Establishing a reference of iron deposition in human brain deep grey matter nuclei using susceptibility mapping

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Purpose: To access iron content of basal ganglia, mid-brain and thalamus in healthy human brains and its correlation with age using quantitative susceptibility mapping (QSM). This data can be used as a baseline while studying the conditions of iron overload and iron deficiencies which are harmful to normal brain function.

Materials and Methods: A total of 180 normal volunteers were recruited with ages ranging from 20 to 70 years old (mean age: 45.3 yr, SD: 14.2 yr). Susceptibility weighted images (SWI) were collected using a 1.5 Tesla GE scanner equipped with an eight-channel phased array head coil. The data was collected using the following imaging parameters: TR/TE = 53 ms/40 ms, flip angle = 20°, bandwidth = 31.25 Hz/pixel, slice thickness = 3 mm, field-of-view = 24 cm and matrix size (Nx x Ny) = 384 x 320, yielding an in-plane resolution of 0.60 mm by 0.75 mm. QSM data were generated using our in-house Matlab based toolbox SMART 2.0 (Saifeng Liu, MRI Institute for Biomedical Research, Detroit, MI, USA). This toolbox contains mainly 4 parts: brain extraction (BET[1]), phase unwrapping (3D-SRNCP[2]), background field removal (SHARP[3]) and iterative Susceptibility Weighted Imaging and Mapping (SWIM) processing[4,5]. The structures of interest included: the Caudate Nucleus (CN), Globus Pallidus (GP), Putamen (PUT), Thalamus (THA), Pulvinar Thalamus (PT), Red Nucleus (RN) and Substantia Nigra (SN). A 3D volume for each structure was traced manually based on the signal contrast in the SWIM images. The measured susceptibility values were converted to iron concentration (C_{Fe}) with unit of μg/g wet tissue based on the correlation of $\Delta\chi=0.6*C_{Fe}$[6].

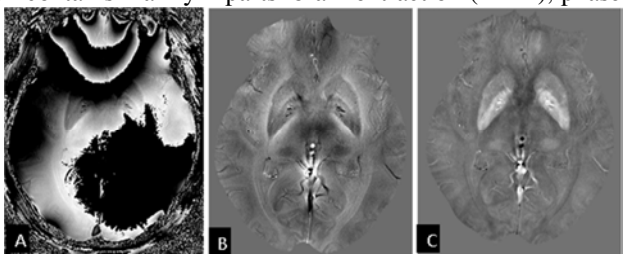

Figure 1. **A**: Original phase. **B**: Phase image after brain extraction, phase unwrapping and background removal. **C**: Iterative SWIM image. Three images are the same slice for a normal case.

Results: An example slice is shown in Fig. 1C. For the 7 brain grey nuclei, the iron deposition concentration was seen to be the highest in the GP (139±2ppb, 232±3μg/g wet tissue), followed decreasingly by the SN (106±2ppb, 177±4μg/g wet tissue), RN (87±2ppb, 145±4 μg/g wet tissue), PUT (60±2ppb, 100±3 μg/g wet tissue), CN (42±1ppb, 69±2 μg/g wet tissue), PT (37±1ppb, 61±2 μg/g wet tissue), and THA (-3±1ppb, -4±1 μg/g wet tissue). The 3D structural average susceptibility values were positively correlated with age in CN, PUT and RN. However, in THA, the average susceptibility decreased with age. No correlation with age was found in GP, SN and PT. Those trends are consistent with what has been shown in ref. (7). PUT is shown as an example of the correlation trend similarity between our measurements and ref. (7) (Fig. 2).

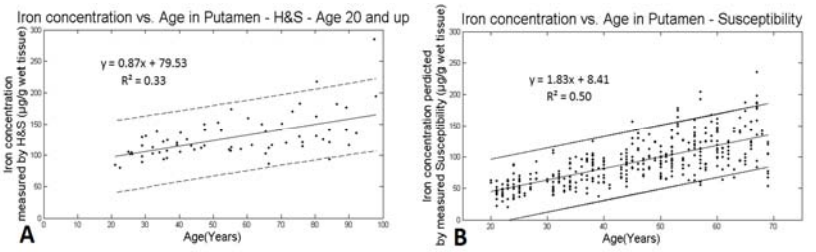

Figure 2. Comparison of correlation between iron concentration in Putamen with age reported by H&S and our study. Both trends are similar. **A**: H&S, iron measured from post mortem human brains including samples with age older than 20yr. **B:** Our study, iron predicted from measured magnetic susceptibility. The lower iron increasing rate in H&S's study may be due to the limited cadaver sample size.

Discussion and Conclusion: Our finding is almost identical to what was reported in H&S's study[7] except for the order between SN and RN. Average iron concentrations agree better with H&S's values in regions with high iron (Fig. 3), which may be caused by less myelin in these iron rich structures[3]. In summary, the age related iron patterns represented by susceptibility show good agreement with post mortem human brain findings[7]. The correlations found in this study can be used as a reference of iron deposition in normal brain aging.

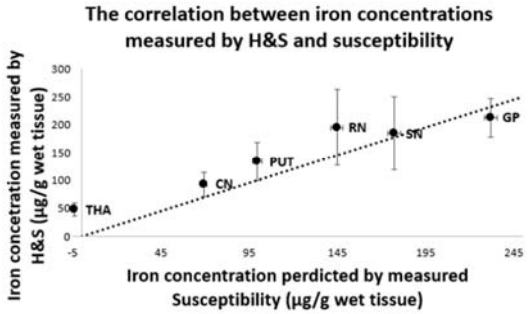

Figure 3. Average iron concentration in each structure cited from H&S and this study. The dashed line represents x=y.

References: 1. S. M. Smith, *Hum Brain Mapp,* 17 (2002), 143-55. **2**. H. S. Abdul-Rahman, *et al*, *Appl Opt,* 46 (2007), 6623-35. **3**. F. Schweser, *et al*, *Neuroimage,* 54 (2011), 2789-807. **4.** E. M. Haacke *et al*, *JMRI,* 32 (2010), 663-76. **5.** J. Tang *et al*, *MRM,* 69 (2013), 1396-407. **6.** W. Zheng, *et al*, *Neuroimage,* 78 (2013), 68-74. **7.** B. Hallgren, and P. Sourander, *J Neurochem,* 3 (1958), 41-51.