Isotropic high-resolution 3D MRI in common marmosets with EAE: A potential marker for the assessment of therapeutic approaches

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Introduction

Experimental allergic encephalomyelitis (EAE) in common marmoset has been shown to present a suitable model for multiple sclerosis (MS) exhibiting common histological subtype II [1]. This model is particularly attractive to study new therapeutic approaches targeting antibody and the complement system. Because the disease is characterized by pronounced clinical heterogeneity, MRI may become an essential tool for intraindividual evaluation of EAE progression and therapy monitoring [2]. So far, however, early lesion detection has been hampered by the use of relatively thick sections of 1 to 3 mm [3]. The purpose of this study was to establish a robust protocol for isotropic high-resolution 3D MRI to characterize EAE progression.

Methods

The animals (n=3) were immunized by intradermal injection of 250 µg recombinant rat myelin-oligodendrocyte glycoprotein (rrMOG). Each animal underwent a MRI examination before immunization, additional measurements were performed about weekly. For MRI animals were anaesthetized, intubated, and maintained under anesthesia by a halothane/N_2O/O_2 gas mixture. MRI studies were accomplished at 2.35 T (Bruker Biospin). For signal detection an elliptical surface coil (40 x 45 mm) adapted to the head of the monkey was used and combined with a Helmholtz coil (100 mm) for signal excitation. T1-weighted (3D FLASH, TR/TE = 17/5.78 ms, α = 25°) and T2-weighted images (3D FSE, TR/TE = 3000/97.01 ms, 16 echoes, interechospacing = 12.28 ms) were obtained with an isotropic resolution of 330 µm resulting in a measurement time of less than 1.5 h. Two animals received an intravenous injection of 0.3 mmol/kg body weight gadolinium-DTPA.

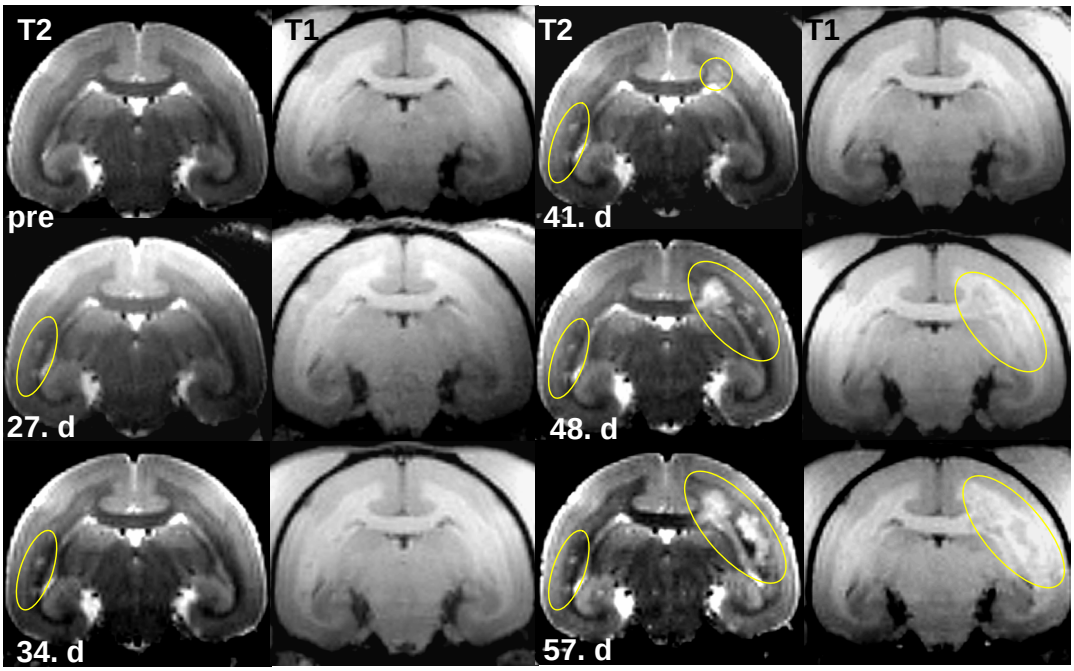

Figure 1: *T2- and T1- weighted images of callitrix jaccus obtained before and weekly after immunization, starting with the time point of the first MRI-detectable lesion in white matter.*

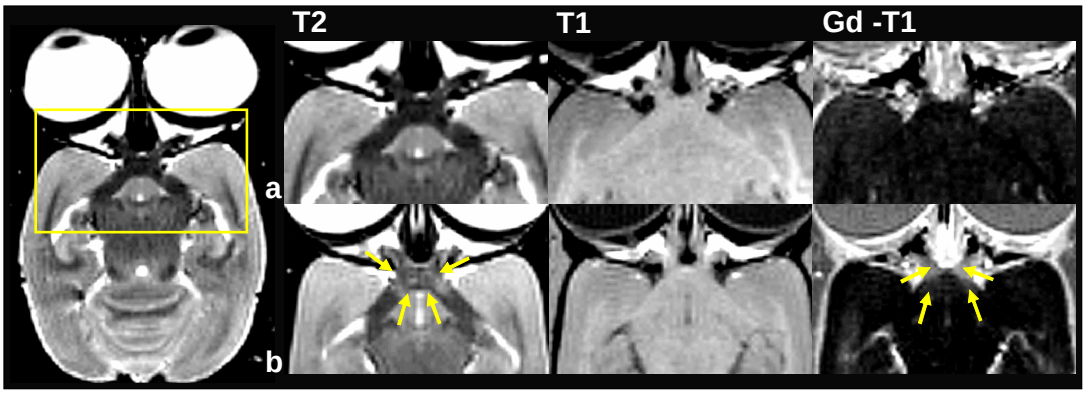

Figure 2: *T2- and T1- weighted images as well as difference images (Gd-T1) of pre- and postcontrast gadolinium-DTPA of normal optic nerve (a) and optic neuritis (b). The MRI section is selected parallel to the optic tract, chiasma, and nerve. Arrows indicate the inflamed nerve regions, which appear hyperintense in T2-weighted and Gd-T1 difference images.*

Results

The animals showed a large heterogeneity with respect to onset and location of the first detectable lesion as well as in terms of disease progression. The lesions appeared as focal hyperintense areas in the white matter in T2-weighted images, whereas respective T1-weighted images not always showed a corresponding signal reduction. Figure 1 illustrates the time course of lesion development of one animal in a selected transverse section. Starting with small focal hyperintensive white matter spots in T2-weighted images, two types of lesions could be differentiated: Persistent lesions with no change in size and intensity and expanding confluent lesions with a corresponding signal decrease in T1-weighted images. In general, a normalization of pathologic contrast or decrease of lesion load was not observed, indicating a continuous degradation during disease progression.

One animal developed a histologically confirmed optic neuritis. Figure 2 shows a slice oriented parallel to the optic tract, chiasma, and optic nerve. In comparison with the unaffected nerve (Figure 2a), optic neuritis (Figure 2b) was indicated by signal increase in the T2-weighted image and by local Gd enhancement illustrated by the post- and precontrast difference image (Figure 2, right).

Conclusion

An isotropic high-resolution MRI protocol was developed as a suitable tool for the assessment of disease progression of EAE in marmosets. Using the present animal model, detection of MRI lesion reduction is expected to become an important marker for therapeutic success.

References

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