Spinal fMRI of Multiple Sclerosis: Comparison of Signal Intensity Changes with Healthy Controls

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Introduction

Functional magnetic resonance imaging of the spinal cord, spinal fMRI, has previously been used to visualize the neurological activity in spinal cord injured patients below the level of injury[1,2]. The SEEP (signal enhancement by extravascular protons) theory, a non-BOLD fMRI contrast mechanism, is based on water crossing over the blood brain barrier to increase extravascular water content in areas of neuronal activity. Using the SEEP theory, we present the first spinal fMRI study involving patients with multiple sclerosis (MS) imaged at the level of an MS lesion or functional deficit. The aim of this study was to further develop spinal fMRI as a clinical tool and to test the SEEP theory in a model with increased permeability of the blood brain barrier.

Methods

Spinal fMRI studies were carried out at 1.5 T (General Electric, Signa Horizon LX) with subjects supine, using a phased-array receiver coil. T2-weighted images were obtained to visualize the lesion load in the spinal cord. Functional time-course data were obtained using a single-shot fast spin-echo sequence (TE = 38 msec), and sets of 8 slices were acquired every 11 seconds. In separate experiments with each subject the imaging location was selected to span the spinal cord segments corresponding to a sensory or motor functional deficit, and also either where an MS lesion was found, or in the cervical or lumbar cord if no lesions were found. Slices were oriented transverse to the spinal cord and were aligned with either the intervertebral discs or the centers of the vertebrae according to established methods[1,2]. Thermal stimulation was applied with a Medoc® TSA-II thermal sensory analyzer. The thermal probe was placed against the skin corresponding to the dermatome associated with the area of the spinal cord being imaged. In each experiment, images were acquired repeatedly while the stimulator was cycled between 32ºC for the baseline and 15 ºC for stimulation. Baseline conditions were held for 66 seconds and stimulation periods were maintained for 44 seconds. The time for the transition from 32ºC to 15ºC was 11 seconds. Studies were repeated with the stimulus applied to both sides of the body. Data were analyzed using custom-made software written in MatLab using a correlation method with a p-threshold of 0.05. The paradigm was defined with the signal higher during stimulation than during the baseline conditions. Only data acquired during the constant temperature periods were used for calculating the correlation to the model paradigm, and no model was assumed for the transitions.

Results

Spinal fMRI was performed on 27 patients with multiple sclerosis; 11 secondary progressive, 6 relapsing remitting, 8 primary progressive, 1 unknown. All but two patients had chronic motor or sensory deficits in the trunk or limbs at the time of the study. Durations since diagnosis of MS ranged from 3 to 32 years. Signal intensity changes in MS patients (11.0% ± 0.1%) were significantly higher than those in healthy controls (6.1% ± 0.9%). Separated into subtypes, the difference remains. The average signal intensity changes for primary progressive, secondary progressive, and relapsing remitting MS were observed to be 9.4% ± 0.2%, 10.6% ± 0.3%, and 12.2% ± 0.7%, respectively.

Discussion and Conclusions

The SEEP theory is based on water crossing the blood-CNS barrier (BCNSB). There is increasing evidence that there are chronic deficits in the BCNSB both before and after macroscopic enhancing MS lesions can be seen by means of T1-weighted MRI. This includes changes in the BCNSB throughout normal appearing white matter in MR images [3,4]. The fact that an increased signal intensity is observed in spinal fMRI of patients with MS, compared to healthy control subjects, gives evidence that we are indeed observing an increase in extravascular water content. This increase was seen both in regions of the spinal cord with and without macroscopic lesions visible on T2-weighted images. These findings suggest that the SEEP contrast mechanism may provide a means of assessing patients with multiple sclerosis, to supplement conventional MRI and other clinical assessment methods.

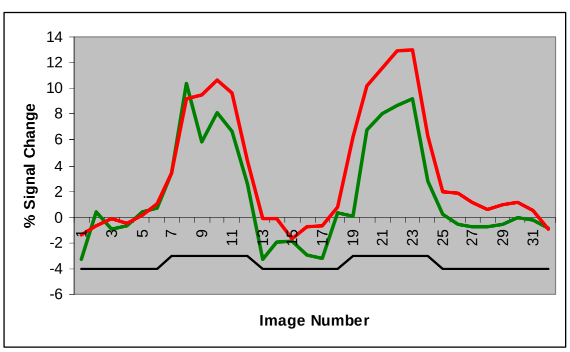

Figure 1. Fractional signal changes observed in spinal fMRI of healthy controls (green) compared to MS patients (red) as they relate to the stimulation paradigm (black)

References

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