Distinguishing Neuromyelitis Optica from Multiple Sclerosis with Myelin Water Imaging

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Background: Neuromyelitis optica (NMO) is a demyelinating disease of the central nervous system that resembles multiple sclerosis (MS) but has distinct pathological features and is likely a separate disorder. A method of clinical differentiation has significant importance since prognosis and optimal treatment for these two diseases diverge; however differentiation can be difficult due to clinical similarities. Multi-component relaxation imaging allows interrogation of the myelin water fraction (MWF), a measure related to myelin content. Multi-component driven equilibrium single pulse observation of T1 and T2 (mcDESPOT) is a high-resolution whole-brain multi-component relaxation imaging technique that affords us the opportunity to study diffuse myelin changes throughout the brain in a clinical setting. In this work, we applied mcDESPOT imaging to cases of both NMO and MS in comparison with healthy controls as a novel marker of demyelination with the aims of furthering understanding of pathology and aiding in differentiating between these diseases clinically.

Methods: Fifteen people with relapsing remitting MS (mean age = 43 years (range 22-62); median Expanded Disability Status Scale (EDSS) = 3.5 (range 0.5-5), mean disease duration = 93 months (range 24-240)), 15 people with NMO (mean age = 48 years (range 20-76); median EDSS = 4 (range 2-6), mean disease duration = 71 months (range 12-186)) and 17 healthy individuals (mean age = 49 years (range 19-76)) were included in the study. Whole-brain mcDESPOT MRI data were acquired on a Siemens Verio 3T scanner with a 1.7mm isotropic resolution in less than 14 minutes. mcDESPOT processing was performed to derive voxel-wise MWF maps for each participant. To compare individual patient MWF maps to the healthy population, a normative 3D ‘atlas’ representing the MWF mean and standard deviation was created from a population of age-matched healthy controls. The healthy MWF maps were non-linearly aligned to the MNI standard space template using a multi-scale approach, and averaged. To restrict our analysis to consistent anatomical voxels (those with a high correspondence between individuals, i.e., white and deep grey matter), voxels with a MWF CoV across subjects of greater than 75% were excluded. Patient MWF maps were non-linearly aligned to the atlas (via registration to the MNI template) following lesion masking. Finally, for each voxel, a Z-score was calculated comparing the individual patient MWF values to the control group distribution. Voxels with a Z-score of less than -4 were considered significantly reduced.

Results: MS patients had a greater volume (p<0.05) of normal appearing tissue with significantly reduced MWF values (see Figure 1). The volume of significantly reduced MWF values correlated significantly with EDSS for MS (R=0.6, p<0.02) but not for NMO (R=-0.3, p=0.2) (see Figure 2).

Conclusions: mcDESPOT demonstrates significantly greater change in normal appearing MS brain tissue than NMO brain tissue, with a strong relationship between this change and clinical disability for MS that is lacking in NMO. This supports differences in pathological mechanisms of disability in these two diseases, and may provide a significant aid in clinical differentiation, particularly for patients at higher EDSS values.