The effect of longitudinal magnetic resonance imaging on the quality of neurophysiological recordings using implanted micro-wire electrodes.

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Introduction. Valuable insights can be gained by combining both invasive and non-invasive schemes for analyzing and activating the central nervous system.. For example, combining fMRI and intracortical recording has yielded important information about metabolic mechanisms that are highly correlated with recorded neural activity[1]. Similarly, combining fMRI with electrical microstimulation has improved understanding on the extent of neural activation [1, 2]. An important step towards combining these technologies is an evaluation of safety and compatibility. Induced currents and associated tissue heating and damage, especially at electrode tips[3], are a major concern. Studies wherein neural tissue is sensed both by the implanted electrodes and MRI are challenging because sensing requires viability of the neural tissue in close proximity to the electrodes. Such requirements are inherently more stringent using, for example, microelectrode arrays recording extracellular multiunit activity (EMUA) since the sensing zone is limited to a couple of hundreds of microns from the metallic electrode tip [4,5]. It is also necessary that the electrodes are MRI-compatible while maintaining a high quality of neural recordings. Previous work presented by Santiesteban et al., [6] addressed important issues related to short-term compatibility of silicon microelectrodes. In order to extend the work of Santiesteban et al. the project described here provides a quantitative assessment of the longitudinal stability and quality of EMUA, comparing animals that have undergone extensive MRI scanning vs. control animals that were not scanned.

Materials and Methods. The microwire electrode assembly typically used in our laboratory, described in [7], was found to give large image artifacts due to the presence of materials with a significant magnetic susceptibility, as shown in Figure 1(a). Individual components were tested by embedding in agarose gel and measuring image distortion (data not shown) and it was found that, in particular, the presence of the standard Omnetic connector and bone-screws produced a large image distortion. Therefore, a modified assembly was developed to replace this connector with a custom-made in-house version using a plastic interconnect (Series 310, MIL-MAX, Oyster Bay, NY) with the electrodes soldered into the pin bases. Brass or PEEK were used as bone screws. Male Sprague Dawley rats (400-500g) were implanted with four 50 µm tungsten microwires in either primary sensory or motor cortical areas. Electrophysiological recordings were carried out in sessions of five minutes with the animal either awake or lightly sedated. Extracellular voltages from each of the 4 electrodes were recorded with respect to a ground wire attached to one of the anchoring bone screws. The signals were boosted with a unity gain FET buffering stage and passed to a lightweight bio-amplifier which digitized the signals (25 kHz) with low-noise 16-bit A/D converters. The signals were multiplexed and transmitted via a fiber-optic cable to rack-mounted TDT modules, digitally band-pass filtered (300 Hz-5 kHz), down-sampled at 12 kHz, and streamed to disk for offline analysis. In order to track the state of the interface, electrode impedances were also measured at 1 kHz. MRI was performed on a horizontal bore 7 tesla magnet, with a 12 cm diameter gradient set and a Varian Direct Drive console. T2 maps were calculated from six spin-echo images acquired with different values of TE (10, 20, 30, 40, 50, and 60 ms, TR=3500 ms for all datasets). Forty contiguous coronal slices were acquired with an acquisition matrix of 128 x 96 and a field of view of 2.1 x 2.1cm giving an in-plane resolution of 164 µm x 220 µm. The slice thickness was 400 µm and two signal averages were acquired. The T2 values were calculated on a pixel-by-pixel basis by fitting a single exponential to the signal intensity as a function of TE. The total data acquisition time was approximately 75 minutes. T2 values were compared for identical regions in the same hemisphere as electrode implantation vs. the contralateral hemisphere using a one-sided t-test assuming equal variance (this process was repeated three times by different individuals).

Results. Figure 1(a) shows the improvement in image quality by making the implanted microwire assembly fully MRI compatible. Figure 1(b) shows that, with the exception of recordings during days 8-14, there is no statistical significance between the quality of the electrophyiology recordings for animals that have undergone MR scannning and those that have not. This gives a good indication that there is no neural/tissue damage very close to the electrodes. Figure 1(c) shows that the T2 values, which are known to be sensitive to neuronal and glial densities as well as edema, are statistically identical in the implanted and control hemispheres, which indicates that there is no significant tissue damage in an extended area within the brain.

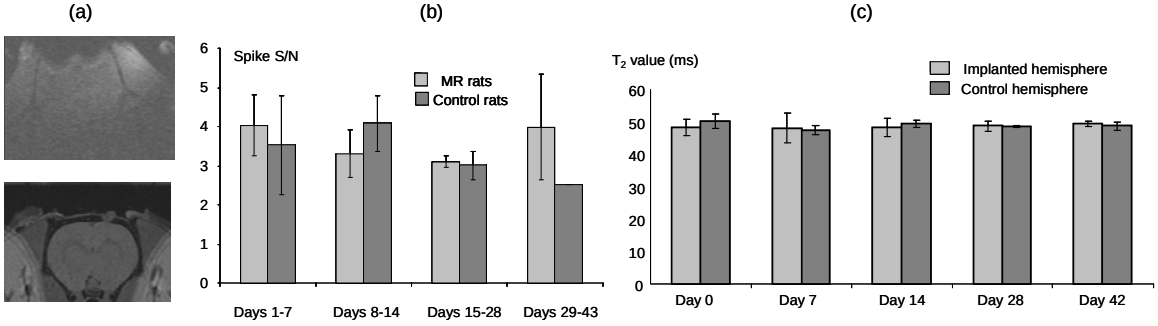

Figure 1: (a) Comparison of gradient echo MR images with implantation of the conventional microelectrode array (above) and one modified for MRI compatibility (below). (b) Measurements of spike signal-to-noise from the electrophysiological recordings over time for both rats that have undergone weekly MRI scans and control animals. (c) T2 values measured over an area of 1 mm posterior to the electrode implantation site. An identical area was analyzed on the contralateral hemisphere. Results are averaged over forty contiguous coronal slices, acquired with an acquisition matrix of 128 x 96 and a field of view of 2.1 x 2.1 cm giving an in-plane resolution of 164 µm x 220 µm. The slice thickness was 400 µm and two signal averages were acquired.

Conclusion. One of the concerns with combined MRI and microelectrode recordings is potential tissue heating local to the electrodes. It has been well established that temperature increases result in irreversible and exponential damage to neural and glial cells. Moreover, temperature changes coupled with damage to endothelial cells of the brain and exposure of serum proteins across the blood-brain barrier causes edema, amplifies cell damage, and in turn severely degrades electrophysiological recordings [8]. The unchanged quality of recordings, together with preliminary histological results, strongly suggests that MR exposure did not induce irreversible changes to neural and glial cell health.

References. [1].N. K. Logothetis et al. Nature, 412, 150, 2001, [2] A. S. Tolias et al. Neuron, 48, 901, 2005. [3] C. J. Yeung et al. Magn Reson Med, 47, 187, 2002. [4] C. Gold et al. J Neurophysiol, 95, 3113, 2006. [5] M. A. Moffitt and C. C. McIntyre, Clin Neurophysiol, 116, 2240, 2005. [6] F. M. Martinez Santiesteban et al.IEEE Trans Biomed Eng, 53, 547, 2006. [7] K. J. Paralikar and R. S. Clement, IEEE Trans Biomed Eng, 55, 2258, 2008. [8] E. A. Kiyatkin, Eur J Appl Physiol, 101, 3, 2007.