Investigating the Association of Cognition with Water and Myelin Content in Neuromyelitis Optica Spectrum Disorder

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Background: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune inflammatory disease of the central nervous system that affects primarily the optic nerves and spinal cord but can also cause focal brain inflammation. Magnetic resonance imaging (MRI) studies have demonstrated abnormalities in cerebral normal-appearing white matter (NAWM) and the thalamus in NMOSD that may contribute to cognitive impairment. However, as findings have been inconsistent, NAWM and subcortical pathology and associations with cognition in NMOSD remain unclear. As such, more investigations using quantitative metrics of myelin content are warranted. Myelin water imaging (MWI), an MRI technique that quantifies myelin content and integrity through myelin water fraction (MWF), can identify subtle myelin changes not visualized on conventional MRI and allow for better characterization of NMOSD brain pathology. Quantitative T_1 measurements can also be extracted to evaluate changes in myelin and water content.

Objective: To investigate cerebral NAWM and thalamus abnormalities and association to cognition in NMOSD participants compared to healthy controls (HC) using MWI.

Methods: 19 NMOSD participants and 21 age- and sex-matched HC were scanned on a 3.0T MRI scanner utilizing a multi-component Driven Equilibrium Single Pulse Observation of T_1 and T_2 (mcDESPOT) protocol. Tissue-compartment and thalamic volumes (normalized to intracranial volume), T_1 relaxation time, and MWF were reported. 12 NMOSD participants underwent the Symbol Digit Modalities Test (SDMT) for evaluation of cognitive performance. Group comparisons were performed using Student's t-test. The association between thalamus metrics and SDMT score was assessed using multiple regression analysis with age as a covariate.

Results: Compared to HC, NMOSD participants had higher T_1 (+2.15%, p=0.024) and lower (though not significantly) MWF (-2.96%, p=0.068) across NAWM. The NMOSD group had reduced (though not significantly) thalamic volumes compared to HC (-5.35%, p=0.084). There was no significant difference in thalamus MWF (p=0.457) or T_1 (p=0.636) between NMOSD and HC groups. There was a significant association of SDMT score with thalamus MWF (R=0.602, p=0.0226) and with thalamus T_1 (R=-0.772, p=0.002).

Conclusion: NAWM in NMOSD reveals diffuse abnormalities with increased water content (T_1) and potentially diffuse demyelination (MWF, T_1) suggestive of a disease process that is overlooked by focal inflammation. Additionally, diffuse thalamic pathology including increased water, demyelination, and atrophy are strong predictors of cognitive performance in NMOSD. Finally, MWI can detect slight changes in myelin content and integrity unlike traditional MRI, which can provide new insight into NMOSD brain pathology.