

# Direct detection of axon firing in the optic nerve and visual cortex using MRI

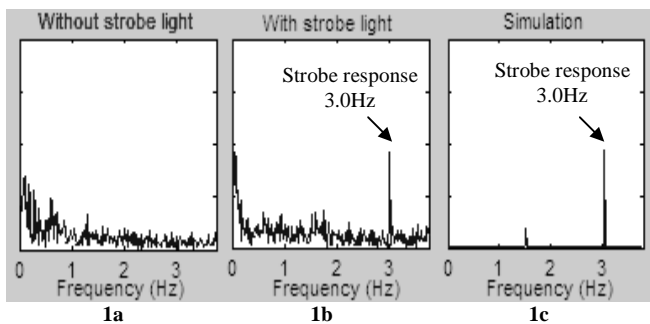
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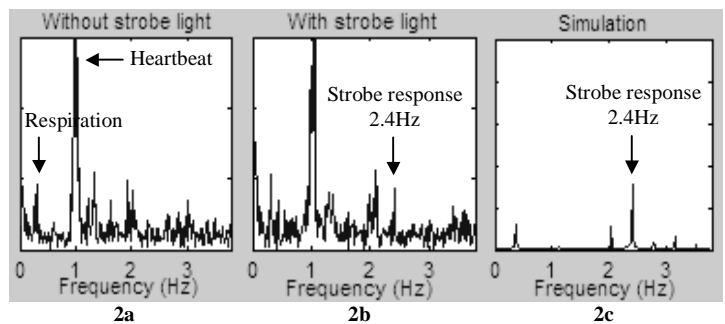
**Introduction:** The aim of this study was to directly detect spectral components of the magnetic fields of neuronal currents caused by firing of the axons in the optic nerve in response to visual stimulation. During firing, the neuronal (ionic) current induces subtle and transient magnetic flux density changes. The component of this magnetic field parallel to the main  $B_0$  field of the MRI scanner locally alters the precession rate of water protons and hence alters the phase of the MR signal. This phase modulation affects successive gradient echo planar image frames, and Fourier theory can be used to analyse the resulting time series from regions of interest. Frequency spectra from experimental data show evidence of the strobe stimulus localised to regions containing the optic nerve and visual cortex, after physiological and motion artefacts have been accounted for, which suggests that direct detection of the magnetic fields emanating from these regions has been achieved. If so, this would be the first time that nerve firing has been detected noninvasively using MRI alone.

**Methods:** All the experiments were performed on a 1.5T MRI scanner using a 10cm surface coil and a 28cm quadrature head coil. Gradient Echo – Echo Planar Imaging (GE-EPI) was used to acquire 500 frames of magnitude images (80 x 80 matrix). Two sets of scanning parameter were used: (a) TR = 66/77ms, TE = 30ms, FOV = 30cm, 8mm slice thickness; (b) TR = 79ms, TE = 32.4ms, FOV = 24cm, 5mm slice thickness. A phantom experiment used a small cylindrical water phantom (33mm diameter, 15mm height) wound with four turns of copper wire fed from an analogue signal generator (Thurlby-Thandar Ltd, Huntingdon, UK), with either sinusoidal or square wave currents between 2.7  $\mu$ A and 33  $\mu$ A at various frequencies. The coil axis was parallel to the  $B_0$  field. In-vivo stimulation of the optic nerve and visual cortex was performed on several occasions in five volunteers (a total of 55 experiments) using a strobe light (Model 250, Soundlab, UK) stimulus in a darkened room over a range of frequencies (0.1-3.3Hz). The strobe light frequency was chosen to be as far away as possible from the heartbeat and respiration rate measured before imaging. A series of control experiments were used together with image registration analysis to ensure that any observed effects were not due to stimulus related motion. Images were processed with software written in-house using MATLAB. The average magnitudes of voxels in a Region Of Interest (ROI) in successive frames were Fourier transformed in a 1D array, to identify any spectral data relating to the strobe stimulus as a function of position in the brain. Frequency maps were also obtained by displaying the same selected spectral component of each voxel in a 2D image.

