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Spike threshold dynamics shape the response of subthalamic neurons to cortical input

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The subthalamic nucleus (STN) is a population of autonomously active glutamatergic neurons within the basal ganglia (BG) that innervates BG output nuclei and is reciprocally connected with the globus pallidus (GP). The STN receives cortical input and so forms a direct bridge to BG output nuclei that bypasses the striatum. The STN's response to cortical stimulation in vivo begins at very short latency (2-5 ms) and consists of two excitatory peaks divided by a brief period of inhibition. The brief inhibition is generally ascribed to disynaptic inhibition from the GP, but signs of cortically-evoked inhibition persist in some STN recordings made in rats with GP lesions. We investigated the contribution of intrinsic properties to the STN's response to cortical excitation by studying their response to cortical fiber stimulation in brain slices in the presence of GABAergic antagonists. Responses to relatively strong stimulation often exhibited two distinct excitatory peaks in the PSTH separated by a gap that resembles inhibition. The distribution of latencies to the first poststimulus spike could also exhibit this gap, so this effect cannot be attributed to the AHP of the first spike. We found that spikes fired shortly after the onset of large EPSPs were triggered at a substantially lowered threshold (2-7 mV). The threshold dropped rapidly (within 1-2 ms of EPSP onset) and rose quickly back to the baseline level (or to a slightly elevated threshold). This drop in threshold can explain the two peaks seen in PSTHs and latency distributions: the cell fires immediately when above the lowered threshold but must otherwise wait until reaching the higher baseline threshold if it misses the narrow low-threshold window. Thus, EPSP-evoked changes in spike threshold can both facilitate a rapid, short-latency response in the STN to strong cortical input and change the firing pattern evoked by that input. Smaller EPSPs advance the time of the next spike but evoke smaller changes in spike threshold that do not produce the appearance of an excitation-inhibition sequence. The change in firing pattern associated with large EPSPs could allow targets of STN projections to distinguish activity driven by sharp increases in cortical drive from autonomous or tonically-driven activity. A model of the STN's response to cortical input suggests that two modes of operation–a coincidence-detecting short latency response to sharp increases in excitation and a more subtle response to smaller fluctuations in synaptic drive–can coexist and operate in parallel.

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