

Age at onset and functional striatal connectivity in drug-naïve patients with Parkinson's disease

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Introduction: Compelling evidence suggests that age at onset may significantly affect the clinical picture of Parkinson's disease (PD), in terms of motor and nonmotor symptoms as well as rate of disease progression and development of complications.

Objective: We investigated the potential effect of age on the regional striatal functional connectivity (FC) in a cohort of early PD patients using resting-state functional MRI (rs-fMRI) data.

Methods: 147 drug-naïve PD patients and 38 healthy controls were enrolled. Non-hierarchical cluster were applied to stratify PD patients according to age at onset in 3 subgroups: 32 "early/young", 69 "early/intermediate" and 46 "early/old". "Early/old" PD were presenting with more severe motor and cognitive impairment relative to "early/young" patients. No differences were detected in terms of disease duration between the study groups. Clinical assessments as well as rs-fMRI were performed at baseline. Longitudinal clinical data were also collected at 4-year follow-up. Using connectivity-based parcellation, we obtained three regions-of-interest (ROIs) for different striatal functional subregions: sensorimotor, limbic and cognitive.

Results: The sensorimotor ROI showed increased FC with the left superior frontal gyrus, precuneus and cerebellum, and decreased FC with right lingual gyrus, paracentral lobule and left inferior frontal gyrus in "early/young" compared to "early/old" PD. The limbic ROI showed increased FC with the right temporal gyrus and decreased FC with the posterior cingulate cortex (PCC) in "early/young" compared to "early/old" PD. The cognitive ROI showed increased FC with the cerebellum and decreased FC with PCC in "early/young" compared to "early/old" PD. "Early-young" PD presented a higher risk to develop treatment-related motor complications after 4 years.

Conclusions: Specific changes in the striatal FC are associated with age at onset in PD patients. This pattern is related with better motor outcome at baseline and increased vulnerability to develop treatment-related motor complications overtime, suggesting the presence of striatal compensatory mechanisms.