

Magnetic Resonance Diffraction Diffractogram in the Assessment of Microstructure Sizes of Rat Corpus Callosum during Brain Maturation

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Abstract

Magnetic resonance (MR) diffusion diffractogram has the potential to probe size of the microstructure. However, realization of this method in the biological tissue is challenging. Previously we have established a q-space diffraction technique to measure microscopic length scales in a phantom. In this work we extended the same technique to a more complex biological system, the rat corpus callosum at different ages. We found that T1 and T2 values of the corpus callosum decreased monotonically from day 10 to day 14, and kept rather constant afterwards. In contrast, the microstructure size of the corpus callosum, defined as the reciprocal of the q position at the first node in the diffractogram, decreased monotonically from day 10 to day 84. Slower change in the microstructure size implies that the change in transmembrane water permeability during brain maturation might be slower than the change in myelinization as indicated by T1 and T2. Further investigation of this technique in monitoring the integrity of the cell membrane in diseased brain is warranted.

Introduction

Magnetic resonance (MR) diffusion diffractogram has the potential to probe size of the microstructure [1]. However, realization of this method in the biological tissue is challenging. The difficulty arises partly from the fact that cells are not perfectly aligned and that water molecules exchange between intracellular and extracellular compartments. To the best of our knowledge, no report was made to reveal coherent diffraction patterns from an intact biological organ. Only one report demonstrated the coherence features in erythrocyte suspensions [2]. Previously we have established a q-space diffraction technique to measure microscopic length scales in a phantom [3]. In this work we extended the same technique to a more complex biological system, the rat corpus callosum at different ages. Axons in the corpus callosum pack themselves in the middle portion and align regularly. Myelin sheath of the axon forms a natural barrier to hinder transmembrane water exchange. These features make it an ideal model to realize diffusion diffraction experiment in an intact organ. To test this model with our technique, rats at different ages were studied to demonstrate the evolution of microstructure size of the corpus callosum derived from the diffraction experiment during the process of brain maturation.

Materials and Methods

Seven male Wistar rats with the age at day 7, 10, 14, 21, 28, 56, and 84 were studied, the body weights being 22, 28, 35, 48, 73, 330, and 400 grams, respectively. T1, T2 and diffusion diffraction measurements were performed in each rat. To test the reproducibility, additional five rats at day 84 were recruited for the diffusion diffraction measurement. The data were acquired on a 3T MRI Biospec system (Bruker, Germany). T1WI of rat brains in sagittal and coronal planes were obtained to localize an axial plane parallel to the middle portion of the corpus callosum. After the imaging plane was defined, a spin echo diffusion weighted sequence was performed to obtain q-space diffractograms. Images were acquired with TR/TE = 1500/67 ms, FOV = 22 mm, slice thickness = 1 mm, matrix size = 16, and number of excitations = 8. The diffusion gradients \mathbf{g} perpendicular to the imaging plane were applied with the gradient duration $\delta = 4$ ms and diffusion time $\Delta = 60$ ms. Magnitudes of the diffusion gradients were incremented from 0 to 950 mTm⁻¹, reaching the maximal diffusion sensitivity $b_{\max} = 6 \times 10^4$ s/mm². After a series of diffusion-weighted images were acquired, a region of interest (ROI) covering the middle portion of the corpus callosum was selected, and the echo intensities of the pixels in the ROI were averaged. The measured echo intensities in each spectral-series were normalized by the value of the largest peak in the series. The T1 and T2 values of the corpus callosum were also measured using TrueFISP and MSME sequences [4].

Results and Discussions

At day 7 the coherent diffraction pattern was not observed. It started to appear at day 10 and became obvious as the age increased (Fig. 1). The diffraction pattern was compatible with the envelope squared sinc curves observed previously in our phantom study [3]. From the curves we determined the reciprocal of the q-distance between the center and the first node to indicate the microstructure size of the corpus callosum. During the process of brain maturation, T1 and T2 values of the corpus callosum decreased monotonically from day 10 to day 14, and kept rather constant afterwards (Fig. 2a & 2b). In contrast, the microstructure size of the corpus callosum decreased monotonically from 70 μm at day 10 to 30 μm at day 84 (Fig. 2c & 2d). The microstructure size at day 84 was $30.67\mu\text{m} \pm 3.79 \mu\text{m}$ (N= 5, Fig. 2c & 2d).

The microstructure size measured by the diffraction pattern is greater than the actual size of an axon, approximately 1 μm . The mismatch can be explained in part by the fact that in addition to the intracellular water, there is significant contribution from the extracellular water to the measured signal. The effect of transmembrane water exchange on the diffractogram can be observed during the process of brain maturation. As shown in Figure 1, as the brain matures, increasing integrity of the myelin sheath hinders the water exchange, leading to progressive stretching of the diffraction pattern to the right, thus a decrease in the measured size (Fig. 2c & 2d). Slower change in the microstructure size implies that the change in transmembrane water permeability during brain maturation might be slower than the change in myelinization as indicated by T1 and T2.

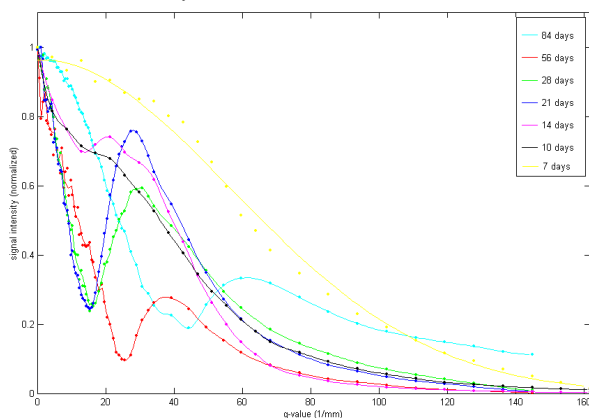


Fig.1 NMR diffusion diffractograms observed in rat corpus callosum at different ages.

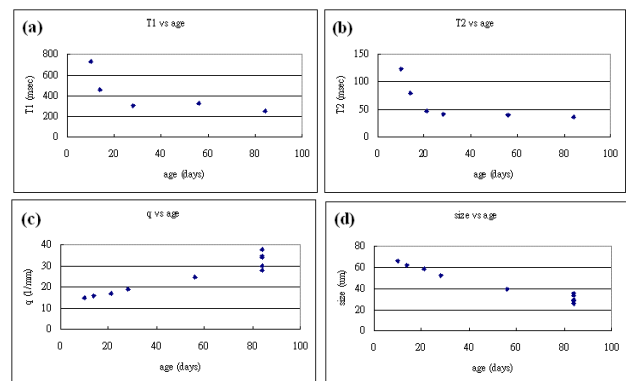


Fig.2 Changes in T1 (a), T2 (b), q-value (c), and microstructure size (d) of the rat corpus callosum during the process of brain maturation.

Conclusions

We have measured the microstructure size of the rat corpus callosum from the coherent features of the q-space diffraction experiment. We have demonstrated progressive change in the microstructure size during brain maturation. The change might correspond to the change in transmembrane water permeability. Further investigation of this technique in monitoring the integrity of the cell membrane in diseased brain is warranted.

References

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