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Deep brain stimulation improves movement amplitude but not hastening of repetitive finger movements

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HIGHLIGHTS

- We examined the effects of STN-DBS on repetitive finger movements.
- Subjects moved faster or slower than the tone rate off stimulation.
- STN-DBS improved movement rate in subjects who moved slower only.
- STN-DBS improved movement amplitude across all subjects.

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ABSTRACT

External pacing cues, dopaminergic medication, and bilateral subthalamic nucleus deep brain stimulation (STN-DBS) improve repetitive movements performed at low rates. When the pacing rate is increased to frequencies near 2 Hz and above, both external pacing cues and Parkinson's medication were shown to be ineffective at improving repetitive finger movement performance. It remains unclear if STN-DBS improves the performance of repetitive finger movements at high pacing rates. This study examined the effects of STN-DBS on the amplitude and rate of repetitive finger movement across a range of external pacing rates. Nine participants with STN-DBS (OFF and ON stimulation) and nine matched healthy adults performed repetitive index finger flexion movements paced by an acoustic tone that increased from 1.0 to 3.0 Hz. OFF stimulation, most subjects moved at rates that were substantially higher (hastening pattern) or lower (bradykinesia pattern) than the tone rate, particularly at high pacing rates. ON stimulation, movement rate improved in subjects with the bradykinesia pattern, but not in those with the hastening pattern. Overall, STN-DBS did not significantly affect movement rate. In contrast, STN-DBS significantly ($p < 0.05$) improved movement amplitude across all pacing rates. These findings demonstrate that STN-DBS improves movement amplitude, but had no effect on the rate of movement in participants with a hastening pattern. Separately testing movement amplitude and movement rate using both high and low rate externally paced cues in the clinical environment may aid in the diagnosis and treatment of people with Parkinson's disease.

1. Introduction

People with Parkinson's disease (PD) have marked impairments in the performance of repetitive movements which contribute to difficulties performing many activities of daily living. The clinical and functional importance of this movement type is reflected by the fact that 30% of the motor score from the Unified Parkinson's Disease Rating Scale (UPDRS) is derived from assessment of repetitive movements. During clinical testing of repetitive movements, patients are usually asked to move "as fast and as wide as possible". These instructions often result in two different behaviors: (1) low

Abbreviations: STN-DBS, subthalamic nucleus deep brain stimulation; STN, subthalamic nucleus; PD, Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale; HOA, healthy older adult.

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rate, large amplitude movements (bradykinetic pattern) or (2) high rate, small amplitude movements (hypokinesia or hastening pattern) [4]. The provision of external pacing cues has been proposed as a method to improve the performance of repetitive movements in people with PD [5,10,13]. Consistent with this idea, several studies have shown that amplitude, rate and inter-movement variability of movements are significantly improved by external pacing cues when the pacing rate is relatively slow (e.g. less than 2 Hz) [20,28]. Yet, when movements are paced by cues presented at high rates (typically near or above 2 Hz) the impairments in repetitive finger movement worsen [6,16,19,20,23,28]. Moreover, it has been shown that impairments in repetitive finger movement at high pacing rates are not improved with optimal medication [20,23] and are not due to peripheral fatigue [22]. This may suggest the involvement of non-dopaminergic systems in the control of externally cued, high rate repetitive finger movements.

Examining the effects of STN-DBS on repetitive finger movements may provide further insight into the control of high rate, externally paced repetitive movement. Despite compelling evidence that STN-DBS improves clinical ratings of motor function [7], the impact of STN-DBS on repetitive movement performance remains unclear. Significant changes in self-paced finger tapping, pegboard and sequential movement tasks have been reported with STN-DBS [2,9,15] with improvements ranging from very modest [2] up to 75% [9,15]. Several studies have provided evidence that STN-DBS improves the maximum amplitude and rate of proximal arm movements, but not repetitive movements of the index finger [27,29] suggesting that STN-DBS may be less effective at improving distal than proximal repetitive movements. However, since the movements examined in these studies were self-paced, subjects used a strategy whereby movements were performed at low rates. To date, no study has examined the effects of STN-DBS on repetitive finger movements paced by external cues delivered at both low and high rates in people with PD.

