L-Dopa and STN-DBS modulate the neural encoding of rhythmic auditory stimulation in Parkinson’s

*Antonio Criscuolo[1], Michael Schwartze[1], Sonja Kotz[1,2]

1. Maastricht University, 2. Max Planck Institute for Human Cognitive and Brain Sciences

In rhythmic auditory stimulation (RAS), temporally regular auditory stimuli (e.g., metronome or music), are utilized to support the precise temporal coordination of motion[1] in people with Parkinson’s disease (pwPD). RAS efficacy is typically associated with the switching from an altered internal pacing system to the intact external cueing system. In doing so, RAS is thought to promote the recruitment of the cerebellar-prefrontal network and recalibrate aberrant β-band synchronization in the striato-thalamo-cortical pathway [1], ultimately mirroring effects observed for dopaminergic replacement therapy (levodopa) and deep-brain stimulation (DBS; [2]) protocols targeting the subthalamic nucleus (STN). Here we asked: Do levodopa/DBS treatments modulate the neural encoding of RAS? Does everyone respond to levodopa/DBS interventions the same way?Our analyses revealed changes in (i-ii) event-locked neural responses (pre- and post-stimulus β-band, as well as event-related potentials), (iii) excitation / inhibition balance (E/I; aperiodic exponent) and (iv) neural tracking of rhythm (δ-band inter-trial phase coherence) in function of the treatment. Furthermore, we characterize the link between changes in E/I balance and motor symptom severity (UPDRS-III) with levodopa administration. Overall, we demonstrate inter-individual variability and differential effects of levodopa, 8-week and 1-year DBS treatments on the neural encoding of basic sounds and rhythm, raising doubts on whether every individual benefits from combinations of levodopa/DBS and RAS. In doing so, we encourage future multimodal imaging and translational studies to better characterize individual responses to treatments. This is a fundamental step if we aim at tailoring rehabilitation protocols and optimize intervention efficacy.

References

Koshimori, Y. & Thaut, M. H. Future perspectives on neural mechanisms underlying rhythm and music based neurorehabilitation in Parkinson’s disease. *Ageing Res Rev* 47, 133–139 (2018).
Sharott, A. *et al.* Spatio-temporal dynamics of cortical drive to human subthalamic nucleus neurons in Parkinson’s disease. *Neurobiol Dis* 112, 49–62 (2018).

Keywords: Parkinson, rhythm, basal ganglia, DBS, dopamine