

# PROCEDURAL MOTOR LEARNING IN PARKINSON'S DISEASE: PRELIMINARY RESULTS

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## Abstract

The purpose of this study is to examine if PD (Parkinson disease) patients present a deficit in procedural motor learning. A portable robotic device is being used to generate forces that disturb subjects' arm movements. Patients and age-matched controls have to learn to manipulate this "virtual mechanical environment." Our preliminary results suggest that, indeed, PD patients present a deficit in the rate of procedural motor learning, particularly in presence of "novelty."

## Introduction

We have been investigating "implicit motor learning". Implicit learning refers to acquisition without awareness of the learned information and its influence. In particular, we have been investigating "procedural learning", which is a form of implicit learning where skill improves over repetitive trials.

Neuroimaging results using a serial reaction time (SRT) paradigm indicated an increase in activation in structures which constitute key

elements of the cortico-striatal loop, thus supporting models that posit the cortico-striatal loop as playing a significant role during implicit learning [Rauch, 1995]. Other neuroimaging studies using a pursuit rotor task indicated an increase of activity in the cortico-cerebellar loop, thus supporting models that hypothesize that procedural learning takes place in the motor execution areas [Grafton, 1994].

We speculated that the apparently different role played by the two brain loops in different paradigms could be related to the different mechanisms associated with procedural learning in a task with prominent motor demands (rotor pursuit) versus a task with more cognitive-perceptual demands (sequence learning). Therefore, we set our goal to design a procedural learning paradigm whose demands might shift from more cognitive-perceptual to motor, and test a hypothesis that the cortico-striatal and cortico-cerebellar loop activities change as the demands of the learning task change.

We pioneered the integration of robotic technology with functional brain imaging [Krebs, 1995 and 1998a]. PET

was used to measure aspects of neural activity underlying learning of the motor task involving the right hand of right-handed subjects, while a portable robotic device was used to generate conservative force fields that disturbed the subjects' arm movements, thereby generating a "virtual mechanical environment" that subjects learned to manipulate [Shadmehr & Mussa-Ivaldi, 1994]. We found that Early Learning activated the right striatum and right parietal area, as well as the left parietal and primary sensory area, and that there was a deactivation of the left premotor area. As subjects became skilled at the motor task (Late Learning), the pattern of neural activity shifted to the cortico-cerebellar feedback loop, i.e. there was significant activation in the left premotor, left primary motor and sensory area, and right cerebellar cortex. These results support the notion of different stages of implicit learning (Early and Late Implicit Learning), occurring in an orderly fashion at different rates. Moreover these findings indicate that the cortico-striatal loop plays a significant role during early implicit motor learning, whereas the cortico-cerebellar loop plays a significant role during late implicit motor learning [Krebs, 1998a].

Our results were in agreement with current theories of human motor learning and memory that consider the brain composed of fundamentally and anatomically separate but interacting learning and memory systems [Schacter & Tulving, 1994]. In fact,

borrowing from computer science, current theories suggest patterns of unsupervised (pre-frontal cortex), supervised (cortico-cerebellar), and reinforcement learning (cortico-striatal) in human motor learning [Alexander & Crutcher, 1990; Graybiel, 1993 & 1995<sup>1</sup>; Houk & Wise, 1995; Houk, 1997; Beiser, 1997; Beiser & Houk, 1998; Berns, 1997; Berns & Sejnowski, 1998].

In view of our neuroimaging results indicating that the cortico-striatal loop plays a significant role in implicit motor learning, we predicted that patients with parkinson disease (PD) should present a deficit in the rate of motor learning while learning to manipulate similar "virtual mechanical environment" generated by a robotic device. In what follows, we present our experimental results to date of aged-matched normal and PD patients.

## Methods

In this pilot study, we used the novel robot MIT-MANUS, which has been designed for clinical neurological applications. Unlike most industrial robots, MIT-MANUS was designed to have a low intrinsic end-point impedance (i.e., back-driveable), with a low and nearly-isotropic inertia and friction [Hogan, 1995; Krebs, 1998b].

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<sup>1</sup> Graybiel suggested a "blend" of unsupervised and supervised learning schemes to describe striatal processing. We suggest that reinforcement learning may be a more appropriate wording.

To date, seven right-handed subjects with parkinsonism (2 females and 5 males) participated in the study. The subjects were between 56 and 78 years old. All subjects were clinically evaluated by a trained movement disorders specialist at the time of testing and found to have mild to moderate Parkinson's disease (Hoehn-Yahr stages 2 and 3) and minimum tremor. Patients were tested early in the morning prior to the administration of any daily medication except for one patient (56 years old female), who could not perform any function due to "freezing." This subject received her medication 30 minutes prior to testing and her results were segregated from

the off-medication patients' group (mean age 70.2). To date, four right-handed healthy age-matched subjects were included for comparison (3 females and one male). The subjects were between 67 and 84 years old (mean 78.5). All subjects were naive to the motor learning task.

