High resolution MR elastography reveals retrograde thalamic tissue degradation in Neuromyelitis optica

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Target audience: Physicians interested in new clinical imaging markers for neuroinflammation and demyelination.

Purpose: Neuromyelitis optica (NMO) or Devic's Syndrom is classified as an autoimmune inflammatory disease of the central nervous system consisting of recurrent inflammation and demyelination of the spinal cord and the optical nerves. It is known from clinical and preclinical MR elastography (MRE) studies that neuroinflammation and demyelination are associated with marked softening of brain tissue (1-3). Here we test if high resolution multifrequency MR elastography (MMRE) (4) can localize the viscoelastic response of the brain to NMO.

Methods: 15 patients with NMO (mean age 48.0 years, range 29 - 68 years, 7 females) and 17 age and sex matched healthy controls (HC) were investigated by multifrequency magnetic resonance elastography (MMRE). The experiments were conducted on a 3T MRI system (Siemens Trio) using a single-shot EPI-based MRE sequence (5). Full 3D wave fields were acquired at 7 mechanical frequencies (25 to 60 Hz, 5 Hz increments) in 15 contiguous slices and by an image resolution of 1.9×1.9×1.9 mm^3 (FoV: 190x160 mm, TR: 2980 ms, TE: 71 ms, 8 dynamics of the wave cycle). For parameter reconstruction, multifrequency dual elasto visco (MDEV) inversion was applied as described in (4). By this method, two independent parameter maps are obtained, which represent the magnitude and the phase angle of the complex shear modulus, $|G^*|$ and φ, respectively. We used ANTs (6) for registering all parameter maps to standard brain atlases in order to better visualize regional effects of the disease.

Results: Fig.1 shows three representative slices of T2-weighted standard brain maps along with elastograms ($|G^*|$-maps) and difference maps $\Delta|G^*|$ obtained by registration and averaging of individual elastograms. It is clearly visible that $|G^*|$ is reduced in patients within the entire brain parenchyma excluding ventricles (ALL, -10%, p=0.006) with accent on thalamic region (TH, -19%, p=0.004) and white matter (WM, -3%, p=0.008) according to the ROI's delineated in Fig.1. No effect was observed in the occipital region (OC) and in the frontal region (FR). The phase angle modulus φ was only significantly altered when considering the whole brain parenchyma (ALL, -6%, p=0.030). Fig.2 compares group averaged $|G^*|$-values between patients and controls in the regions shown in Fig.1. $|G^*|$-ALL correlated with the presence of AQP-4-Ab (R=0.612, p=0.015), a serum marker for NMO.

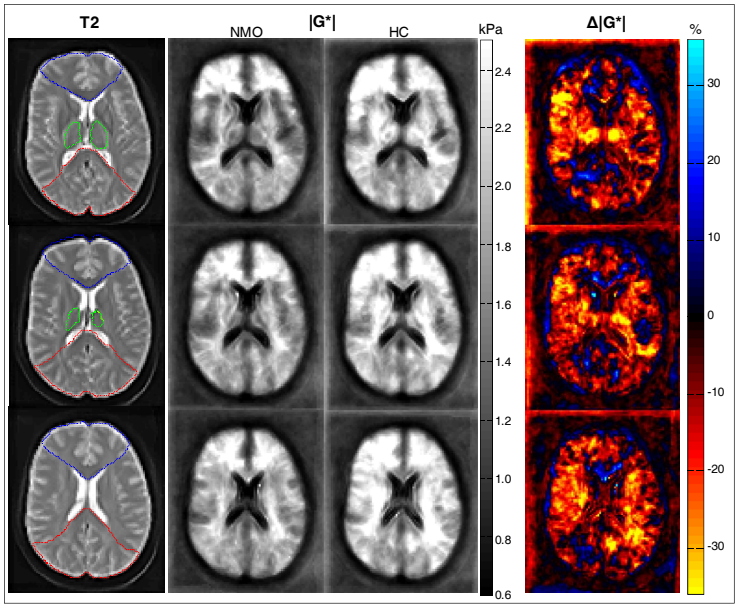

Fig.1: Normalized viscoelasticity changes in brain tissue due to NMO: The magnitude modulus |G*| clearly decreases from patients to healthy controls (HC) as represented by the relative ratio maps $\Delta|G^*|$. The regions in the T2-maps illustrate the delineated ROI's: frontal (FR, blue), occipital (OC, red) and thalamus (TH, green). The white matter ROI was manually segmented.

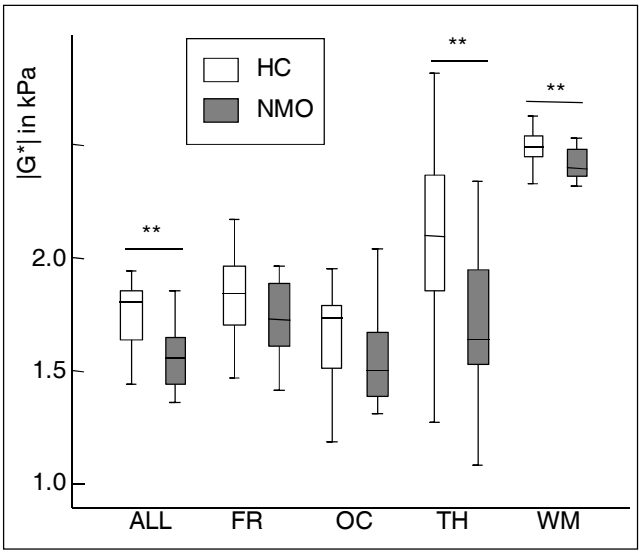

Fig.2: Group averaged $|G^*|$-values in patients and healthy controls (HC) averaged over the ROI's shown in Fig.1. **p<0.01, *p<0.05

Discussion: Despite scientific advances in the classification and understanding of NMO since its first description in 1870 by Thomas Clifford Allbutt and its distinction from Multiple Sclerosis following the identification of the AQP4-Ab (7), little is known about the pathomechanisms of the disease. Beyond the affection of the myelon and optical nerves typically identified by lesions in the spinal cord region, disseminated neurodegenerative processes as revealed by volumetric changes and cognitive deficits have been considered as part of the NMO pathology. The present study supports the hypothesis of a widespread cerebral neurodegeneration in NMO and provides further details about regional effects of the disease. The pronounced involvement of the thalamus and WM in NMO indicates retrograde effects due to neuronal cell loss through reoccurring myelitis.

Literature: (1) Schregel et al. PNAS 2012;109:6650-5 (2) Riek et al. NeuroImage: Clinical 2012;1:81-90 (3) Streitberger et al. PLoS One 2012;7(1):e29888. (4) Guo et al. PLoS One 2013;8(8):e71807. (5) Braun et al. Neuroimage, 2014;90:308-14. (6) Avants et al. Neuroimage 2011;54:2033-2044 (7) Lennon et al. Lancet 2004;364:2106-12.