Finding NAMO (Neuroelectric Activity under Magnetic-field Oscillations) with MRI *in vivo*

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Introduction

Neuroimaging techniques are among the most important tools for investigating the function of the human nervous system, but are invasive (single-cell recordings) and/or limited in their ability to accurately localize neural activity in space (EEG, MEG) or in time (PET, fMRI). There is hence a need to develop novel techniques that allow non-invasive imaging of neural activity with a high accuracy both spatially and temporally. Several studies have explored the feasibility of using MRI for detecting the magnetic field changes induced by electrical currents in phantoms[1–3] or neuronal currents in humans[4–8], thereby combining the high temporal resolution of electrical recording methods with the high spatial resolution and non-invasiveness inherent in MRI. Despite some encouraging results in phantoms, the direct imaging of neural activation *in vivo* has been challenging, because of the extremely small activation-induced magnetic field changes as well as synchronized confounding signals in the brain reflecting cerebral blood oxygenation, blood volume, and blood flow changes or physiological noise.

Here, we address these two fundamental issues and demonstrate the capability of MRI to directly image neuroelectric activity *in vivo*. First, to boost the signal detectability, we propose a novel acquisition strategy based on the Lorentz effect induced by neuroelectric activity. Although the contrast mechanism of Lorentz effect imaging was previously validated in phantoms[9], the original technique was not sensitive enough for *in vivo* applications. Here, we incorporate a series of oscillating magnetic field gradients applied in synchrony with the neural stimulation to drastically increase its sensitivity. Second, to isolate neuroelectric activity from potential confounds, we perform our experiments in the human median nerve using electrical stimulation of the wrist to induce sensory nerve action potentials propagating proximally in the median nerve.

Methods

A current-carrying conductor exposed to a magnetic field experiences a Lorentz force equal to the cross product of the current and the field. If the conductor is surrounded by an elastic medium, this force induces a displacement of the conductor, resulting in a spatially incoherent displacement of the elastic medium in adjacent regions. In the presence of a magnetic field gradient, the spins in these regions experience a loss of phase coherence proportional to its amplitude and duration, resulting in a destructive signal summation within a voxel and causing a signal loss. Here, we apply a series of oscillating gradients (with positive/negative lobes of same duration to avoid a global signal loss) in synchrony with the neural stimulation such that the neuroelectric activity occurs only during the negative lobes (Fig. 1). The loss of phase coherence is thus drastically amplified and the sensitivity enhanced.

Electrical stimulation of the median nerve was achieved by applying a series of biphasic current pulses (with a duration of 1 ms and an amplitude below the motor threshold to avoid motion artifacts) triggered at the onset of the negative lobes of the oscillating gradients. A duration of 5 ms was chosen for each lobe to ensure that sensory nerve action potentials propagating in the median nerve between the wrist and the elbow would be fully contained within one lobe. Three cycles of oscillating gradients were used to generate sufficient loss of phase coherence while minimizing TE and consequently the global signal attenuation due to T_2^* relaxation.

The studies were performed on a 4 T GE scanner using a surface coil and a gradient echo spiral sequence with TR 2 s, TE 36 ms, FOV 20 cm, matrix 64×64, and three 15-mm sagittal slices (with respect to the forearm, which was orthogonal to the main magnetic field to maximize the Lorentz effect). The activation paradigm was a block design consisting of seven alternating rest and stimulation periods, each lasting 20 s during which ten image volumes were acquired. Five runs were acquired per experiment and averaged to increase the SNR.

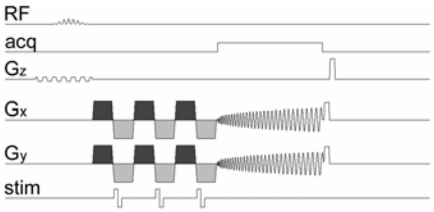

Fig. 1: **Pulse sequence** showing the RF pulse, acquisition window, gradients on the slice (z), readout (x), and phase (y) axes, and current applied by the stimulator to the wrist for three cycles of oscillating gradients (shaded) and three electrical pulses triggered at the onset of the negative lobes.

