# MRI visualization of MOG-induced opticus neuritis in a rat model of EAE

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**Introduction**

Multiple sclerosis is an inflammatory and demyelinating disease of the central nervous system, which is frequently accompanied by neuritis of the optic nerve. The experimental autoimmune encephalomyelitis (EAE) induced by injection of myelin oligodendrocyte glycoprotein (MOG) in female brown Norway (BN) rats is an animal model which commonly results in *nervus opticus* neuritis [1]. The purpose of this 3D MRI study was to develop MRI protocols in order to visualize both the healthy and inflamed optic nerve and to assess the potential of MRI to evaluate new therapeutic strategies

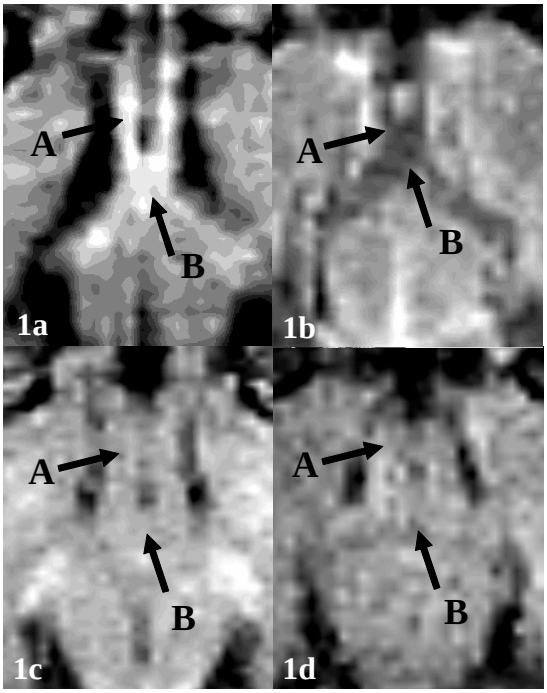


Fig. 1: T1-weighted (left column) and T2-weighted (right column) images of the optic nerve before (top) and 2 week after immunization (bottom). Slice selection was parallel to optic nerve (A) and chiasm (B)

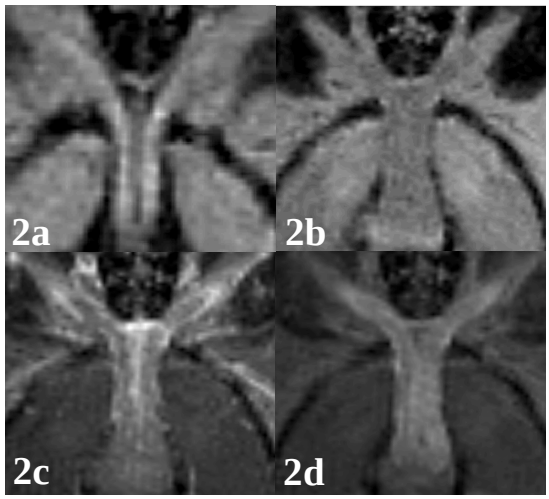


Fig. 2: T1-weighted images (a) before and (b-d) 2 weeks after immunisation (b) without a contrast agent, (c) 10 min after Gd-DTPA, and (d) after additional $MnCl_2$.

**Methods**

Adult BN rats (n = 6) were injected intradermally at the base of the tail with 50 µg of rr $MOG^{IgD}$ emulsified in complete Freund's adjuvant containing 200 µg heat inactivated mycobacterium tuberculosis [1]. At 1, 2, and 3 weeks after immunization T1-weighted (3D FLASH, TR/TE= 17/4.38 ms, $\alpha$ = 25°) and T2-weighted images (3D FSE, TR/TE = 3000 ms/98.75 ms, 16 echos) were obtained at 2.35 T (Bruker Biospin) with an isotropic resolution of 230 µm [2]. The relative short TE for T1-weighted MRI was chosen to ensure opposed-phase conditions for fat and water. Animals were either injected intravenously with Gd-DTPA (0.5 mmol/kg Magnevist™, Schering, Berlin, Germany) or with a $MnCl_2$ solution (7 mg/kg). T1-weighted MRI was started 10 min after injection. In addition, some animals received $MnCl_2$ about 1 hour after Gd-DTPA administration.

**Results**

One week after immunisation T1-weighted and T2-weighted images revealed normal soft issue contrast. However, 2 weeks after immunisation more than 80% of the animals exhibited a signal reduction in T1-weighted images (1c) and a corresponding signal increase in T2-weighted images (1d) of one ore both optic nerves as shown in comparison to images obtained before immunization (1a,b). MRI revealed an increased diameter of the optic nerve. Together with the T2 hyperintensities this can be interpreted as inflammation, matrix loss, and edema which are typical histolopathological findings in this animal model.

In the affected animals Gd-DTPA resulted in an enhancement of the borders of the inflamed optic nerves most likely reflecting a disturbance of the blood-brain barrier (2c). At 48 h after injection, Gd-DTPA was almost completely washed out (3a). Interestingly, manganese enhanced the central parts of the optic nerve, probably reflecting influx of manganese ions into the cytoplasm of the nerve fibers. The manganese enhancement was detectable 10 min after i.v. injection (2d) and was still persistent 48 h (3b) as well as 1 week after injection and allowed for a clear delineation of the optic nerve. Thus, both methods may complement each other by depicting different parts of the optic nerve. Increased manganese enhancement of the inflamed optic nerve may reflect the increased penetration of manganese through a disrupted blood brain barrier or increased influx of bivalent cations like calcium and manganese into neurons affected by inflammatory lesions.

**Conclusion**

Despite the large number of MRI studies of EAE, only few focused on the *nervus opticus*. This study demonstrated that adapted MRI protocols result in a robust visualization of both healthy and inflamed optic nerves. In particular, neuritis was clearly detectable by decreased T1 and increased T2 MRI signals at 230 µm isotropic resolution. While Gd-DTPA mainly contrasted the borders of the affected optic nerves, manganese stained the central parts of the optic nerve possibly showing the cytoplasm of the neurons. Further studies will correlate MRI data with electrophysiological methods such as measurement of visual evoked potentials.

**References**

[1] Meyer R et al, 2001:J Neurosci 21, 6214-6220.
[2] Natt O et al, 2002, J Neurosci Methods 30;120(2):203-9.

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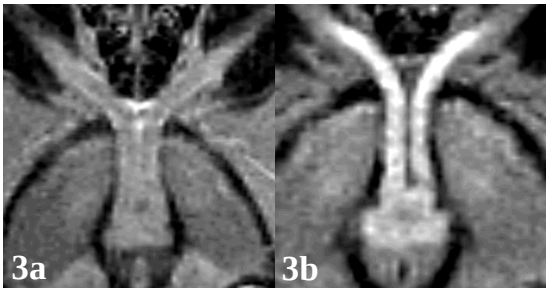


Fig. 3: T1-weighted images (a) 48 h after Gd-DTPA and (b) 48 h after Gd-DTPA and additional $MnCl_2$