Assessing Iron Load in Deep Grey Matter Brain Nuclei of Parkinson's Disease with L2-Regularized Quantitative Susceptibility Mapping

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Target audience

Clinical scientist who are interested in the application of magnetic susceptibility imaging in neurodegenerative disease.

Purpose

Parkinson's disease (PD) patient were often observed with excessive iron deposition in substantia nigra[1]. Abnormal iron accumulation was postulated to be the cause of neuronal cell loss in PD. In this study, we aimed to examine the brain iron loading of PD patients with regularized quantitative susceptibility mapping (QSM) method.

Methods

22 subjects of ethnics Chinese were recruited, with 11 PD patients (5 female, age = 62 ± 10y, duration of illness = 8 – 14 years) and 11 healthy control (5 female, age = 63 ± 10y). All images were acquired with the following parameters: 3D-FFE sequence at 3.0T MR system, TR/TE = 28/23 ms, flip angle = 15°, NEX = 1, FOV = 230 x 201 x 180 mm^3, resolution = 0.9 x 0.9 x 1 mm^3. The reconstructed phase images were unwrapped with PRELUDE in FSL and filtered with iterative SHARP algorithm. Susceptibility maps χ were generated from the corrected phase by regularized L_2-norm approach[2,3], where $\chi = \text{argmin}_\chi \|F^{-1}DF\chi - \Phi\|_2^2 + \lambda \|G\chi\|_2^2$, where D denotes the dipole kernel in Fourier space, F refers to the Fourier operator, Φ corresponds to the map of frequency shift and G is the differential operator. Closed-form solution was computed with a fixed λ of 7×10^{-3} which was selected based on the L-curve method[2,3]. Region-of-interest (ROI) were manually drawn on 6 brain nuclei, including the bilateral caudate nucleus (CN), putamen (PT), globus pallidus (GP), substantia nigra (SN), red nucleus (RN), dentate nucleus (DN) (fig. 1). ROI drawing was performed with reference to the same session magnitude images. Independent-samples t-test assuming unequal variance was performed to examine the difference of susceptibility value of the brain structures between PD patient and healthy subjects.

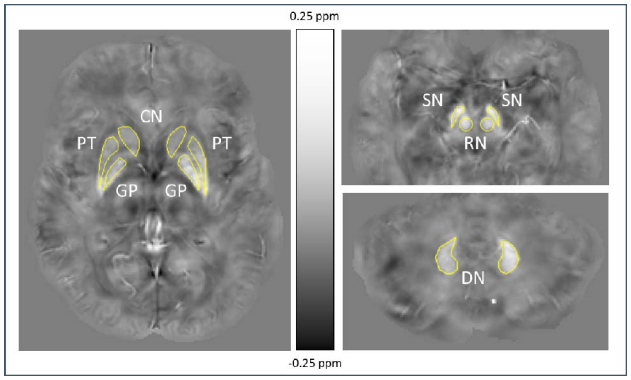

Fig. 1 L2-regularized QSM image from one of the subjects, with the defined ROIs of the 6 brain structures

Results

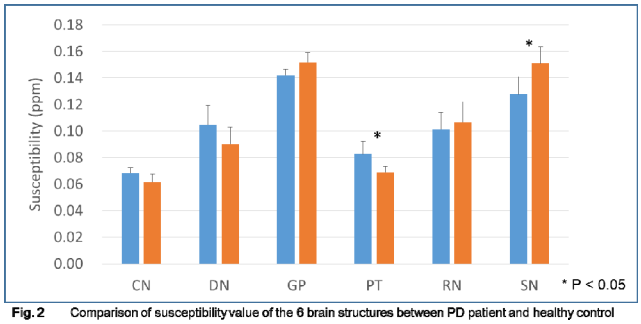

Fig. 2 Comparison of susceptibility value of the 6 brain structures between PD patient and healthy control

The reconstructed susceptibility map displayed better contrast of blood vessels and brain nuclei which were hardly observed in the corresponding magnitude images. Mean susceptibility values measured from the 6 brain nuclei were shown in figure 2. Error bar of the graph indicated two standard errors from the mean. Measured mean susceptibility of healthy control were comparable with the previously published data[2]. Statistical analysis revealed higher susceptibility in the substantia nigra of PD patients when compared with healthy control ($p = 0.033$), suggesting possible increment of iron accumulation in the mid-brain nuclei. No statistical significances were found when assessing the iron content of caudate nucleus ($p = 0.225$), globus pallidus ($p = 0.054$), dentate nucleus ($p = 0.183$) and red nucleus ($p = 0.639$). Lower susceptibility and possible lower iron content was observed in putamen of PD patients ($p = 0.016$).

Discussion and Conclusion

Previous studies indicated that magnetic susceptibility was linearly associated with iron concentration[1,2,4]. In this study, we explored the application of QSM to assess the iron concentration in different deep brain nuclei in PD, and the result confirmed the clinical findings of abnormal iron content in PD patients. Abnormal iron content in substantia nigra was postulated to be the cause of degeneration of dopaminergic neuron in PD, and studying pathophysiology of PD inevitably required the understanding of iron metabolism, which QSM is the potential tool for such purpose. QSM offers a quantitative approach to quantify *in vivo* iron concentration in which each pixel represents a real physical quantity. The method presented is this study hence provides a more reliable result than the traditional phase-based method. QSM is also superior to other *in vivo* method due to its easy and fast acquisition (less than 5 minutes per case in our study) and the emergence of fast processing routine[2,3]. This study also presents the first batch data of the *in vivo* iron content of Hong Kong ethnic Chinese PD patients, which contribute to the completeness of the worldwide study of iron deposition in PD patients.

Reference

1. Gowland PA, et al. High Resolution Magnetic Susceptibility Mapping of the Substantia Nigra in Parkinson's Disease. J Magn Reson Imaging. 2012 Jan; 35(1):48-55.
2. Bilgic B, et al.. MRI estimates of brain iron concentration in normal aging using quantitative susceptibility mapping. NeuroImage 2012; 59: 2625-2635.
3. Bilgic B, et al. Fast Quantitative Susceptibility Mapping with L1-Regularization and Automatic Parameter Selection. Magn Reson Med. 2014 Nov; 72(5): 1444-59.
4. Langkammer C, et al. Quantitative Susceptibiliy Mapping (QSM) as a means to measure brain iron? A postmortem validation study. Proc. Intl. Soc. Mag. Reson. Med. 20. 2012