The visually-evoked and visually-guided task is similar to the one used in our neuroimaging studies [Krebs, 1998a] and it consisted of moving the robot end-effector from its initial position towards a target, in a point-to-point movement. The target set had a fixed number of positions in a horizontal plane as shown in figure 1.

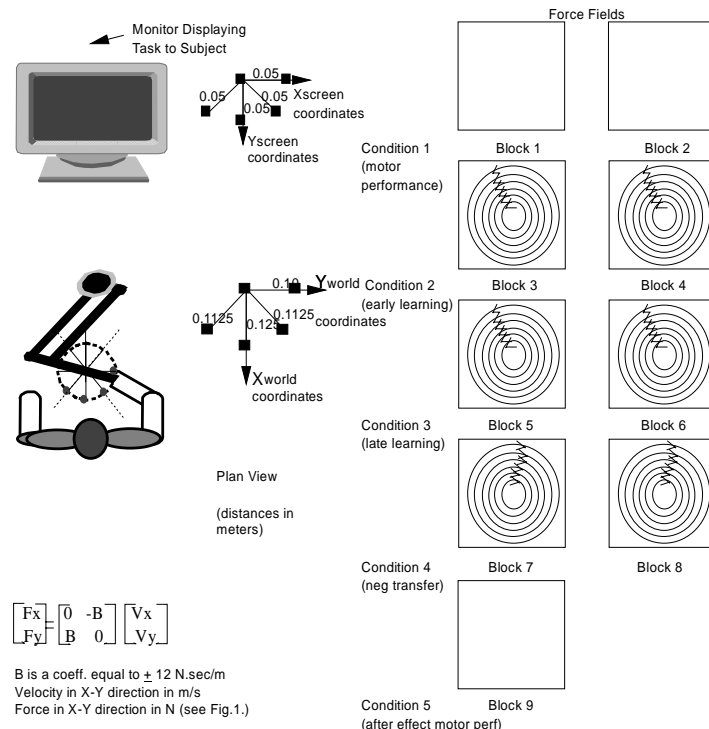


FIG.1. General Arrangement and Force Fields in Different Conditions Subject while sitting, moved the robot end-effector in a point-to-point task in a virtual haptic environment with different force fields for each condition.

The outward targets 1 to 4 were randomly presented. The inward homing target 0 was presented following each of the outward targets. Every outward target was presented an equal number of times. Note that the hand coordinates were different from the visual coordinates, in order to compensate for the rectangularity of the monitor. The subject sat in a chair in front of the robot and monitor, and grasped a handle on the end-effector of the robot. He was instructed to move the end-effector to the presented target within 0.8 sec. The color of the target changed for the subsequent 0.8 sec, and a new target was presented. Note that the monitor screen was positioned perpendicular to the subject's line of sight, therefore moving the end-effector handle towards the subject corresponded to moving down on the monitor. The subject's movement was performed predominantly with the arm and forearm.

The robot measured the kinematics and dynamics of the subject's hand motions, and imposed perturbation forces as follows:

**Condition Motor Performance:** the robot generated no perturbation, but recorded the behavior of the subject (blocks 1 & 2). The subject practiced as needed to become fully comfortable with the task.

**Condition Early Motor Learning:** the robot measured the behavior, and also perturbed the movement of the subject (blocks 3 & 4).

**Condition Late Motor Learning:** the robot measured the behavior, and

also perturbed the movement of the subject (blocks 5 & 6). This condition differs from Condition 2 by the degree of smoothness of the motor response.

**Condition Negative Transfer:** the characteristic of the perturbation forces was reversed (blocks 7 & 8).

**Condition After-Effect Motor Performance:** the robot generated no perturbation, but recorded the behavior of the subject (block 9). The objective was to determine the influence of fatigue.

The perturbation forces were velocity-dependent, generating a conservative force field according to the following relations:

$$\begin{bmatrix} F_x \\ F_y \end{bmatrix} = \begin{bmatrix} 0 & -B \\ B & 0 \end{bmatrix} \begin{bmatrix} V_x \\ V_y \end{bmatrix}$$

where B is a coefficient equal to 12 (or -12) N.sec/m; the velocity in X-Y direction ( $V_x$ ,  $V_y$ ) are given in m/sec; and the forces in the X-Y direction ( $F_x$ ,  $F_y$ ) are in Newtons with X-Y directions indicated in figure 1.

