Improved detectability of experimental allergic encephalomyelitis in pig spinal cord by high b-value q-space DWI

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Synopsis

Experimental allergic encephalomyelitis (EAE) is an immune-mediated inflammatory demyelinating animal model affecting the CNS. In this study nine EAE diseased pig spinal cords and three controls were studied by T_1-, T_2- weighted MRI and high b-value q-space Diffusion MRI (q-space DWI). In all nine EAE diseased spinal cords the q-space DWI maps were different from that of the control maps. Diffusion MRI showed that abnormalities in the EAE diseased spinal cords exceed the areas of the plaques. This study provides the first characterization of the EAE model in pig spinal cords using conventional and high b-value q-space diffusion MRI.

Introduction

Experimental allergic encephalomyelitis (EAE) is an immune-mediated inflammatory demyelinating animal model affecting the central nervous system. EAE pathology has similarities to multiple sclerosis (MS) in humans and its main features are inflammation and loss of the insulating sheath around nerve fibers, known as demyelination. Here, we used T_1-, T_2- and diffusion weighted MRI to study EAE in excised pig spinal cords.

Methods

Tissue samples of control (N=3) and EAE diseased (N=9) pig spinal cords (cervical) were used in this study. The EAE model was induced by immunization with bovine myelin basic protein, complete Freund's adjuvant and *M. tuberculosis*. The experiments were performed on excised spinal cords fixed in Formalin using an 8.4T NMR spectrometer (Bruker, Germany) equipped with a minimaging accessory capable of producing pulse gradients of up to 20 gauss/cm in each of the three directions. Rdio frequency transmission and signal receiving was done using a home built surface coil of 15 x 10 mm. The *in vitro* MRI protocol included T_1-, T_2- and diffusion-weighted images. The transverse T_1- and T_2- weighted images were acquired using the spin-echo imaging sequence with TR/TE of 700/20ms and 3500/50ms, respectively. Diffusion-weighted data were acquired using the stimulated-echo diffusing imaging sequence with the following parameters: TR/TE=1000/46ms, Δ/δ=200/10ms, G_{max}=12 G/cm resulting in b_{max} and q_{max} of $2x10^6$ s/cm^2 and 511 cm^{-1}, respectively. Diffusion was measured perpendicular and parallel to the long axis of the spine. In each experiment 16 b-values were acquired, and the displacement and probability maps were calculated as previously described [1].

Results

Five EAE diseased pig spinal cords showed well defined plaques in the white matter, which were characterized by areas of increased intensity in the T_1-weighted images. The plaques were variable in size and their areas occupied 0.7 – 8.4 % of the transverse area of the spinal cord. T_2-weighted images also identified the lesions and demonstrated lesion heterogeneity in some cases. Figure 1 shows T_1- and T_2-weighted images and a q-space diffusion displacement map (measured perpendicular to long axis of the spine) of a representative control and two representative EAE diseased spinal cords. Figure 1 shows that abnormalities were observed in the q-space DWI displacement maps in EAE diseased spinal cord even in cases where plaques were not detected by the T_1- and T_2-weighted images. The mean q-space displacement in the white matter of the control and "normal appearing white matter" (NAWM) of the EAE diseased spinal cord were 5.80±0.13 μm and 6.39±0.20 μm, respectively. The mean displacement of the EAE diseased spinal cords were different from that of the controls both in the plaques ($p<0.0001$) and in the NAWM ($p<0.0001$) of the EAE diseased spinal cords. The mean displacements for the controls, the plaques and the NAWM of the EAE diseased spinal cords in both orientations are shown in Figure 2.

Discussion

This study provides the first identification of EAE abnormalities in pig spinal cords using a combination of conventional and q-space diffusion MRI. The q-space displacement maps, obtained from DWI, showed abnormalities in the NAWM of the EAE diseased spinal cords that T_1 and T_2-weighted images could not identify.

References

[1] Assaf Y, Mayk A, Cohen Y. Magn Reson Med 2000;44:713-722.

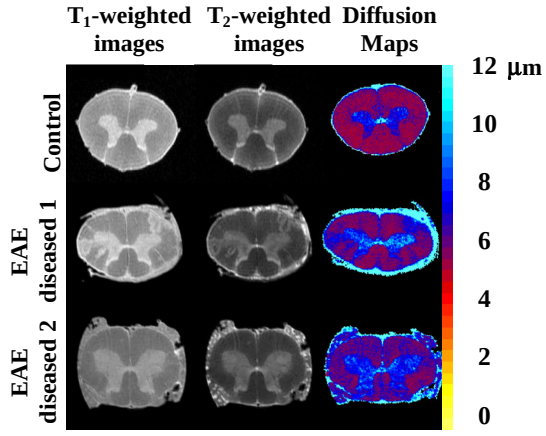

Figure 1. T_1-, T_2-weighted images and displacement maps of one control and two EAE diseased pig spinal cords.

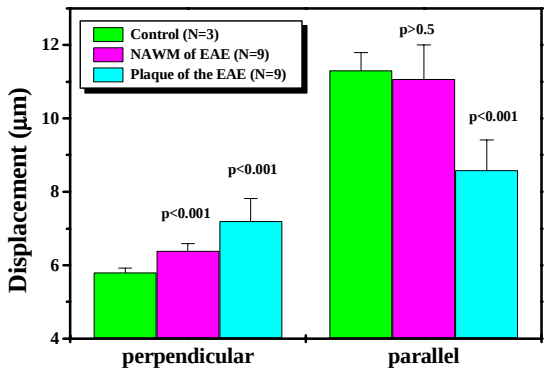

Figure 2. The mean displacement extracted from the q-space DWI maps for the controls, the plaques and the NAWM of the EAE diseased spinal cords both directions.