Assessing Demyelination and Remyelination using MRI Texture Analysis

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Introduction

Significant advances have been made in the use of MR imaging to evaluate multiple sclerosis (MS). However, while gadolinium-enhancing activity is a standard measure of inflammatory pathology there is no established MRI strategy to evaluate remyelination or repair. The lack of a marker of remyelination confounds the translation of potential remyelinating agents to clinical practice[1]. MRI texture analysis is a measure of the local characteristic pattern of image intensity. Preliminary data suggest that T2 MRI texture is a sensitive measure of tissue injury and recovery[2,3], and that the degree of coarse texture relates to the severity of pathological damage in MS[4]. The goal of this study was to identify MRI texture footprints in evolving de- and re-myelination induced in mouse spinal cord.

Method

Thirteen 3-month-old, 129/SvEv mice were examined in this ongoing prospective study. Focal demyelination was induced by depositing 1.5μL of a 1% lysolecithin solution, a myelin disrupting agent, into the dorsal column of mouse spinal cord at the level of C5/6. MR imaging was performed before (day 0) and 7, 28, and 35 days after lysolecithin injury using a Bruker 9.4T scanner. According to experience[5], such MRI timepoints correspond to phases of demyelination (day 7) and significant remyelination (days 28 and 35) in histology. MRI protocol included an axial T2 RARA sequence (TR/TE=2500/15 ms, number of averages=12, matrix=256x256, FOV=2x2 cm^2, slice thickness=0.75 mm, 7 slices) conducted around lesion epicenter (C5/6). The mice were anaesthetized during imaging with respiratory rate and body temperature monitored in real time. At each timepoint, lesion texture was calculated in multiple MR images that contain the lesion, which was averaged per mouse for group analysis. Texture in the lateral spinal cord white matter was used as control. MRI lesion area was computed in a similar manner using a semi-automatic algorithm.

Results

Three to 4 mice were imaged at each timepoint. One focal hyperintense lesion was identified in the dorsal column of each spinal cord at C5/6 after injury (Fig. 1). It was the largest at day 7 ($p<0.01$); some extended to the adjacent white and gray matter, which decreased significantly at days 28 and 35 (top right plot). Moreover, the heterogeneity of lesion texture tended to increase during demyelination, which became remarkably finer with remyelination ($p>0.05$) at day 28. Such a fine texture pattern was maintained at day 35; however, the texture was still coarser than that at day 0 (bottom plot). Lesion texture was coarser than the lateral white matter texture ($p<0.05$).

Discussion

This pilot study demonstrates that the coarseness of MRI texture evolves in concordance with the time course of demyelination and remyelination. While this is consistent with the change in lesion area texture analysis further reveals that coarse texture maintains at day 35 compared to day 0, suggesting residual tissue injury despite significant remyelination. This signifies the sensitivity of texture analysis and is corroborated by our earlier results [2,3,4] and ongoing histological analysis (unpublished). MRI texture analysis may be a promising measure of de- and re-myelination, which should benefit the discovery of novel reparative therapies for MS patients.

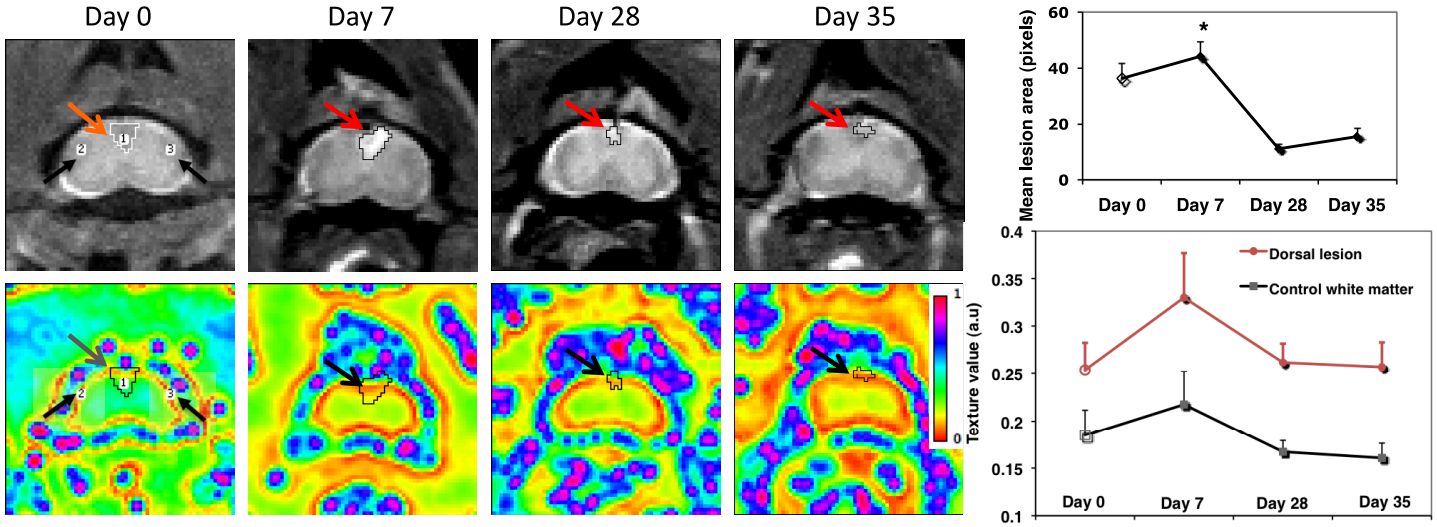

Fig 1: Sample T2 MR images and corresponding texture maps of dorsal lesions (arrows) over time (left panel). Highlights at day 0 reflect normal area (top) or texture (bottom) of dorsal column, and control white matter (black arrows) of the spinal cord. Quantitatively, lesion size (top right panel) decreased more prominently with remyelination than texture heterogeneity (bottom right) which remained coarser than intact myelin (day 0). It also appears that dorsal column was initially coarser than lateral spinal white mater, which is subject to confirmation. Bars are standard error.

References: [1] Fancy SP et al., *Exp Neurol* 2010; 225:18-23. [2] Zhang Y et al., *Neuroimage* 2009; 47:107-111. [3] Zhang Y et al., *Multi Scler J* 2011; 17: 532-40. [4] Zhang Y et al., *Ann Neurol* 2011, under revision. [5] Greg et al., *J Neurosci* 2007: 27: 1812-23.