Quantitative mechanical stimulator for fMRI and microPET studies

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Synopsis

The present study developed a fully MR-compatible, computer-controlled, pneumatic stimulator to deliver quantitative tactile stimulation. Mechanical stimulation of the hindpaw of rat significantly increased BOLD signal intensity in the primary somatosensory cortex of the hindlimb region (S1HL). The results validated the feasibility of this stimulator and were coincident with the microPET experiment.

Introduction

BOLD fMRI is widely used as a noninvasive tool for functional brain mapping in both humans and animals. The device that can elicit adequate stimuli for tactile sensation is an indispensable tool for studying the somatosensory projection, nociceptive responses, and brain functional rehabilitation [1]. A mechanical stimuli delivery system that can be driven in parallel with MR imaging sequences and compatible with the MRI environment has considerable impact on the functional brain mapping. However, the size of MR compatible mechanical stimulator is difficult to reduce [2] and thus restricted the applications in high filed MR system with small bore size. In this study, a computer-controlled, small-sized, MR-compatible stimulator was constructed and demonstrated that the tactile stimuli can be successfully delivered. In addition to the BOLD fMRI study, the brain metabolic changes following tactile stimulation using microPET was also investigated.

Material and Methods

The mechanical stimulation system is composed of the following components (Fig. 1): a function generator, a relay, an electromagnetic valve, a N_2 gas cylinder, a pneumatic control module (diameter<3 cm), and the VonFrey filament. The electromagnetic valve was mounted on the gas cylinder. The power line was connected in serial with the relay used as a switch to turn on and off the valve. The relay was triggered by the signals generated by the function generator. The piston in the pneumatic control module was pushed by the flow supplied through the gas cylinder to force the VonFrey filament to move back and forth, hence provided the tactile stimuli. The stimulation parameters for the following imaging studies were 1 Hz and 18 gw/cm^2. For the animal experiments, 10 adult Wistar rats of 250 g body weight were initially anesthetized by 3% isoflurane. After that the rats were positioned on a stereotaxic holder and α-chloralose (70 mg/kg) was given through the tail lateral vein for subsequent anesthesia. The body temperature was maintained using a warm-water circulating system. MR images were performed in a 4.7 T Biospec 47/40 spectrometer. A 72 mm volume coil was used as the RF transmitter and a quadrature surface coil placed on the head was used as the receiver. Gradient echo EPI was used and the imaging parameters were: TR=2500 ms, TE=25 ms, NEX=2, SLTH=1.5 mm, FOV=2.4 cm^2, repetition=60. The first and last 20 time frames were categorized as baseline, whereas the middle 20 were collected during stimulation. For the microPET studies, 90 mg/kg ketamine was given intraperitoneally for anesthesia and 2 mCi [^{18}F]fluorodeoxyglucose was injected through the tail lateral vein as a radiotracer. Static imaging was then simultaneously captured with the tactile stimulation by the microPET R4 for 50 min. All images were analyzed using the MATLAB and custom-built ISPMER image analyzing interface [3].

Results and Discussion

The mechanical stimulator was fully MR-compatible and can be calibrated using a pressure sensor (PSM-2M, model AB, KYOWA) and a bridge circuit. By changing the size of filaments, different stimulation intensity can be correspondingly produced (18 gw/cm^2 for 0.65 mm in diameter, 9 gw/cm^2 for 0.40 mm in diameter, 4 gw/cm^2 and for 0.35 mm in diameter). The results showed that mechanical stimulation induced significant BOLD signal increase in the S1HL (Fig. 2B), while in this area the glucose metabolic increase was also observed in Fig. 2C. Although electrical stimulation was widely used for mapping cortical functions, it tends to non-specifically excite the Aβ, Aδ, and C fibers and generates less specific brain activation patterns [5]. This system overcome the potential confoundings of using traditional electrical stimulator and should be useful for further investigation of specific tactile somatotopic organization [1], hyperalgesia [4], and stroke recovery [6] in both small animal MRI and PET environment.

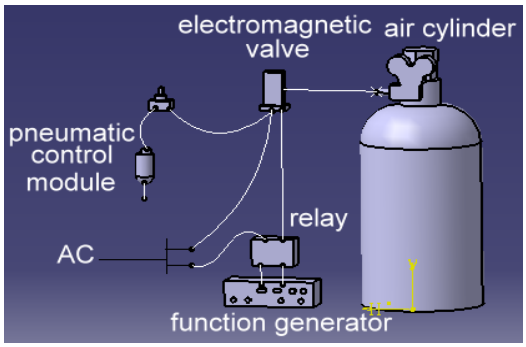

Fig. 1 The schematic view of the mechanical stimulation system. All metallic and electronic components in the system stayed outside the magnet, and only the pneumatic control module and the plastic tubes entered the MR environment.

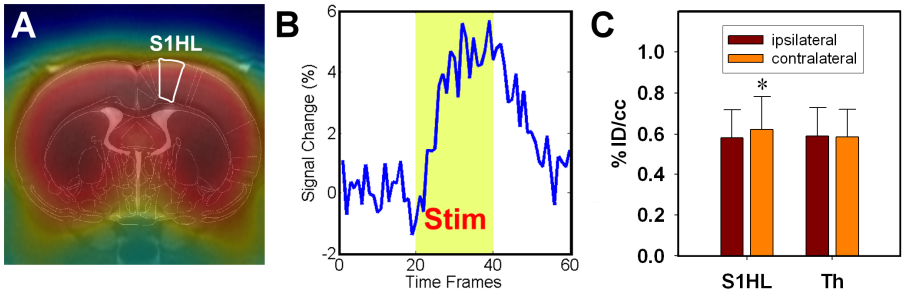

Fig. 2 (A)FDG-microPET and T2-weighted MR images were registered and fused with the rat atlas providing anatomical alignment and corresponding ROI. The location of the image is 0.7 mm anterior to the bregma. (B) The BOLD signal changes in contralateral S1HL (C) In the FDG microPET studies, paired t-tests was performed to compare the differences between two hemispheres, where * denotes p<0.05 and error bars represent mean ± standard deviation. Clear lateralization was observed in the S1HL.

Conclusion

The MR compatible tactile stimulator developed in the present study allowed identification of the brain levels involved in tactile responses. It not only facilitates the studies of sensory system using both small animal fMRI and PET, but is also useful for pre-clinical evaluation of the complex hyperalgesic responses and the brain functional rehabilitation as well.

Reference

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