

Preliminary Findings of Elevated Iron Deposition in the Substantia Nigra in Patients With Idiopathic Parkinson's Disease Using Quantitative Susceptibility Mapping With a Two-region Approach

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Background

- Iron deposition in the brain has been implicated in the role of neurodegenerative disease and normal aging, and thus is of great interest to researchers and clinicians. Assessing iron content in the brain with MR imaging is frequently performed using R2*, which is a sum of the relaxation due to spin-spin interactions and local susceptibility effects¹.
- More recently, a technique called quantitative susceptibility mapping (QSM) has been of interest for researchers and clinicians studying brain iron. The technique uses magnitude and unfiltered phase SWI data to create a map which shows true susceptibility of the tissue, which is directly proportional to iron content, and also has uses in blood oxygen saturation, and assessing cerebral microbleeds^{2,3}.
- Our group has previously used this technique on 174 healthy controls to establish an age-based baseline of iron deposition in the midbrain and basal ganglia⁴.
- In this work, we assessed iron content in the midbrain in Parkinson's Disease using a similar approach, which will show whole region, and a thresholded high-iron region.

Methods

- Twenty PD patients with mean age of 66.5 +/-10 years with mild to moderate Idiopathic Parkinson's Disease (IPD) were imaged with a 3T Skyra system (Siemens, Erlangen, Germany) with a 20-channel head/neck coil with a venous imaging protocol.⁵
- Multi-echo SWI imaging was performed and magnitude and phase images were processed using in-house softwares.^{6,8}
- The substantia nigra (SN) and the red nucleus (RN) were traced in all of the images and susceptibility means were reported for global (whole) and high iron (RII) regions.

Quantitative Susceptibility Map Flow Chart and ROI Tracing

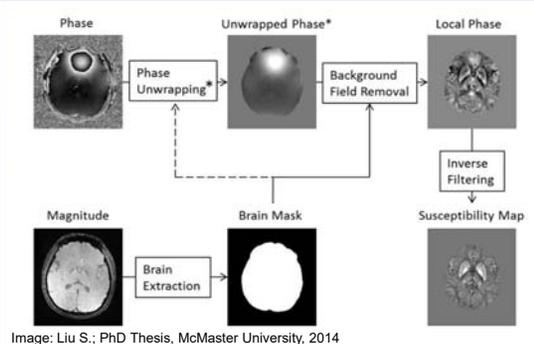


Figure 1. Illustration of the proposed algorithm. Four steps were applied to generate the resulting QSM images: brain extraction⁷, phase unwrapping⁸, background field removal⁹, and an iterative QSM approach^{2,10}. Upon QSM generation, the boundaries for the SN and RN were manually traced and global and regional iron content was calculated using previously established methods⁴.

In vivo data results

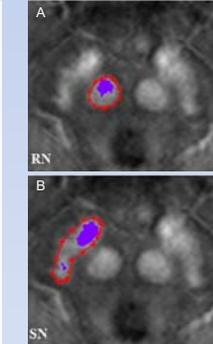
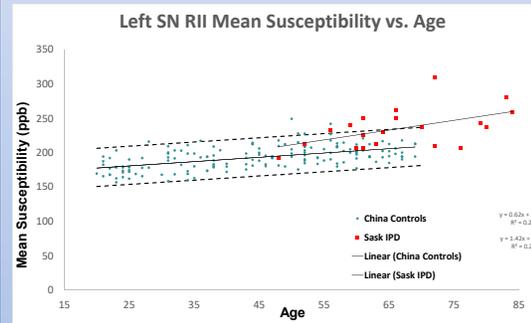
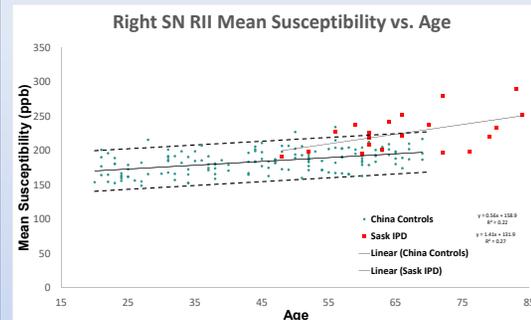


Figure 2: Example ROI drawings of the RN (A) and SN (B), with high-iron region thresholded by age colored purple.

Figure 3.

Plots showing high-region mean susceptibility as a function of age for the right (top) and left (bottom) red nucleus and substantia nigra. IPD subjects are plotted in red, and 174 healthy controls from Liu et. al⁴ are plotted in green.

The linear regression model of right SN showed mean RII iron increasing at a higher rate compared to controls starting at 50 years. The left SN data showed a similar trend with a regression line of $y = 1.42x + 140$, and an $R^2 = 0.25$.

Results

- Global susceptibility means for the right and left SN were 161.01 ppb (SD=25) and 152.85 ppb (SD=34.2), respectively. For the right and left RN, global susceptibility means were 113.78 ppb (SD=36.0) and 108.40 ppb (SD=33.4).
- RII susceptibility means for the right and left substantia nigra were 225.98 ppb (SD=27.5) and 235.14 ppb (SD=28.7). For the right and left RN, RII susceptibility means were 180.41 ppb (SD=21.3) and 180.05 (SD=17.97).
- Plots depicting RII mean susceptibility vs. age, along with their regression lines compared to controls⁴ are shown for the right SN (Fig. 3).

Discussion and Conclusion

- No apparent differences in iron were observed globally and regionally for the RN. The SN, however, not only had higher global iron content, but also much higher regional iron content compared to controls.
- An advantage of using RII compared to global regions is that the variability of the results decreases and is generally a more robust result. Any errors in tracing extra boundaries may also be mitigated by thresholding out surrounding low-iron tissues.
- QSM using a two-region approach was a robust method in showing elevated iron content in IPD compared to healthy controls in the substantia nigra. This may serve as a biomarker for future studies.

References

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