

More than meets the Eye-Myelinated axons crowd the subthalamic nucleus.

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Source

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Abstract

High frequency deep brain stimulation (DBS) of the subthalamic nucleus (STN) is a successful treatment for patients with advanced Parkinson's disease (PD). Although its exact mechanism of action is unknown, it is currently believed that the beneficial effects of the stimulation are mediated either by alleviating pathological basal ganglia output patterns of activity or by activation of the axons of passage that arise from the cerebral cortex and other sources. In this study, we show that the anatomical composition of the primate STN provides a substrate through which DBS may elicit widespread changes in brain activity via stimulation of fibers of passage. Using quantitative high-resolution electron microscopy, we found that the primate STN is traversed by numerous myelinated axons, which occupy as much as 45% of its sensorimotor territory and 36% of its associative region. In comparison, myelinated axons occupy only 27% of the surface areas of the sensorimotor and associative regions of the internal segment of the globus pallidus (GPi), another target for therapeutic DBS in PD. We also noted that myelinated axons in the STN, on average, have a larger diameter than those in GPi, which may render them more susceptible to electrical stimulation. Because axons are more excitable than other neuronal elements, our findings support the hypothesis that STN DBS, even when carried out entirely within the confines of the nucleus, mediates some of its effects by activating myelinated axons of passage.