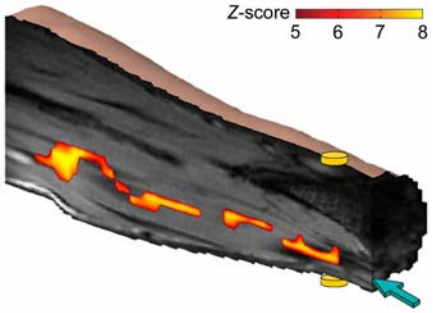

Fig. 2: **Activation map** showing the effect of neuroelectric activity *in vivo* in the human median nerve (arrow). The discs represent the electrodes placed on the wrist.

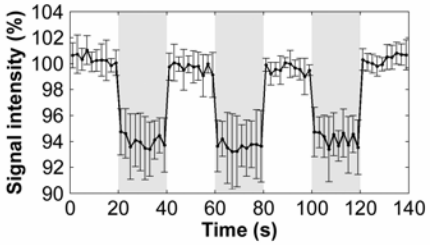

Fig. 3: **Time course** in the activated region during alternating rest (white) and stimulation (gray) periods averaged over five experimental sessions and normalized to the mean signal intensity during rest.

Results and Discussion

A first experiment was performed using three cycles of oscillating gradients and three electrical pulses synchronized with the negative lobes for each image acquisition (Fig. 1). It was repeated in five different sessions to demonstrate the reproducibility of the results. A representative activation map shows highly significant activation along the median nerve (Fig. 2). The time course in the activated region averaged over the five sessions shows a systematic signal decrease of (6.1 ± 1.9)% during the stimulation periods (Fig. 3). The transitions between rest and stimulation periods exhibit no delay, demonstrating that our technique has a better temporal resolution than BOLD fMRI, which is limited by a hemodynamic delay of 3 to 6 s.

A second experiment was performed using only two cycles of oscillating gradients and two electrical pulses synchronized with the negative lobes. Less significant activation was detected, illustrating that the sensitivity can be significantly decreased when there is insufficient loss of phase coherence. Furthermore, since this experiment is equivalent to the first one with a one-cycle offset between the oscillating gradients and the electrical stimulation, this also shows that our technique is sensitive to temporal offsets of the stimulation on the order of milliseconds, thus demonstrating its high temporal resolution.

Finally, two control experiments, identical to the first one but with the electrical pulses delayed by 50 ms with respect to the oscillating gradients or without oscillating gradients, were performed. No activation was detected in either experiment, which further validates the contrast mechanism of our technique by demonstrating that the observed activation is due to the loss of phase coherence generated by the oscillating gradients rather than to the actual displacement of the nerve, and that there are no artifacts due to eddy currents induced in the stimulation circuit by the oscillating gradients or electrical interference from the stimulation pulses.

In this work, we have demonstrated the capability of a novel MRI technique to image neuroelectric activity *in vivo* in the human median nerve with a high temporal resolution. Such a direct, real-time, and non-invasive neuroimaging technique will likely find broad applications, as it can potentially characterize nerve conductivity in various neuropathies, but also be applied to white matter tracts to study functional connectivity, and, although experimentally more challenging, ultimately be extended to image dendritic neuroelectric activity in gray matter (since the currents do not have to be unidirectional), which would have a significant impact in neurosciences.

References: 1. Bodurka, JMR 1999;137:265. 2. Bodurka, MRM 2002;47:1052. 3. Konn, MRM 2003;50:40. 4. Kamei, IEEE Trans Magn 1999;35:4109. 5. Xiong, Hum Brain Mapp 2003;20:41. 6. Chu, Neuroimage 2004;23:1059. 7. Bianciardi, MRI 2004;22:1429. 8. Konn, MRI 2004;22:1413. 9. Song, MRI 2001;19:763.

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