Neuromyelitis optica spinal cord has increased T1 and decreased myelin water fraction

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BACKGROUND: Neuromyelitis optica (NMO) is an autoimmune disease characterised by demyelination of the optic nerve and the spinal cord. Clinically, NMO strongly resembles multiple sclerosis (MS), but it has recently been shown that a specific water channel is affected in NMO and the mechanism of demyelination differs[1]. In brain, conflicting studies have not found clear differences in MRI measures between diseases. Differences in pathology may be more evident in the spinal cord, which is highly affected in NMO. We hypothesized that NMO spinal cord would show changes in myelin and total water content compared to healthy controls. Multi-component driven equilibrium single pulse observation of T1 and T2 (mcDESPOT) is a rapid high-resolution multi-component relaxation imaging technique that affords us the opportunity to study diffuse water changes[2]. It can be used to estimate the myelin water fraction (f_M) as well as T1, which is related to total water content. mcDESPOT in spinal cord has been successfully demonstrated in healthy controls and MS in previous studies[3,4]. *The goal of this study* was to determine whether differences in myelin or total water content, as measured with mcDESPOT, can be detected between NMO and MS in cervical spinal cord.

METHODS: *Subjects:* 14 MS patients (mean age 41, range 22-62; Expanded Disability Status Scale (EDSS) median 2, range 0.5-5), 14 NMO patients (mean age 47, range 28-76; EDSS median 4, range 2-7.5) and 17 healthy controls (mean age 49, range 19-76) were included in the study. *MRI Data Acquisition:* mcDESPOT MRI data were acquired on a Siemens Verio 3T scanner over the whole cervical cord with 0.9x0.9x1.8mm voxels (22 minutes) as well as whole brain with 1.7mm isotropic voxels (14 minutes). The mcDESPOT data set consisted of a series of spoiled gradient echo (SPGR) and balanced steady state free procession (bSSFP) scans each acquired over a range of flip angles[2]. An inversion recovery-prepared SPGR scan was also acquired for correction of B1 inhomogeneity effects[5], and 2 phase-cycling patterns (0° and 180°) were acquired for the bSSFP data to correct for off-resonance effects[5]. *MRI Data Analysis:* Three-pool mcDESPOT processing was performed to derive voxel-wise f_M and T1 maps for each participant[6]. The spinal cord was extracted using the fsl tool FAST[7] on a 3D T1-weighted SPGR image from the mcDESPOT data set (flip angle=9°). f_M and T1 values were averaged across the entire cervical spinal cord, and across all brain tissue. *Statistics:* Non-parametric statistics were used with p-values < 0.05 considered significant.

RESULTS: Compared to healthy controls, cervical spinal cord f_M was significantly reduced in NMO (on average 12.5% reduction, p=0.007) and MS (9.8%, p=0.02) (FIG 1). T1 maps revealed an increase in total water compared to control cervical spinal cord in both NMO (10.6%, p=0.009) and MS (6.7%, p=0.06), although it only reached significance in NMO (FIG 2). Contrarily, in brain whole tissue no significant difference between the three groups was found (p-values: f_M: 0.08; T1: 0.4).

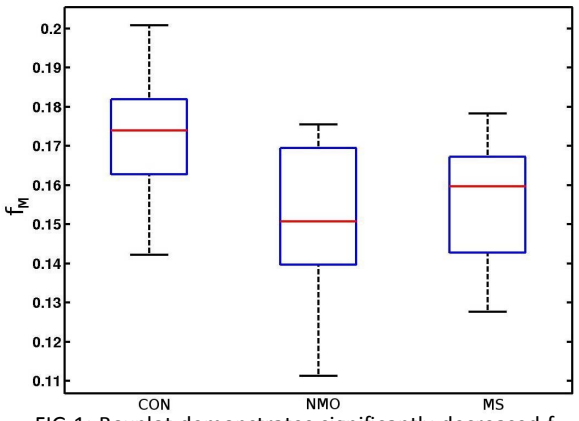

FIG 1: Boxplot demonstrates significantly decreased f_M in both NMO and MS cervical spinal cord compared to healthy controls.

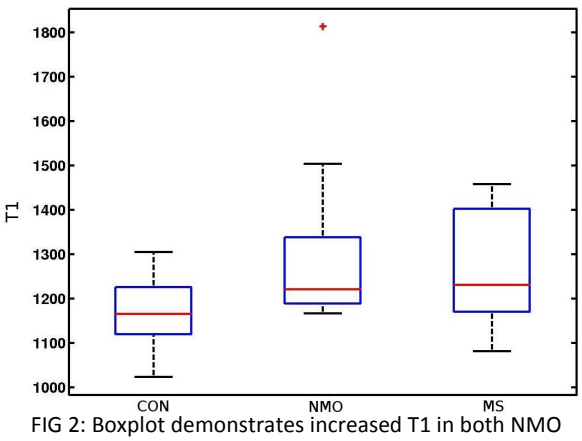

FIG 2: Boxplot demonstrates increased T1 in both NMO and MS cervical spinal cord compared to healthy controls, only reaching significance in NMO.

DISCUSSION AND CONCLUSIONS: Surprisingly, the application of mcDESPOT to NMO and MS patients showed little difference in f_M or T1 between NMO and MS. Our results are not likely to be driven by differences in lesion burden between groups as nearly all patients had two or more lesions in spinal cord, and there was no significant difference in spinal cord volume (p=0.2). Thus our findings suggest that differences between MS and NMO spinal cord pathology are not reflected by myelin or total water content changes. Comparing spinal cord whole tissue with brain whole tissue, it is easier to detect differences in myelin and total water content between controls and MS or NMO in spinal cord than in brain.

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