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Short paper

Parkinson's disease: a motor control study using a wrist robot

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Abstract—Deep brain stimulation (DBS) is the most common surgical procedure for patients with Parkinson's disease (PD). DBS has been shown to have a positive effect on PD symptoms; however, its specific effects on motor control are not yet understood. We introduce the novel use of a wrist robot in studying the effects of stimulation on motor performance and learning. We present results from patients performing reaching movements in a null field and in a force field with and without stimulation. We discuss special cases where robotic testing reveals otherwise undiagnosed impairments, and where clinical scores and robot-based scores display opposing trends.

Keywords: Wrist robot; Parkinson's disease; deep brain stimulation; motor control; motor learning.

1. INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disease, often characterized by tremor, slowness of movement and rigidity. The degeneration of neurons in the substantia nigra creates a shortage in the neurotransmitter dopamine, resulting in movement impairments that characterize the disease. In the US, at least 500 000 people are thought to suffer from PD and about 50 000 new cases are reported annually; the average age of onset is around 60 [1]. Aging of the society will likely lead to a larger prevalence of the disease in the population. At this time, there is no cure for PD. After initial diagnosis, many patients have only a mild manifestation of the symptoms and need no treatment for several years. When the severity of symptoms increases, doctors usually prescribe levodopa to help replace the brain's lost dopamine [1]. For those patients for whom pharmacological treatment loses efficacy, the most common therapeutic surgical procedure is deep brain stimula-

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tion (DBS) of the subthalamic nucleus (STN). In 1987 the first deep-brain high-frequency stimulation of the thalamus was performed to treat tremor and in 1993 the technique was applied to the subthalamic nucleus for treatment of advanced PD [2].

STN DBS has been demonstrated to be effective in mitigating the primary disease symptoms. An average improvement of about 52% over baseline is reported, using the unified PD rating scale (UPDRS) motor score, in the 'off medication' condition. However, the literature suggests an incidence of adverse effects related to the surgery in approximately 11% of the cases [3].

While DBS demonstrates a high rate of success as a PD treatment, its mechanism of action is not yet well understood. Robotic technology has been used extensively in studying unimpaired subjects (e.g., Refs [4–7]). It has also been employed in studying stroke [8–10], Huntington disease [11] and PD [12]. It has been used in combination with imaging techniques [13], and may similarly assist in elucidating specific effects of stimulation on motor performance and motor learning.

To investigate motor learning, we used an implicit learning task: explicit learning refers to the acquisition of information accompanied by awareness of the learned information and its influence; implicit learning refers to similar acquisition without awareness of the learned information and its influence. In particular, we are investigating procedural learning, which is a form of implicit learning where skill improves over repetitive trials. Imaging results with healthy young males showed an increase in activation of the striatum during early phases of implicit motor learning and decreased activation during the skill-transfer phase [12, 13]. As the striatum is a component of the basal ganglia, which are affected in PD, we set out to test PD patients in the 'off medication' state on the same task and compare them with age-matched controls [12].

Here, we expand upon our previous studies, and employ a novel wrist robot to study motor performance and motor learning in PD patients with DBS, comparing the stimulation 'on' and stimulation 'off' conditions, in the 'on medication' state. While significant contributions to the study of motor control and to neuroscience were achieved *via* studies involving more proximal limb segments, i.e., shoulder-and-elbow, devices that allow similar kinds of studies with more distal limb segments such as the wrist and hand offer certain advantages as these areas have larger cortical representation, which are more lateralized and thus will facilitate our future tests with cortical stimulators.

To test motor performance, we examine the characteristics of subjects' movements in a null force field (see Methods)—we evaluate their point-to-point wrist movements, and score the movements based on their accuracy, smoothness and timing. We compare the scores of PD patients with DBS turned on to their score when the DBS is turned off. We also compare those scores to those of age-matched controls. After performing the point-to-point movements in the null force field, subjects' movements are examined in the presence of a force field. Their rate of adaptation to the field is assessed and compared among the groups. As mentioned

earlier, one goal of the research is to evaluate the effect of stimulation on motor learning. Another goal is to use the wrist robot as a patient-evaluation device to provide a non-invasive, objective, accurate and reproducible method of scoring patients' performance, based on which adjustments to stimulation parameters could be made.

