Sensitivity of Myelin Water Imaging in Focal Spinal Cord Demyelination: a Combined Neurophysiological and Neuroimaging Study of Cervical Spondylotic Myelopathy

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Introduction

Cervical spondylotic myelopathy (CSM) is the leading cause of spinal cord dysfunction in people over 55 years of age in North America, yet the relationship between the degree of stenosis and the tissue damage that leads to symptoms is poorly understood. Diagnosis of CSM is primarily based on the clinical signs and symptoms, and increased signal intensity changes on conventional MRI of the spinal cord. Somatosensory evoked potentials (SSEP)[1] are diagnostic measures of spinal cord impairment that assess changes in neural impulse conduction of the posterior cord (dorsal column), and are sensitive to demyelination. Recently, a novel MRI technique, myelin water imaging, has been developed to directly measure the fraction of water trapped between myelin bilayers, called the myelin water fraction (MWF) and has applied to investigate the role of myelin degradation in CSM[2]. In the present study the relationship between changes in MWF and tibial SSEP was studied in subjects with CSM to assess the sensitivity of MWF to clinical findings of demyelination.

Methods

Subjects: 10 subjects diagnosed with CSM as characterized by established clinical deficits (5 m, 5 f, mean age 60, range 50-69) and 17 age-matched healthy adults (7 m, 10 f, mean age 59, range 51-75) were recruited in accordance with the local institutional review board.

SSEP Measurement: Standard tibial SSEP were retrieved by stimulation of the posterior tibial nerves at the medial ankle with combined recordings at the popliteal fossa (to assure appropriate stimulation and exclude impairment of peripheral nerve conduction) and cortical levels. Changes in amplitude, latency and configuration were calculated to score SSEP recordings[3].

MRI Measurement: Subjects were scanned on a 3.0T MRI system (Philips Healthcare, Best, The Netherlands) with a phased array spine coil using only the first four channels. Myelin water imaging was performed by a T_2 relaxation experiment using a 3D 32-echo sequence (1st echo =10ms, echo spacing=10ms, TR=1300ms, six 5mm thick axial slices perpendicular to the spinal cord, 256×128 matrix, FOV 180mm×135mm, one acquisition)[4]. The stack was centered at the level of stenosis in CSM subjects, and at the C5 level in controls. Data analysis was performed by a non-negative least squares algorithm as described previously[2], to produce maps of the MWF for each pixel. For each subject, the average MWF in the dorsal column was calculated by drawing regions of interest (ROI) on T_2 weighted images and combining the ROIs over all slices to yield a volume of interest (VOI).
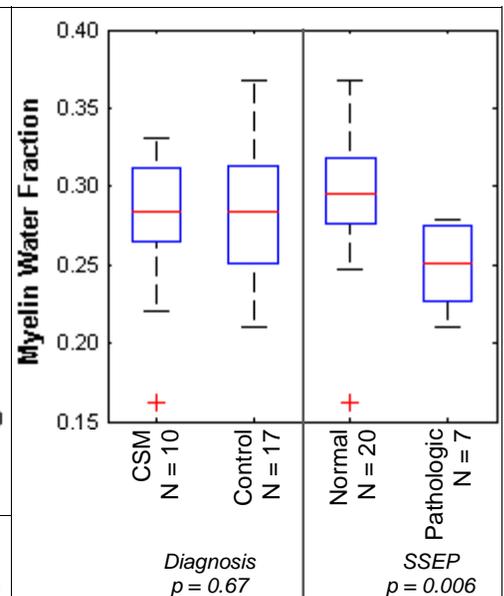
Results

Figure 1 shows the relationship between MWF and SSEP cortical latency for both the right and left tibial nerves. The Spearman's rank coefficient was significant for a negative trend between MWF and both cortical latencies (right rho = -0.486, left rho = -0.574), however the coefficients for trends with the fossa latencies were not significant (right rho = -0.263, left rho = -0.227). Figure 2 highlights the differences in MWF between CSM and controls, as well as the same data grouped by subjects with normal SSEPs versus subjects with at least one SSEP classified as pathologic by a neurologist. In particular, there was a significant difference in MWF when subjects were grouped by SSEP results (p=0.006), as opposed to nearly identical MWF values when subjects were grouped by diagnosis.
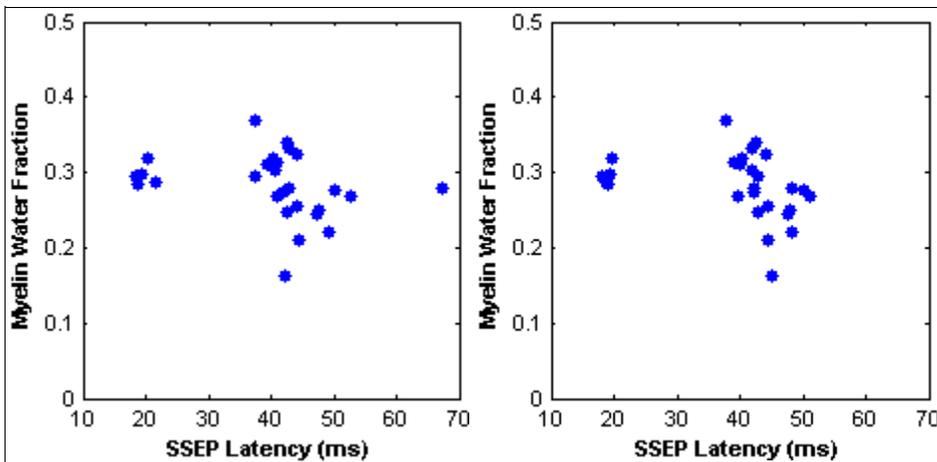
Fig 1. *Left:* MWF versus tibial SSEP latency at the left sensory cortex.
Right: MWF versus tibial SSEP latency at the right sensory cortex.

Fig 2. Differences in MWF data grouped by diagnosis (*left*) or SSEP classification (*right*). Subjects with at least one pathologic SSEP were classified as pathologic. P values reflect the Student's T-test statistical difference between groups.

Conclusions

The combined assessment of dorsal column function by neurophysiological and neuroimaging recordings reveal a significant correlation between changes in SSEP latency and MWF. A reduction in MWF was specifically related to subjects who presented delayed SSEP latencies, and there was a clear agreement between SSEP classification and MWF values, indicating a relationship between MWF and SSEP as measures of demyelination. The lack of relationship between SSEP latencies at the fossa and MWF indicates that SSEP results were mainly affected by the stenosis at the cervical level. The presented findings indicate for the first time that MWF in the cervical spinal cord is sensitive to focal demyelination in humans and might provide a novel tool to assess clinical interventions aimed at treating diseases and disorders of myelin in spinal cord white matter.

References 1. Baba, H. *Paraplegia* 34:100-106 (1996). 2. MacMillan, E. *Proc ISMRM* #2290 (2008). 3. Curt, A. *J Neurotrauma* 25(6): 677-685 (2008). 4. Mädler, B. *Magn Reson Imaging* 26(7):874-88 (2008).