Short latency activation of cortex during clinically effective subthalamic deep brain stimulation for Parkinson's disease.

Subthalamic deep brain stimulation (DBS) is superior to medical therapy for the motor symptoms of advanced Parkinson's disease (PD), and additional evidence suggests that it improves refractory symptoms of essential tremor, primary generalized dystonia, and obsessive-compulsive disorder. Despite this, its therapeutic mechanism is unknown. We hypothesized that subthalamic stimulation activates the cerebral cortex at short latencies after stimulus onset during clinically effective stimulation for PD. In 5 subjects (six hemispheres), EEG measured the response of cortex to subthalamic stimulation across a range of stimulation voltages and frequencies. Novel analytical techniques reversed the anode and cathode electrode contacts and summed the resulting pair of event-related potentials to suppress the stimulation artifact. We found that subthalamic brain stimulation at 20 Hz activates the somatosensory cortex at discrete latencies (mean latencies: 1.0 ± 0.4, 5.7 ± 1.1, and 22.2 ± 1.8 ms, denoted as R1, R2, and R3, respectively). The amplitude of the short latency peak (R1) during clinically effective high-frequency stimulation is nonlinearly dependent on stimulation voltage (P < 0.001; repeated-measures analysis of variance), and its latency is less variable than that of R3 (1.02 versus 19.46 ms; P < 0.001, Levene's test). We conclude that clinically effective subthalamic brain stimulation in humans with PD activates the cerebral cortex at 1 ms after stimulus onset, most likely by
antidromic activation. These findings suggest that alteration of the precise timing of action potentials in cortical neurons with axonal projections to the subthalamic region may be an important component of the therapeutic mechanism of subthalamic brain stimulation.

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