Increased midbrain iron deposition in Parkinson's disease measured by quantitative susceptibility mapping

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Target audience: Neuroscientists and clinicians interested in movement disorders; MRI researchers interested in quantitative susceptibility mapping (QSM).

Purpose: Parkinson's disease (PD) is the second most common neurodegenerative disorder that is marked by the loss of dopaminergic neurons in the substantia nigra (SN) of the basal ganglia. Both the understanding of the etiology of PD and evaluation of potential neuroprotective therapies have been hindered by the lack of objective, easily obtainable, in vivo marker(s) for PD-associated pathological changes. Increased iron content in the SN of PD patients has been consistently reported in pathological studies, which may be reflected indirectly by higher R2* values [1-4]. Quantitative susceptibility mapping (QSM), a new MRI post-processing technique, has been proposed to directly quantify iron content in human brain [5,6]. In this work, we examine the potential use of QSM as an in vivo marker(s) of PD related pathology in nigrostriatal structures.

Methods: Brain MRIs (Trio, Siemens Magnetom, Erlangen, Germany, with an 8-channel head coil) were obtained from 25 PD (13/12 males/females, mean age 66±10 years, mean UPDRS-III score 29.7±23.8, mean disease duration 6.1±6.0 years) and 21 healthy control subjects (8/13 males/females, mean age 63±8 years). T1-weighted images were obtained using an MPRAGE sequence (TR/TE = 1540/2.34, FOV = 256 mm, matrix = 256, slice thickness = 1 mm, slice number = 176). T2-weighted images were collected using a fast-spin-echo sequence (TR/TE = 2500/316, with the same resolution settings used for T1-weighted images). A multiecho gradient-echo sequence was used to collect images for QSM (TR/TE = 55/6.2, 12.4, 18.6, 24.8, 31.0, 37.2, 43.4, 49.6; FOV = 240 mm, matrix = 240, slice thickness = 2mm, slice number = 64). QSM images were generated by using the morphology-enabled dipole inversion with the nonlinear formulation method [6]. AutoSeg 2.9, a probabilistic atlas-based segmentation software (Neuro Image Analysis Laboratory, UNC Chapel Hill, NC) [7], was used on T1-, and T2-weighted images to generate regions-of-interest (ROIs) for nigrostriatal nuclei, namely caudate (CN), putamen (PUT), global pallidus (GP), substantia nigra (SN) and red nucleus (RN). An affine registration (3D Slicer) then was used to propagate segmented ROIs to QSM image space. The median of each striatal ROI then was acquired using an in-house matlab program. Regional QSM values were compared between PD and control subjects using ANCOVA with age and gender as covariates.

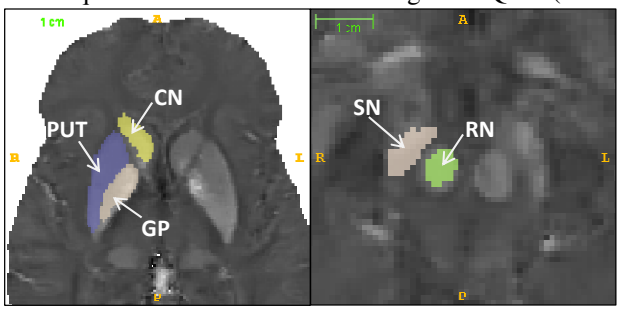

Fig 1. A typical QSM image with segmented ROIs. Only right side shown for demonstration purposes.

Results/Discussion: QSM images provided superb contrast for all nigrostriatal structures of interest (Fig. 1). Compared to controls, PD subjects showed increased susceptibility in the SN ($p = 0.026$) and the RN ($p = 0.039$; Fig. 2), but there was no significant difference between groups in the CN, PUT, or GP. Susceptibility values did not correlate with clinical measurements (disease duration and UPDRS-III scores). Increased susceptibility in the SN might reflect increased iron associated with PD pathology, which is consistent with previous studies [2,3]. Elevated susceptibility in the RN, distinct from the SN, might suggest the involvement of cerebellar-related structures in PD [4].

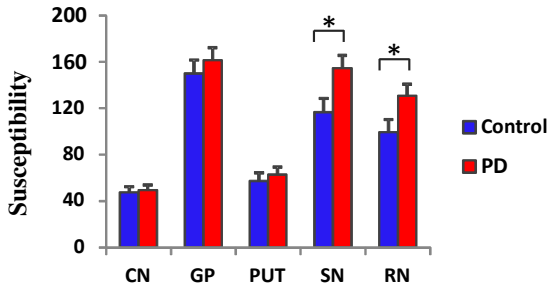

Fig 2. Comparison between PD and controls.

Conclusion: The current results support the hypothesis that QSM can measure iron accumulation associated with the PD-related pathological process. Future studies are warranted to explore using this technology in developing clinically useful biomarker(s) for PD diagnosis and progression.

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