

Asymmetry of bradykinesia features in Parkinson's and interhemispheric inhibition imbalance

*Martina De Riggi*¹, G. Paparella², D. Colella¹, A. Cannavacciuolo², A. De Biase¹, L. Angelini¹, D. Birreci¹, D. Costa¹, A. Guerra², A. Berardelli^{1,2}, M. Bologna^{1,2}

¹Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy

²IRCCS Neuromed, Pozzilli, IS, Italy

Introduction: Bradykinesia and other motor symptoms in Parkinson's disease (PD) are predominantly asymmetric [1,3]. An asymmetrical reorganization and an altered connectivity between the two primary motor cortices (M1) have previously been demonstrated in PD [1,2,3,4]. Whether the asymmetry of motor manifestations relates to the imbalance of the inhibitory interhemispheric connections, however, is still unknown.

Aims: To investigate the relationship between the asymmetry of bradykinesia, quantified by kinematic analysis of finger tapping, and the asymmetry of the interhemispheric inhibitory connections in PD, tested by transcranial magnetic stimulation (TMS).

Methods: Twelve PD patients (1 female, 69.75±9.9 years) and 10 age- and gender-matched healthy controls (HCs) were enrolled. Objective bradykinesia measurements during finger tapping were obtained using a motion analysis system from both sides. Paired-pulse TMS was used to measure the interhemispheric inhibition (IHI) between the hand areas of the two M1, with an interstimulus interval (ISI) between the conditioning (CS) and the test stimulus (TS) of 10 ms (short-latency IHI, sIHI) and 40 ms (long-latency IHI, lIHI)^{[1][2][4]}. Asymmetry indices (AI) were calculated for all neurophysiological data. We then tested possible relationship between kinematic and TMS data in patients.

Results: PD patients were slower than in HCs during finger tapping ($p=0.01$). In PD there was a more severe progressive reduction of movement amplitude during movement repetition, i.e., sequence effect ($p=0.04$). When testing IHI (from the most affected to the less affected hemisphere), we found a reduced sIHI in patients. The amount of interhemispheric disinhibition, i.e., interhemispheric imbalance quantified by the sIHI-AI, correlated with the sequence effect of the less affected side ($p<0.001$).

Conclusions: we here provided novel evidence on the role of interhemispheric disinhibition in the pathophysiology of bradykinesia asymmetry in PD. The results support the hypothesis that the sequence effect has pathophysiology mechanisms distinct from those underlying other bradykinesia features.

References:

- [1] Li JY, Espay AJ, Gunraj CA, Pal PK, Cunic DI, Lang AE, Chen R. Interhemispheric and ipsilateral connections in Parkinson's disease: relation to mirror movements. *Mov Disord.* 2007 Apr 30;22(6):813-21. doi: 10.1002/mds.21386. PMID: 17290459.
- [2] Lizarraga KJ, Saravanamuttu J, Baarbé JK, Lang AE, Chen R. Interhemispheric pathways in agenesis of the corpus callosum and Parkinson's disease. *Brain Stimul.* 2020 Mar-Apr;13(2):360-362. doi: 10.1016/j.brs.2019.11.003. Epub 2019 Nov 4. PMID: 31727582.
- [3] Malling ASB, Morberg BM, Wermuth L, Gredal O, Bech P, Jensen BR. The effect of 8 weeks of treatment with transcranial pulsed electromagnetic fields on hand tremor and inter-hand coherence in persons with Parkinson's disease. *J Neuroeng Rehabil.* 2019 Jan 31;16(1):19. doi: 10.1186/s12984-019-0491-2. PMID: 30704504; PMCID: PMC6357382.

[4] Bologna M, Caronni A, Berardelli A, Rothwell JC. Practice-related reduction of electromyographic mirroring activity depends on basal levels of interhemispheric inhibition. *Eur J Neurosci.* 2012 Dec;36(12):3749-57. doi: 10.1111/ejn.12009. Epub 2012 Oct 4. PMID: 23033874.