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Measurement of Upper Limb Kinematics and Joint Angle Patterns During Deep Brain Stimulation for Parkinson's Disease

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Abstract- **Therapeutic benefits of subthalamic nucleus (STN) deep brain stimulation (DBS) for motor symptoms of Parkinson's disease (PD) are well-documented. However, the mechanisms underlying motor improvement with DBS remain poorly understood. We tested the hypothesis that STN-DBS-related improvements in voluntary arm movement kinematics are mediated by changes in the velocity and temporal sequencing of proximal joint angles. We evaluated a 56 year old male and 66 year old female with idiopathic Parkinson's disease chronically implanted with bilateral STN-DBS. Patients performed a button press task while off medication in the DBS-on and DBS-off conditions. Movements of the upper limb were recorded using a 3-D motion analysis system, and detailed kinematic measures were obtained for the arm and forearm. As expected, reaction and movement times were improved in the DBS-on compared to DBS-off condition. The two subjects differed with regards to the magnitude of their changes in peak linear velocity and peak angular velocities (shoulder flexion extension, shoulder abduction adduction and elbow flexion extension). Surprisingly, both PD patients increased the frequency with which they used a preferred sequence of shoulder and elbow joint activations when in the DBS-on condition. This preferred pattern was adopted with twice the frequency than in the DBS-off condition, and with increased frequency relative to a control group of 9 age-matched controls. These results suggest that STN-DBS may improve movement execution at the cost of flexibility in movement execution strategy.**

I. Introduction

Impaired voluntary movement is a cardinal feature of Parkinson's disease (PD), a disease that results from disrupted neurochemical and physiological function of the basal ganglia. Deficits in the timing and overlap of movements across multiple joints [1-3] and in synchronizing or switching between multiple motor programs [4-6] have been observed. Many current hypotheses about altered joint motion during voluntary arm movements in PD focus upon a disruption of timing of agonist-antagonist muscle sequencing and resultant deterioration in the timing of changes in joint angles [7-10].

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Possible mechanisms underlying the efficacy of DBS relate to the improved sequencing of agonist-antagonist muscle activation patterns yielding significant alterations in the temporal sequencing and amplitude of joint angle changes [1, 11]. Electrophysiological studies support the notion that the facilitation or inhibition of cued movements is mediated by changes in the synchronization of STN neuron firing [12-17]. Thus, the STN has emerged as a robust therapeutic target for ameliorating the motor symptoms in PD. Studies quantifying changes in voluntary movement following STN-DBS have revealed improvements in both reaction and movement time [16, 18, 19]. Although these changes are well-documented, the underlying mechanisms of STN-DBS remain poorly characterized. In this case study, we evaluated changes in the gain and temporal sequencing of proximal joint angles. We quantified proximal and distal arm segment kinematics and joint angle changes at the shoulder and elbow to characterize the relationship between STN-DBS, changes in proximal and distal limb movement patterns, and improvements in motor outcome measures.

II. Methods

A. Subject Demographics

All procedures were approved by the Research Subjects Review Board under the direction of the Office for Human Subjects Protection at the University of Rochester. All 11 participants (two individuals with PD and 9 age-matched controls) provided informed consent prior to study procedures. Individuals with idiopathic PD and no other neurological or musculoskeletal disorders affecting upper extremity function were recruited from the Movement Disorders Clinic at Strong Hospital. The first subject was a right-handed 56 year-old male with disease duration of 11 years, who underwent STN-DBS implantation 20 months (left side, more affected) and 15 months (right side, less affected) prior to testing. The second subject was a right-handed 66 year-old female with disease duration of 19 years, who underwent bilateral STN-DBS implantation 20 months prior to testing. Both subjects stopped medication 12 hrs prior to testing. For DBS-off testing, the stimulator was turned off at least 30 minutes prior to clinical assessment and data acquisition. Unified Parkinson Disease Rating Scale motor scores on the testing day were 58.5 and 55.5 (DBS-off) and 30 and 40.5 (DBS-on) for PD subjects one and two, respectively. Control subjects with no history of neurological disease were recruited from the community in accord with regional census statistics for gender, race, and ethnicity. We used data from 9 control subjects whose ages were ± 5 years of the two PD subjects (age range: 54-71).

