Inflammation, axonal loss and trans-synaptic degeneration affect the visual system in multiple sclerosis – a preliminary 7 Tesla MRI and optical coherence tomography study.

Tim Sinnecker1, Timm Oberwahrenbrock1, Hanna Zimmermann1, Jan Dör2, Caspar Pfue1,2, Lutz Harms2,3, Thoralf Niendorf4,5, Alexander U Brandt1,2, Friedemann Paul1,2, and Jens Wuerfel1,6

1NeuroCure Clinical Research Center, Charité - Universitätsmedizin Berlin, Berlin, Berlin, Germany, 2Clinical and Experimental Multiple Sclerosis Research Center, Charité - Universitätsmedizin Berlin, Berlin, Berlin, Germany, 3Department of Neurology, Charité - Universitätsmedizin Berlin, Berlin, Berlin, Germany, 4Experimental and Clinical Research Center, Charité - Universitätsmedizin Berlin and Max Delbrueck Center for Molecular Medicine, Berlin, Berlin, Germany, 5Berlin Ultrahigh Field Facility (B.U.F.F.), Max Delbrueck Center for Molecular Medicine, Berlin, Berlin, Germany, 6Institute of Neuroradiology, Universitätsmedizin Göttingen, Göttingen, Niedersachsen, Germany

Introduction: Axonal loss is common in multiple sclerosis (MS)1,2 and detectable from the earliest clinical stages3,4 However, the underlying neurodegenerative pathomechanisms in MS have not been fully understood, a factor that impedes the development of neuroprotective drugs. Today, the optic radiation - a structure highly susceptible to MS related damage5 – can be visualized with near microscopic resolution in vivo by ultrahigh field MRI at 7 Tesla (7T). We studied the extent of focal inflammatory damage within the optic radiation in clinically isolated syndrome (CIS) and MS patients. Our findings were correlated with atrophy of the optic radiation, retinal nerve fiber layer thinning measured by optical coherence tomography (OCT), visual evoked potentials (VEP), and functional acuity contrast testing (FACT).

Methods: We investigated 31 patients (13 women, mean±SD age 36±8 years, including 8 CIS and 23 MS patients) and 10 matched healthy controls (HC) using 7T MRI (Siemens Magnetom, Erlangen, Germany), OCT and FACT. Our MRI protocol included T2*-weighted FLASH as well as T2-weighted TIRM sequences. Transmission and reception was performed using a 1TX/24RX brain coil (Nova Medical, Andover, USA). We quantified the lesion volume affecting the optic radiation (ORV), and the optic radiation thickness (ORT). A subset of 17 patients additionally underwent VEP examination.

Results: High spatial resolution 7T MRI revealed neuroinflammatory lesions affecting the optic radiation in 25 of 31 patients (figure 1). Statistical analysis revealed a strong association between focal damage of the optic radiation as indicated by ORV and thinning of the optic radiation as indicated by ORT (figure 2; p<0.001). Furthermore, ORV correlated inversely with the retinal nerve fiber layer thickness (p<0.001), and we observed a dependency between ORV and delayed VEP latency (p=0.029). Regarding visual disability, we observed an association between ORV and impaired visual perception as indicated by FACT under photopic (p=0.016) and mesopic (p=0.012) conditions as well as visual acuity (p=0.005).

Conclusion: Damage of the optic radiation is a frequent finding in MS often causing visual disturbances. The high incidence might be partially explained by the anatomical congruency of the optic radiation passing through a predominantly affected area of MS related demyelination, namely the periventricular white matter. In alignment with recent reports6-9, the significant correlation between focal damage of the optic radiation and retinal nerve fiber layer thinning in MS suggests retrograde trans-synaptic degeneration. Furthermore, acute inflammatory lesions within the optic radiation should be considered as a differential diagnosis of acute optic neuritis in patients with bilateral visual disturbances.