All conditions described above were divided into two blocks. Each block entailed a total of 80 movements (40 movements to the outward positions and 40 movements to the homing position).

## **Preliminary Results**

Normal subjects make unconstrained point-to-point movements in approximately a straight line with bell-shaped speed profiles [Flash & Hogan,

1985]. Kinematic analysis of subjects' movements was performed including the mean squared difference between the movement and the minimum-jerk speed profiles described above.

This index showed a consistent pattern while learning the task. The baseline condition (block 1 & 2) was followed by deterioration of the performance as the force field was applied (block 3). The subsequent results showed a progressive reduction of the difference, indicating learning (block 4 to 6). Similar patterns can be observed as subjects were challenged with a new force field with reverse characteristics (block 7 & 8). Subjects' performance resembled baseline condition after the force field was eliminated suggesting that fatigue is not a primary factor (block 9). Figure 2 shows the learning rate assessed by the slope of the regression to the normalized mean squared speed difference averaged across subjects of the age-matched control group and across subjects of the PD group. We used the mean squared speed difference of each group during blocks 1 and 2 as the normalizing factor. Figure 2 also shows the ratio between the learning rate of the age-matched control group and the PD patients. Note that the mean learning rate is faster for the age-matched group than the PD groups for all conditions. The control group learns on average 18% faster during Early Learning (condition 2), 3% faster during Early + Late Learning (conditions 2 and 3), and 433% faster during Negative Transfer (condition 4).

## Conclusion

Existing evidence strongly suggest a role of the striatum in learning novel motor tasks. If this is actually the case, we should expect that patients with PD should present a deficit in the rate of procedural motor learning, particularly in presence of "novelty". Indeed, this appears to be the case. Our results indicate the largest difference between the learning rate of the age-matched subjects and the PD patients groups during the Early Learning and Negative Transfer (conditions 2 & 4). These conditions correspond to "novelty" scenarios. Consistent with our view of different stages of procedural motor learning, we observed minimal learning rate difference during Late Learning (condition 3) for which neuroimaging results posits a significant role to the cortico-cerebellar loop [Grafton, 1994, Krebs, 1998a].

While PD subjects achieve normal accuracy under a wide variety of feedback conditions, including remembered targets acquired without visual feedback [Poizner, 1998], they have particular difficulty in a novel task where they are required to transform from visual to proprioceptive space [Adamovich, 1997]. Our results for procedural motor learning are similar to results of procedural cognitive learning in Parkinson's disease [Brown & Marsden, 1990; Saint-Cyr, 1988; Taylor, 1986] indicating learning deficiencies.

This result raises questions about the role of the direct and indirect pathways (i.e., the excitatory and inhibitory loops within the basal ganglia “circuitry”). One possible explanation is that the direct pathway reinforces the appropriate cortical motor pattern, while the indirect pathway brakes it

[Alexander & Crutcher, 1990]. In view of our results, one might speculate that for our PD patients, “braking or switching” motor patterns is the primary learning deficiency. If so, this raises important questions about optimal rehabilitation strategies.

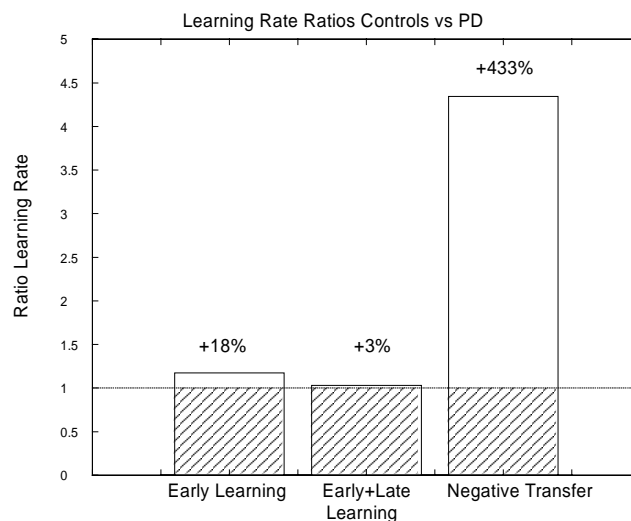


FIG.2. Learning Rate Ratios -- Four Age-Matched Controls versus Six PD Patients  
The plot shows the learning rate ratio between the age-match and PD groups. The number at the top of each column represents how much faster the Age-Match Controls learned.

### Grant Support

Supported in part by The Burke Medical Research Institute and NSF under Grant 8914032-BCS to MIT, and NIH 5-R01-NS-36449-02 and 2-R01-NS-28665-07 to Rutgers University.

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