

Gait Regulation by Nested Phase-Locked Inhibit-and-Fire Neuronal Circuits

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OBJECTIVE: To propose a neuronal model for gait regulation, to validate it by examination of neurophysiological and clinical evidence and to evaluate its implications in gait therapy.

BACKGROUND: The gait regulation mechanism has long been a subject for research and debate. Roles for internal cuing and for sensory information in open and closed-loop have been proposed and disputed. Yet, analytic examination of neurophysiological and clinical evidence shows that solving the gait cuing enigma reduces to understanding the bursting activity of the midbrain dopamine neuron.

METHODS: Neurophysiological evidence was compressed into analytically plausible models of the basal ganglia and the dopamine neuron bursting mechanism. Cross-examination of clinical data obtained for healthy individuals and for patients with movement disorders involving different information pathways, Parkinson's disease and multiple sclerosis in particular, was used to validate the proposed models.

RESULTS: A control-theoretic model of the basal ganglia was constructed, showing that the bursting activity of the dopamine neuron is regulated by three topologically and functionally nested mechanisms, phase-locking proprioceptive and sensory (visual auditory and tactile) feedback signals from the subthalamus nucleus. The internal phase-lock is self-inhibition of the dopamine neuron. The intermediate phase-lock is cross-inhibition of dopamine and GABA neurons of the substantia nigra. The external phase-lock is the dopamine-glutamate feedback loop connecting the dopamine neuron and the subthalamus. All three phase-locks are modulated by behavioral activities, such as movement with respect to earth-stationary visual objects. Nesting makes the inhibit-and-fire phase-locks highly fault-tolerant. Loss of dopamine, as in Parkinson's disease (PD), reducing the efficacy of the self-inhibitory phase-lock, is compensated by GABA cross-inhibition and vice versa. Loss of proprioception, as in multiple sclerosis (MS), is compensated by sensory feedback, and vice versa. Long-term potentiation and depression, hence, memory, makes dopamine neuron bursting possible without dopamine. A comparative analysis of clinical data obtained for healthy individuals and for PD and MS patients using artificially enhanced sensory feedback shows age and disease-related benefits, conforming with the proposed model.

CONCLUSION: Gait is regulated by the bursting activity of the midbrain dopamine neuron. Nested phase-locked circuits regulate neuronal bursting by self-inhibit-and-fire and cross-inhibit-and-fire mechanisms, providing a high degree of fault tolerance. Movement disorders are compensated by sensory feedback enhanced by memory, which makes dopamine neuron bursting possible with and without dopamine.