Award Presentation (Oral)

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Subthalamo-pallidal interactions underlying parkinsonian neuronal oscillations in the primate basal ganglia

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Parkinson's disease (PD) is characterized by degeneration of nigral dopaminergic neurons, leading to psychomotor dysfunctions. Accumulated studies suggest that abnormal oscillations in the basal ganglia contribute to the expression of PD symptoms. However, the mechanism that generates abnormal oscillations in a dopamine-depleted state remains poorly understood. We addressed this question by examining basal ganglia neuronal activity in two MPTP-treated parkinsonian monkeys. We found that systemic administration of L-DOPA (dopamine precursor) diminished abnormal oscillations (8-15 Hz) in the internal pallidum (GPi) and subthalamic nucleus (STN) when PD signs were alleviated. GPi oscillations and PD signs were suppressed by silencing of the STN with infusion of muscimol. Neuronal oscillations in the STN were suppressed after intrasubthalamic microinjection of CPP (NMDA receptor antagonist) and NBQX (AMPA/kainate receptor antagonist) to block glutamatergic afferents of the STN. The STN oscillations were further eliminated by muscimol inactivation of the external pallidum (GPe) to block GPe GABAergic inputs. These results suggest that, in the dopamine-depleted state, glutamatergic inputs to the STN and reciprocal GPe-STN interconnections are both important for the generation of the oscillatory activity of STN neurons, which is subsequently transmitted to the GPi, thus contributing to the symptomatic expression of PD.