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MAGNETIC RESONANCE IMAGING TECHNIQUE AND PERIPHERAL NERVE ACTIVITIES

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ABSTRACT. During the last decade many medical investigators have attempted to measure neural currents directly using magnetic resonance imaging (MRI). The action currents of a peripheral nerve create their own magnetic field that can cause the phase of the spins to change. Our goal in this paper was to use the measured magnetic field of several nerves to estimate the resulting phase shifts in the magnetic resonance signal. We examine four cases: frog sciatic nerve, crayfish medial giant axon, squid giant axon, and human median nerve. In each case, the phase shift is much less than one degree, and will be very difficult to measure with current technology.

Keywords: MRI, action currents, phase shift, nerve

Several investigators (Bodurka & Bandettini 2002; Cassara et al. 2008; Kamei et. al 1999; Paley et al. 2009) have attempted to detect neural currents directly using magnetic resonance imaging (MRI). The action current of a nerve creates its own magnetic field (Wikswo et al. 1980; Roth & Wikswo 1985) that can act like a gradient field during magnetic resonance imaging, causing the frequency or phase of the nuclear spins to change because of the presence of the action current. However, this magnetic field is very small; and it is not clear if this effect can be measured. Therefore, our goal in this paper was to use the measured magnetic fields of peripheral nerves to estimate the resulting phase shifts in the magnetic resonance signals.

Magnetic measurement of action currents using magnetic resonance would be a significant diagnostic tool because it would allow true functional imaging of action currents using all the power and resolution of MRI. Researchers have developed functional MRI to detect brain activity, which measures the blood oxygenation level-dependent (BOLD) signal (Ogawa et al. 1990). However, BOLD is an indirect measurement of perfusion rather than a direct detection of neural activity. Ideally, measurement of the magnetic field of action currents would provide a signal that better follows the spatial and temporal distribution of neural activity. Biomagnetic measurements using magnetometers outside the body have been used to measure neural activity directly (Hamalainen et al. 1993; Romani 1989). However, MRI measurements would detect the magnetic field inside the body, eliminating the ill-posed and difficult inverse problem that normally plagues biomagnetic studies. For this reason, magnetic resonance detection of action currents has generated much interest in the past few years.

Previous studies (Cassara et al. 2008; Paley et al. 2009) have attempted to calculate the magnetic field associated with action currents from first principles. However, a large body of research exists in which magnetic fields of nerves, and even single axons were directly measured using ferrite-core, wire-wound toroids (Gielen et al. 1986; Wijesinghe et al. 1991). Our goal was to use these measurements to estimate the MRI signal caused by action currents.

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METHODS

Action currents in nerves have been directly measured using neuromagnetic current probes by us and our former colleagues (Gielen et al. 1991; Wijesinghe et al. 1991; Wikswo & van Egeraat 1991; Wikswo et al. 1990). From these measurements of the current, I, and the radius of the fiber, r, we can calculate the magnetic field created by this current at the surface of the

fiber using Ampere's law,

$$B = \frac{\mu_0 I}{2\pi r} \quad (1)$$

where μ_0 is the magnetic permeability of free space. Equation 1 neglects return currents (Woosley et al. 1985) and is strictly valid only for unmyelinated axons, although myelinated axons should behave continuously to a good approximation (Basser 1993).

Even though this expression represents an approximation for evaluating the magnetic field created by a nerve axon in the body, it is not a poor approximation for distances very close to the fiber (Woosley et al. 1985). In the magnetic resonance signal, this magnetic field will induce a phase shift, ϕ, of

$$\phi = \gamma B \Delta t \quad (2)$$

where γ is the gyromagnetic ratio of a proton (2.7×10^8 s^{-1} T^{-1}), B is the strength of the magnetic field created by the nerve, and Δt is the duration of the rising phase of the magnetic field. (Strictly, the phase is found by integrating the magnetic field over time, but Equation 2 should be a useful approximation. To be quantitatively correct, one should use the component of the magnetic field parallel to the static field in Equation 2). This phase shift is an invaluable tool in investigating whether a noticeable event occurs in the MR signal due to action currents in nerves.

RESULTS

We have investigated the phase shifts due to four different measured action currents, from the frog sciatic nerve, the crayfish medial giant axon, the squid giant axon, and the human median nerve.

