Brain softening - a hallmark of neurodegeneration: Cerebral MR elastography in patients with supranuclear palsy and idiopathic Parkinson's disease.

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Background: Neurodegenerative disorders are defined by a progressive loss of function and structure of neurons, synaptic alterations and inflammation. The loss of neurons and oligodendrocytes results in gross atrophy of affected brain regions that can be assessed by volumetric MRI, diffusion weighted MRI or MR elastography (MRE). In particular, MRE [1] has been proven sensitive to disseminated degradation of brain tissue due to physiological aging [2], Multiple Sclerosis (MS) [3], Alzheimer's disease [4], and Hydrocephalus [5].

Problem: The differential diagnosis of neurodegenerative Parkinson syndromes is clinically challenging. Although routine T1- and T2-weighted MRI can help to exclude symptomatic Parkinsonism, it is of limited use for detecting and discriminating predominantly neurodegenerative Parkinson syndromes.

Objective: We used 2D multifrequency MRE as well as 3D MRE to assess the sensitivity of cerebral viscoelastic properties for discriminating two neurodegenerative disorders with overlapping clinical presentation, but different underlying neuropathology - namely progressive supranuclear palsy (PSP) and idiopathic Parkinson's disease (PD) – in comparison to healthy controls.

Methods: The study cohort comprised 52 participants including 18 patients with mild to moderate PD (6 female; mean age 63 years), 16 patients diagnosed with PSP (8 female; mean age 70 years), and 18 age-matched healthy controls (8 female; mean age 64 years). After routine clinical MRI, two additional MRE experiments were conducted, 2D multifrequency MRE (MMRE) [2,3,5] and 3D MRE [4] applying the identical mechanical actuator - a head cradle attached to a distant loudspeaker. MMRE was used to measure the shear modulus μ and the powerlaw exponent α, according to the springpot model, in the frequency range between 25 and 62.5 Hz. 3DMRE was used to reconstruct the complex shear modulus represented by the magnitude |G*| and the phase angle ϕ at 50 Hz harmonic excitation. By 3DMRE normalized maps of |G*| and ϕ could be calculated in order to compare regional effects of PD and PSP on the brain's viscoelastic properties.

Results and Discussion: Among PD cases, eight patients presented with an akinetic-rigid phenotype, three were tremor dominant, and seven suffered equally from both symptoms. Among PSP cases, eight met the criteria for Richardson subtype, and eight for the Parkinson subtype of PSP. Clinical severity in PD and PSP can be assessed by motor part of UPDRS as well as the Golbe scale, respectively. In our group, PD patients suffered from a mean $UPDRS_{III\text{-}ON}$ of 16.7 pts., ranging from 4 to 36 pts. *MMRE:* When compared to the matched healthy control group, no significant change in global MMRE parameters μ and α was found in PD. In contrast, PSP was associated with a significant reduction of both, μ and α. This effect was pronounced in the periventricular region. Considering this region in PD patients, only a weak reduction of α was discernable, while μ remained unchanged (**Fig.1a**). **Fig.1b** addresses the local variation of *3DMRE* parameters. Since φ reflects the duality of fluid-solid properties of tissue, it is highly affected by the heterogeneous distribution of fluid-filled spaces in the brain. In contrast, |G*| presented with less in-plane variation than φ. Both |G*|- and φ-image intensities decay from the healthy state to PD and PSP. A pronounced signal deterioration is seen in the basal ganglia, demarcated by dashed red lines superposed to the |G*|-maps in **Fig.1b**. As can be appreciated in **Fig.1c**, 3DMRE reproduced our primary findings of a stronger reduction of viscoelastic constants in PSP compared to PD with pronounced effect in the periventricular region. *Correlation of disease severity and MRE parameters:* There was a strong correlation between $UPDRS_{III\text{-}ON}$ and 3DMRE obtained in both, global brain as well as basal ganglia (all $r < -0.5$, all $P < 0.05$, **Fig.1d**). In PSP, 3DMRE parameters correlated with disease stage (PSP staging system, $P < 0.05$), and less robust with the clinical symptom score ($P = 0.04$).

