

## Midbrain Degeneration and Cognition in Parkinson's Disease

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Neuromelanin imaging is an emerging biomarker for PD as it captures degeneration of the midbrain. Currently, it is unknown whether this degeneration contributes to cognitive dysfunction in PD beyond dysfunction associated with fronto-subcortical systems. Here, we examine whether neuromelanin signal is associated with broader cognitive dysfunction in PD patients with varying degrees of cognitive impairment: PD with normal cognition (PD-NC), PD with mild cognitive impairment (PD-MCI), and healthy controls (HC).

12 PD-NC, 18 PD-MCI and 19 HC underwent an MRI scan that included a neuromelanin-sensitive (NM-MRI) sequence. Contrast-to-noise-ratio of the substantia nigra pars compacta (SNc) and ventral tegmental area (VTA) was calculated.

Analyses indicated a significant main effect of group ( $p < 0.001$ ) for both SNc CRmode and VTA CRmode. PD-MCI patients exhibited significantly reduced SNc CRmode relative to HC. The same pattern was observed for the VTA CRmode whereby PD-MCI exhibited significantly reduced VTA CRmode relative to HC.

PD patients exhibited decreased neuromelanin in the SNc and VTA relative to healthy controls, confirming the ability of the NM-MRI sequence to map neurodegeneration in Parkinson's Disease. There is a generally consistent relationship between SNc and VTA degeneration in PD, with SNc degeneration more strongly associated with worse cognitive performance in working memory and executive functioning tasks than VTA degeneration. These findings warrant further examination of the SNc and VTA in PD patients with varying levels of cognitive impairment.