In Vivo MRS Monitor Delayed Neurodegeneration in Experimental Spinal Cord Injury

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INTRODUCTION Since axonal loss ultimately results in neurologic deficit, the ability to noninvasively monitor axonal loss/dysfunction will have significant clinical implications in spinal cord injury (SCI). ^{1}H MRS is most commonly used for measuring the levels of N-acetylaspartate (NAA), total creatine (Cr, includes both phosphocreatine and creatine), choline (Cho), lactate and lipids. Of these NAA has attracted the greatest attention since it is considered to be a neuronal/axonal marker. Because of many technical challenges, relatively few *in vivo* MRS studies of spinal cord have been reported[1,2,5]. In this study, we measured the changes of NAA and other metabolites in the spinal cord of rats at day 14 after injury using *in vivo* ^{1}H MRS.

MATERIALS and METHODS These studies were performed on Sprague Dawley rats weighing between 300-350g. They were divided into two groups of five each: normal-uninjured and injured. The spinal cords injury and RF coil implantation procedure were performed as described previously[2,3]. MR scans were performed on day 14 post-injury. For MRI/MRS studies rats were intubated and maintained under anesthesia with a mixture of 2.5% isoflurane, 30% oxygen and air. All MR studies were performed on a Bruker Biospec 7T/30cm spectrometer. PRESS sequence was used to acquire localized ^{1}H spectra from the epicenter of the injury (0 mm), rostral (+3 mm from epicenter) and caudal (-3 mm from epicenter) spinal cord with a voxel size 2 mm×2 mm×3 mm, TR = 4000 ms, TE = 20 ms, spectral width of 10000 Hz, 4k data points, and 128 averages. All spectra were manually phased, and corrected for baseline before quantitative measurements for peak areas by the standard routines provided by the Bruker software TOPSPIN. Integrated peak areas were measured and normalized to that of the water resonance in rostral spinal cord without water suppression. Statistical comparisons were carried out by analysis of variance (ANOVA) and Student's *t*-test routines.

RESULTS Fig.1 shows the proton MRS of normal and injured cord at different locations. Quantitative analysis indicated that the relative NAA peak area in the epicenter, rostral and caudal to the injury site decreased significantly by about 70%, 50% and 50%, respectively. The relative Cr peak area at the epicenter, rostral and caudal to the injury site decreased significantly by about 60%, 25% and 30%, respectively. The relative lipid peak area at 0.85 ppm in the epicenter, rostral and caudal to the injury site increased two or three fold compared to control rats.

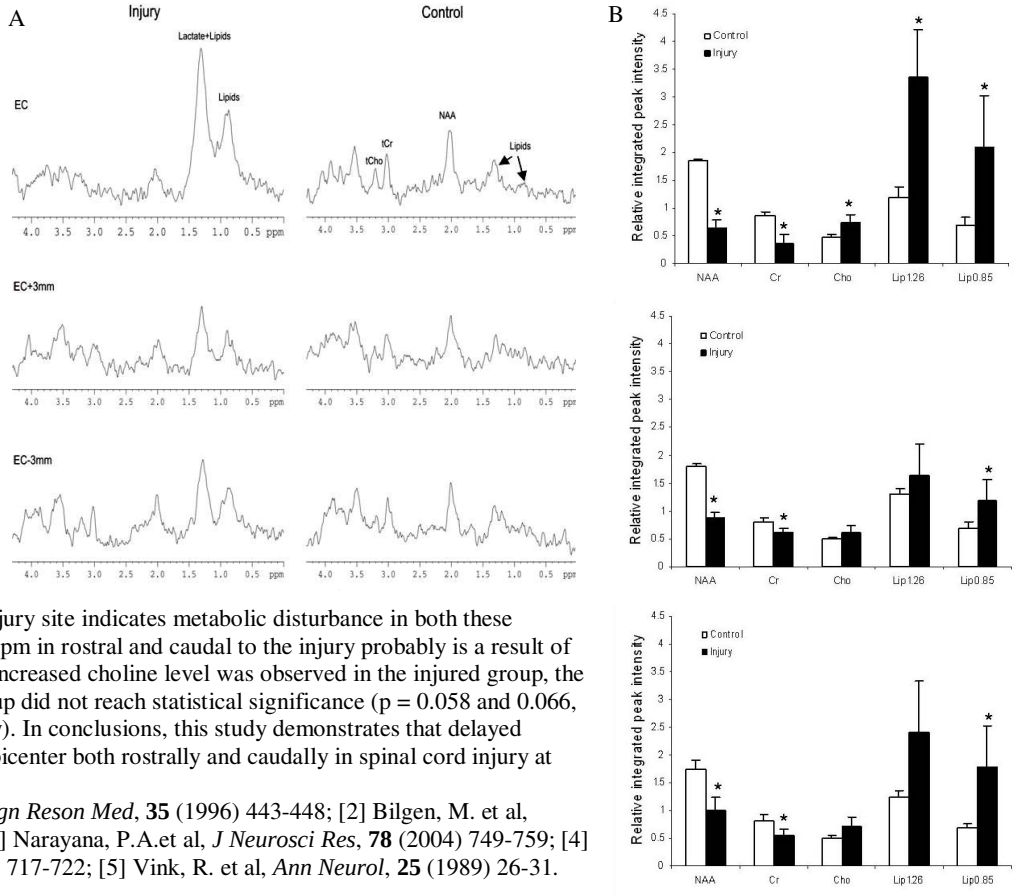

Fig 1. (A) ^{1}H MR spectra acquired from three segments in a control and a spinal cord injured rats at day 14 after injury. EC: epicenter; EC+3mm: rostral to epicenter; EC-3mm: caudal to epicenter; (B) Changes of relative signal intensities of NAA, creatine (Cr), Choline (Cho), Lipid at 1.26 and 0.85 ppm in spinal cord injured and control rats. From top to bottom, epicenter, 3 mm rostral and caudal to the injury site, respectively. *p < 0.05, compared to control group.

DISCUSSION The NAA changes in the epicenter and rostral to the injury site observed in this study agreed well with the previous studies that measured NAA using gas chromatography-mass spectrometry[4]. The reduction in creatine concentration in rostral and caudal to the injury site indicates metabolic disturbance in both these regions. The increased lipid signal at 0.85 ppm in rostral and caudal to the injury probably is a result of demyelination. Although a strong trend of increased choline level was observed in the injured group, the difference between injured and control group did not reach statistical significance (p = 0.058 and 0.066, rostral and caudal to the injury, respectively). In conclusions, this study demonstrates that delayed neurodegeneration occurs away from the epicenter both rostrally and caudally in spinal cord injury at day 14 post-injury.

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