Frog sciatic nerve.—The frog sciatic nerve consists of thousands of individual small axons. Experiments were performed to record action currents from the bull frog (*Rana catesbeiana*) sciatic nerve bundle *in vitro*. The frogs were dissected approximately one hour before the experiments were started. During the dissection, frog Ringer's solution was used to keep the nerve moist. The nerve remained immersed in circulating, oxygenated frog Ringer's solution at 20 °C throughout the experiment. The action currents were recorded magnetically by threading the nerve through a wire-wound, ferrite-core toroid that served as a pick-up coil. The nerve and toroid were immersed in saline solution, and the induced emf in the coil was measured using a sensitive room-temperature amplifier. A more detailed experimental procedure pertaining to this experiment has been published by Wijesinghe and his colleagues (Wijesinghe et al. 1991). The measured action current from a frog sciatic nerve bundle is shown in Fig. 1. This signal was recorded using a strong stimulus so that it excited most of the axons in the nerve bundle. Therefore, the measured current, I, as can be seen in the signal is 0.2 μA, and the bundle radius, r, is 0.75 mm. Thus, B is 0.05 nT. The rise time is about 1 ms, so the induced phase shift is about 0.0007°.

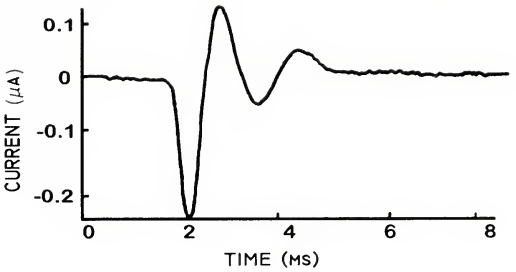

Figure 1.—The recorded action current from a frog sciatic nerve bundle at 21 °C.

Squid giant axon.—The squid axon is historically one of the most important bioelectric systems studied (Hodgkin & Huxley 1952), and is one of the largest single axons known. Wikswo & van Egeraat (1991) measured the action current associated with a propagating action potential along a squid giant axon using the same method described for the frog sciatic nerve bundle, and obtained $I = 6$ μA. Hodgkin & Huxley (1952) reported that the radius of the squid giant axon, r, was about 0.5 mm. Thus, the calculated value of B at the surface of the axon, from Equation 1, is 2.4 nT. The rise time is approximately 0.4 ms, so the induced phase shift, from Equation 2, is about 0.00026 radians, or 0.015°.

Crayfish medial giant axon.—The crayfish medial giant axon, even though it is not as large as the squid giant axon, has been studied in several important experiments including the first ever axonal current recordings using the magnetic technique (Roth & Wikswo 1985) and using the same procedure described above for the frog sciatic nerve bundle. As shown in Fig. 2, the measured action current associated with propagating signal, I, was about 2 μA.

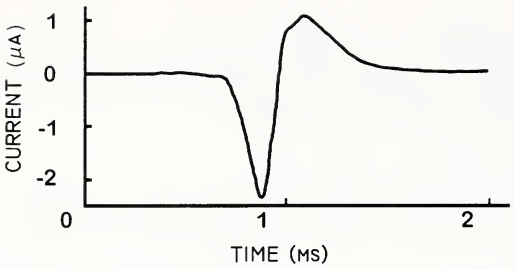

Figure 2.—The recorded action current from a crayfish giant axon at 20 °C.

The radius of this giant axon, r, was about 0.1 mm. Therefore, the calculated value of B at the surface of the axon is 4.0 nT. The rise time of the signal is about 0.3 ms. Therefore, from Equation 2, the induced phase shift is about 0.00032 radians, or 0.018°.

Human median nerve.—The first intraoperative recording of the action current of the human median nerve bundle was reported by Wikswo et al. (1990) using a toroidal pickup coil. This recording was performed on patients undergoing surgical section of flexor retinaculum for decompression of carpal tunnel at the Vanderbilt University Medical Center. The median nerve was exposed proximal to the flexor retinaculum and followed distally to demonstrate the lateral and medial branches. The nerve was immersed in physiological saline for the duration of the recording procedure. They found the recorded current using a toroidal pickup coil to be $I = 0.35$ μA. The radius of the median nerve bundle is $r = 2$ mm. Therefore, the corresponding magnetic field at the surface of the bundle is 0.035 nT. The rise time is about 0.75 ms. The calculated phase shift is about 0.0004°.

All these phase shifts are very small, much less than one degree. We can look at the size of the phase shifts from another point of view. In NMR spectroscopy, one often measures the chemical shift, which specifies the fractional change in the resonant frequency for different chemical species and is typically on the order of a few parts per million. In our case, the static magnetic field during MRI was about 1 T, and the magnetic field of the nerve was about 1 nT, implying a fractional change of magnetic field (analogous to a chemical shift) of about one part per billion. Thus, we expect a frequency resolution of about one thousand times that of NMR spectroscopy would be required to detect the magnetic signal of the nerve.