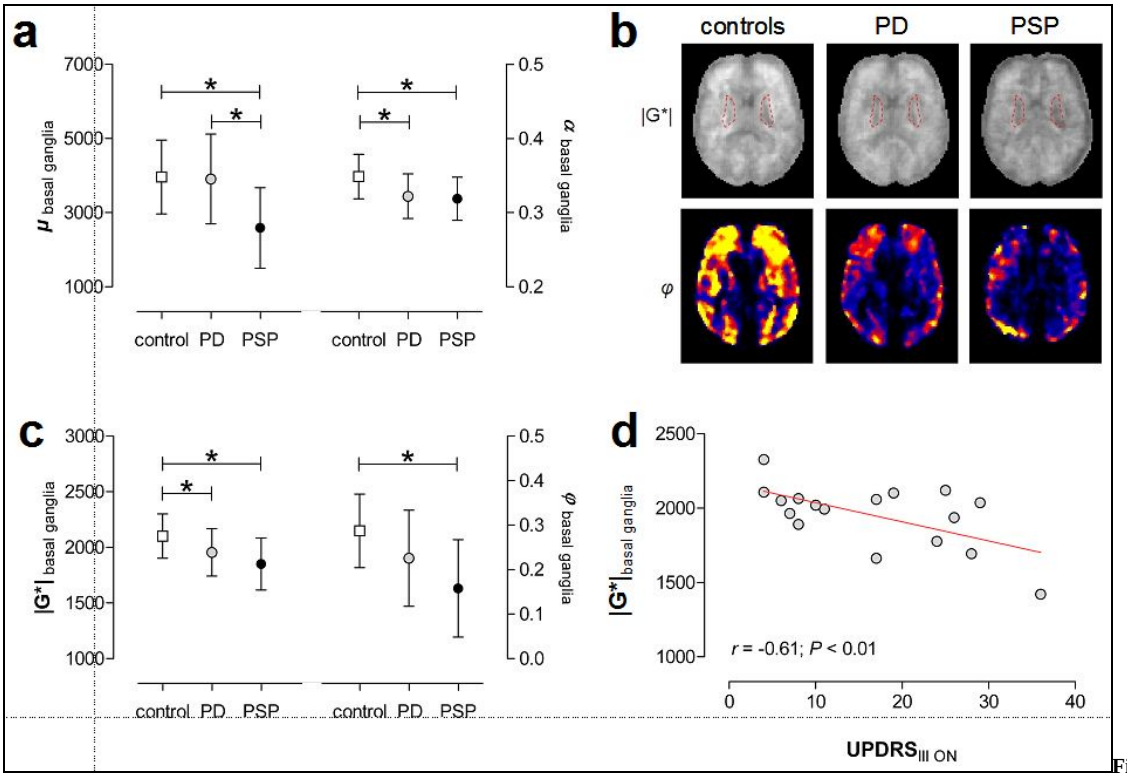

Fig.1

Conclusion: We observed a close negative correlation between MRE constants and measures of clinical severity in PD and PSP, emphasizing the capability of MRE to detect and quantify ongoing brain parenchymal degradation due to neurodegeneration. Moreover, we showed that brain viscoelasticity in PSP and PD is differently affected, depending on the underlying neurodegenerative pathology; whereas in PSP all MRE constants are reduced, changes in PD are limited to declining the parameters μ and |G*| , while network density (α and φ) remains intact.

Literature: [1] Muthupillai et al. Science 1995;269(5232):1854-1857. [2] Sack et al. Neuroimage 2009;46(3):652-657. [3] Wuerfel et al. Neuroimage 2010;49(3):2520-2525. [4] Murphy et al. J Magn Reson Imaging 2011;34(3):494-498. [5] Streitberger NMR Biomed 2011;24(4):385–392.