B. Experimental setup

Subjects sat facing a horizontal array of five pushbutton targets. The array was positioned at a fixed distance from each subject measured from the front of the array to the 1st carpal-metacarpal joint with both arms fully extended. A shoulder harness maintained uniform trunk posture during testing. Subjects were required to move from the center target to a single illuminated target (near=3 inches from center; far = 6 inches from center) to the left or right of center. Movements were instructed to be as quick and accurate as possible following an auditory go cue. Behavioral trials were computer-controlled (National Instruments, Austin, TX) using a custom LabView program (1 kHz sampling rate).

Reflective markers were placed on anatomical landmarks on the trunk, arm, forearm, hand, and index finger of all subjects in order to acquire 3-D motion profiles of the trunk and upper limbs (60 Hz sampling rate; Vicon Motion Systems, Oxford, CA). This motion analysis system captures motion data with an error < 1mm in all 3 dimensions. The LabView program controlled data acquisition while time-stamping and storing all behavioral events (e.g. start of trial, button lighting, button press, button release).

C. Three-Dimensional Analysis of Upper Limb Motion

Marker displacement data were acquired from the distal phalanx, styloid processes of ulna and radius, lateral epicondyle of the humerus, acromion process of the scapula, and manubrium of the sternum. All movement traces were filtered with a 5-sample moving average. Linear displacement and joint angle (elbow flexion-extension, shoulder flexion-extension and shoulder abduction-adduction) were differentiated to obtain velocity and angular velocity, respectively. A threshold criterion (7% of the peak) was used to identify movement onset in linear and angular velocity traces. Movement end was defined by the button press event in LabView. Kinematic data from all successful trials for each target type were temporally aligned with the auditory "go" cue that initiated movement. The following values were calculated: reaction time (time from go cue to movement onset), movement time (time from movement onset to button press), peak velocity (maximum), average velocity (total distance traveled divided by movement time), acceleration time (movement onset to peak velocity) and deceleration time (peak velocity to button press). The sequencing of joint movements was determined by examining the relative onset of angular velocity change for shoulder flexion-extension, shoulder abduction-adduction, and elbow flexion-extension.

D. Statistical Comparisons

Within-subject comparisons revealed that kinematics of near and far ipsilateral button presses are mirrored by the contralateral movements. Despite a few subject-specific differences in the attainment of statistical significance for kinematic measures for movements to near and far ipsilateral and contralateral targets, the trends apparent in these data were identical. We therefore collapsed these data in Table 1 for simplicity. A multivariate analysis (MANOVA) was performed for the PD subject data (*Statistica*, StatSoft, Inc., Tulsa, OK) using DBS status and target types as repeated measures for each hand. Post hoc analyses were performed after Bonferroni correction.

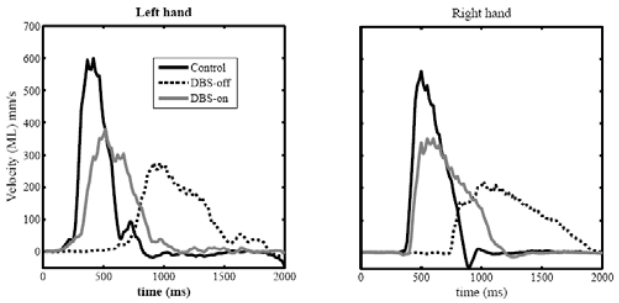

Fig. 1. Representative traces of index finger velocity for PD subject 1 and their closest age-matched control during single trials to the far contralateral target with each hand. Time zero corresponds to the go cue for movement onset.

III. Results

A. Kinematic Analysis of Index Finger *Motion*

Representative single trial index finger velocity traces from PD subject 1 are shown in Figure 1. Bradykinesia is reflected in lower peak velocity and longer total trial time in the PD subject compared to control, and is more severe in the DBS-off compared to DBS-on condition. Reduced reaction time, increased peak velocity, and reduced time spent in deceleration are apparent in the DBS-on versus DBS-off conditions for this subject. Once movement was initiated, neither the rate of acceleration (slope of velocity trace) nor the duration of acceleration changed as a function of DBS condition.