DISCUSSION

We found that in four common bioelectric systems, the phase shift induced during MRI is small (often less than one tenth of a degree), and would probably not be measurable with current technology. Therefore, we are not optimistic about the future of such techniques. In fact, we believe our results above overestimate the MRI signal for the following reasons: (1) The magnetic field of an action potential consists of a biphasic signal with both depolarization and repolarization signals. The repolarization current lasts somewhat longer than the depolarization current, but is also weaker, so the integrated phases from depolarization and repolarization have the same magnitude but opposite sign. The net signal of the action current is nearly zero, as the phase shifts of depolarization and repolarization cancel. The entire action potential is over in just a few milliseconds, which is a short time compared to most MRI imaging pulse sequences. Thus, action potentials will be more difficult to detect than predicted above, unless very brief, carefully timed pulse sequences are developed. (2) In the case of the nerve, the action potentials in different axons propagate at different speeds, so that the compound action potential results from the summation of many single axon signals (Wijesinghe et al. 1991). Therefore, the measured signal will decrease as the action potentials propagate and become less well synchronized. (3) We calculated the magnetic field just outside a nerve, where it was largest. In general, the field falls off with distance outside the fiber (Equation 1). A typical MRI signal represents an average over a pixel or voxel, which often has a size on the order of a millimeter. Thus, only part of a voxel may experience a large magnetic field, with other parts experiencing a weaker field. (4) In most cases, the entire nerve will not be simultaneously active. Whereas for a frog sciatic nerve it is fairly easy to stimulate most or all of the axons using a strong electrical pulse, in an experiment on a human median nerve under normal physiological conditions only a small fraction of the axons in a nerve will be active. This can be confirmed by comparing the data presented in this paper for the frog sciatic nerve bundle and the human median nerve. Even though the

radius of the human median nerve is much larger than that of the sciatic nerve, the current recorded in the human median nerve was much smaller than that of the frog sciatic nerve. Even though the total number of fibers in the human median nerve is much larger than that in the frog sciatic nerve bundle, the "active fibers" in the median nerve bundle were fewer than that in the frog sciatic nerve bundle. For these reasons, we suspect that detecting neural activity will be even more difficult than our calculated phase shifts suggest.

Troung & Song (2006) recently introduced another method called "Lorentz Effect Imaging" for detection of action currents using MRI. This method is based on the principle that when a current is placed in a magnetic field, there exists a force–the Lorentz force–on the current. This Lorentz force causes a current-carrying nerve to shift from its original position in the body. If there simultaneously exists a magnetic field gradient during the MRI, this movement of the axon causes the spins to diphase, resulting in an artifact in the magnetic resonance signal. Roth & Basser (2009) recently investigated this effect using a mathematical model and found that the Lorentz displacement was too small to be detected using MRI techniques. In fact, they concluded that the Lorentz force effect will be even smaller than the effect examined in this paper.

Our analysis focused on peripheral nerves. Other systems that might give larger results are the brain and the heart. In the heart, a very large volume of cardiac tissue is simultaneously active, and this may provide a good starting place to search for action currents recorded using MRI (although motion artifacts will certainly be a problem). If large regions of the brain are simultaneously active, the magnetic field around these active regions may be larger than we estimate here. Moreover, if the signal is caused by dendritic currents, it may not have the rapid repolarization currents to cancel the depolarization signal (Park & Lee 2007). These two systems need to be examined in more detail.

Our estimates of the fractional change in magnetic field strength or frequency caused by action currents assume that the magnetic resonance study is performed using a typical static magnetic field strength on the order of 1 T. However, action currents might be detected more easily using ultra-low field MRI systems (Cassara & Maraviglia 2008). The ability of these systems to detect biomagnetic signals is yet to be explored on living tissues. Because the biomagnetic field is not proportional to the static magnetic field (as it would be for chemical shift or susceptibility effects), a lower static field means a larger fractional change in frequency caused by action currents. Thus, ultra-low field measurements may be one way to better detect action currents.

In conclusion, we find that MRI measurements of action current in nerve are unlikely using current technology. Bandettini et al. (2005) asked if detecting neural activity using MRI is "fantasy, possibility, or reality?" Our results suggest that, at least for peripheral nerves, "fantasy" may be closer than "reality".

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