

Deep neurobehavioral phenotyping uncovers neural fingerprints of locomotor deficits in PD.

Garulli EL, Merk T, El Hasbani G, Kabaoğlu B, De Sa R, Behrsing R, Doll D, Schellenberger MF, Hanafi I, Vogt A, Neumann WJ, Palmisano C, Isaias IU, Peng Y, Endres M, Harms C, Wenger N. *NPJ Parkinsons Dis.* 2026; 12(1): 65. doi: 10.1038/s41531-026-01280-4. PMID: 41654501.

Parkinson's Disease (PD) is characterised by diverse neural and behavioural deficits, and complex motor deficits, like Freezing of Gait (FoG), remain a therapeutic challenge. The limited success in addressing these symptoms led to the exploration of adaptive DBS protocols and the search for suitable biomarkers to guide the intervention. In this study, we employed a data-driven approach to identify novel neural correlates of akinetic episodes in a 6-OHDA unilateral rodent model, and explored the translational value of our findings in two Parkinson's patients. We identified Hjorth Complexity and Mobility as two novel parameters that correlate with the onset of akinetic episodes, both for rodents and humans.

We trained hemiparkinsonian rats to traverse a runway while recording 3D kinematics and neural data from ECoG screws over the Motor Cortex. Then, we labelled their locomotion sequences with three distinct locomotor states: gait, stationary movement (e.g. grooming) and akinesia. Using the self-developed toolbox neurokin, we extracted relevant kinematic features, and using `py_neuromodulation` (developed in the B03 project), we computed an extensive set of neural features. To pinpoint salient features characterising locomotor states, we compared two complementary machine learning models. We identified features that were consistently relevant in constructing a low-dimensional embedding space, indicating their modulation across locomotor states.

We corroborated the validity of this bottom-up pipeline by confirming that it retrieved known correlates of akinesia and bradykinesia (such as beta band amplitude), as well as known correlates of prokinetic activity (such as gamma band amplitude). However, most interestingly, it also identified novel features such as Hjorth Complexity and Mobility as playing an important role in characterising the locomotor states.

Finally, the translational relevance of these findings was supported by validation in two Parkinson's patients with FoG, using STN recordings during walking tasks (the data were kindly provided by the B04 project).

In one patient, STN activity reproduced the modulation profile of the novel biomarkers observed in rodents, with an increase

in Hjorth Complexity and a decrease in Hjorth Mobility during FoG. Although the second patient showed no clear modulation, this was likely due to suboptimal electrode placement.

Overall, we propose these novel neural fingerprints as potential biomarkers of akinetic states, which could be further explored as targets for precision interventions such as closed-loop stimulation. ■



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Elisa Garulli is a PhD student in the Translational Neuromodulation Group at Charité in the lab of Prof. Wenger. She investigates novel neurobehavioral markers in a rodent model of Parkinson's and develops closed-loop paradigms for spinal cord stimulation to improve gait deficits.



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