2. METHODS

2.1. Wrist robot

The wrist robot is configured for safe, stable and compliant operation in close physical contact with humans. This is achieved using backdrivable hardware and impedance control—a key feature of the robot control system. The robot can move, guide or perturb movements of a subject's limb, and can record motions and mechanical quantities such as the position, velocity and torques applied. It is designed with 3 d.o.f., corresponding to those of the human wrist: abduction–adduction (AA), flexion–extension (FE) and pronation–supination (PS). A curved rail sits between four guide wheels, which allow it to rotate. Figure 1 shows the wrist robot.

AA and FE motions are accomplished by a differential mechanism with a total speed reduction of 8:1, while PS movement is accomplished by a curved rail geared to 10:1. A key aspect of the design is combining these speed-reduction ratios in a compact, low-friction transmission, as it permits the use of smaller and lighter actuators than a direct-drive design of comparable performance, while maintaining a low robot output impedance (i.e., the device is highly 'backdrivable'). Ideally, a subject attempting to move the robot at speeds from 0 to 38 rad/s should encounter

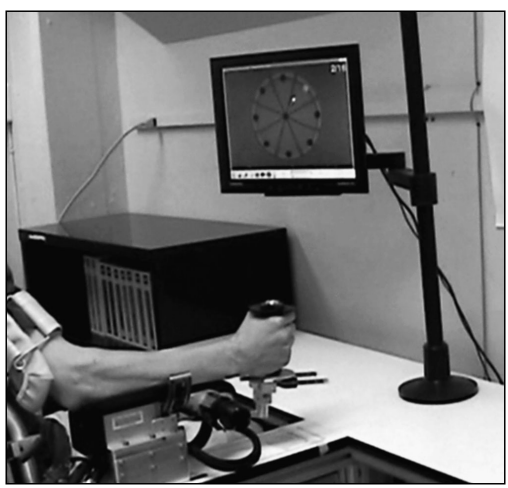

Figure 1. The wrist robot. Here, used to control a cursor on the screen and move it to a presented target.

no significant friction, inertia or stiffness. In this design, the apparent stiffness is zero, the maximum apparent inertia for each wrist d.o.f. is estimated to be (30–45) $\times 10^{-4}$ kg m^2 and the maximum apparent static friction torque is 0.29 N m for PS, 0.075 N m for FE and 0.075 N m for AA. The device accommodates the range of motion of everyday tasks: FE 60°/60°, AA 30°/45° and PS 70°/70°. The torque output from the device is capable of lifting the person's hand against gravity, accelerating the inertia and appears to be able to overcome most forms of hypertonicity. The device can produce a range of continuous stall torques with no cogging (1.85 N m for PS, 1.43 N m for FE and 1.43 N m for AA), impedances (0 to 60 N m/rad for PS, 0 to 40 N m/rad for FE and 0 to 40 N m/rad for AA) and damping (0 to 1 N m s/rad for PS, 0 to 0.45 N m s/rad for FE and 0 to 0.45 N m s/rad for AA). For more details on the device, see Refs [14–16].

2.2. Protocol

Ten subjects diagnosed with PD and with bilaterally implanted DBS participated in the experiment after giving their informed consent. Subjects were seated in a chair, resting their arm on an armrest, while holding the robotic manipulandum's end-effector in their hand. They used the end-effector to control a cursor on a computer screen positioned in front of them. They were presented with one center target and eight peripheral ones (see Fig. 1). A different target was highlighted every 1.6 s, alternating between a randomly selected peripheral target and the center target. This duration was chosen to allow enough time for subjects who may have a long reaction time and move at a slow speed to complete the movement. We asked the subjects to reach the targets with the cursor as they changed color. Each set of 80 movements out to the periphery and back to the center is termed a block. Some of the blocks were performed in a null force field and some in the presence of a curl force field. The forces used are proportional to the subject's wrist velocity, and are perpendicular to it:

$$\begin{bmatrix} \tau_{\mathrm{FE}} \\ \tau_{\mathrm{AA}} \end{bmatrix} = \begin{bmatrix} 0 & 0.15 \\ -0.15 & 0 \end{bmatrix} \begin{bmatrix} \dot{\theta}_{\mathrm{FE}} \\ \dot{\theta}_{\mathrm{AA}} \end{bmatrix}, \tag{1}$$

where τ is the torque vector (Nm), $\dot{\theta}$ is the wrist velocity vector (rad/s) multiplied by constant matrix representing the imposed viscosity (Nm s/rad).

After an initial practice block (null perturbation forces), subjects performed one block in the absence of perturbation forces (null), six blocks within a curl force field (A), two blocks with a curl field in the opposite direction (B) and, finally, one more block in a null force field. The null block is used to study baseline performance. The set of blocks in the A field is used to study motor learning. The set of blocks in the B field is used to study skill transfer, i.e., the effect that learning one task (compensating for force field A) has on the rate of learning of another task (compensating for force field B). The final null block is used to verify that no effects of fatigue are present. Subjects performed the entire set of null–A–B–null blocks

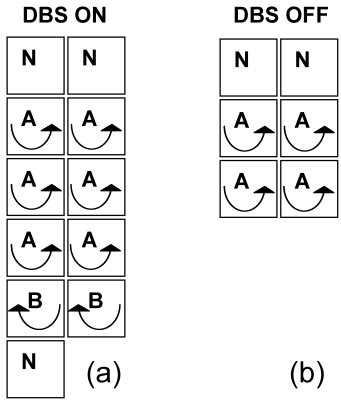

Figure 2. Order of blocks in the DBS ON (a) and DBS OFF (b) conditions. Each block comprises a set of 80 movements to a peripheral target and back to the center target. N = null field, A = force field in one direction (clockwise or counter clockwise; controlled by the sign of the B matrix in (1) and B = force field in the opposite direction to A. Half of the subjects experienced a clockwise force field in A and half experienced a counterclockwise forced field in A.

with stimulation on (DBS ON; see Fig. 2a). After a 1-h break, their stimulators were turned off bilaterally and testing resumed 15 min later. With stimulation off (DBS OFF) patients performed only the practice block, the baseline null block and four blocks of the A field (see Fig. 2b). Subjects continued to follow their normal medication regimen throughout the experiment. When in the stimulation 'on' state, patients were evaluated using a battery of neuropsychological tests, including the UPDRS and the modified Hoehn and Yahr scale (H&Y). When in the stimulation 'off' state, they were re-evaluated only on the H&Y scale and on Part 3 (Motor) of the UPDRS.

We analyzed the movement traces generated by the subjects and scored each movement based on parameters that reflect movement quality. Here, we present two of these measures of performance: path length and lateral deviation.

2.3. Robot-based performance metrics

Reaching movements involving the shoulder and elbow have been shown to follow a straight trajectory [4], and performance measures were developed based on this observation. Measuring total path length to a target and deviation from a straight line to the target as indicators of movement quality has been a common approach [12, 17]. Wrist movements have not yet been similarly characterized. However, we see a very clear pattern indicating these two measures are relevant for wrist movements: when healthy subjects are exposed to a force field which perturbs their movements, they suffer an increase in both path length and lateral deviation, but learn to compensate for the force field, which is manifested in a shorter path length and less deviation (unpublished observations).

We use the following equations for calculating these measures:

$$\text{Path length:} \quad S = \int_{s_0}^{s_N} \mathrm{d}s, \tag{2}$$

where S is the total path length and s_0 and s_N are the first and last position points, respectively. We, thus, measure the total length of the subject's wrist movement as the subject reaches from the central target to a peripheral one. This value is assigned as the path length score for that movement. The score per block is the average score for the 80 individual movements in the block.

$$\text{Lateral deviation:} \quad D = \sqrt{\sum_{i=1}^{N} (s(i) - p(i))^2}, \tag{3}$$

where D is the total lateral deviation, N is the total number of samples, $s(i)$ is the wrist position at sample i and $p(i)$ is the point of intersection between the straight line connecting the targets and a normal to that line, passing through $s(i)$. That is, for each movement, we pass an imaginary line connecting the center point to the peripheral target and calculate by how much the subject's wrist deviated laterally from that line. This value is the assigned lateral deviation score for the movement.

3. RESULTS

We are currently pursuing our initial goal of recruiting and testing 40 subjects. Here, we present several cases that exemplify the versatility of the robotic apparatus in identifying various facets of the disease. We have so far encountered five distinct categories of patients in the experiment: one typical and four atypical; we discuss each separately below.

3.1. Patient A—typical

A 62-year-old right-handed male, diagnosed with PD 14 years prior to the experiment, had bilaterally implanted STN DBS 1.5 years earlier. The subject had no problem performing the task with stimulation on (see Fig. 3a). With stimulation off, the subject was still able to perform the task, although with less agility (see Fig. 3b). When forces were introduced in the DBS OFF state, performance deteriorated further (*cf.*, Fig. 3c and d), yet improved over successive blocks (*cf.*, Fig. 3d and e). Five out of the 10 patients we tested so far fit this overall pattern.

3.2. Patient B—clinical scores and robotic scores do not agree

A 65-year-old left-handed male, diagnosed with PD 17 years prior to the experiment, had bilaterally implanted STN DBS 2.5 years earlier. The patient had been

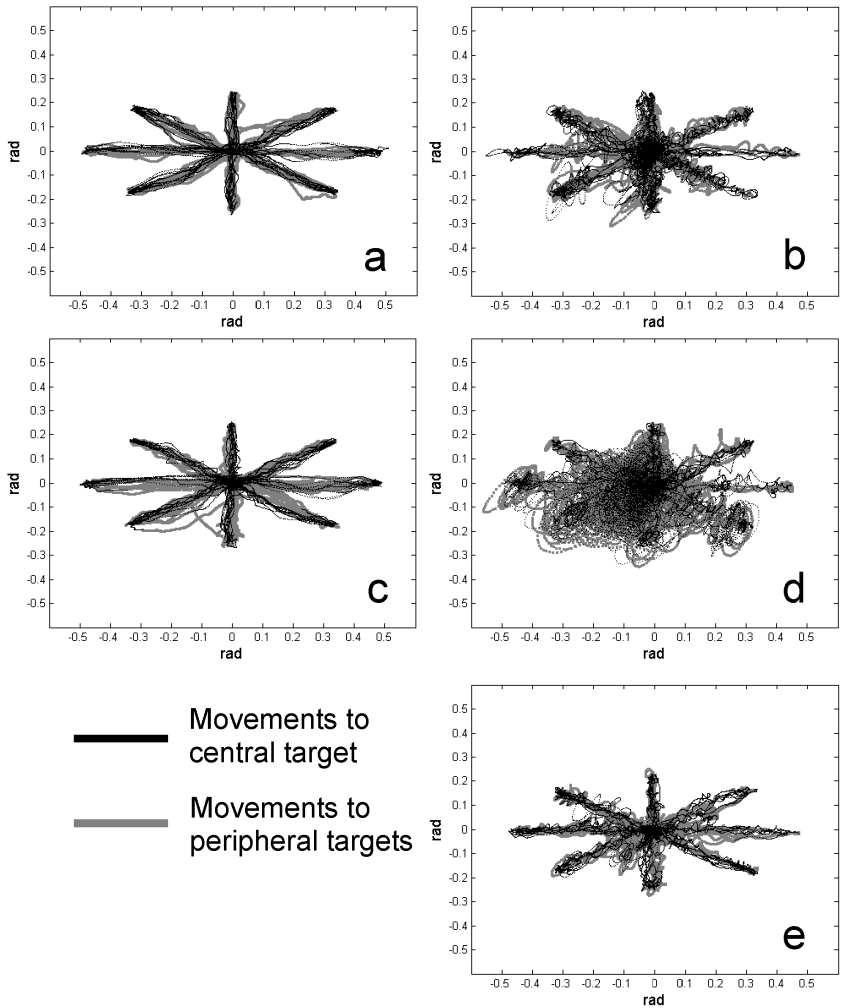

Figure 3. Movement traces of patient A in the DBS ON (left column) and DBS OFF (right column) conditions. (a) DBS ON, block 2 (null field); (b) DBS OFF, block 2 (null field); (c) DBS ON, block 3 (A field); (d) DBS OFF, block 3 (A field) and (e) DBS OFF, block 6 (A field).

suffering from a severe bipolar disorder when off stimulation. This subject's performance appeared to improve according to the robot-based measures when stimulation was turned off, yet his UPDRS Part 3 and H&Y scores indicated a decline (see Table 1 and Fig. 4).

3.3. Patient C—inability to perform task

A 62-year-old right-handed male, diagnosed with PD 15 years prior to the experiment, had bilaterally implanted STN DBS 1 year earlier. The subject's clinical scores were not abnormal for his condition (see Table 1). He verbally confirmed understanding the task, but was unable to execute it as required. The task can be de-

Table 1.
ON/OFF clinical scores

Patient	UPDRS On	UPDRS Off	H&Y On	H&Y Off
A	9	35	2	3
B	10	17	0	2
C	11	22	2.5	2.5
D	9	29	0	3
E	27	32	3	3

The Motor section (Part 3) of the UPDRS and the modified H&Y. Higher scores indicate increased impairment.

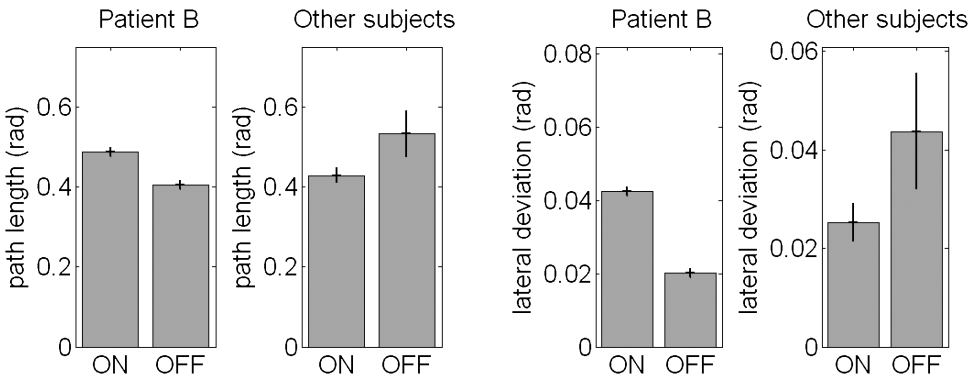

Figure 4. Robot-based performance measures demonstrating an improvement in patient B's performance when stimulation is turned off. Patient B's results are plotted next to the average performance of seven other PD patients.

composed into random and predictable movement directions. When the movement direction is random, the subject must wait for a visually displayed target before initiating movement. The predictable movement was the return back to the center target after each reach to a peripheral one. Cursor location was recorded during the 1.6 s allocated for each movement. Inspecting Fig. 5, one would notice that the patient was not moving the wrist at all during times that were allocated for 'back to the center' movements (black line), but only during times allocated for 'out to a peripheral target' movements (gray line). This pattern persisted in both the DBS ON and DBS OFF states. Inspection of Fig. 5 reveals the subject had no physical problem with reaching the targets or visual impairment that prevented him from detecting the highlighted target. It appears the presence or absence of a randomness component played a role in his ability to respond to stimuli. This impairment, readily evident using the robotic task, was not otherwise detected with the conventional clinical scales. We speculate that may be due to a difficulty with executing concatenated tasks.

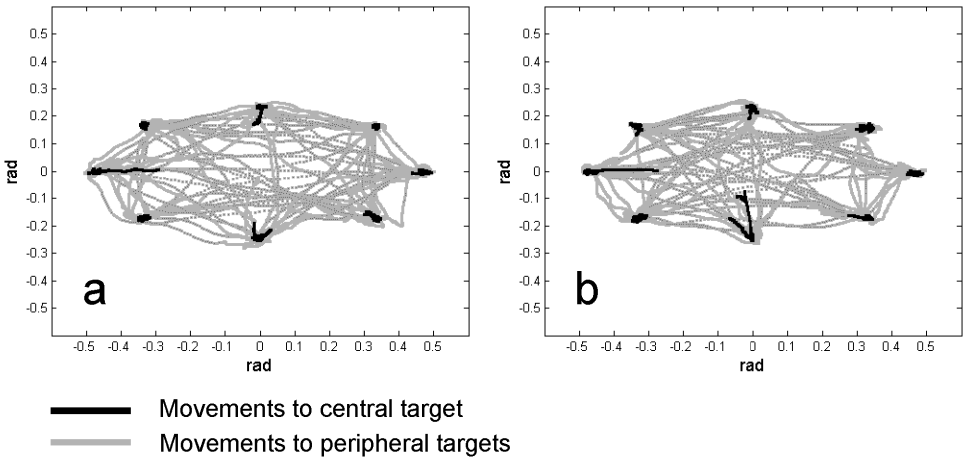

Figure 5. Movement traces of patient C, demonstrating his inability to perform the task in either the 'stimulation on' (a) or 'stimulation off' (b) state.

3.4. Patient D—inability to perform task only in the DBS OFF state

A 66-year-old left-handed male, diagnosed with PD 12 years prior to the experiment, had bilaterally implanted STN DBS 1.5 years earlier. The subject had no particular difficulty performing the task with stimulation on (see Fig. 6a). With stimulation off, the subject was unable to perform the task as required (see Fig. 6b).

3.5. Patient E—long wear-off period, mostly gait affected by PD

An 80-year-old right-handed male, diagnosed with PD 14 years prior to the experiment, had bilaterally implanted STN DBS 5 years earlier. This subject's PD symptoms manifested themselves mostly in the lower limbs. From DBS ON to DBS OFF, his UPDRS Part 3 score worsened by 3 points and his H&Y score did not change (see Table 1). We also found no statistically significant difference in his performance between the two conditions using the robot-based measures. The patient anecdotally mentioned days-long periods for the stimulation effects to wear off. This is a case where (i) evaluation shortly after turning the stimulation off may not be relevant and (ii) using the wrist robot for evaluation when symptoms manifest themselves mostly in the lower limb may be less relevant.

4. DISCUSSION

We introduce the use of a wrist robot, able to measure wrist position and exert forces on it, in evaluation of PD patients with implanted DBS. We test subjects in a null field to evaluate their baseline performance, and then in the presence of a force field to examine their capacity for motor learning and their rate of motor learning. We survey five distinct cases that exemplify the breadth of the patient spectrum that was

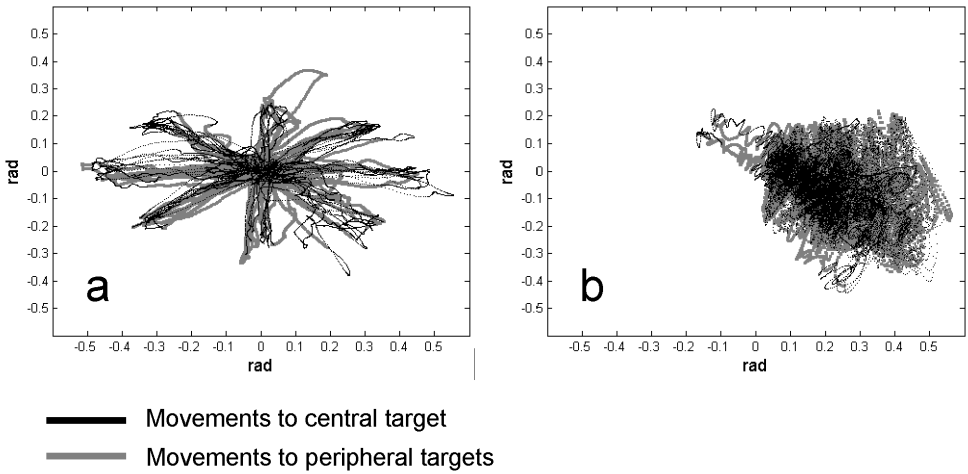

Figure 6. Movement traces of patient D, demonstrating his ability to perform the task in the 'stimulation on' (a) state, but not in the 'stimulation off' (b) state. Both figures depict the patient's movements in a null field.

tested: (i) one which displayed a 'typical' behavior when stimulation was turned off (five out of 10 subjects), (ii) one which scored better on robotic-based measures, but worse on clinical scales when stimulation was turned off, (iii) one who was unable to perform the task in either stimulation setting, (iv) one who was unable to perform the task only when in the stimulation 'off' setting, and (v) one who displayed no significant difference between the 'on' and the 'off' states, possibly due to a combination of factors—long stimulation-effects wear-off periods and primary symptom manifestation on the lower limbs. The initial results from these cases suggest that the wrist robot may serve as a complimentary tool to clinical scales—to detect different aspects of movement not covered by the clinical scales. To further investigate this possibility, we are currently testing more patients as well as healthy controls.

Our robotic technology opens the door to a variety of applications within the patient care realm. One such application that we are presently studying is the possibility of using the robot to update stimulation parameters: each patient's performance is evaluated at baseline before stimulators are implanted. After stimulators are implanted and turned on, as the patients perform reaching movements using the wrist robot, their trajectories are analyzed, and new stimulation settings are identified and transmitted to the pulse generator for optimized performance (gain scheduling).

5. CONCLUSIONS

We report the novel combination of two well-established and validated technologies, i.e. DBS and the wrist robot, to study the effects of stimulation on motor control in patients with PD. In particular, our goals are to evaluate specific parameters of

movement in a null field—timing, accuracy and smoothness—as well as rate of motor learning, manifested as adaptation to the presence of a force field. With stimulation parameters as the input and robot-based measures of performance as output, we might be better able to optimally adapt the DBS parameters to the patients' needs over time even as the neuro-degeneration process progresses. The wrist robot provides a novel platform for studying the effects of neurological diseases and their treatments on motor performance and motor learning.

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