Evoked and Spontaneous High-Frequency Biomarkers for DBS Surgery and Programming

WSSFN 2025 Interim Meeting. Abstract 0031

Alan Bush,[1] Matteo Vissani,[1] Abigail Zuckerman,[1,2] German Abrebaya,[3] Clemens Neudorfer,[1] T. Herrington,[1] Helmut Strey,[1,4] Lilianne Mujica-Parodi,[1,4] Robert Mark Richardson.[1]

[1] Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
[2] Harvard Medical School, Cambridge, MA, USA
[3] Harvard Medical School, MA, USA
[4] State University of New York at Stony Brook, Stony Brook, NY

Corresponding author: Alan Bush. email: alan.bush@mgh.harvard.edu

How to Cite: Bush A, Vissani M, Zuckerman A, Abrebaya G, Neudorfer C, Strey H, et al. Evoked and Spontaneous High-Frequency Biomarkers for DBS Surgery and Programming: WSSFN 2025 Interim Meeting. Abstract 0031. NeuroTarget 2025;19(2):15-6.

Abstract

Introduction: Beta oscillations are established biomarkers of rigidity and bradykinesia in Parkinson's disease (PD).[1-3] However, beta-band exhibits considerable intra- and inter-patient variability and correlates only partially with the spectrum of PD motor signs or clinical response to DBS.[4] More reproducible biomarkers, directly tied to network dynamics evoked by stimulation, are needed to optimize DBS frequency, waveform, and spatial patterns of stimulation for individual patients. Here we assess two promising biomarkers - high-frequency oscillations (HFOs)[5-7] and evoked resonant neural activity (ERNA),[8-12] examining their spatial distribution and co-occurrence in the BG.

Method: We recorded intraoperative LFPs from directional DBS leads in PD patients undergoing awake surgery. Passive and evoked potentials (EP), obtained after bursts of DBS-like stimulation, were recorded. Cohort 1, 29 subjects (University of Pittsburgh, 2017–2019); Cohort 2, 9 subjects (MGH, 2024–2025). We quantified resting-state power spectra and evoked responses, focusing on HFOs and ERNA in STN, GPi, and VIM. Spectral features were extracted via a custom implementation of specparam,[13,14] and EP were analyzed using MATLAB and R. Statistical analyses employed linear mixed-effects models. We developed two computational models of the BG network in Neuroblox: a biophysically detailed H-H model,[15] and a Next-Generation Neural Mass Model.

Results: Both HFOs and ERNA were robustly detected in both the STN and GPi, but not in VIM. Within the STN, HFOs exhibited clear spatial clustering, with "fast" (300-350 Hz) oscillations localized ventrally to "slow" (250-300 Hz) oscillations. ERNA waveforms, measured across the ventral and dorsal ring contacts, were remarkably consistent across stimulation from directional segments, suggesting activation of a single circuit. Failure to evoke ERNA in the STN was predictive of suboptimal lead placement. Our computational models of the STN and GP network successfully recapitulated spontaneous HFOs and the temporal dynamics of ERNA.

Discussion: HFOs and ERNA coincide in frequency and co-occur across patients, suggesting a common neural substrate. We hypothesize that spontaneous HFOs reflect intrinsic STN<=>GP dynamics, which are enhanced by DBS, manifesting as ERNA. Our computational models capture these dynamics, providing mechanistic insight.

Conclusions: High-frequency intraoperative biomarkers could help confirm accurate lead placement. ERNA can be recorded in less than 200ms per trial, enabling time-efficient exploration of stimulation parameters. Model-based fitting of patient-specific HFO and ERNA data can enable in-silico optimization of DBS settings, streamlining DBS programming.

References

1. Brown P. et al. Dopamine Dependency of Oscillations between Subthalamic Nucleus and Pallidum in Parkinson's Disease. J Neurosci. 2001; 21:1033–1038.
2. Neumann W. et al. Subthalamic synchronized oscillatory activity correlates with motor impairment in patients with Parkinson's disease. Mov. Disord. 2016;31:1748–1751.
3. Kühn A, Kupsch A, Schneider G, & Brown P. Reduction in subthalamic 8–35 Hz oscillatory activity correlates with clinical improvement in Parkinson's disease. Eur J Neurosci. 2006;23:1956–1960.
4. Little S, et al. Adaptive deep brain stimulation in advanced Parkinson disease. Ann. Neurol. 2013;74:449–457
5. Foffani G. et al. 300-Hz subthalamic oscillations in Parkinson's disease. Brain. 2003;126, 2153–2163.
6. López-Azcárate J. et al. Coupling between Beta and High-Frequency Activity in the Human Subthalamic Nu-

cleus May Be a Pathophysiological Mechanism in Parkinson's Disease. J. Neurosci. 2010;30:6667–6677
7. Aman JE. et al. Directional deep brain stimulation leads reveal spatially distinct oscillatory activity in the globus pallidus internus of Parkinson's disease patients. Neurobiol. Dis. 2020;139:104819.
8. Sinclair NC. et al. Subthalamic nucleus deep brain stimulation evokes resonant neural activity. Ann Neurol. 2018;8:1027–1031.
9. Sinclair NC et al. Deep brain stimulation for Parkinson's disease modulates high-frequency evoked and spontaneous neural activity. Neurobiol. Dis. 2019;130: 104522.
10. Awad M. Z. et al. Subcortical short-term plasticity elicited by deep brain stimulation. Ann. Clin. Transl. Neurol. 2021;8:1010–1023.
11. Johnson KA, et al. Globus pallidus internus deep brain stimulation evokes resonant neural activity in Parkinson's disease. Brain Commun. 2023. doi:10.1093/braincomms/fcad025.
12. Wiest C. et al. Evoked resonant neural activity in subthalamic local field potentials reflects basal ganglia network dynamics. Neurobiol Dis. 2023: 106019 doi:10.1016/j.nbd.2023.106019.
13. Donoghue T, et al. Parameterizing neural power spectra into periodic and aperiodic components. Nat Neurosci. 2023 23:1655–1665.
14. Bush A, Zou JF, Lipski WJ, Kokkinos V & Richardson. RM. Aperiodic components of local field potentials reflect inherent differences between cortical and subcortical activity. Cereb. 2024; Cortex 34, bhae186.
15. Adam EM, Brown EN, Kopell N & McCarthy MM. Deep brain stimulation in the subthalamic nucleus for Parkinson's disease can restore dynamics of striatal networks. Proc. Natl. Acad. Sci. 2022;119:e2120808119
16. Chen L & Campbell SA. Exact mean-field models for spiking neural networks with adaptation. J. Comput. Neurosci. 2022;50:445–469.
17. Byrne Á, O'Dea RD, Forrester M, Ross J & Coombes S. Next-generation neural mass and field modeling. J. Neurophysiol. 2020;123:726–742.