

## Lesions distribution and normal appearing white matter in demyelinating diseases

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**Background:** previous non-conventional imaging studies comparing Neuromyelitis Optica Spectrum disorder (NMOSD) and Multiple Sclerosis (MS), has yielded differing results, partly explained by cohort heterogeneity (i.e. antibodies status). No studies are available in MOG-Ab disease (MOGAD).

**Objectives:** we compared in MOGAD, NMOSD and MS: brain volume, lesion-load, and tissue damage (in and outside of lesions) using diffusion-measures (fractional anisotropy-FA, mean diffusivity-MD).

**Methods:** 18 relapsing-remitting MS, 18 MOGAD, 19 NMOSD-aquaporin-4 positive (NMOSD-AQP4) and 18 HC were included. We performed 3T structural-brain-MRI and multi-shell DWI. The brain volume was calculated using SIENAX and FA-voxel-wise statistical analysis was carried out using Tract-Based-Spatial-Statistic (TBSS), both part of FSL. Lesions were segmented manually on an axial-FLAIR.

### Results:

MS had the highest lesion-load compared to NMOSD-AQP4 and MOGAD ( $p < 0.0001$ ), and lesions increased with disease duration, not seen in the other diseases.

Brain volume was not significantly abnormal in any group compared to HC ( $p = 0.08$ ), although there was a trend for lower volumes in NMOSD-AQP4 and MS compared to MOGAD.

Lesional-FA was not different between groups, but lesional-MD was higher in the three diseases compared to HC ( $p < 0.0001$ ).

The normal-appearing-white-matter (NAWM)FA was lower in NMOSD-AQP4 compared to MOGAD ( $p < 0.05$ ) and not significantly different compared to HC. NAWM-MD was similar between diseases and HC.

Between lesions and NAWM; FA was different in MOGAD ( $p = 0.008$ ), while MD was different in all the three diseases (NMOSD-AQP4,  $p = 0.0001$ ; MOGAD,  $p = 0.002$ ; MS,  $p < 0.0001$ ).

The FA-voxel-wise comparison analysis showed reduced NAWM in NMOSD-AQP4 compared to HC and MOGAD, and in MS compared to HC. There is no difference between MOGAD and HC.

**Conclusions:** MOGAD showed normal brain volume, NAWM integrity and fewer lesions, compared to other diseases. FA is able to discriminate between lesional and non-lesional area only in MOGAD. The lack of lesion-load increase with disease duration is a pointer towards antibodies-mediated disease.