THE IONIC MECHANISM UNDERLYING THE PATHOLOGICALLY INCREASED BURST DISCHARGES IN THE SUBTHALAMIC NUCLEUS IN PARKINSON’S DISEASE

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Introduction: Neural circuits involving the basal ganglia are related to motor functions, the impairment of which may result in clinical diseases including Parkinson’s disease (PD). The pathological oscillations in the pallido-subthalamic network seem to assume an important role in the pathophysiology of PD, as deep brain stimulation on the subthalamic nucleus (STN) has proved an effective treatment of PD-related symptoms in neurological clinics. However, the ionic mechanism underlying the synchronized rhythmic activity in STN is not fully clear.

Aims: With in-vivo electrophysiological recordings and behavioral tests in parkinsonian rats, we have established a causal role of increased subthalamic burst discharges in parkinsonian motor symptoms. Accordingly, the aim of this study is to explore the ionic mechanism underlying the increased bursting activities in STN and thus the pathophysiology of PD.

Methods: Pharmacological and electrophysiological characterizations were done with whole-cell patch-clamp and cell-attached extracellular recordings in STN neurons that is either acutely dissociated or located in acute brain slices.

Results: We characterized low-voltage activated Ca2+ conductances or T-type Ca2+ currents in acutely dissociated STN neurons. Moreover, pharmacological interventions that inhibit T-channel currents in dissociated neurons would dramatically diminish, whereas the other Ca2+ channel blockers without observable effects on T-channels did not affect, STN burst discharges in slices.

Conclusions: These findings demonstrate that T-type Ca2+ channels are essential for the genesis of the subthalamic burst discharges. Inhibition of subthalamic T-type Ca2+ currents would decrease subthalamic bursting discharges, and may thus constitute a novel strategy for the treatment of Parkinson’s disease.