Circuit-Inspired Strategies to Improve Treatments for Parkinson's Disease

October 29

Tuesday, 12:30 pm

Billings Building—Rosedale Room

SPEAKER:

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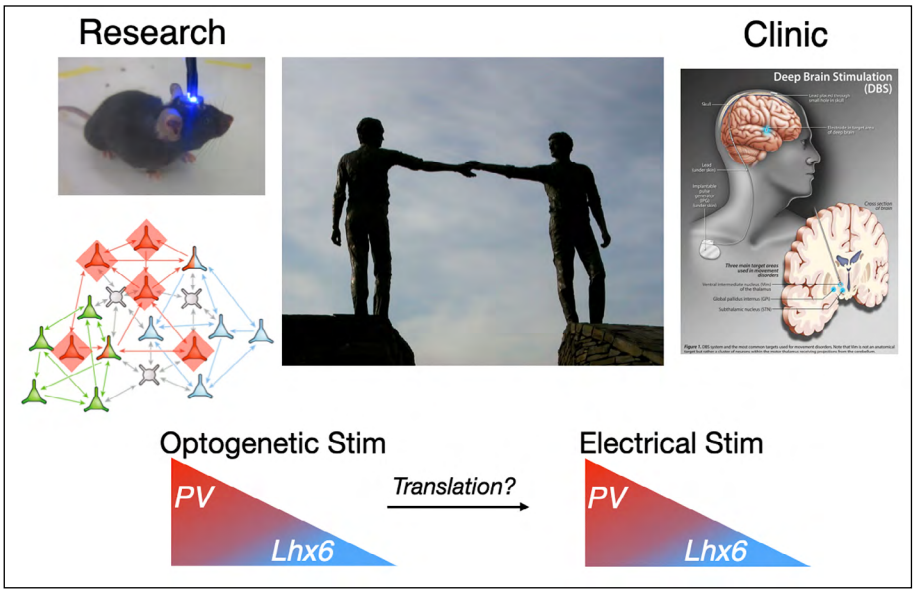
Abstract

Symptoms of neurological diseases emerge through the dysfunction of neural circuits whose diffuse and intertwined architectures pose serious challenges for delivering therapies. Deep brain stimulation (DBS) improves Parkinson's disease symptoms acutely but does not differentiate between neuronal circuits, and its effects decay rapidly if stimulation is discontinued. Recent findings suggest that optogenetic manipulation of distinct neuronal subpopulations in the external globus pallidus (GPe) provides long-lasting therapeutic effects in dopamine-depleted (DD) mice. We used synaptic differences to excite parvalbumin-expressing GPe neurons and inhibit lim-homeobox-6–expressing GPe neurons simultaneously using brief bursts of electrical stimulation. In DD mice, circuit-inspired DBS provided long-lasting therapeutic benefits that far exceeded those induced by conventional DBS, extending several hours after stimulation. These results establish the feasibility of transforming knowledge of circuit architecture into translatable therapeutic approaches.



Publications

Dopamine depletion weakens direct pathway modulation of SNr neurons,A Aristieta, JE Parker, YE Gao, JE Rubin, AH Gittis. Neurobiology of Disease 196, 1065121 2024

Population-specific neuromodulation prolongs therapeutic benefits of deep brain stimulation, TA Spix, S Nanivadekar, N Toong, IM Kaplow, BR Isett, Y Goksen, Science 374 (6564), 201-206

The indirect pathway of the basal ganglia promotes transient punishment but not motor suppression, BR Isett, KP Nguyen, JC Schwenk, JR Yurek, CN Snyder, MV Vounatsos, Neuron 111 (14), 2218-2231. e421 2023