A functional MRI study can show neuronal pathway interruption by inserting acupuncture needle in a dog model of Parkinson¡¯s disease

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Introduction:

Functional MRI (fMRI) techniques have been used to study neurophysiology in animals. Previous fMRI studies of acupuncture needling have shown that acupuncture can activate multiple analgesic systems and stimulate the pain modulation system through the neuromodulation of input into the central nervous system (1, 2). However, the underlying mechanism of acupuncture remains unclear. Parkinson's disease (PD) is currently regarded as the second most common degenerative disorder of the aging brain after Alzheimer's dementia. Several studies found the evidence of the acupuncture effects in the nigrostriatal dopaminergic pathway in PD-modeled rat brain (3, 4). People usually perform fMRI studies by using active tasks by subjects.

Passive moving task (PMT) is one method of inducing proprioceptive stimulation to investigate human kinesthesia (5). We hypothesized that the acupuncture has acupoint specific effects and it can affect afferent proprioception. In addition, we also hypothesized that the acupuncture effect on the proprioception can be affected by damages of the dopaminergic neurons. Thus, the purpose of this study was to investigate the interruption of a neuronal pathway during PMT by acupuncture insertion at a certain acupoint in the normal and PD dog model.

Materials and Methods:

We developed a novel method to model PD dog because a previous method had severe acute toxicity. MPTP-HCl (Sigma-Aldrich, St Louis, MO, USA) was diluted with 0.9% saline (0.05mg/ml solution) to prevent acute systemic damages, including death. The group of MPTP-treated dogs was injected three times with 2.5 mg/kg MPTP-HCl every second day by a syringe pump (1.25 mg/(kg·h)) rather than injecting a single dose. Eight healthy beagle dogs were divided into two groups of four dogs each, a normal control (NC) and a PD model (PDM) group.

After 6 days from the first injection, anatomical and functional images were obtained on a 3T MRI system. During fMRI, the PMT was performed in the right tarsal joint during three different sessions, which consisted of PMT only (**MO**), PMT while being inserted with an acupuncture needle at the ST36 acupoint (**TA**), and PMT while being inserted with the needle at a sham point (**SA**). During the SA session, the same needle was inserted 1.5 cm lateral of ST36 in the same manner as the true acupuncture insertion. This site was a sham acupuncture point and was used as a control. After that, PMT of the hind limb was also performed on the same side as the sham acupuncture needling.

Blood oxygenation level-dependent (BOLD) fMRI signals were collected using a T2*-weighted, gradient-echo EPI sequence with an eight channel sensitivity encoding (SENSE) knee coil. SPM8 software was used for the preprocessing and analyzing of fMRI data. In order to investigate the BOLD signal changes during PMT from the acupuncture insertion in a certain acupoint, the effects of PMT during three different sessions were calculated by using a one-sample t-test of the full factorial design for each group. Therefore, the group effects of MO, TA, and SA were obtained for each group. In order to compare BOLD signal differences between the two groups, we performed ANOVA tests of the full factorial design for between-group comparisons of the three conditions of MO, TA, and SA, separately.

Results :

Fig. 1 shows the results of neurologic examinations of consciousness, gait and placing, and brain stem reflexes before and 5 day after modeling. In the NC group, BOLD signals during PMT increased in the reticular formation and cerebellum during the MO session, decreased in these areas and in dopaminergic pathway regions during the TA session, and increased in these areas during the SA session. In the PDM group, BOLD signals during PMT increased only in the primary somatosensory area, while the activities of most areas of the dopaminergic pathway decreased during the MO session. BOLD signals slightly decreased in dopaminergic pathway regions during the TA and SA sessions. **Fig. 2** shows the results of BOLD fMRI studies for each experiment. Compared to the NC group, the PDM group exhibited higher BOLD signal intensities in the ipsilateral motor-sensory area, while lower BOLD signal intensities were found in the contralateral somatosensory area and dopaminergic pathway regions during the MO session. The PDM group exhibited higher BOLD signal intensities during the TA session, but lower BOLD signal intensities during the SA session.

Conclusion: Insertion of an acupuncture needle at a specific acupoint can interrupt the related neuronal pathway. However, the interruption from the specific acupoint decreases its specificity in the PD brain. The dog model can be useful to investigate PD and acupuncture may be useful to stimulate certain fibers in PD brain in human.

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Fig. 1. Results of neurologic examinations

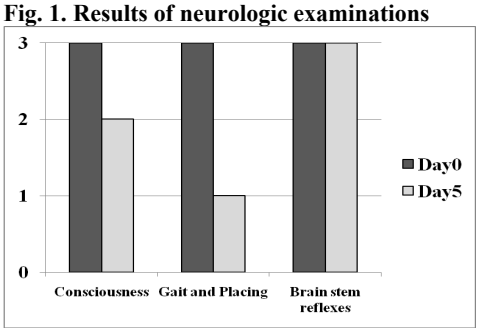
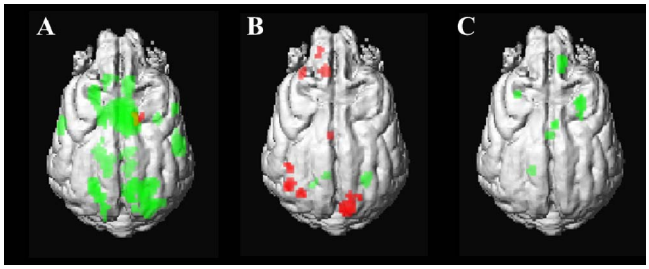


Fig 2. Results of BOLD fMRI



Green, NC>PD and Red, NC<PD