Detection of Neuronal Activity by Motion Encoding Gradients: A Snail Ganglia Study

Tae S. Park[1], Ji-Ho Park[2], Min H. Cho[1], Soo Y. Lee[1]

[1]*Dept. of Biomedical Engineering, Kyung Hee University, Korea*
[2]*Graduate School of East-West Medical Science, Kyung Hee University, Korea*
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Abstract

Presuming that firing neurons have motions inside the MRI magnet due to the interaction between the neuronal magnetic field and the main magnetic field, we applied motion encoding gradients to dissected snail ganglia to observe faster responding MRI signal than the BOLD signal. To activate the snail ganglia in synchronization with the MRI pulse sequence, we used electrical stimulation with the frequency of 30 Hz and the pulse width of 2 s. To observe the fast responding signal, we used the volume selected MRI sequence. The magnetic resonance signal intensity, measured with 8 ms long motion encoding gradient with a 20mT/m gradient strength, decreased about 3.46±1.48 % when the ganglia were activated by the electrical stimulation.

Key words : neuronal currents, lorentz effect, motion encoding gradient, extracellular potential recording, snail ganglia, electrical stimulation, volume selection MRI

I. INTRODUCTION

Because fMRI technique detects regional cerebral hemodynamics such as cerebral blood volume (CBV) and cerebral blood flow (CBF), it has limited by slow response function of cerebral hemodynamics and the complex vascular geometry in spatial resolution (Bandettini and Wong 1997; Kim S-G *et al* 1997). Recently, some groups have proposed new fMRI methods to prove a feasibility of direct observation of neuronal activities with MRI. Visualizing the neuronal current effects is one of them. Neuronal currents make neuronal magnetic fields which could have effects on the MRI signal. Based on the fact that the neuronal magnetic fields make local field inhomogeneity and in turn attenuate the MRI signal intensity in the vicinity of firing neurons, several experiments have been performed on phantoms (Bodurka and Bandettini 2002; Kamei *et al* 1999; Konn *et al* 2003), animals (Park *et al* 2006, Pertidou *et al* 2006) and human brains (Xiong *et al* 2003). However, the field inhomogeneity effect seems to be minimal. The activated neurons can experience small displacement due to the Lorentz force in main magnetic field of the MRI. The displacement induced intra voxel phase changes due to Lorentz force would be incoherent. A signal loss of this voxel will be caused by the integrated effect of these incoherent phase change with the voxel and can be weighted with motion encoding gradients just like the diffusion effect in MRI. (Song and Takahashi 2001). Recently, fMRI utilizing the Lorentz force effect has been tried on human subjects to get faster temporal response than the BOLD effect (Li and Song 2003, Truong 2006).

In this study, we applied motion encoding gradients to dissected snail ganglia to observe faster responding MRI signal than the BOLD signal. We have used dissected snail ganglia which have nonmagnetic hemocyanin as oxygen carrying protein (Park *et al* 2004). Experimental results indicating the MRI signal change to the motion encoding gradient strength are presented.

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Corresponding Author :Soo Yeol Lee, Ph.D.
Dept. of Biomedical Engineering, Kyung Hee University, 1 Seochun, Kiheung, Yongin, Kyungki 449-701, Korea
Tel : +82-31-201-2980 / Fax : +81-31-201-3666
E-mail : sylee01@khu.ac.kr

II. MATERIALS AND METHODS

We have used visceral ganglia dissected from *Achatina fulica*, African agate snails, weighing 30-40g. We prepared the dissected snail ganglia in the same way as described in the previous work (Park *et al* 2004, 2006). To activate the snail ganglia in synchronization with the MRI pulse sequence, we have used electrical stimulation with the frequency of 30 Hz, the pulse width of 2 s and the amplitude of 3 V. The activated states have been confirmed with extracellular potential recording

