

## Grey matter loss in cognitively impaired Parkinson's disease

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**Objectives:** To characterize grey matter changes associated with clearly defined stages of cognitive impairment in PD using structural MRI.

### Methods:

Ninety-six PD subjects were classified using detailed cognitive testing as PD with normal cognition (PD-N, n=57), mild cognitive impairment (PD-MCI, n=23), or dementia (PD-D, n=16);<sup>1</sup> thirty-four controls matched for mean age and sex ratio participated. Disease severity was assessed using the UPDRS-III. 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. Structural images were segmented and grey matter images were normalized to a probabilistic elderly template.<sup>2</sup> Voxel-based morphometry was used to compare grey matter concentration among the PD cognitive groups and controls, and multiple linear regression assessed the relationship between cognitive and motor impairments and grey matter concentration (false discovery rate-corrected  $p < 0.05$ ).

### Results:

No grey matter differences were identified in PD-N compared to controls. PD-MCI showed some grey matter atrophy in temporal, parietal, and prefrontal cortex as well as bilateral hippocampi, amygdala, and right putamen. PD-D subjects exhibited far more extensive atrophy of the temporal lobe, in particular the intracalcarine gyri, lingual gyri, posterior cingulate gyrus, and parahippocampi, as well as prefrontal cortex (figure 1). Grey matter loss in PD was associated with global cognitive score but not motor impairment in most of these regions.

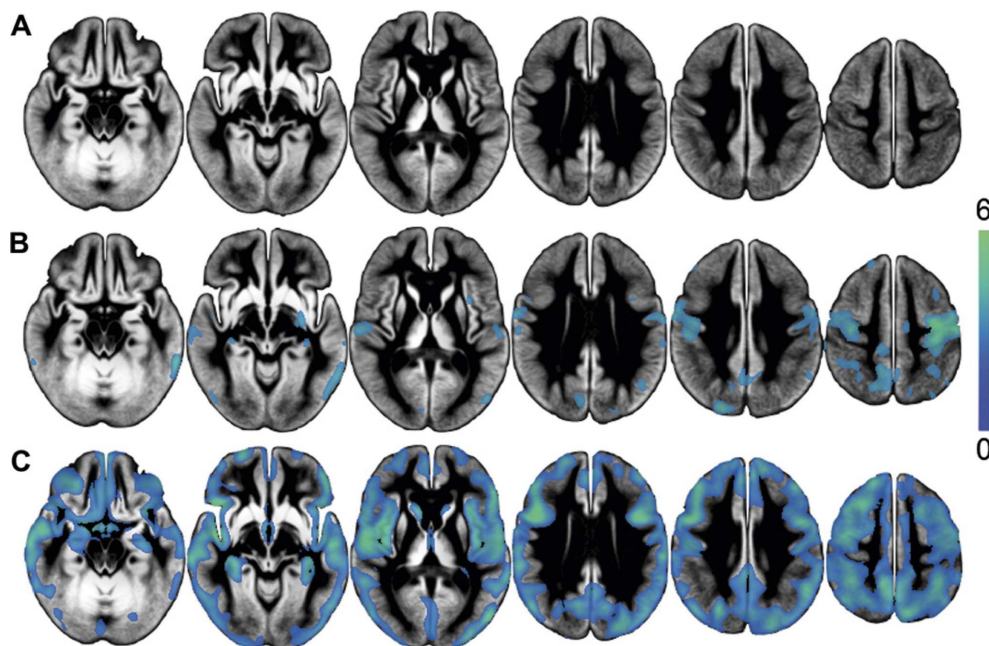


Figure 1: Regions displaying any areas of significant grey matter atrophy in patients with (A) Parkinson's disease with normal cognition (PD-N), (B) Parkinson's disease with mild cognitive impairment (PD-MCI) and (C) Parkinson's disease with dementia (PD-D), relative to controls, displayed on the study-specific average grey matter image (neurological convention). Significant clusters (FDR,  $p < 0.05$ ) indicate atrophy in PD-MCI ( $t > 2.84$ ) and PD-D ( $t > 2.06$ ). Colour bar displays  $t$  statistic scale. Slices displayed are  $z = (-18, -8, 7, 27, 37, 52)$ .

### Discussion:

Marked grey matter atrophy occurs in PD dementia and less extensive changes are also evident in PD-MCI. Thus atrophy may precede the development of frank dementia. Detailed neuropsychological testing and structural MRI of well-defined cognitive groups may help clarify the process of structural degradation associated with cognitive decline in PD. Longitudinal follow-up of this cohort will be important to clarify the utility of structural MRI in describing and predicting PD-related cognitive decline.

### References:

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2. Lemaître, H., Crivello, F., Grasset, B., Alperovitch, A., Tzourio, C., & Mazoyer, B. (2005). Age- and sex-related effects on the neuroanatomy of healthy elderly. *Neuroimage*, 26(3), 900-11.