Direct MR Detection of Neuronal Electrical Activity In Vitro at 7T

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Introduction: Present fMRI methods reflect underlying neuronal activity indirectly, via coupling with blood flow and metabolic processes. A preferable alternative method would be to measure neuronal electrical activity directly. The possibility of direct MR-based detection of neuronal electrical activity has been recently suggested [1-4], however the feasibility of the technique has yet to be confirmed. Here we present further evidence of MR-based detection of local magnetic fields originating from intrinsic spontaneous neuronal activity in organotypic rat-brain cultures in vitro [5]. This physiologic model is ideal, as it contains active neuronal tissue but no blood flow or physiologic pulsations that may also contribute to the MR signal.

Methods: Organotypic tissue cultures were obtained from coronal sections of newborn-rat somatosensory cortex (in-plane:1-2mm^2, thickness:~100μm). The slices contained a network of 50000-100000 neurons, equivalent to a human cortical unit. The neuronal networks exhibited spontaneous synchronized activity with local field potential (LFP) burst frequency <5Hz (LFP duration:100-200ms). The cultures were prepared on multi-electrode arrays (MEA; 64 electrodes, Multichannelsystems), immersed in 0.8ml culture medium. The culture preparations were scanned at 7T/21cm (Bruker Biospin MRI Corp) using a custom-made ~1" surface coil. One 2mm thick axial slice was prescribed covering the entire neuronal culture and MR data were obtained using a Free Induction Decay (FID) acquisition (TE:30ms, TR:100ms, FOV:2cm, readout~41ms, 1024 points per FID). Each MR session involved two acquisitions (10,100 FID's / ~17minutes each): 1) *MR PRE*: neuronal activity present and 2) *MR TTX*: neuronal activity suppressed by TTX injection (tetrodotoxin: sodium channel blocker). MEA electrical recordings were obtained prior and after each MR session, also corresponding to the PRE and TTX states for the given neuronal network (64x1million samples, ~17min (1KHz) per state). A total of five experiments were performed. An additional MR experiment was also performed as control, in identical conditions but without neuronal tissue on the MEA.

The first 100 FID's per data set were discarded to ensure signal steady state. The remaining 10,000 FID's were phase corrected, apodized, and reconstructed into magnitude and phase. The mean magnitude and phase FID of each data set was subtracted from each FID in the respective data set. The resulting FID's were integrated per TR, yielding a 10,000-point time course (*MR Trace*) of the net magnitude or phase change per TR. EEG traces were calculated as the average of the 64-electrode/MEA electrical recordings, resampled at 10Hz (1/TR) to allow for direct comparison between EEG and MR. Spectra were computed for the average EEG, MR magnitude and phase traces. The total signal power was computed for all spectra. Differences in signal power between *PRE* and *TTX* states were then calculated for both EEG and MR spectra as a measurement of the strength and/or presence of neuronal activity.

Results: MR signal changes associated with neuronal activity were observed in all experiments. An increase in MR signal power was observed during the active state of the neuronal networks, corresponding to the range of the individual neuronal network burst frequency, as measured from the EEG traces. In the TTX state, both EEG and MR measurements showed a decrease in signal power localized to the burst-activity frequencies as compared to the active state. Figure 1 illustrates the PRE and TTX spectra (MR and EEG) for one culture. Figure 2 shows the signal power decrease (0-5Hz) between PRE and TTX states, for MR vs. EEG (all experiments).

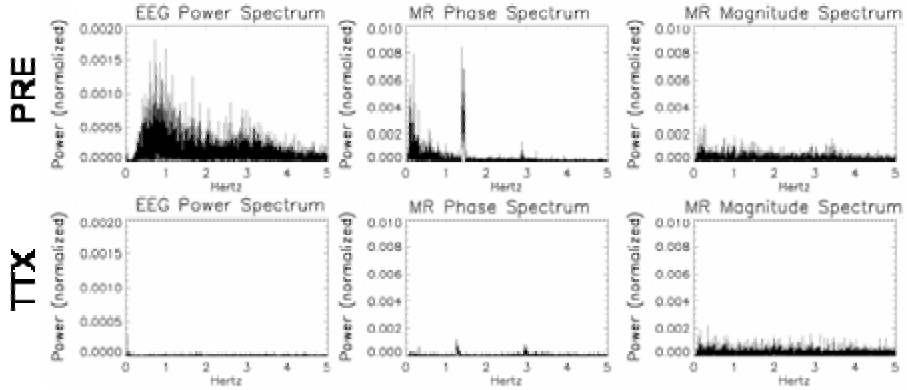

Figure 1. EEG power spectra and MR phase/magnitude spectra for one culture for PRE (top row) and TTX (bottom row) states. Yaxis: power normalized to total spectral power

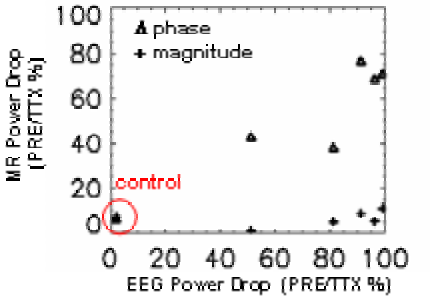

Figure 2. Signal power decrease (0-5Hz) between PRE and TTX states, for MR magnitude (+) and phase (Δ) vs. EEG (n=5, plus control)

The decrease in MR magnitude power between PRE and TTX was on the order of, or below, noise, which may be expected if neuronal activity induces a phase shift in the MR signal [2,3]. The decrease in MR phase power between PRE and TTX was comparable to that observed in the EEG. Overall, an effect was observed in both MR phase and magnitude and ranged from 0.1-1.7 degrees and 0.01%(below noise) -0.4 % respectively. The resulting magnetic field changes were on the order of ~0.2 to ~3.5nT, which is in the range expected for the neuronal networks used.

Conclusion: The present study suggests that MR detection of neuronal activity directly is possible. Based on the localization of EEG and MR spectra in frequencies up to 5 Hz, as well as the decrease in signal power with TTX for both methods, we believe that the most likely origin of the observed MR signal changes is due to synchronized electromagnetic activity across synapses.

References: [1] Bodurka et al. *Magn Reson Med*. 2002;47(6):1052-8, [2] Bodurka et al. *J Magn Reson.* 1999;137(1):265-71, [3] Xiong et al. *HBM* 2003;20(1):41-9, [4] Petridou et al. *NeuroImage Supp* 2003;20(2) [5] Plenz et al. *Neurosci* 1996; 70(4): 861-924.