Central Nervous Pathway for Heating Pain and Acupuncture Stimulation: Localization of Processing with Functional MR Imaging of the Brain -Preliminary Experience

Department of Biomedical Engineering, School of Medicine, The Catholic University of Korea

Moon-Hyun Yoon, Bo-Young Choe, Gi-Soon Choi, Sung-Ik Yoon, Dong-Cheol Woo

The effects of acupuncture are complex and how it works is not entirely clear. Research suggests that the needling process, and other modalities used in acupuncture, may produce their complex effects on a wide variety of ways in the brain and the body. For example, it is theorized that stimulated nerve fibers transmit signals to the spinal cord and brain, thus activating parts of what is called the central nervous system. The spinal cord and brain then release certain hormones responsible for making us feel better overall and, more specifically, feel less pain. In fact, a study using images of the brain confirmed that acupuncture increases our pain threshold, which may explain its ability to produce long-term pain relief. Also, acupuncture may increase blood circulation and body temperature. It may also affect white blood cell activity (responsible for our immune function).

Key words: Acupuncture, Psychosomatic, fMRI, Acupoint LR3 · LI4, Tteum (뜸)

INTRODUCTION

Acupuncture has effects on multiple physiological systems. It is a promising complementary therapy for affective and psychosomatic disorders such as anxiety, depression, substance abuse, pain and visceral dysfunctions. We used fMRI to monitor its action on normal human brain, with the focus on the limbic system and subcortical gray structures that are intimatelyinvolved in the regulation of emotions, autonomic and endocrine functions. The imaging studies also showed increased activation in two other brain structures - the left anterior cingulate cortex and the basal ganglia. The researchers speculate that increased activity in these two regions may be part of an inhibition pathway that blocks the pain signal from reaching the higher cortical structures responsible for pain perception. However, Schulz-Stubner noted that more detailed fMRI images are needed to definitively identify the exact areas involved in hypnosis-induced pain reduction, and he hoped that the newer generation of fMRI machines would be capable of providing more answers. We demonstrated prominent and coordinated effects in these neural circuits. The pattern of response observed with acupuncture sensation was distinctly different from that observed with tactile stimulation or with pain sensation. Follow-up study confirms reported findings and reveals involvement of additional brain regions that are closely related to the limbic system.

METHODS

All research subjects signed a written consent form. This research project was reviewed the experience which Cho ZH had done in the University of California-Irvine Institutional Review Board. After studying pain dynamics as discussed above, we directed our attention to acupuncture analgesia by extending our pain study paradigm to include acupuncture administration. LR3 was chosen because of its accessibility for fMRI scanning techniques; namely, insertion of a needle in the foot does not require moving the subject's head. In addition, LR3 is a major acupuncture point: it is to the foot as LI 4 is to the hand.

Thermal stimulation (putting a tteum on the index finger at a temperature of 52°C for 30 seconds) was used as pain stimulation. Putting the tteumr on the finger results in several steps of different sensations from feeling heat to unpleasantness to extreme pain. To maximize exposure to hot temperature (pain), we pre-warmed the finger with 43°C water. Care was taken not to injure the subject's skin and no damage was observed. Acupuncture stimulation at LR3 was accomplished by (a) manually rotating (twirling) the needle for 30 seconds, needling 30 seconds without twirling, and finally, removing the needle, and (b) repeating the same paradigm 5 times without removing the needle, after which the needle was removed for the remainder of the data acquisition period. These "pain" and "acupuncture with pain" stimulation paradigms are shown in Fig. 1a and 1b. For the first part of study with the meridian acupuncture, a single set of twirling was applied (paradigm Fig. 1b(1), the "weak" stimulation). In the latter part of the experiments with sham acupuncture, we applied "strong" stimulation, as shown in Fig. 1b(ii).

