670-2673.
12. Kwong KK, Belliveau JW, Chesler DA et al. Dynamic resonance imaging of human brain activity during primary sensory stimulation. Proc Natl Acad Sci (USA) 1992;89:5675-5679.
13. Wiseman N, Boss K, Ellis AW, Feit R (Editor), Fundamentals of Chinese Acupuncture, Redwing Books Co. 1991 Brookline, MA.
14. Kwong KK, Belliveau JW, Chesler DA, Goldberg IE, Weisskoff RM, Poncelet BP, Kennedy DN, Hoppel BE, Cohen MS, Turner R, Cheng HM. Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation Proc Natl Acad Sci USA 1992;89:5675-5679.
15. Hui KKS, Liu J, Makris N, Gollub RL, Chen AJW, Moore CI, Kennedy DN, Rosen BR, Kwong KK Acupuncture modulates the limbic system and subcortical gray structures of the human brain: Evidence from fMRI studies in normal subjects. Human Brain Mapping 2000;9:13-25.
16. Friston KJ, Holmes AP, and Poline JB. Analysis of fMRI time-series revisited. *Neuroimage*, 1995;2:45-53.
17. Warren Boling, André Olivier, Richard G. Bittar, and David Reutens, Localization of hand motor activation is localized in Broca's pli de passage moyen. J Neurosurg. 1999;91:903-910.