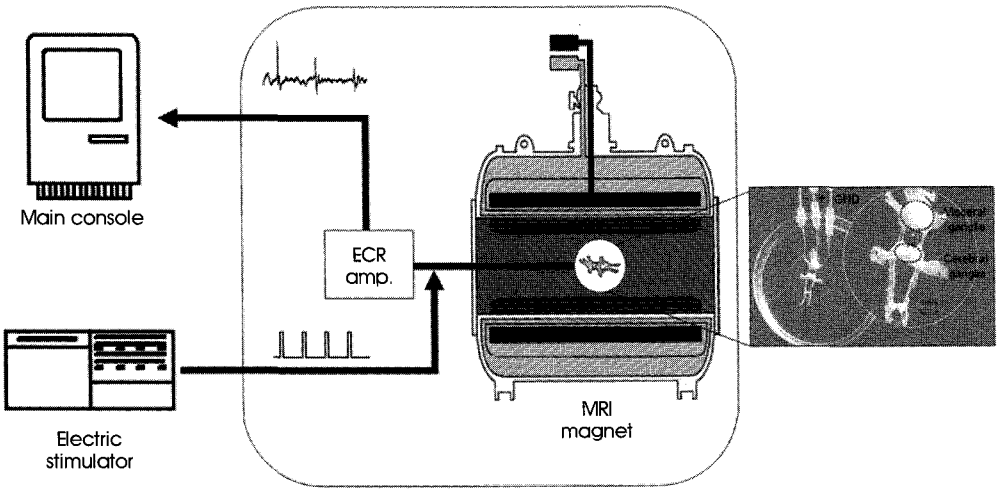

Fig. 1. Schematic diagram of the ECR and electrical stimulation system

(ECR). Figure 1 shows a schematic diagram of the ECR, MRI and the electrical stimulation system. The electrical stimulator has a synchronization trigger output and it is fed to the MRI spectrometer for synchronization between the electrical stimulation and MRI scan. For ECR, a high input-impedance amplifier (BrainAmp, Brain Products GmbH, Germany) which could use in MRI was positioned 1m away from the micro-electrode to amplify the extracellular potential signals. To minimize interference of the microelectrode in receiving MRI signals from the ganglia region, we put the micro- electrode into the axon bundle 0.5-1.0 cm of intestinal nerve from the ganglia region. For electrical stimulation, we used a commercial electrical stimulator (S88, Grass, U.S.A.) and the same micro-electrode as in ECR. That is, the output of the electrical stimulator and the input of the ECR amplifier were tied in parallel. When the electrical stimulation was applied, the ECR amplifier was gated to a high input impedance state. To verify the extracellular potential signal changes to the electrical stimulation, the ECR with the electrical stimulation has been performed outside the MRI magnet. We did not perform ECR during the MRI signal measurement with the electrical stimulation because of excessive noise couplings on the long electrical wires from the electrical stimulator to the micro-electrodes. An air-tight rubber lid was placed over the saline, in the Petri-dish, in order to prevent any kind of vibration during MRI recording. Moreover, to prevent possible wire motions

