

**Neurophysiological markers of motor reserve in Parkinson's disease**

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*Introduction:* Motor reserve (MR) is defined as the resilience mechanisms of the brain coping with neurodegeneration in idiopathic Parkinson's disease (PD) [1]. No investigation of MR focused on lateralized PD with bilateral binding reduction at dopamine transporter (DAT) imaging.

*Methods:* In this cross-sectional case-control study, we included 16 PD patients and 28 healthy control. Patients were included if their motor signs were unilateral (Hoehn and Yahr stage =1/5, two independent raters) but DAT density ([123I]-Ioflupane-SPECT, DATQUANTTM) was significantly reduced in bilateral putamina (Putamen z-score>0.5). Subjects were extensively investigated using the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS; part-III was videorecorded), Hoehn & Yahr (H&Y) stage. Transcranial magnetic stimulation (TMS) was performed on primary motor cortices (M1) in presymptomatic (PH) and symptomatic hemispheres (SH) for patients and on dominant hemisphere for HC. TMS measured cortical excitability, plasticity and interhemispheric-inhibition (IHI).

*Results:* TMS testing revealed asymmetries in corticospinal excitability with higher values in the PH. SH demonstrated lower M1-plasticity (compared to the asymptomatic hemisphere). Finally, we found reduced IHI from PH to SH. Interestingly, reduced putamen binding was predicted by reduced ICF in SH and by higher plasticity and reduced IHI in PH. Reduced putamen binding was predicted by enhanced plasticity and reduced IHI in PH, and by reduced ICF in SH. Putamen/caudate ratio was directly associated with corticospinal excitability in PH and inversely associated with cortical plasticity in symptomatic hemisphere. MRC distinguished PH from SH (AUC 0.9844). It was associated in SH with PAS increment, IHI and corticospinal excitability reduction.

*Conclusions:* Response to PD neurodegeneration involves a M1-putamen network, and cortico-M1 connections, responsible for excitability and plasticity changes, depending on caudate activity and becoming more effective with binding reduction in putamen. Further insight on PD MR networks is relevant for novel neuromodulation approaches, aimed at reducing motor burden in daily life.

**References:**

[1] Hoening, M.C., Dzialas, V., Drzezga, A., van Eimeren, T., 2022. The Concept of Motor Reserve in Parkinson's Disease: New Wine in Old Bottles? *Mov. Disord. Off. J. Mov. Disord. Soc.* <https://doi.org/10.1002/mds.29266>.