The purpose of this study was to examine the effects of STN-DBS across a range of externally paced rates. We hypothesized that (1) in the OFF stimulation state, participants with STN-DBS would demonstrate a significant decrease in movement amplitude and increase in movement rate at or above pacing rates near 2 Hz and (2) movement amplitude and movement rate at or above pacing rates near 2 Hz would not be improved with the stimulators turned ON.

2. Methods

2.1. Subjects

Nine participants with bilateral STN-DBS (6 male/3 female, mean age = 54 ± 11, 6 right handed/3 left handed) were tested after a 12-h withdrawal from all parkinsonian medications. Nine age-, gender-, and handedness-matched healthy older adults (HOA) (6 male, 3 female, mean age = 59 ± 12, 6 right handed/3 left handed) were also tested. Participants with STN-DBS were tested one hour after the stimulators were turned off (mean UPDRS score OFF stimulation = 44 ± 10) and one hour after the stimulators were turned on during the same day (mean UPDRS score ON stimulation = 27 ± 9). All subjects gave their written informed consent prior to inclusion into the study, and the Institutional Review Board of Northwestern University approved the procedures.

2.2. Data collection

Participants completed an incremental frequency task, performing a finger flexion-extension movement synchronized with an acoustic tone for approximately 90 s [11,23] (Fig. 1). A tone was initially presented at a pacing rate of 1 Hz and then increased by 0.25 Hz until reaching 3.0 Hz. Fifteen intervals were presented for each of the nine pacing rates. The forearm, wrist, hand, thumb, and fingers 2–4 were supported with a brace maintaining the forearm in a pronated position with the elbow flexed at 90 degrees. The index finger remained unconstrained to allow for full range of motion without tactile feedback (i.e. no thumb contact). An accelerometer (Measurement Specialties EGAXT3-15-/L2M) was placed on the index finger between the first and second joints. Participants with STN-DBS used their most affected hand and HOAs used the matched counterpart. Three participants with STN-DBS and three HOAs completed the task with their non-dominant hand. HOAs completed 5 trials and participants with STN-DBS completed 5 trials in each stimulation state.

The acceleration signal was collected (Power 1401, Cambridge Electronic Design, UK; Signal 2 software, Cambridge Electronic Design, UK) and double integrated to derive finger displacement. Movement rate and peak-to-peak amplitude was calculated for each detectable movement, and then averaged across all 5 trials for each pacing rate. Both the difference and absolute value of the difference between the mean movement rate and pacing rate were calculated. Movement amplitude was normalized to data collected at 1 Hz to allow for comparisons across pacing rates and between-subjects since no constraints were placed upon range of motion.

2.3. Statistical analyses

For all primary dependent variables (absolute movement rate difference and normalized movement amplitude), a repeated measures ANOVA was used to test for differences in the between-subjects factor of group (HOAs vs. STN-DBS OFF; HOAs vs. STB-DBS-ON) and within-subjects factor of pacing rate (1.0–3.0 Hz). Comparisons between the OFF and ON STN-DBS conditions were tested separately using a repeated measures ANOVA with within subjects factors of stimulation state (OFF vs. ON) and pacing rate. Assumptions of sphericity were tested using Mauchly's Test and the degrees of freedom were corrected accordingly using Greenhouse–Geisser estimates of sphericity. Tukey's Honestly Significantly Difference Test was used for post hoc analysis of interaction effects.

3. Results

Data from one participant OFF and ON STN-DBS and one HOA is shown in Fig. 1. Note the marked decrease in movement amplitude and increase in movement rate (hastening), when the pacing rate increased from 2 to 2.25 Hz in the OFF stimulation state. ON stimulation, this participant showed a clear improvement in movement amplitude across all pacing rates, but still hastened at pacing rates of 2.25 Hz and above. The HOA was able to perform the entire task at the required movement rate with little decrement in movement amplitude.

Fig. 2A (OFF stimulation) and 3B (ON stimulation) show the mean movement rate at each pacing rate for all participants with STN-DBS. Two features of movement rate in the OFF stimulation state were noteworthy. First, 4 of 9 participants moved at a rate more than two standard deviations higher than the HOA mean rate beginning at the pacing rate of 1 Hz. Second, as the pacing rate increased, the variance in movement rate across participants increased, with a more pronounced increase at pacing rates of 2 Hz and above. The increase in movement rate variance across participants at high pacing rates reflects that hastening of movement was enhanced for some participants whereas other participants showed a decline in movement rate. ON stimulation, participants that moved slower than the tone rate in the OFF stimulation state