

Theme: Cognitive Neuroscience

The impact of putamen dopamine in the prefrontal cortex connectivity during executive functioning in Parkinson's disease

Isabel Catarina Duarte^{1,2*}, Ricardo Martins^{1,2}, Filipa Júlio^{2,4}, Íris Almeida³, Joana Marques³, Cristina Januário^{2,4} and Miguel Castelo-Branco^{1,2,4}

1 ICNAS, University of Coimbra, Portugal

2 CIBIT, University of Coimbra, Portugal

3 Department of Physics, University of Coimbra, Portugal

4 Faculty of Medicine, University of Coimbra, Portugal

*presenting author

Abstract:

We investigated the link between presynaptic dopamine synthesis capacity and storage in the putamen and the executive functioning (EF) decline in Parkinson's disease (PD). PD is triggered by the loss of dopaminergic neurons in the substantia nigra that project to the putamen. PD patients often experience EF impairments, where dlPFC seems to play a key role. We have previously assessed executive function in PD using EcoKitchen, a virtual reality tool simulating daily kitchen tasks, which is sensitive to subtle EF changes.

We used dynamic [18F]FDOPA PET to assess dopamine in the putamen and fMRI to measure connectivity between the dlPFC and other brain regions during performance of the EcoKitchen task. Eighteen participants (6 females; age 55.2 ± 8.1 ; disease duration 4.3 ± 3.0 years) with mild PD (UPDRS score 21.1 ± 6.5) were recruited. Dopamine synthesis capacity and storage was quantified by determining K_i , the net influx rate constant, using the Patlak plot method. Standard fMRI preprocessing pipeline was applied. The right dlPFC was selected as the seed for psychophysiological interaction (PPI) connectivity analysis.

Results showed a correlation between dopamine synthesis in the putamen and motor function, as assessed by UPDRS ($r=0.59$, $p=0.008$). Using PPI, we calculated task-related connectivity between the dlPFC and other brain regions during EcoKitchen, then performing whole-brain voxel-wise correlations with dopamine synthesis capacity in the putamen. A link between dopamine synthesis and EF via dlPFC connectivity was found in the frontal pole (BA9/10) and anterior cingulate cortex (BA32) ($r(16) > 0.73$, $p \leq 0.05$ FDR cor.). This result shows that the higher the synthesis capacity in the putamen, the stronger the connectivity between these prefrontal regions.

While dlPFC is pivotal in executive function, the frontal pole and the ACC are also heavily involved, specifically in planning task switching, and error monitoring. This work sheds light on the extent and nature of executive dysfunction in PD.

Keywords: Parkinson's Disease; Dopamine; Executive Function; Functional Connectivity; [18F]FDOPA PET; fMRI