Data from index finger kinematic analyses from both PD subjects are summarized in Table 1. Trends for both subjects are the same (reductions in reaction and movement times, increases in peak velocity, and decreased time spent in acceleration and deceleration) with some metrics reaching statistical significance. Since movement time and peak velocity are potentially related, we calculated the correlation coefficient for peak velocity and time spent in acceleration and deceleration ($r^2<0.29$ for both hands in DBS-on and DBS-off conditions for all measures) revealing an absence of correlation.

B. Changes in Joint Angle Velocity

To characterize how distal arm processes (e.g. kinematics of index finger motion) relate to strategies of proximal arm movement, we quantified joint angle changes from the relative motion of the trunk, shoulder and elbow markers. Movements were largely restricted to the horizontal plane and were comprised mainly of shoulder flexion/extension, shoulder abduction/adduction, and elbow flexion/extension. Peak angular velocities (mean ± SE) for each joint obtained from multiple trials to ipsilateral and contralateral targets are shown in Figure 2. Data for PD subjects 1and 2 are plotted in DBS-on and DBS-off conditions. The mean ± SE for the age-matched control population is plotted for reference. The predominant trend is for increased peak angular velocity. However, the peak angular velocities attained even in the DBS-On condition reach

Variable	Hand	DBS	PD1	PD2	Control
Reaction Time	R	Off	537±22	311±23	282±23
		On	**322±13**	275±11	
	L	Off	493±16	366±16	288±22
		On	**369±18**	322±16	
Movement Time	R	Off	1385±157	667±23	631±44
		On	**644±27**	**561±18**	
	L	Off	1442±137	744±30	598±39
		On	**685±32**	**661±20**	
Peak Velocity	R	Off	262±15	437±19	562±23
		On	**339±15**	**557±23**	
	L	Off	271±16	410±19	601±43
		On	**360±20**	**462±17**	
Time in Accel	R	Off	309±26	202±11	180±07
		On	**230±10**	**148±8**	
	L	Off	301±14	213±16	193±8
		On	**265±9**	**161±10**	
Time in Decel	R	Off	1075±157	464±18	400±42
		On	**414±23**	**412±16**	
	L	Off	1141±140	530±29	432±45
		On	**420±32**	500±21	

Table 1. Kinematic data summary from 3-D motion analysis of index finger marker from two PD patients. Data are shown for each hand (R,L) during DBS-on and DBS-off conditions. Data from the group of 9 age-matched controls is included. Performance measures reflect mean ± standard error (SE). Within-subject comparisons of DBS-on versus DBS-off metrics with significance of $p<0.01$ are indicated in **Bold.**

only about 50% of the peak angular velocity achieved by the control subject population.

C. Selection of Preferred Sequences of Joint Angle Changes

Both PD patients exhibited increases in the frequency of the selection of a specific proximal joint movement sequence when in the DBS-on condition. Based on the joint angles that we measured, there are 6 possible sequences of onset of joint angle changes. The probability of any one sequence of proximal joint movements would be 0.17 (1/6) if none is preferred. Based on the task design, the first movement is likely to be elbow flexion (in order to retract the hand from the center button prior to horizontal movement to the lit target). Therefore, the conditional probability of a sequence with elbow flexion / extension occurring first is 0.33. We identified the sequence that was performed with greatest frequency during ipsilateral and contralateral movements with right and left arms when in the DBS-on condition. This frequency was compared for the same movements when in the DBS-off condition and when performed by controls (Table 2). Similar frequencies were observed for both PD subjects in the DBS-off and the control population. However, in the DBS-on condition, the frequency with which a preferred sequence was selected approximately doubled, increasing from 38% and 24% to 72% and 48% for subjects PD1 and PD2, respectively.