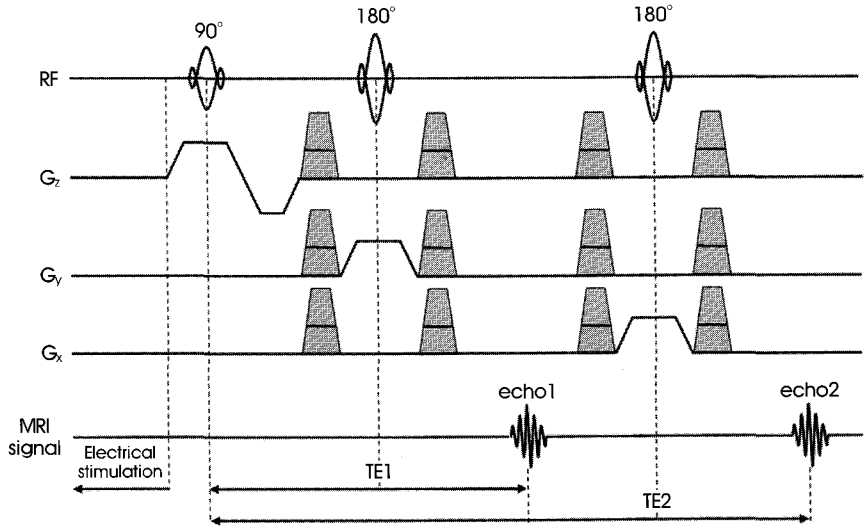

Fig. 2. The volume selected MRI pulse sequence with motion encoding gradients

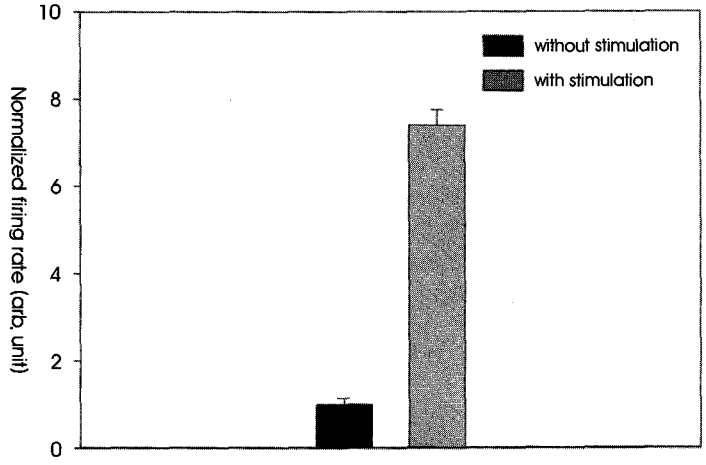

Fig. 3. The average firing rate of three snail ganglia before and after the electrical stimulation

inside the MRI magnet during the electrical stimulation, we aligned the electrode wires to main magnetic field direction and fixed them to a supporting frame with cable ties.

To investigate the faster responding MRI signal, we used a volume selected MRI pulse sequence as shown in Fig. 2 (Bottomley *et al* 1984). To observe the Lorentz force effect of firing neurons on the MRI signal, we incorporated motion encoding gradients into the volume selected MRI pulse sequence. Motion encoding gradients of 0, 10 and 20mT/m with the pulse width of 2ms were placed symmetrically with respect to the 180° pulses. The motion encoding gradients sensitize any kinds of spin motions including the Lorentz-force-induced motion and diffusion. We presumed that the Lorentz-force-induced motion is randomly oriented, hence, vector sum of magnetizations of large number of firing neurons would result in MRI signal attenuation. The time scale of an action potential, ~ ms, is far shorter than the minimum second echo time (TE2) of the volume selected MRI pulse sequence, usually longer than several tens of ms.

Targeting the volume of interest to the visceral ganglia region, we observed the second echo signal intensity (echo 2 in the figure) with and without applying the electrical stimulation at 0, 10 and 20mT/m gradient strength. The volume selected MRI signal measurement was performed with a 3.0 Tesla whole body MRI scanner (Magnus 3.0, Medinus Inc., Korea) equipped with a gradient system capable of 35 mT/m. We developed a dedicate RX surface coil with diameter of 5cm in order to receive the MRI signal from the snail brain and positioned the dish containg the snail ganglia on RX coil. A birdcage TX RF coil with the diameter of 30 cm was used for

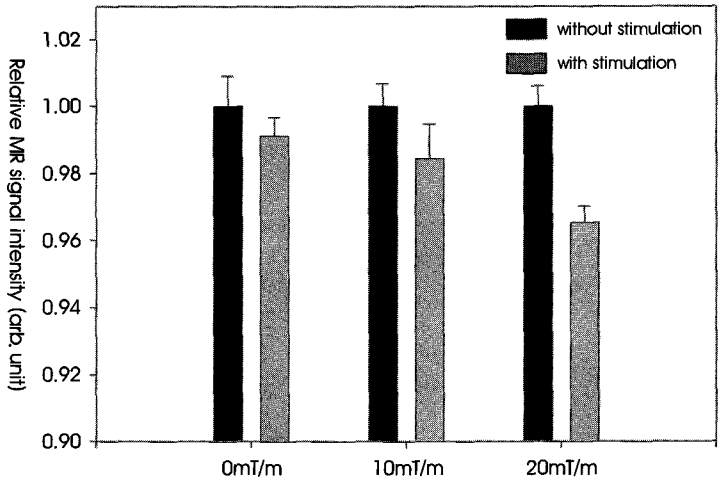

Fig. 4. The average MRI signal intensities of three snail ganglia

the spin exitation. After acquiring the planar and cross-sectional images of the snail ganglia, we positioned the volume of interest in the center of visceral ganglia. In this region, the MRI signal intensity has been measured and integrated during the second echo signal in the time domain. The number of sampling points was 2048 and sampled every 0.4 ms. The MRI signal intensity, then, mostly represents the amount of water molecules in the volume of interest, and any signal intensity changes reflect phase changes of the water molecules' nuclear spin.

