Decrease of brain stiffness compared to loss of brain volume in Multiple Sclerosis patients

K. J. Streitberger[1], F. Paul[2], D. Krefting[3], D. Klatt[1], S. Papazoglou[1], S. Hirsch[1], J. Braun[3], and I. Sack[1]
[1]Institute of Radiology, Charité - University Medicine Berlin, Berlin, Berlin, Germany, [2]Neurocure, Charité - University Medicine Berlin, Berlin, Berlin, Germany,
[3]Institute of Medical Informatics, Charité - University Medicine Berlin, Berlin, Berlin, Germany

Background: Chronic inflammatory diseases of the CNS such as Multiple Sclerosis (MS) lead to demyelinization and to widespread degradation of neurons and axons. The loss of neurons and axons alters the mechanical structure and therefore the elasticity of the brain, a process which may be useable for early recognition of diffuse pathological degeneration [1].
Problem: Current knowledge of biomechanical properties of in vivo human brain is very limited. Nothing is known about the relationship between brain atrophy associated with MS and viscoelastic properties of the brain. To date magnetic resonance elastography (MRE) [2] is the only method capable to measure in vivo viscoelastic properties of the brain without intervention [3-6]. However, since MRE is sensitive to geometrical boundary conditions, it is important to systematically investigate volume effects in MRE of MS patients.
Objective: Multifrequency magnetic resonance elastography (MRE) [4] and MRI volumetry [7] was applied to 17 MS patients and 42 age- and sex-matched healthy volunteers.

Methods:
Experiments were run on a standard 1.5T clinical MRI scanner (Siemens, Erlangen, Germany). A custom-made head cradle was used for multifrequency head stimulation. Four transverse images slices with through-plane motion-encoding direction were chosen in a central slab through the cerebrum. 32 time-resolved phase-difference wave images, $u(x,y,t)$ were Fourier-transformed for decomposition into complex wave images at driving frequency: $U(x,y,\omega)$, ($\omega / 2\pi$ = 25, 37.5, 50 and 62.5 Hz). Complex modulus images were obtained by wave inversion ($G(x,y,\omega)=-\rho\omega^2 U/\Delta U$) and spatially averaged [4]. The resulting global modulus function was fitted by the springpot model $G=\kappa(i2\pi f)^{\alpha}$ with κ and α as variables. κ was transformed to a parameter related to shear elasticity μ taking η = 3.7 Pas as the mean viscosity of all volunteers according to [6]. Volume data were acquired by a 3D Magnetized Prepared Rapid Gradient Echo (MPRAGE) sequence (TR/TE = 2110/4.4 milliseconds, TI 1100 ms, flip angle 15°, resolution 1 mm³). Normalized volumes of the whole brain parenchyma were calculated using a method for total brain volume measurement (SIENAX software) using the default BET options (Brain Extraction Tool; part of FSL4.0 Software Library; www.fmrib.ox.ac.uk/fsl).

Results: Averaged shear moduli (μ) and brain volumes (V) are listed in the table. The results show a clear softening of brain parenchyma in the course of MS with a highly significant effect in female patients and a less significant trend in men. Similarly, disease-related brain atrophy is discernable for women while in men no such clear effect appeared in our study. Comparing μ and V, brain elasticity showed a more than three time higher sensitivity to MS than atrophy.

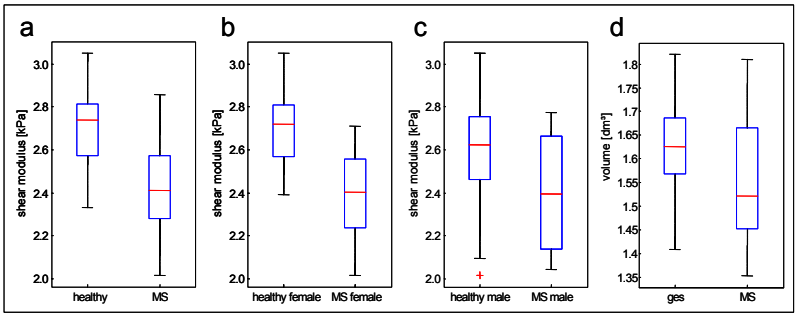

Figure: Shear elasticity of the brain in healthy volunteers and MS patients (a-c). The disease-related decrease of elasticity is significant with P < 0.0001 whereas brain volume changed with P = 0.021 (d). The plots depict the lower and upper quartiles as well as the 50th percentile (median). Full data range is presented by the whiskers.

Table: Description of the groups of volunteers and patients and corresponding averaged data of elasticity (μ) and brain volume (V). SD denotes the standard deviation.

	healthy all	MS all	healthy females	MS females	healthy males	MS males
N	42	17	23	12	19	5
age	49.14	52.82	50.30	55.92	47.74	45.40
SD	10.98	8.41	8.68	5.74	13.37	9.71
range	33 - 69	33-64	36 - 69	45 - 64	33 - 69	33-53
μ [kPa]	2.54	2.11	2.52	2.06	2.57	2.22
SD	0.25	0.35	0.23	0.29	0.27	0.48
$\Delta\mu$	430 Pa (17%)		451 Pa (18%)		347 Pa (13%)	
P	< 0.0001		< 0.0001		0.049	
V [dm³]	1.623	1.548	1.646	1.541	1.595	1.572
SD	0.096	0.133	0.084	0.147	0.104	0.090
ΔV	75 cm³ (5%)		105 cm³ (6%)		23 cm³ (1%)	
P	0.021		0.010		0.118	

Discussion and conclusion: Our results indicate that the biomechanical properties of the brain are connected in a highly sensitive manner with diffuse processes of neuronal degeneration. MS-related atrophy measured by MRI volumetry [7] is less sensitive indicating the stability of MRE against changes in geometrical boundary conditions. MRE could represent a new method for early recognition of neuronal and axonal damage in MS and other neurodegenerative diseases, as well as a possible tool for evaluating therapeutic approaches to neuroprotection.

Literature:
[1] Wuerfel et al. Neuroimage. 2009 Jun 16. [Epub ahead of print]; [2] Muthupillai et al. Science 1995;269(5232):1854-1857. [3] McCracken et al. Magn Reson Med 2005;53(3):628-639. [4] Klatt et al. Phys Med Biol 2007;52(24):7281–7294. [5] Green et al. NMR Biomed 2008;21:755-764. [6] Sack at al. Neuroimage 2009;46:652-657. [7] Sanfilipo et al. Neuroimage 2005;26:1068-1077.