Quantitative Susceptibility Mapping (QSM) as a means to measure brain iron? A postmortem validation study

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1. Introduction

Abnormally increased brain iron concentrations have been found in a variety of neurological disorders including Alzheimer's disease, Parkinson's disease and multiple sclerosis [1,2]. Quantitative susceptibility mapping (QSM) is a novel technique which aims at calculating the magnetic susceptibility of tissue from gradient echo phase images [3,4]. Although iron has a strong paramagnetic effect in the magnetic field [5], it is currently unclear if and to what extend QSM can serve as a means for the reliable assessment of brain iron levels. Contributions of myelin, calcium and other metals, for example, may confound interpretation of magnetic susceptibility of tissue, especially in white matter regions of the brain [3]. Therefore, the goal of this study was to investigate the relationship between brain iron concentration and magnetic susceptibility in unfixed (in situ) postmortem brains.

2. Subjects and Methods

Twelve deceased subjects (age at death: 38-81years) without a history of a neurologic disorder underwent in situ MRI at 3T (TimTrio, Siemens) within 72 hours after death. Brain temperature at the start of the scan was between 4 ° and 24°C. Gradient echo MR data were acquired with a 3D FLASH sequence (TR/TE1/TE2/FA = 30ms/9.2ms/20ms/20°, resolution= 0.5x0.5x2mm³). Bulk susceptibility maps without streaking artifacts were reconstructed from unwrapped MR phase data using the HEIDI algorithm described in [6]. The maps were normalized for each subject by using the susceptibility of occipital white matter as reference because this region was considered to have low iron concentration [7,8]. After MRI, brains were extracted and fixed in 4% neutral buffered formalin. Tissue specimens were taken from several prespecified gray matter (globus pallidus, putamen, nucleus caudate, and thalamus) and white matter (frontal-, occipital- and temporal) structures and iron concentrations were determined with an inductively coupled plasma mass spectrometer (Agilent 7500ce) at m/z 56 in He-mode. According to the position of the dissected tissue specimens, regions of interest were outlined in the susceptibility maps and an univariate regression analysis was employed to investigate the relation between chemical determined iron concentration and the bulk tissue susceptibility.

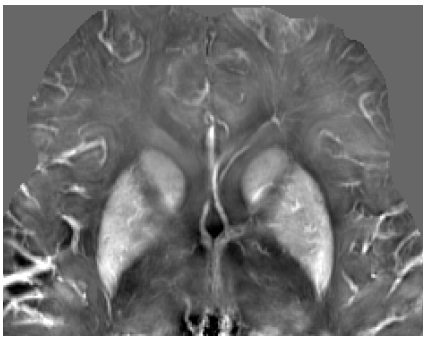

Figure 1: Representative postmortem QSM map. The basal ganglia with known high iron concentrations appear bright (windowing =-2.4 ppm - 0.36 ppm).

3. Results

Regional iron concentrations were found to be in good agreement with results from other postmortem work [7,8]. The reconstructed susceptibility maps (Fig. 1) were largely comparable with maps from in vivo measurements although significantly more small vessels were visible. A strong positive linear correlation between chemical iron concentration and bulk magnetic susceptibility was found when all regions were regarded ($r=0.88$, $p<0.001$) but also when only gray matter structures (green in Fig. 2) were included ($r=0.86$, $p<0.001$) in the analysis. The correlation coefficient of white matter structures (diamonds in Fig. 2) was significantly lower ($r=0.22$, $p<0.001$). Including all regions, linear regression yielded $\chi = 0.0012*[Fe]-0.0416$, where [Fe] is given in mg/kg wet mass.

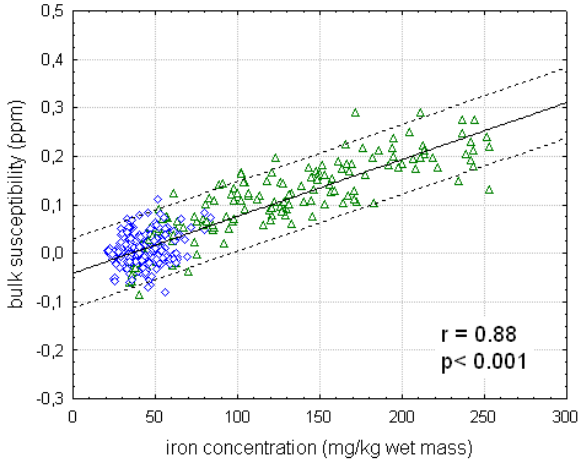

Figure 2: Correlation of regional bulk susceptibility with iron concentration. White matter regions are shown as blue diamonds, while the green triangles represent gray matter structures.

4. Discussion and Conclusion

In this study, a strong linear relation between brain iron and bulk susceptibility was found. The slope of the correlation found herein (0.0012*[Fe]) is consistent with theoretical considerations [5]. The results demonstrate that QSM is a sensitive means for investigating brain iron concentrations in deep gray matter regions. The moderate scattering of the measured values may be attributed to mismatch of dissected tissue specimens and analyzed regions in the MR data as well as confounding biophysical effects such as deoxygenated heme, myelin content and orientation dependency of the susceptibility [9,10]. Further work is required to disentangle these effects by accounting for the myelin content as well as for the fiber orientation in white matter.

References:

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