

Source separated susceptibility maps reveal iron accumulation in substantia nigra and cortex in Parkinsons disease

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Background

Quantitative Susceptibility Mapping (QSM) is a powerful MRI technique for non-invasively measuring tissue magnetic susceptibility, providing insights into iron deposition and myelin content. However, conventional QSM cannot characterise sub-voxel susceptibility distribution. Paramagnetic (iron) and diamagnetic (myelin) sources may coexist within voxels, with opposing contributions potentially masking pathological changes in Parkinson's disease (PD). DECOMPOSE-QSM addresses this by decomposing bulk susceptibility into Paramagnetic (PCS), Diamagnetic (DCS), and Composite (CompS) maps. We examined source-separated susceptibility in PD and controls, identifying regional differences and clinical associations.

Methods

59 PD patients aged 50–80 (age=66.9±7, 20 female) within 10 years of diagnosis and 17 age-matched controls (age=67.7±6, 8 female) underwent 3T multi-echo multiparameter mapping.

QSM Pipeline: Phase unwrapping (ROMEO), two-pass brain masking, per-echo background field removal (PDF), and dipole inversion (STAR-QSM) were applied to generate susceptibility maps. These were processed using DECOMPOSE-QSM to produce PCS, DCS, CompS maps, co-registered and across multiparameter acquisitions.

Regions of Interest (ROI): Cortical ROIs were defined using the Schaefer atlas; subcortical ROIs used MRICloud. Subcortical ROIs included the caudate, globus pallidus (interna/externa), putamen, subthalamic nucleus, substantia nigra, and red nucleus.

Statistics: ANOVAs were used to assess group differences and multiple linear regression models were used to examine associations with cognition (MoCA) and motor severity (UPDRS-III), controlling for age and sex. Significant associations were examined at $p < 0.05$ for subcortical ROIs and $FDRp < 0.05$ for cortical ROIs.

Conclusions

Source-separated susceptibility mapping revealed both cortical and subcortical differences between PD patients and controls that are not apparent using conventional QSM approaches.

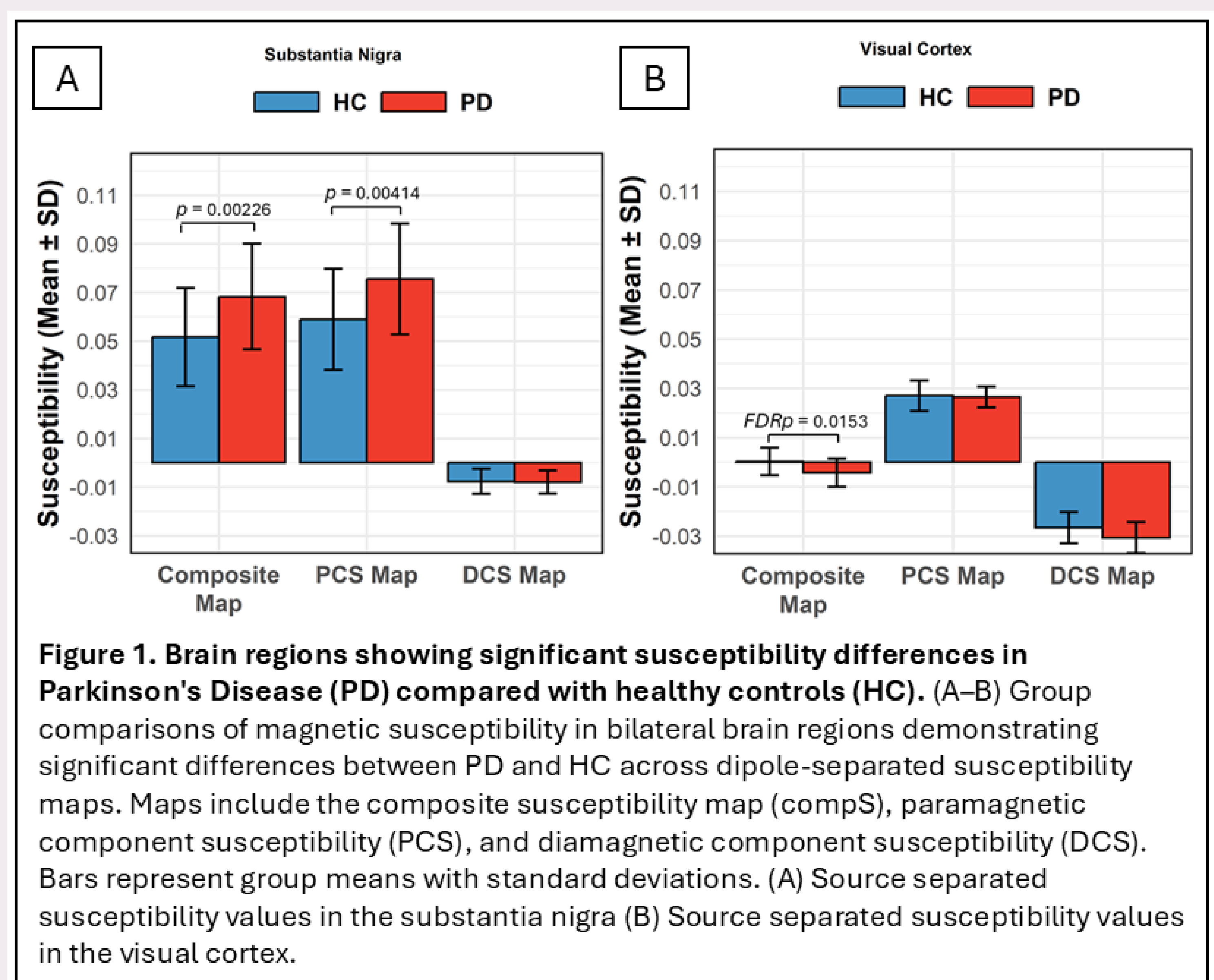
Increased substantia nigra paramagnetic susceptibility replicated prior findings, while reduced composite susceptibility was observed in visual cortex. Critically, cortical susceptibility measures associated with both cognitive (MoCA) and motor severity (UPDRS-III), underscoring the clinical relevance of examining paramagnetic and diamagnetic components separately.

Results

Group Differences

Analysis of subcortical regions revealed increased susceptibility in the substantia nigra in PD patients compared to controls. This difference was significant in both the composite and paramagnetic susceptibility maps (PCS: $p = 0.0041$; CompS: $p = 0.0023$) (see Figure 1A). No other subcortical regions showed significant differences between PD and control participant brains.

In the composite susceptibility (CompS) map, the visual cortex demonstrated significantly lower susceptibility values in the PD group compared to controls ($FDRp = 0.015$) (see Figure 1B). While no significant differences were observed in the paramagnetic or diamagnetic maps after FDR correction, the diamagnetic map showed a trend toward significance in this region ($p = 0.014$, uncorrected). No other cortical regions exhibited significant differences after multiple-comparison correction.



Associations with cognition and motor severity

Within the PD group, higher MoCA scores correlated with increased diamagnetic ($FDRp = 0.0098$) and composite ($FDRp = 0.022$) susceptibility in the temporal pole. Additionally, higher UPDRS-III scores correlated with increased composite susceptibility in the visual area ($FDRp = 0.038$) (Figure 2).

