쥐에서 말초 자극에 따른 뇌피질 활성화의 자기공명 영상

MR imaging of cortical activation by painful peripheral stimulation in rats

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ABSTRACT

As imaging technology develops, magnetic resonance imaging (MRI) techniques have contributed to the understanding of brain function by providing anatomical structure of the brain and functional imaging related to information processing. Manganese-enhanced MRI (MEMRI) techniques can provide useful information about functions of the nervous system. However, systematic studies regarding information processing of pain have not been conducted. The purpose of this study was to detect brain activation during painful electrical stimulation using MEMRI with high spatial resolution. Male Sprague-Dawley rats (250-300 g) were divided into 3 groups: normal control, sham stimulation, and electric stimulation. Rats were anesthetized with 2.5% isoflurane for surgery. Polyethylene catheter (PE-10) was placed in the external carotid artery to administrate mannitol and MnCl2. The blood brain barrier (BBB) was broken by 20% D-mannitol under anesthesia mixed with urethane and a-chloralose. The hind limb was electrically stimulated with a 2Hz (10V) frequency while MnCl2 was infused. Brain activation induced by electrical stimulation was detected using a 4.7 T MRI. Remarkable signal enhancement was observed in the primary sensory that corresponds to sensory tactile stimulation at the hind limb region. These results suggest that signal enhancement is related to functional activation following electrical stimulation of the peripheral receptive field.

Keywords: MRI, manganese enhanced MRI, brain activity, somatosensory stimulation

1. INTRODUCTION

There is growing interest in delineating brain function in human and animal models in vivo by using non-invasive imaging technique [1]. Among them, manganese-enhanced MRI (MEMRI) has been successfully utilized to detect brain activity and depict neuronal architecture by systemic administration of manganese ion [2, 3].

In MEMRI, signal intensities depend on the uptake and accumulation of the contrast agent manganese in neurons. Manganese ions can enter neurons through several ways: 1) via transferrin binding and transferrin-receptor–mediated internalization, 2) via divalent metal ion transpoters, and 3) via L-type voltage-gated calcium channels [4].

A recent study demonstrated that MEMRI represents a sensitive in vivo method for monitoring neuronal activity and functionality in mouse and rat brain [5]. However, MEMRI studies regarding information processing of pain were rare. Therefore, the present study was conducted to detect brain activation during painful electrical stimulation using MEMRI.

2. MATERIALS AND METHODS

Male Sprague-Dawley rats (250-300g) were divided into 3 groups: normal control, sham stimulation and electric stimulation. Rats were anesthetized with 2.5% isoflurane for surgery. Polyethylene catheter (PE-50) was placed in the external carotid artery to administration mannitol and $MnCl_2$. Blood brain barrier (BBB) was broken by 20% D-mannitol under anesthesia mixed with urethane and α-chloralose.

Electrical stimulations were stimulated hind limb with approximately 2Hz (10V) frequency during the $MnCl_2$ (25 mM) infusion.

Experiments were performed in a Biospec 4.7 T MRI system (Bruker, Germany). Coronal and sagittal scouts were acquired using a RARE T2-weighted sequence. To analyze Mn distribution, a set of noncontiguous T1-weighted (T1W) images were obtained. The set consisted of a spin-echo sequence using the following imaging parameters: TR = 200 ms, TE = 10 ms, 10 averages, slice thickness = 1 mm, field of view = 40 × 30 mm^2, and matrix = 256 × 256.

3. RESULTS AND DISCUSSIONS

In the manganese-enhanced response, more enhanced regions were observed in somatosensory area. However, there is no statistical significance among three groups.

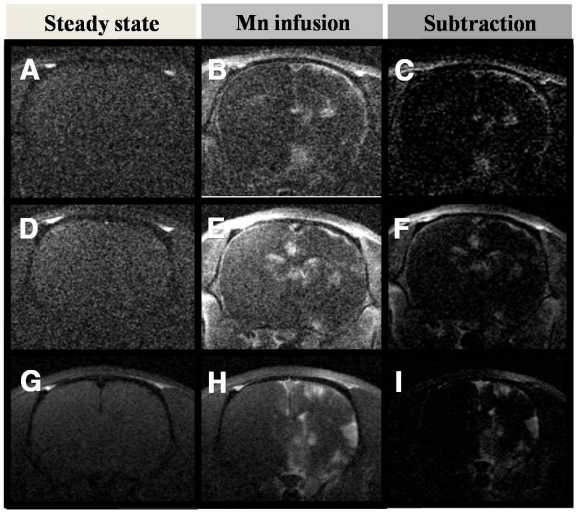

Figure 1: MEMRI of the normal control, sham stimulation and electric stimulation rats (A, D, G: before MnCl2 injection; B, E, H: 20 min after MnCl2 injection; C, F, I: subtraction of B-A, E-D and H-G respectively).

In the present study, remarkable signal enhancement was observed in the primary somatosensory area corresponding to sensory tactile stimulation of the hind limb region. These results suggest that signal enhancement is related to functional activation following electrical stimulation of the peripheral receptive field. MEMRI is useful for functional brain imaging study.

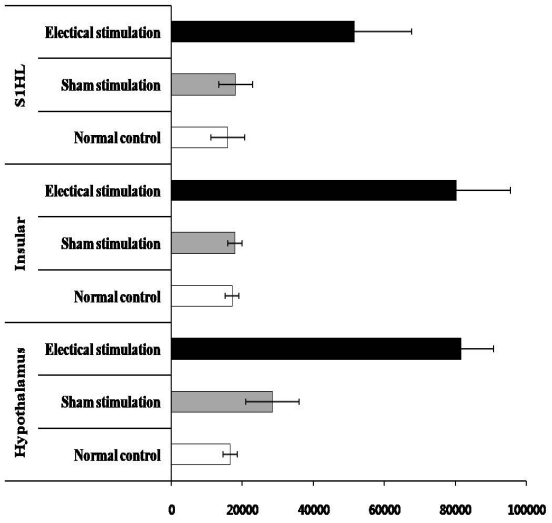

Figure 2: Comparison of signal intensities in different brain areas (S1HL: primary somatosensory hind limb).

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REFERENCES

1. Aoki I, Naruse S, Tanaka C. Manganese-enhanced magnetic resonance imaging (MEMRI) of brain activity and applications to ealry detection of brain ischemia. NMR Biomed. 2004; 17: 569-580.
2. Koretsky AP, Silva AC. Manganese-enhanced magnetic resonance imaging (MEMRI). NMR Biomed. 2004 17(8):527-31.
3. Aoki I, Tanaka C, Takegami T, Ebisu T, Umeda M, Fukunaga M, Fukuda K, Silva AC, Koretsky AP, Naruse S. Dynamic activity-induced manganese-dependent contrast magnetic resonance imaging (DAIM MRI). Magn Reson Med. 2002 48(6):927-33
4. Weng JC, Chen JH, Yang PF, Tseng WY. Functional mapping of rat barrel activation following whisker stimulation using activity-induced manganese-dependent contrast. Neuroimage. 2007 15;36(4):1179-88
5. Silva AC, Bock NA. Manganese-enhanced MRI: an exceptional tool in translational neuroimaging. Schizophr Bull. 2008 34(4):595-604.