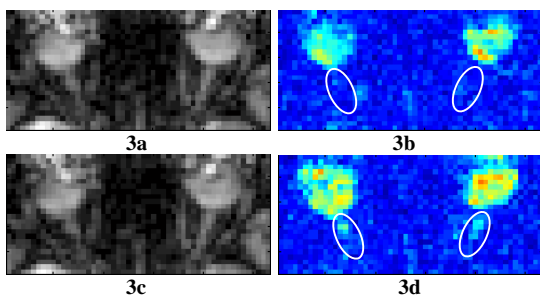
**Results:** The phantom experiment successfully produced spectra consistent with detection of the fluctuating magnetic field resulting from the sinusoidal or square wave current. The lowest detectable magnetic field measured with this phantom was  $4 \times 10^{-10}$  T corresponding to 2.7 $\mu$ A current at a SNR of 2:1. Figures 1 and 2 show the in-vivo frequency spectra of the optic nerve (obtained with the surface coil) and visual cortex (obtained with head coil) respectively. The strobe responses were detected at frequencies similar to the applied strobe light, and they did not appear in the same Region Of Interest (ROI) without stimulation under dark-adapted control conditions. The simulated spectra of the phase modulation caused by the nerve bursts show frequency components consistent with those obtained experimentally. In Figure 3, the regions corresponding to the optic nerves within the oval markers generally show a greater response when both eyes were being strobe stimulated, compared to the control experiments without stimulation. All the in-vivo experiments are summarized in Figure 4. A time of flight venogram and angiogram were acquired from the same volume as the GE-EPI images. It was found that the major vessels do not cross the ROI in the optic nerve and visual cortex and thus should not contribute to the response. The maximum spatial correlation coefficient for successive frames was found for the optic nerve. The result confirms that the strobe response was not due to synchronised motion of the optic nerve.



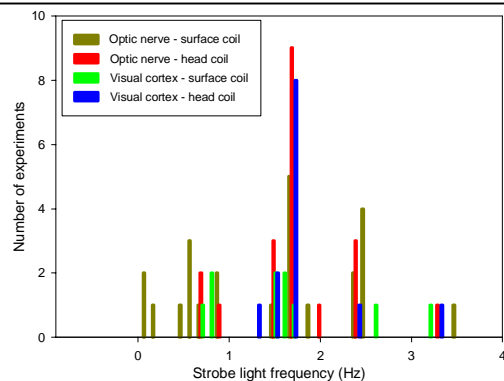
**Figure 1:** Frequency spectra for a ROI in the optic nerve: (a) without strobe light. (b) at 3.0Hz strobe stimulus, obtained with surface coil. (c) Simulated spectrum with 3.0Hz nerve-burst modulation.



**Figure 2:** Frequency spectra for a ROI in the visual cortex: (a) without strobe light. Respiration (0.3Hz) and heartbeat (1.0Hz) were detected. (b) at 2.4Hz strobe stimulus, obtained with head coil. (c) Simulated spectrum with 2.4Hz nerve-burst modulation.



**Figure 3:** (a) GE-EPI magnitude image without strobe light and (b) its frequency map at 1.6Hz; (c) GE-EPI magnitude image with both eyes exposed to 1.6Hz strobe stimulus and (d) its frequency map at 1.6Hz.



**Figure 4:** Summary of data from all in-vivo experiments

**Conclusions:** Based on all the in-vivo experimental results (Figure 4), this study shows preliminary evidence for detection of a perturbation of the MR signal caused by the magnetic field from axons in the optic nerve and leading to the visual cortex, due to strobe light stimulation. The GE-EPI image spectra contain strobe frequency components localised to regions of the optic nerve and visual cortex consistent with a phase modulated MR signal, which are not thought to be due to physiological or motion responses. Future studies are planned to corroborate this preliminary data with improved detection sensitivity at higher field with more sophisticated stimuli, and by investigating other cranial nerve fibres such as those found in the corpus callosum.