Ⅲ. RESULTS

The MRI signal acquisition and ECR with the electrical stimulation at a laboratory bench are performed with three dissected snail ganglia. Before the three snail ganglia expe-riments, we had verified with three other snails that the survival state of dissected snail ganglia is maintained as long as several hours without special treatment. After dissecting a snail, we waited 30 min to perform ECR for the dissected snail ganglia to be stabilized. We performed ECR 10 times every 2 minutes for each snail ganglia with and without electrical stimulation, and each ECR period was 20 s. All three snail ganglia showed similar responses to the electrical stimulation, i.e., increase of neuronal activity after the electrical stimu-lation. Figure 3 shows firing rate change of snail ganglia during the electrical stimulation. The numbers of peaks were counted in the initial period of 2s out of the ECR period of 20 s, and the ten measured results were averaged. All the snails show significant increase in firing rates after the electrical stimulation. The average increase of the firing rate in the three snail experiments is about 720%.

Figure 4 shows MRI signal intensities observed in volume selected snail ganglia region. These data also acquired every 2 min for 20 min in the three snail experiments. In the MRI signal measurements, the volume of interest was set to 2×2×2 mm^3 with TE1 and TE2 of 68 ms and 136 ms, respectively. The MR data acquisition was carried out 500 ms after the end of the electrical stimulation. The experiments were performed consecutively, that is, without the electrical stimulation first and then with the electrical stimulation on each gradient strength. In the two minute time interval, a single volume selection sequence was applied with no averaging. Therefore, the effective repetition time (TR) was 2 min. The black and gray bars represent the MRI signal intensities without and with the electrical stimulation in each gradient strength, resp-ectively. The MRI signal intensities were normalized with the average MRI intensity in the case of no stimulations in each snail experiment. When the motion encoding gradients were not applied there were no significant MRI signal decreases. However, when we applied 10 mT/m and 20mT/m gradients for 8ms, the average MRI signal decreased due to the electrical stimulation was about 1.73 and 3.46% respectively. When we applied 20mT/m gradient strength, p-value was under 0.000001 while p-value was just 0.4 in without gradient expe- riments. Consequently, we can get the statistical significance in strong gradient experiments.

Ⅳ. CONCLUSIONS AND DISCUSSIONS

In this study, electrical stimulation is applied to the dissected snail ganglia in order to control neuronal activity. The firing rate is increased 7 times compared to the normal state. This result indicates the efficacy of the electrical stimulation. To evaluate Lorentz force effect of neurons in MRI, we applied motion weighting gradient to volume selection sequence and observed the dependence of the MRI signal intensity on gradient strength. Increase of applied motion encoding gradient strength resulted in decrease of the MRI signal intensity during snail brain activated. Applied motion encoding gradient in this study can give weighting to incoherent displacement in intra-voxel. This method indicates the feasibility of enhanced new fMRI under fast time resolution condition and enhances the signal contrast in functional study with MRI. The recent report that the diffusion weighted fMRI on human subjects showed decrease of pixel intensity in the activated regions, opposite to the BOLD effect, which indicates possible couplings between the Lorentz force effect and MRI signal intensity (Li and Song 2003, Troung 2006). We think these results indicate that the Lorentz force effect can be one of the mechanism of MR signal changes to neuronal activity. Around 3% MRI signal attenuation corresponds to a maximum spatial disp-lacement of neurons by approximately 15um in one direction, when the motion is calculated with these results using referred equation (Song et al, 2001).

However, other potential sources and mechanisms of the signal change are still controversial such as magnetic field effect (Xue et al, 2006), cell volume change (Tasaki et al, 1985), temperature changes due to metabolic activity and so on. The negative response, also, will be troublesome in brain function studies where low SNR is often of great concern.

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