What Characterizes and Drives Cognitive Changes in Parkinson's Disease? The Roles of Brain Structure and Connectivity Enabled by a Novel Data Integration Tool

Malireddy, Vennela (School: Caddo Parish Magnet High School)

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor symptoms such as tremor, rigidity, and bradykinesia, as well as widespread cognitive and behavioral deficits, including impairments in memory, processing speed, cognitive flexibility, visuospatial judgment, and global cognition. Sex may also influence the severity and pattern of these cognitive deficits, but these differences along with cognitive aspects remain under-researched. To facilitate efficient analysis of complex databases relevant to PD, we developed PPMIExplorer, a graphical application designed to streamline organization and analysis of multimodal data from the Parkinson's Progression Markers Initiative (PPMI) database. Using PPMIExplorer, we compiled and analyzed cognitive performance and cortical thickness measures from individuals with PD (n = 358) and healthy controls (n = 849). A univariate analysis of covariance (ANCOVA) revealed that the PD group performed significantly worse than controls across all cognitive domains, confirming cognitive and behavioral impairments. Across the PD group, females generally exhibited less pronounced cognitive deficits than males: females outperform males in verbal memory, processing speed, cognitive flexibility and global cognition, whereas males perform better in visuospatial judgment. Cortical thinning correlates with cognitive performance, and these structural patterns highlight gender differences in PD. These findings confirm the presence of measurable cognitive and behavioral deficits in PD and demonstrate the potential of PPMIExplorer as a scalable, time-efficient tool for integrating and analyzing large, multimodal datasets. This work provides insights into the role of cognition and sex differences in PD.

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