REGION-SPECIFIC DISTURBED IRON DISTRIBUTION IN EARLY IDIOPATHIC PARKINSON'S DISEASE MEASURED BY QUANTITATIVE SUSCEPTIBILITY MAPPING

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Target audience: Researchers and clinicians interested in movement disorders and iron deposition; MRI researchers interested in susceptibility mapping.

Purpose: Parkinson's disease (PD) is a common neurodegenerative disorder whose major pathologic features of PD include selective loss of the dopaminergic neurons, presence of α-synuclein, and iron elevation in specific brain regions. A reliable in vivo quantitative evaluation of iron deposition is important, especially in early PD, because iron-mediated PD can be targeted by iron chelation, such as deferiprone[1]. Although the conventional gradient-echo (GRE) imaging approaches (magnitude, phase, R2*) have been widely used to characterize the susceptibility change in PD[2], the observations didn't reach a consensus, which may be partially contributed by the technical problems. To overcome the non-locality of the magnetic field distribution in conventional GRE approaches, a novel post-processing method, quantitative susceptibility mapping (QSM)[3] has been introduced. A recent postmortem study has validated the high sensitivity and reliability of the QSM technique to indicate brain iron accumulation in vivo[4]. In this work, we aimed to investigate the iron deposition changes with QSM in deep grey matter structures of patients with early PD, and explore the relationships of these changes with clinical futures.

Methods: MRI scans of forty-four patients with early PD (25/19males/females, mean age 58±8 years, mean UPDRS-III score 15.57±6.22, mean disease duration 2.8±1.6 years) and sixteen age-matched healthy controls (5/11 males/females, mean age 61±6 years) were performed on a 3T scanner (Signa HDxt, GE Healthcare; eight-channel head coil). A multiecho GRE sequence (TR/TE1=54.6/5.468ms, 8echoes with inter-echo spacing=6.408ms, resolution 0.47×0.47×2.0mm^3, 62 slices) was used to obtain the susceptibility weighted images. QSM images were reconstructed using the Morphology Enabled Dipole Inversion (MEDI) method[3]. A neuroradiologist blinded to the diagnosis of each subject measured the regions of interest on susceptibility maps twice with five weeks apart, namely the bilateral head of caudate nucleus（CN）, globus pallidus (GP), putamen （PUT）, substantia nigra （SN）, and red nucleus（RN）. The means of the two measurements were used for the final analysis. Statistical analysis included Mann-Whitney U tests to assess group differences between PD and controls and linear regression analysis to assess the relationships between iron deposition and clinical features. The present study was approved by the local ethics committee.

Results: QSM images clearly reflected the shape of the deep grey matter nuclei. The results demonstrated a strong positive relationship between the susceptibility values in healthy controls of this study and iron concentrations as previously assessed by biochemical methods[5] in each measured brain region (r =0.983, *P* =0.0026) **.** Susceptibility values were elevated within the SN and RN, either contralateral (SN: *P*=0.0096; RN: *P*=0.0071, Fig 1) or ipsilateral (SN: *P* =0.0111; RN: *P*=0.0091, Fig 1) to the most affected limb in early PD when compared with healthy controls. Moreover, increased susceptibility levels within both the bilateral SN (*P*=0.0103; *P*=0.0187 respectively) and RN (*P*=0.0187; *P*=0.0325 respectively) were also observed in the subgroup of patients at the earliest clinical detectable state (Hoehn & Yahr, Stage I). The QSM values in PUT contralateral to the predominant clinical syndromes were decreased (*P*=0.0449, Fig 1) in early PD. Other measured regions failed to show difference on a group level. Furthermore, regional magnetic susceptibilities within the bilateral SN in early PD were positively correlated with disease duration (r=0.326, *P*=0.0308; r =0.322, *P*=0.0329 respectively) and UPDRS-III scores (r =0.359, *P* =0.0166; r =0.404, *P*=0.0065 respectively).

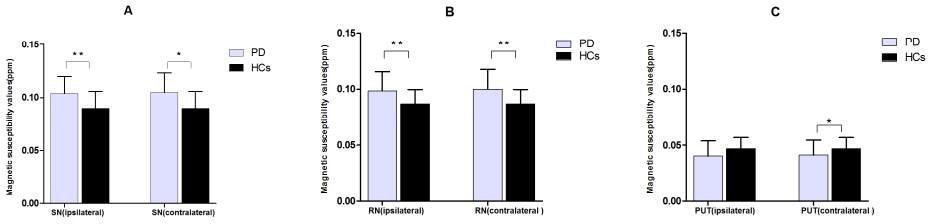

Fig 1. Comparison of susceptibility values in PD and controls. Significant differences between PD and control subjects are represented as: *P < .05; **P < .01.

Discussion and Conclusion: Elevated SN susceptibility and decreased PUT susceptibility values in this study are consistent with previously published neuropathologic evidence of selective degeneration in PD and previous MRI studies[6]. The elevated susceptibility in RN might suggest the cerebellar-related structures are involved in PD[7]. These findings indicate that QSM is useful for quantitatively detection of iron alteration, which might be an early event in the progression of PD.

References: [1] Devos D, et al. Antioxid Redox Signal 2014;21:195-210. [2] Martin WR, et al. Neurology 2008;70:1411-1417. [3] de Rochefort L, et al. Magn Reson Med 2010;63:194-206. [4] Langkammer C, et al. Neuroimage 2012;62:1593-1599. [5] Hallgren B, et al. Journal of neurochemistry 1958;3:41-51. [6] Ryvlin P, et al. Arch Neurol 1995;52:583-588. [7] Lewis MM, et al. Neurobiol Aging 2013;34:1497-1503.