Suppression of parkinsonian tremor with deep brain stimulation and auditory cueing

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DESPITE extensive research, the detailed pathophysiology of parkinsonian tremor remains unknown. It has been hypothesized that the generation of parkinsonian tremor is related to abnormal activity within the basal ganglia. The cerebello-thalamocortical loop has also been suggested to indirectly contribute to the expression of parkinsonian tremor [1,2]. 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 [3]. Furthermore, hyperactivity 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 external timekeeper can be achieved in the absence of intact basal ganglia function [3,4].

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) may significantly reduce tremor. While DBS directly influences neuronal activity patterns in the basal ganglia loops, it may be expected that modulation of the cerebellar loops may 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, tremor occurrence in both hands and both feet was sequentially tested in seven PD patients receiving STN-DBS while performing repetitive movements cued by an auditory signal. Inertial sensors attached to the hands and feet registered any movements and tremor. Each patient performed the following test: moving the hand or foot between two dots indicated on the table or on the floor with a distance of 30 cm between them. The movement frequency was dictated by a metronome which sequentially beat at a frequency of 1.6, 3.2 or 4.8 Hz for a duration ranging between 10 and 16 seconds. This test was subsequently performed by the right arm, left arm, right leg, left leg. The sequence of metronome frequencies was randomized. Each test was performed both for stimulation "on" and "off"; stimulator settings were applied according to the settings normally used by each individual patient with stimulation amplitudes in the range from 2 to 4.2 V, and a frequency of 140 or 145 Hz.

Tremor often is present intermittently. Since tremor frequency is rather constant it may be recognized within short time intervals on the basis of the power spectral density of movement signals. All recorded signals were divided into windows of 2 s and each window was classified as a tremor or non-tremor window based on the spectral properties [5]. The Chi-square test was used to compare the occurrence of tremor, i.e. the occurrence of at least one tremor window during the test, in any of the extremities for the different cueing frequencies and DBS "on" and "off" states. The number of extremities showing tremor under cued conditions were compared to the occurrence of rest tremor and action tremor during self-paced movements.

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

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