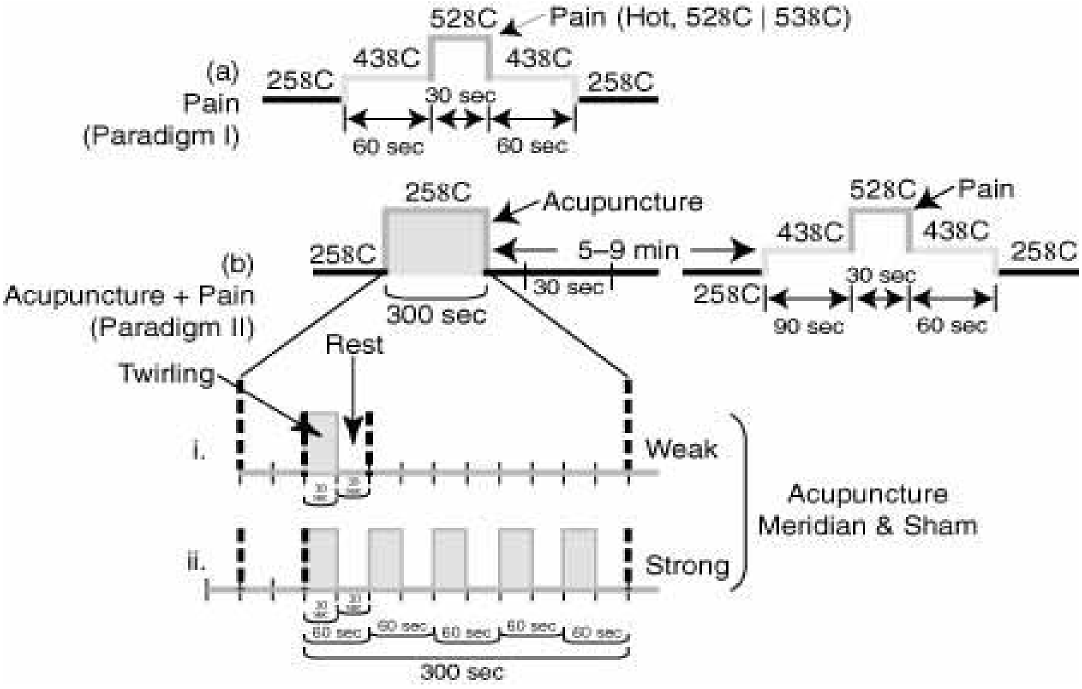

Fig. 1. Stimulation paradigms used in the pain and acupuncture + pain experiments (a) Paradigm I: Pain is achieved by immersing the index finger into a hot bath of water (52°C) for 30 seconds. (b) Paradigm II: Acupuncture + pain stimulation is further divided into: (i) a weak stimulation for the meridian acupuncture + pain experiment while (ii) a strong stimulation was used for the sham acupuncture + pain experiment. This paradigm consists of pain stimulation after 9 minutes from the initial start of acupuncture stimulation.

Averaging the data of many individuals often obscures the fine details of time-dependent activation due to the widely varying response time delays as well as differences in the pain perception pattern of each individual. Summary data presented in this article are mixed with intrapersonal and interpersonal averages of 3 experiments that show a similar pattern of pain perception as well as the acupuncture analgesia effect. Many variables are inherent in acupuncture, including uncertainty of localization of the acupuncture point, the differences in nerve distributions for different subjects, needling methods, responses of the individual as a responder or non-responder, the individual's mental status and health condition, and pain perception pattern or differences in pain tolerance. Due to such variability as well as the technical difficulties such as the movement associated with painful stimuli (both the heating pain stimulus and acupuncture needling), data sets with severe motion artifact. We selected and averaged 3data sets of similar patterns for each mode out of 50 experimental sets. The fMRI pulse sequence used was the gradient echo planar imaging sequence with 3 seconds repetition time, 35 milliseconds echo time, and 24 slices with a Gimens 1.5-T scanner. Three experiments were performed on each subject: (1) pain stimulation only, (2) meridian acupuncture followed by pain stimulation, and (3) sham acupuncture followed by pain stimulation. Their corresponding stimulation paradigms are shown in Fig. 1a and 1b, respectively. For each set, consisting of 24 axial slice images or data, 60 image data sets/slice image at 3-second intervals were collected. To further visualize the dynamic or time-dependent physiological responses of cortical activation. The total activation data or images obtained for each experimental set were 24 (slices) × 60 (time course images/ slice) × 3 (pain, meridian acupuncture, sham acupuncture) = 4,320 image data. The total activation images processed were 24 (slices) × 12 (processed activation data) × 3 (pain, meridian acupuncture + pain, sham acupuncture + pain) × 3 (axial, sagittal, coronal) = 2,592. Among these vast amounts of activation data, we selected a data set of 4 representative time-dependent responses (d = 0 seconds, 9 seconds, 18 seconds, and 27 seconds, respectively) and displayed 3 representative selected slices for each time response for each mode (pain, meridian acupuncture + pain, sham acupuncture + pain). Each image data set is made of axial, coronal, and sagittal images for visualization. In each image data, P values are indicated at the upper left corner and response time d is given in the final column of each data set. Our data processing was performed by SPM99. In SPM99, the option was available to superimpose the activation data on SPM standard template images such as EPI. In general, acupuncture appears to transmit its effects via electric, neurologic, hormonal, lymphatic, and electromagnetic wave pathways.

