Characterizing Neural Representation and Sleep Architecture in Early Motor Sequence Learning Using a Chronic Neural Interface in Patients with Parkinson's Disease

K. Presbrey[1*], J. Bernabei[2], S. Kondapavulur[1], K. Louie[1], A. Giff[1], P. Starr[1], D. Wang[1]
[1]*University of California San Francisco, San Francisco, CA, USA;*
[2]*University of Pennsylvania, Philadelphia, Pennsylvania, USA*
*505 Parnassus Ave, Moffitt Hospital M779, San Francisco, CA, 94143, USA | kara.presbrey@ucsf.edu

Introduction. The neural encoding of motor sequences over prolonged practice and consolidation of the corresponding memories during sleep are poorly understood in Parkinson's (PD) patients and healthy subjects alike. This is due to low spatiotemporal recording resolution and difficulties separating learned neural encoding changes from changes in neural activity as a byproduct of changing behavior. Our solution: (1) Use chronic multisite neural implants to record high spatiotemporal resolution local field potentials (LFPs) from the motor control network of PD patients while they practice typing two sequences for multiple days on (2) in-house custom equipment that precisely captures movement.

Methods and Results. Five PD patients were implanted with chronic, multisite bidirectional implants (Summit RC+S), with one quadripolar lead over motor cortex and one quadripolar lead in the basal ganglia (subthalamic nucleus or globus pallidus).

We recorded neural activity while patients performed a 5-day typing task and while they slept each night after the task. Each day, patients practiced typing sequences S1 and S2 in response to visual stimuli. An in-house keypad captured precise movement onset times using proximity and force sensors. A photodiode and additional eeg monitor (used to detect neurostimulation transients) soldered to the keypad motherboard allow for alignment of movement data with the visual stimuli and neural interfaces respectively. Patients demonstrated learning across days.

To assess pre-movement sequence-specific neural activity for learned sequences, we compared Day 4 neural activity for S1 vs. S2 during the 200ms prior to the onset of sequence execution in our first patient. Ridge classifiers trained on oscillatory power of dorsal STN (dSTN) (65.1%, $p = 0.001$), but not ventral STN (vSTN) (53.8%, $p = 0.21$) or M1 (50.0%, $p = 0.50$), predicted the identity of the upcoming sequence better than chance. Shuffling any frequency band largely decreased dSTN decoding accuracy; shuffling gamma caused the greatest drop (alpha: -12%, beta: -15%, gamma: -24%).

In our preliminary sleep analysis, we built a model to classify sleep stages using neural data and built spindle, slow oscillation (SO), and replay detectors. Early results suggest there is more spindle-SO coupling during sleep after the task relative to the null distribution and that spindles occur predominantly during slow wave sleep.

Discussion. Our early results show that single-trial classification on dSTN alpha, beta and gamma, collectively, can predict the identity of an upcoming movement sequence before movement has begun, suggesting dSTN may encode a motor planning or sequence-specific initiation signal for learned motor skills in PD patients. The failure of M1 activity to predict identity of a planned sequence is consistent with recent findings that M1 does not represent sequence identity, a high-level movement property, in healthy subjects either [1]. Our initial sleep analysis results show learning-related changes consistent with other work [2]. Our forthcoming analysis on additional behavioral epochs, sessions, patients, and treatment conditions (DBS ON) will help define a systems neurophysiological framework for understanding motor sequence learning, representation and offline consolidation in PD.

Significance. This is the first, that we know of, electrophysiological investigation of the role of the cortico-basal ganglia motor control network in human multi-day dexterous motor sequence learning at sufficient spatiotemporal resolution and the first electrophysiological investigation of prolonged motor sequence learning in PD at *any* spatiotemporal resolution. We provide evidence that low frequency aggregate neural activity can provide useful information for BCI decoders for hand movement.

References. [1] Berlot, Eva et al. "Combining Repetition Suppression and Pattern Analysis Provides New Insights into the Role of M1 and Parietal Areas in Skilled Sequential Actions." *The Journal of neuroscience : the official journal of the Society for Neuroscience* vol. 41,36 (2021): 7649-7661. doi:10.1523/JNEUROSCI.0863-21.2021
[2] Solano, Agustín et al. "Motor Learning Promotes the Coupling between Fast Spindles and Slow Oscillations Locally over the Contralateral Motor Network." *Cerebral cortex (New York, N.Y. : 1991)* vol. 32,12 (2022): 2493-2507. doi:10.1093/cercor/bhab360.