Magnetic Field Correlation Measurement in the Mouse Brain at High Magnetic Field

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INTRODUCTION

Alteration of iron contents in CNS has been implicated in a variety of neurodegenerative pathologies, including Alzheimer's and Parkinson's diseases. Magnetic Field Correlation (MFC) is a recently developed MRI contrast mechanism that is sensitive to the presence of microscopic magnetic field inhomogeneities produced by, for example, the presence of iron in the tissue (1). MFC can provide information of tissue microstructure, which is beyond what is contained in the standard NMR relaxation times, such as T2 and T2*. In this study, we have developed an MFC measurement technique suitable for high magnetic field to investigate alterations in iron contents in the mouse brain of AD models in relation to Aβ plaque pathology.

METHODS

All experiments were performed on a 7 T MR system (SMIS, Guilford, UK). MFC images were acquired using an asymmetric dual spin echo pulse sequence. Imaging parameters were TE/TR = 30/3000 ms, spatial resolution = 200 x 200 x 200 μm, FOV = 25.6 x 25.6 mm, slice thickness 200 μm, matrix = 128 x 128, echo time shift = 0, ±2, ±4, ±6, ±8, and ±9.6 ms. MFC maps were calculated by a quadratic polynomial fitting of log-transformed signal intensities on echo time shifts, based on the relationship between MFC and asymmetric echo shift time (1). Phantoms containing a contrast agent (GdDTPA) and yeast cells in 0.25% agarose solutions were used to compare MFC and T_2 contrasts, since the presence of yeast cells in the media creates microscopic magnetic field inhomogeneities in otherwise homogeneous medium through the exclusion of contrast agent from the cells. To investigate the MFC contrast in the brain at high magnetic field, a total of 7 mouse brains fixed with formalin were imaged.

RESULTS AND DISCUSSION

To demonstrate the difference between MFC and T_2 contrasts, phantoms containing GdDTPA and yeast cells were imaged. Figure 1 shows MFC maps (A) and the corresponding T_2 maps (B) of phantoms containing either a contrast agent + yeast cells or contrast agent (GdDTPA) alone. Phantoms containing both yeast cells (**1a** and **2a**) and GdDTPA showed ~3 times higher MFC values compared to the phantoms without yeast cells (**1b** and **2b**), whereas T_2 values were not altered with the addition of yeast cells. In addition, the dependence of MFC and T_2 contrasts on the concentration of the contrast agent can be seen in **1a,b** (20 mM GdDTPA) and **2a,b** (10 mM GdDTPA). These observations demonstrate the sensitivity of MFC to the microscopic magnetic field inhomogeneities, especially in the water diffusion length scale in a given TE. Figure 2 shows MFC maps and T_2 maps of a fixed non-transgenic mouse brain. Highly enhanced MFC contrasts for iron rich structures including corpus callosum, anterior commissure, and fornix can be seen. Cortex and ventricle showed very low MFC values, which is consistent with very low iron content in those structures. The overall contrast of MFC maps was very similar to the distribution of ferritin binding sites in the mouse brain (3), suggesting MFC contrast is related to the distribution of iron in the brain. Typical MFC values at inter echo time of 30 ms were ~3000 s^{-1} for white matter tracts (corpus callosum, fornix, and anterior commissure), and 300 – 400 s^{-1} for cortex. The observed MFC values in white matter tracts were much higher than those measured at lower magnetic field (e.g. globus pallidus human brain at 3 T ~ 500 s^{-1}), consistent with the quadratic dependence of MFC on external magnetic field, by definition.

In conclusion, we have demonstrated that MFC is sensitive to microscopic inhomogeneities and provides a distinct MR contrast from T_2. In addition, MFC showed pronounced enhancements in the structures with high iron contents, suggesting that MFC imaging is a promising tool for assessment of iron contents in the brain and other organs using MRI.

REFERENCES

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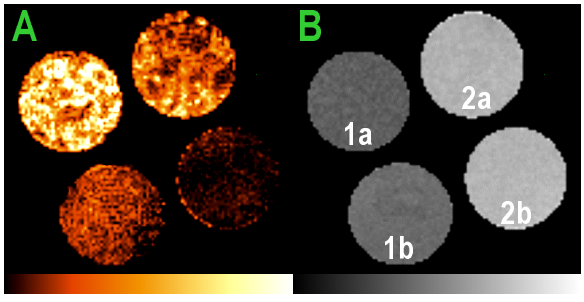

Fig. 1 Comparison of MFC (A) and corresponding T_2 maps (B) of pantoms containing GdDTPA and yeast. Color scale bar: MFC 0- 5000 s^{-1}; gray scale bar: T_2 5 - 35 ms. (**1a**: 20 mM GdDTPA + yeast; **1b**: 20 mM GdDTPA; **2a**: GdDTPA 10 mM GdDTPA + yeast; **2b**: 10 mM GdDTPA)

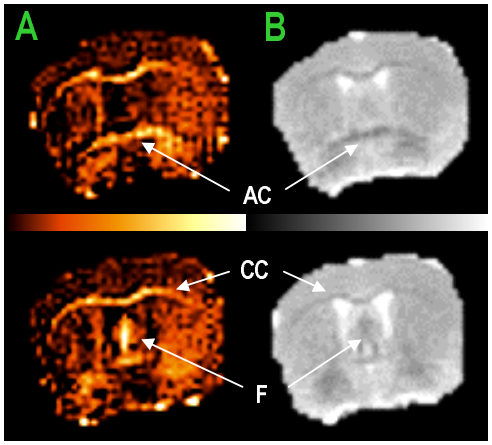

Fig. 2 MFC (A) and T2 maps of a non-transgenic mouse brain Color scale bar: MFC 0- 5000 s^{-1}; gray scale bar: T_2 5 - 35 ms. (AC: anterior commissure; CC: corpus callosum; F: fornix)