RESULTS

Signal increases occurred in the primary and secondary somatosensory cortices both in acupuncture and in heating pain. A marked contrast was observed in the deep structures. The 11 subjects who experienced *deqi* demonstrated prominent *decreases* of fMRI signals in limbic and subcortical regions as the amygdala, hippocampus, parahippocampus, hypothalamus, septal nucleus, caudate, putamen, nucleus accumbens, anterior cingulate gyrus, anterior insula, temporal pole and fronto-orbital cortex The 2 subjects who had painful sensation during acupuncture demonstrated signal increases in these regions instead. Acupuncture evoked *deqi* in both subjects. The former demonstrated signal *decreases* in the limbic and subcortical gray structures as before. The latter showed a reverse in the direction of signal changes, from signal increases with pain before to signal *decreases* with *deqi* in the repeat study. Whole brain imaging revealed prominent signal *decreases* with *deqi* sensation in additional brain regions that are closely linked to the limbic system, such as the frontal pole, prefrontal cortex and cerebellar vermis.

CONCLUSION

The study provides evidence that supports a coordinated effect of acupuncture on a network of cortical and subcortical limbic and paralimbic structures including the frontal pole, the prefrontal cortex and cerebellar regions that are connected to the limbic system. in the human brain. Modulation of this neuronal network could initiate a sequence of effects by which acupuncture regulates multisystem functions. The effects on the limbic system could well contribute to its efficacy for the treatment of diverse affective and psychosomatic disorders.

REFERENCES

1. Cho ZH, Chan JK, Ericksson L: IEEE Trans Nucl Sci 23:613-22 (1976)

2. Ogawa S, Tank DW, Menon R, et al: Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. Proc Natl Acad Sci USA 89:5951-5 (1992)
3. Cho ZH, Chung SC, Jones JP, et al. New findings of the correlation between acupoints and corresponding brain cortices using functional MRI. Proc Natl Acad Sci USA 95:2670-3 (1998)
4. Cho ZH, Na CS, Wong EK, Lee SH, Hong IK. In: Stux G, Hammershlag R, eds. Clinical Acupuncture: Scientific Bases. Berlin, Germany: Springer, (2000), pp. 83-96
5. Cho ZH, Na CS, Wong EK, Lee SH, Hong IK. In: Litscher G, Cho ZH, eds. Computer Controlled Acupuncture. Lengerich, Austria: Pabst Science Publishers, (2000), pp. 45-64
6. Hui KK, Liu J, Makris N, et al: Acupuncture modulates the limbic system and subcortical gray structures of the human brain: evidence from fMRI studies in normal subjects. Hum Brain Mapp 9:13-25 (2000)
7. Cho ZH, et al: fMRI Neurophysiological evidence of Acupuncture Mechanisms. A Journal for the American Academy of Medical Acupunture