Perfusion deficits predate grey matter atrophy in cognitively-impaired Parkinson's disease

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Aim: To investigate the evolution of perfusion deficits and grey matter atrophy in relation to cognitive decline in Parkinson's disease (PD).

Methods:

The MR protocol included a T1-weighted, three-dimensional inversion recovery spoiled gradient echo sequence acquired on a 3T General Electric HDx scanner with an eight-channel brain coil. Perfusion was measured quantitatively using pseudo-continuous arterial spin labeling and background suppression.[1] Sixty PD and 29 control subjects completed comprehensive neuropsychological testing which was used to classify PD patients as cognitively normal (PD-N; n = 33), with mild cognitive impairment (PD-MCI; n = 16), or with dementia (PD-D; n = 11).[2] Disease severity was assessed using the UPDRS-III. Structural images were segmented and grey matter and perfusion images were normalized to a probabilistic elderly template.[3] Voxel-based morphometry was used to compare grey matter changes and an ANCOVA implemented in biological parametric mapping[4] was used to compare perfusion changes among the PD cognitive groups and controls (false discovery rate-corrected $p<0.05$).

Results:

In comparison to controls and PD-N, both PD-MCI and PD-D showed decreased perfusion in extensive cortical areas (Fig 1A). Subcortical reduction occurred in left caudate and in PD-MCI only, anterior thalamic region. PD-MCI did not show significant atrophy apart from one small cluster in the right postcentral gyrus, whereas PD-D exhibited widespread cortical atrophy and in bilateral caudate (Fig 2A). Perfusion correlated with global cognitive status in PD in regions consistent with those showing perfusion changes across the groups.

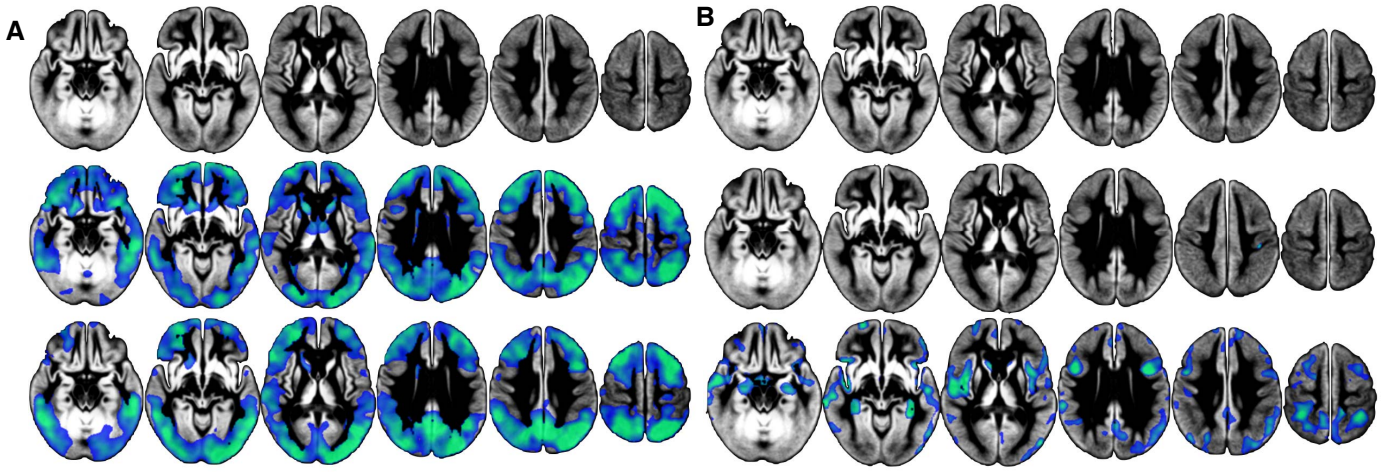

Figure 1: A) Significantly decreased perfusion in PD-N (upper), PD-MCI (middle), and PD-D (lower) relative to controls, displayed on the study-specific average grey matter image in neurological convention (FDR $p<0.05$). B) Significant grey matter atrophy in PD-N (upper), PD-MCI (middle), and PD-D (lower panel) relative to controls.

Discussion:

Functional perfusion decreases in PD-MCI and PD-D, not explained by underlying grey matter atrophy, were identified in extensive cortical and subcortical regions, while PD-N was indistinguishable from controls. Conversely, only PD-D exhibited widespread atrophic changes. The structure-function dissociation in PD-MCI suggests that functional blood flow changes occurred before detectable structural changes in cognitive decline associated with PD. Furthermore, this dissociation provides a promising biomarker sensitive to cognitive status in PD. A study is underway to follow these changes longitudinally.

References:

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