

volumetric brain differences in a diverse sample of pwMS.

Participants and Methods: The sample (n=79) was compiled from multiple neuroimaging datasets and divided into three groups- Latinx (n=19), NHB (n=29), and NHW (n=32)- based on self-reported race/ethnicity. Participants completed demographic interviews and structural magnetic resonance imaging (MRI) scans. Neuroimaging data was visually inspected and processed in FreeSurfer (7.3.2). Volumetric measures for total gray matter, cortical gray matter, total white matter, and subcortical gray matter were used as the primary outcome measures.

Results: A multivariate general linear model was used to examine volumetric brain differences across groups. Age and total intracranial volume were included as covariates. Results showed a significant effect of race/ethnicity (Pillai's Trace=0.175, $F(6, 148)=2.36$, $p=.033$), indicating significant differences in volumetric brain metrics across race/ethnicity, namely for subcortical gray matter, total gray matter, and total white matter volumes. Post-hoc testing showed the Latinx group to have less subcortical gray matter, total gray matter, and total white matter than NHWs. There was a trend for the NHB versus NHW, with NHBs having less brain volume. No significant differences were observed between the Latinx and NHB groups. Lesion volume and regional gray matter volumes were also examined.

Conclusions: To the authors' knowledge, this is among the first studies to investigate structural brain differences across race/ethnicity in pwMS. Results point to disparities in brain volume across racial/ethnic groups with MS. These differences may partially underlie the differing trajectories observed in clinical characteristics across race/ethnicity. Future studies should include larger samples of diverse pwMS and examine the intersection of psychosocial and systemic factors (i.e., social determinants of health) and brain metrics to better understand the divergent disease trajectories observed across groups.

Categories: Multiple Sclerosis/ALS/Demyelinating Disorders

Keyword 1: neuroimaging: structural

Keyword 2: diversity

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4 Compensatory Functional Activation During Motion Discrimination in Parkinson's Disease

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Objective: PD patients commonly exhibit executive dysfunction early in the disease course which may or may not predict further cognitive decline over time. Early emergence of visuospatial and memory impairments, in contrast, are more consistent predictors of an evolving dementia syndrome. Most prior studies using fMRI have focused on mechanisms of executive dysfunction and have demonstrated that PD patients exhibit hyperactivation that is dependent on the degree of cognitive impairment, suggestive of compensatory strategies. No study has evaluated whether PD patients with normal cognition (PD-NC) and PD patients with Mild Cognitive Impairment (PD-MCI) exhibit compensatory activation patterns during visuospatial task performance.

Participants and Methods: 10 PD-NC, 12 PD-MCI, and 14 age and sex-matched healthy controls (HC) participated in the study. PD participants were diagnosed with MCI based on the Movement Disorders Society Task Force, Level II assessment (comprehensive assessment). Functional magnetic resonance imaging (fMRI) was performed during a motion discrimination task that required participants to identify the direction of horizontal global coherent motion embedded within dynamic visual noise under Low and High coherence conditions. Behavioral accuracy and functional activation were evaluated using 3×2 analyses of covariance (ANCOVAs) (group [HC, PD-NC, PD-MCI] \times Coherence [High vs. Low])

accounting for age, sex, and education. Analyses were performed in R (v4.1.2(Team, 2013)).

Results: PD-MCI (0.702 ± 0.269) patients exhibited significantly lower accuracy on the motion discrimination task than HC (0.853 ± 0.241 ; $p = 0.033$) and PD-NC (0.880 ± 0.208 ; $p = 0.039$). A Group \times Coherence interaction was identified in which several regions, including orbitofrontal, posterior parietal and occipital cortex, showed increased activation during High relative to Low coherence trials in the PD patient groups but not in the HC group. HC showed default mode deactivation and frontal-parietal activation during Low relative to High coherence trials that was not evident in the patient groups. **Conclusions:** PD-MCI patients exhibited worse visuospatial performance on a motion discrimination task than PD-NC and HC participants and exhibited hyperactivation of the posterior parietal and occipital regions during motion discrimination, suggesting possible compensatory activation.

Categories: Neurodegenerative Disorders

Keyword 1: Parkinson's disease

Keyword 2: cognitive functioning

Keyword 3: neuroimaging: functional

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5 Midbrain Degeneration and Cognition in Parkinson's Disease

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Objective: Neuromelanin imaging is an emerging biomarker for PD as it captures degeneration of the midbrain, a process which is associated with the motor symptoms of the disease. Currently, it is unknown whether this degeneration also contributes to cognitive dysfunction in PD beyond dysfunction associated with fronto-subcortical systems, as quantitative examination of substantia nigra (SN) degeneration could not be studied until recently.

In the current study, 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).

Participants and Methods: 11 PD-NC, 16 PD-MCI and 14 age and sex-matched healthy controls (HC) participated in the study. PD participants were diagnosed with MCI based on the Movement Disorders Society Task force, Level II assessment (comprehensive assessment). In addition, all participants underwent an MRI scan that included a T1-weighted sequence and a neuromelanin-sensitive (NM-MRI) sequence. Contrast-to-noise-ratio of the substantia nigra pars compacta (SNc) was calculated and a distribution-corrected z-score was used to identify the number of extrema voxels for each individual, suggestive of the number of voxels that have exhibited significant degeneration (extrema_count). An analysis of covariance (ANCOVA) was used to evaluate group differences between HC, PD-NC, and PD-MCI in the extrema_count accounting for age, sex, and education. A multiple regression for each cognitive variable with extrema_count as the dependent variable adjusting for age, sex, and education were conducted.

Results: A significant main effect of group ($F(2, 33) = 33.548$; $p < 0.001$) indicated that PD-NC (21.55 ± 12.57) and PD-MCI (43.64 ± 32.84) patients exhibited significantly greater extrema_counts relative to HC (3.36 ± 3.61 ; both $p < 0.001$). Regression results indicated that higher extrema_counts were associated with worse cognitive performance across cognitive domains, including working memory (Digit Span Backward; $R^2 = .357$, $F(1,20) = 5.295$, $p = .032$), (Hopkins Verbal Learning Test – Revised, Trials 1 to 3; $R^2 = .432$, $F(1,20) = 5.819$, $p = .026$).

Conclusions: PD patients (PD-NC and PD-MCI) exhibited decreased neuromelanin in the SNc relative to healthy controls, confirming the ability of the NM-MRI sequence to differentiate PD from HC. There was no significant difference in SNc neuromelanin levels between PD-NC patients and PD-MCI patients, however, this is likely due to the small sample size. In addition, significant SNc degeneration was associated with worse cognitive performances in tasks associated with working memory and executive functioning. These results warrant further