Does white matter, grey matter or lesion multi-component relaxation differ between neuromyelitis optica and multiple sclerosis brain?

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Background. Neuromyelitis optica (NMO) and multiple sclerosis (MS) are demyelinating diseases of the central nervous system with clinical resemblance. However, the discovery of an antibody against the aquaporin-4 water channel in NMO has revealed that NMO has pathological characteristics distinct from those in MS, and likely a different mechanism of demyelination[1]. Illustrating these differences with MRI has proven challenging. Recently we applied a rapid approach to whole-brain multi-component relaxation imaging to investigate the fraction of fast-relaxing signal (f_M, thought to be linked to myelin) in NMO and MS; we demonstrated that MS patients had a greater proportion of normal appearing white matter (NAWM) with significantly reduced f_M values than NMO patients, and that this reduction correlated with clinical disability in MS but not in NMO[2]. In this study, we hypothesized that this effect of greater damage in MS normal appearing tissue would extend to grey matter (GM), but that NMO lesions would be more severe than MS lesions, and that this would be reflected in respective average f_M values. As NMO is a disease linked to changes in water, we also investigated T1, which is strongly influenced by total water content.

Methods. The study incorporated 16 NMO patients (mean age = 48 years (range 20-76); median Expanded Disability Status Scale (EDSS) = 4 (range 2-7.5); mean disease duration = 72 months (range 12-186); median lesion volume = 1748 mm^3 (range 17 – 16625)), 15 relapsing remitting MS patients (mean age = 43 years (range 22-62); median EDSS = 2 (range 0.5-5); mean disease duration = 93 months (24-240); median lesion volume = 5969 mm^3 (range 634 – 29046)) and 17 healthy controls (mean age = 49 years (range 19-76)). A Siemens Verio 3T scanner with a 1.7mm isotropic resolution was used to acquire whole-brain mcDESPOT[3] MRI data of the subjects. Conventional images included T1W (for segmentation) and FLAIR (for lesion identification) images. NAWM and GM masks were created with the FSL tool SIENAX[4] using lesion filling. Three-pool mcDESPOT analysis[3] was employed to obtain voxel-wise maps of f_M and T1. Non-parametric statistics were used to determine difference between the groups with $p<0.05$ considered significant.

Results. *f_M (FIG 1):* Compared to healthy controls, f_M was significantly decreased in NMO NAWM (on average 4.7% reduced, $p = 0.02$) as well as in MS NAWM (6.1%, $p = 0.0008$) and MS GM (4.5%, $p = 0.02$) (Fig 1). NMO lesions showed a trend to have higher f_M values than MS lesions (9.2% higher in NMO than MS, $p = 0.06$). *T1 (FIG 2):* NAWM T1 was significantly increased compared to controls for NMO (3.9%, $p = 0.02$), and MS (5.3%, $p = 0.0004$). No significant differences were found for T1 in GM or lesions.

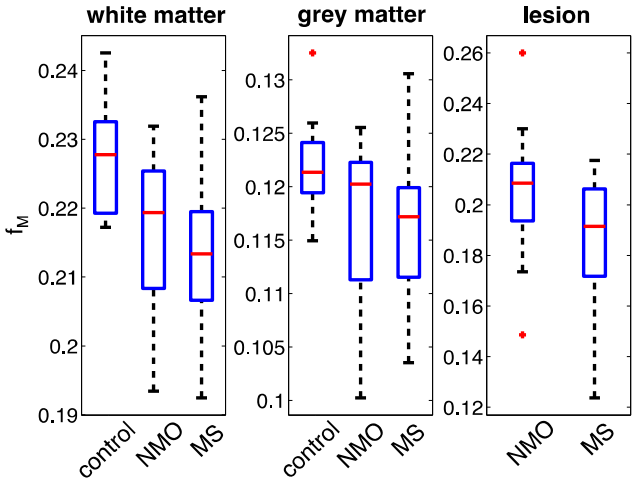

FIG 1: Boxplots illustrate significantly reduced f_M compared to controls for NMO NAWM, and MS NAWM & GM. f_M was higher in NMO lesions than MS though it did not reach significance (p=0.06).

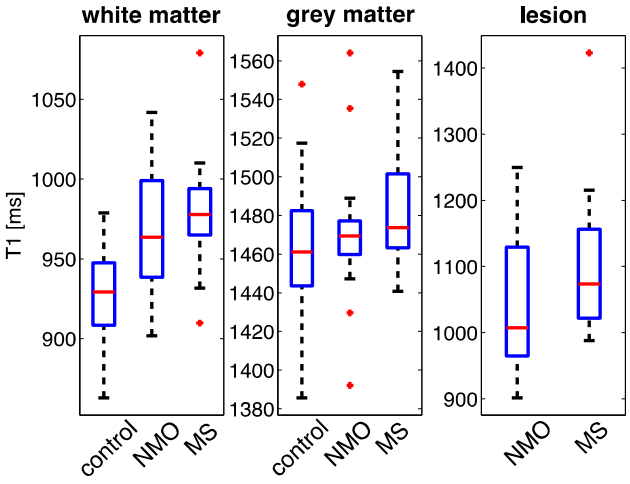

FIG 2: Boxplots illustrate significantly longer T1 in both NMO and MS NAWM. No significant differences were found in GM or lesion.

Discussion and Conclusions. Both NMO and MS exhibited a greater difference from controls in NAWM than in GM, suggesting that damage is more acute in NAWM than in GM in both diseases. While neither f_M nor T1 demonstrated a significant difference between MS and NMO in average values in any tissue type, MS consistently demonstrated lower mean f_M and higher mean T1 values. This is consistent with our hypothesis of more diffuse damage in normal appearing tissue in MS, but the interesting finding of greater change in MS lesions than NMO lesions suggests that the mechanism driving the severe clinical symptoms in NMO is not likely to be greater demyelination in lesion.

References. [1] Morrow et al. J Neuroopthamol 2012;32:154. [2] Gorodezky et al. Proc. ISMRM 2013; 1084. [3] Deoni et al. MRM 2013;70:147. [4] Smith et al. Neuroimage 2002;17:479.

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