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. 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). 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. Voxel-based morphometry was used to compare grey matter changes and an ANCOVA implemented in biological parametric mapping 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.

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: