Dynamic Diffusion MRI Signal Changes Accompany Electrical Activity in Myelinated Axons

William M Spees1,2, Tsen-Hsuan Lin1, Peng Sun1, Sam E Gary1, Sheng-Kwei Song1,2

1Mallinckrodt Institute of Radiology and 2Hope Center for Neurological Disorders, Washington University School of Medicine, St. Louis, MO, USA

Abstract

Brain functional studies with standard BOLD (Blood Oxygen Level Dependent) fMRI rely upon coupling of hemodynamic response to functional activation, but are essentially limited to grey matter. On the other hand, a number of neurological disorders originate with white-matter pathology, and white matter accounts for approximately half of the volume of the human brain. Thus, a technique for non-invasive assessment of white-matter functionality would be a valuable tool for basic neuroscience and clinical diagnostic purposes. This has motivated our work in developing white-matter diffusion fMRI.

By way of introduction, this talk begins with an overview of our previous work, which demonstrated the utility of diffusion fMRI to assess function and dysfunction in healthy and diseased mouse optic nerves in vivo [1, 2]. However, the majority of this presentation will focus on mechanistic studies involving perfused ex vivo frog sciatic nerves. Because of its exceptionally robust nature, the ex vivo frog sciatic nerve has been the subject of numerous electrophysiology and MRI studies over the years. We report on diffusion fMRI signal changes resulting from repetitive in-magnet electrical stimulation in this model test system.

We have developed and implemented an inexpensive perfusion system allowing for good long-term in-magnet stability and simultaneous MRI/electrophysiology studies in perfused nerves. Decreased diffusivity of tissue water and reduced compound action potential conduction velocities accompany prolonged periods of repetitive electrical stimulation. The electrophysiology and diffusion fMRI results are both consistent with hypothesized microstructural alterations of the PNS myelinated fibers. Recent T2 spectral analyses also shed light on this interesting biophysical phenomenon. Finally, perfused nerves were fixed in-magnet in attempts to “lock in” microstructural alterations for electron microscopy imaging.

References.