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Modulating basal ganglia and cerebellar activity to suppress parkinsonian tremor

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Despite extensive research, the detailed pathophysiology of the parkinsonian tremor is still unknown. It has been hypothesized that the generation of parkinsonian tremor is related to abnormal activity within the basal ganglia. The cerebello-thalamic-cortical loop has been suggested to indirectly contribute to the expression of parkinsonian tremor. However, the observed tremor-related hyperactivity in the cerebellar loop may have a compensatory rather than a causal role in Parkinson's disease (PD) by preventing tremor from spilling over into voluntary movement. Furthermore, observed overactivation in cerebellar loops has also been associated with a higher ability of PD patients to perform repetitive movements that are cued by auditory or visual stimuli, suggesting that rhythmic synchronization with an auditory timekeeper can be achieved in the absence of intact basal ganglia function. Deep brain stimulation (DBS) in the subthalamic nucleus (STN) is currently an accepted treatment for advanced PD that may significantly improve motor complications and reduce tremor. While DBS directly influences neuronal activity patterns in basal ganglia loops, it may be expected that modulation of the cerebellar loops have an additional effect on parkinsonian tremor if both loops are involved in tremor generation and expression.

The aim of this pilot study is to test whether the combination of DBS and auditory cueing has an enhanced effect on tremor reduction. Therefore, in a group of seven PD patients receiving STN-DBS, tremor occurrence in both hands and both feet was sequentially tested while performing repetitive movements cued by an auditory signal. The frequency of the auditory cues ranged from 1.6 Hz, which is within the range of frequencies that can be found during normal movements, and 4.8 Hz, which is near the average PD tremor frequency. Movements and tremor were registered by inertial sensors attached to the hands and feet. The Chi-square test was used to compare the occurrence of tremor in any of the extremities for the different cueing frequencies and DBS "on" and "off".

Compared to the resting condition and the performance of self-paced hand or foot movements, the number of extremities showing tremor was significantly reduced under external cueing conditions when stimulation was "on". With DBS "off", only the lower cueing frequencies (1.6 and 3.2 Hz) provided a beneficial effect.

From the results it may be hypothesized that modulation of the pathological patterns in basal ganglia (by DBS) and cerebellar activity (by auditory cueing) provides enhanced suppression of action tremor in PD.