Quantitative Susceptibility Mapping (QSM) in Wilson′s Disease

Andreas Schäfer[1], Dominik Fritzsch[2], Peter Günther[3], Robert Trampel[1], Robert Turner[1], and Karl-Titus Hoffmann[2]

[1]Max-Planck-Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [2]Department of Neuroradiology, University of Leipzig, Leipzig, Germany, [3]Department of Neurology, University of Leipzig, Leipzig, Germany

PURPOSE: Accumulation of metallic compounds in the human brain has been shown in some neurodegenerative diseases. In Parkinson's disease iron content seems to be increased in the basal ganglia [1], whereas in Alzheimer's disease zinc and iron are increased [2]. Recently it was shown that quantitative susceptibility mapping (QSM) is very sensitive to paramagnetic effects of iron [3], supporting the differentiation of Parkinson patients from healthy controls using MRI and QSM [4]. Wilson's disease is a neurodegenerative disease with symptoms rather similar to Parkinson's disease and other movement disorders, but in Wilson's disease the copper content is increased [5]. The aim of this study is to investigate whether copper accumulation in the brain of Wilson's patients can be detected using QSM, by comparison with healthy controls.

METHODS: 8 patients with Wilson's disease (23-64 years, mean 44 years, 4 female) and 10 age-matched healthy controls (27-61 years, mean 45 years, 5 female), who gave informed consent, were examined on a whole body 7T scanner using a 24 channel phased array coil. The study was approved by the local ethics committee. For imaging a 3D spoiled gradient multi-echo sequence (TR=40 ms; TE=9.76/19.19/28.62 ms; bw=150 Hz/pixel; voxel=0.6x0.6x0.8mm³) was used.

The phase data, which show the effects of a field perturbation $B_{dz}(\mathbf{r})$, were unwrapped using a 3D best-path phase unwrapping algorithm [6]. The SHARP algorithm was used to remove any B_0 inhomogeneities and thus obtain high-pass filtered phase data [7]. The filtered phase data were divided by γB_0TE to convert the field-shift to units of ppm. The data were re-sampled to 0.6 mm isotropic resolution. The susceptibility was then calculated by $\chi(\mathbf{r})=\mathrm{FT}^{-1}(-3\cdot B_{dz}(\mathbf{k})/B_0\cdot C^{-1}(\mathbf{k}))$, where $B_{dz}(\mathbf{k})$is the field perturbation in *k*-space, B_0 the main magnetic field and $C(\mathbf{k})=3k_z^2/|\mathbf{k}|^2-1$ the convolution kernel. Before inverse Fourier transform values of the convolution kernel smaller than 1.3 were set to signum($C(\mathbf{k})$)·1.3 to reduce noise amplification and minimise streaking artefacts [8]. So far we only analysed the Substantia Nigra (SN).

RESULTS: Figure 1 shows an example of the gradient echo magnitude image, phase image and the calculated QSM for one patient. The average value of the susceptibility of the SN is 0.23±0.08 ppm and 0.13±0.03 ppm for patients and healthy controls, respectively. Figure 2 shows the susceptibility of the SN of the Wilson's patients (red) and healthy controls (green). 6 out of 8 patients show an increased susceptibility within the SN compared to healthy controls.

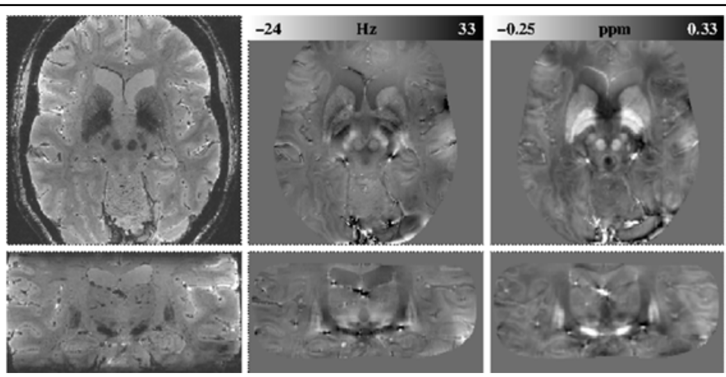

Fig 1: The T2*-weighted magnitude image (left column), the filtered phase image (middle column) and the QSM of one patient. The axial and coronal orientation is shown in the top and bottom row, respectively.

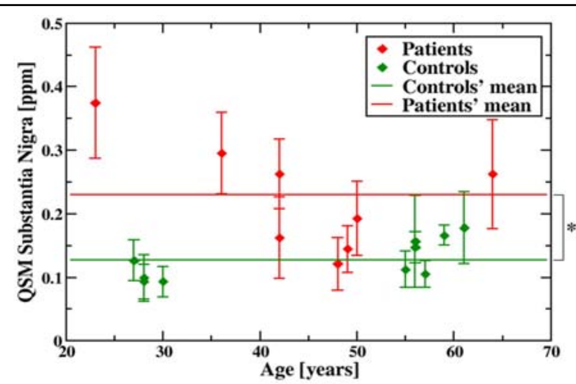

Fig 2: Quantitative susceptibility values of the substantia nigra for all patients and healthy controls. The mean QSM values are significantly different.

DISCUSSION: Our data clearly show that the SN is more paramagnetic in Wilson's disease patients compared to healthy controls. The remaining question is: What induces the change in magnetic behavior? The element copper is only slightly more paramagnetic than water, and copper(I)-compounds are even more diamagnetic than water [9]. One possible explanation is that copper(II)-compounds, which mostly have strong paramagnetic behavior, yield the increased paramagnetic behavior of Wilson's patients.

CONCLUSION: We have successfully applied QSM to Wilson's disease patients. There is a trend that paramagnetic copper(II) induces the magnetic susceptibility changes in patients as compared to controls. Further investigations will include quantitative T1 mapping, since copper(II) also enhances the longitudinal relaxation rate [10].

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