IV. Conclusions

Both PD patients exhibited improvements in clinical and kinematic measures in the DBS-on versus DBS-off conditions. The magnitude of change was different for the two subjects. Several subject-specific factors may account for this difference, including degree of baseline bradykinesia in the DBS-off

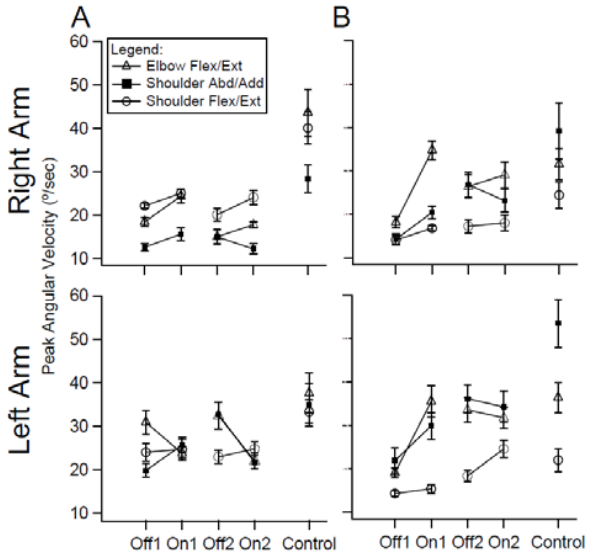

Fig. 2. Plot of mean ± SE of the peak angular velocities of joint angle changes for all trials in which ipsilateral (A) and contralateral (B) targets were successfully acquired with right and left arms. Data for PD subjects 1 (Off1, On1) and 2 (Off2, On2) are shown during DBS-off and DBS-on conditions. The mean ± SE values for the control subject population are shown for comparison.

		Right Arm		Left Arm	
Subject	**Means**	**Ipsi**	**Contra**	**Ipsi**	**Contra**
PD1 off	0.38	0.13	0.57	0.47	0.36
PD1 on	0.72	0.80	0.93	0.47	0.67
Control	0.35	0.50	0.43	0.13	0.34
PD2 off	0.24	0.0	0.46	0.27	0.23
PD2 -on	0.48	0.27	0.67	0.50	0.47
Control	0.31	0.11	0.29	0.51	0.34

Table 2. Frequency of stereotyped joint angle activation sequence selection in both PD subjects (DBS-off and DBS-on) and the control population.

condition, and differences in active DBS contact location and stimulation parameters. Additional subjects are currently being tested in our laboratory to determine the shared mechanisms of improved motor function across all subjects receiving STN-DBS therapy as a treatment for PD, as well to clarify the determinants of variability in kinematic responses to DBS in subgroups of patients. In particular, the relationships between estimated volume of STN tissue activated (based on DBS contact location and stimulation parameters) and motor outcomes are currently being investigated by other laboratories [20-22], and can be examined in relation to kinematic outcomes in our subjects. An improved understanding of the relationship between DBS stimulus parameters, active contact location, and

the mechanisms of motor function improvement is a necessary step in extending the clinical benefits of this technology.

Despite the clear improvements in the DBS-on condition, there were residual deficits in the generation of proximal limb peak angular velocities measured at the shoulder and elbow. For both subjects, some increases in joint angle peak velocity were noted, but even the most improved measures remained less than half that observed in the age-matched controls. Vaillancourt and colleagues reported similar outcomes when ankle joint velocity measured from individuals with STN DBS for PD was compared to their off-treatment condition and to healthy controls[[23]]. Relative to off-treatment conditions, both medications and DBS increased ankle velocity, yet these values remained 45% decreased relative to healthy controls.

Our findings have many possible interpretations. The improvement in the kinematics of the index finger between the DBS-off and DBS-on conditions may not be as prominently reflected at the level of the proximal limb. Other groups have reported greater changes in proximal arm movements relative to finger movements in a grip-lift task [11]. The button press task used in our study requires simultaneous coordination of proximal and distal joint movements to direct the index tip to the target, versus sequential distal followed by proximal movements implemented in a grip-lift task. The effects of STN-DBS on proximal and distal joint angle coordination for index finger targeting thus warrants further examination in a larger population of PD patients and during the performance of more diverse tasks. Behavioral task requirements and the context in which they are performed may have unique influences upon the results obtained.

The relative overrepresentation of a particular joint activation sequence that we observed during the DBS-on condition may represent a mechanism by which performance improvements are ensured. When executing a sequence in a stereotyped manner, trial-to-trial variability can be greatly reduced. This was reflected in our data as a reduction in the standard error in the timing of joint angle movement onset in the DBS-on condition (data not shown). Alternatively, this may suggest the introduction of a bias in movement pattern selection introduced by DBS influences. This may represent a connection between the motor functions of the basal ganglia circuitry and its putative relationship to repetitive behaviors [24], an observation that warrants further examination.

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