The increase of burst discharges in the subthalamus is essential for the genesis of locomotor deficits in Parkinson's disease

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Introduction: Parkinson's disease (PD) is a common neurodegenerative disorder with characteristic motor disabilities. The pathophysiology of PD may be contributed by abnormal electrophysiological activity in the subthalamic nucleus (STN). This idea arises from the increased burst firings of STN neurons in PD, and is also in part suggested by the symptomatic relief of PD with electrical stimulation (deep brain stimulation, DBS) of STN. However, neither the molecular mechanisms underlying DBS nor the causal relation between the abnormal subthalamic firings and motor symptoms in PD has been established.

Aims: This study is aimed to explore whether or not the increased burst activity in STN has a direct casual relation with parkinsonian motor disabilities. In other words, could direct modulation of STN bursts readily remedy parkinsonian motor deficits?

Methods: We did in-vivo single-unit extracellular recordings and behavioral tests of locomotor activities in 6-OHDA-induced parkinsonian rats. The effects of different chemical and electrical interventions on neuronal discharges and locomotor behavior were documented.

Results: Administration of specific electrophysiological maneuvers or chemical agents (e.g. Ni2+) that decrease STN burst discharges would readily alleviate the locomotor deficits in parkinsonian animals, whereas those which do not reduce burst discharges (e.g. Cd2+) showed little or no effect on locomotor deficits.

Conclusions: Our findings demonstrate that increased burst discharges in STN has an essential contribution to, or even is the direct cause of, the locomotor deficits in the parkinsonian state. This may serve as a critical base for more sophisticated electrophysiological and novel pharmacological therapies of parkinsonian symptoms.