

P19

Effects of dopaminergic medication on reactive and proactive inhibitory control

Giovanni Mirabella^{1,2}, C. Mancini¹, E. Olivola², A. Rizzardi¹, V. Di Caprio², E. Ferrari¹, N. Modugno², A. Pilotto¹, A. Padovani¹

¹Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy

²IRCCS Neuromed, Pozzilli (IS), Italy

Objective: In this study, we addressed the effects of dopaminergic treatment (DT) on the two domains of motor inhibition [1], i.e., reactive (the ability to react to a stop signal) and proactive inhibition (the ability to adapt the motor strategies according to the current context flexibly) according to the stage of Parkinson's disease (PD).

Methods: We recruited cognitively unimpaired PD patients under dopaminergic treatment in the early (H&Y 1/1.5, n=20), intermediate (H&Y 2, n=20), and moderate/advanced (H&Y 2.5/3, n=20) stages and 30 age-matched healthy controls. Each participant underwent a standardized motor and cognitive assessment and stop-signal task (SST). Covariance analyses adjusted for the effect of age, sex, and UPDRS3 evaluated the differences between the performance in the SST (in terms of reactive and proactive inhibition) in DT ON and OFF and each stage of the disease as well as in comparison with controls.

Results: We found that both reactive and proactive inhibition is progressively impaired along the disease. However, the DT negatively affects reactive inhibition in the early and proactive inhibition in the intermediate PD stage. By contrast, DT does not impact motor inhibition in moderate/advanced patients.

Conclusion: In PD's early and intermediate stages, the DT negatively impacts reactive and proactive inhibition, respectively, despite improving motor symptoms. Such evidence supports the dopamine overdose hypothesis [2], which suggests that the administration of DT in the first stages of PD benefits dopamine-depleted dorsal striatal circuitries improving motor symptoms but overdose the more intact dopamine-dependent circuitries of the ventral striatum, impairing executive functions relying on it. Such findings suggest that the DT has to be titrated carefully to maximize patients' quality of life in the first stages of PD.

References:

- [1] Mirabella G. Inhibitory control and impulsive responses in neurodevelopmental disorders. *Dev Med Child Neurol.* 2021 May;63(5):520-526. doi: 10.1111/dmcn.14778. Epub 2020 Dec 19. PMID: 33340369.
- [2] Vaillancourt DE, Schonfeld D, Kwak Y, Bohnen NI, Seidler R. Dopamine overdose hypothesis: evidence and clinical implications. *Mov Disord.* 2013 Dec;28(14):1920-9. doi: 10.1002/mds.25687. Epub 2013 Oct 9. PMID: 24123087; PMCID: PMC3859825.