

## Motor learning processes in a movement-scaling task in olivopontocerebellar atrophy and Parkinson's disease

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## **Abstract**

Nine Parkinson's disease (PD), seven olivopontocerebellar atrophy (OPCA) patients and two age-matched control groups learned a linear arm movement-scaling task over 2 days, requiring movements proportional in length to visually presented target-bars. Scaling was acquired through knowledge of results (KR concerning the direction and magnitude of errors) following every second acquisition trial. Initial acquisition of both groups was significantly worse than their respective controls (poorer movement scaling), but rapidly improved to nearly identical levels. Retention for the PD group's movement scaling was as good as controls initially, but markedly poorer after 24 h. The OPCA group did not show this deficit. Both patient groups extrapolated accurately to longer, previously unpracticed target distances (no KR provided), suggesting an unimpaired capacity to generate and use an internal representation of the movement scaling. They also rapidly learned a new scaling relationship when the gain was changed. Overall, the learning of this movement-scaling task was not adversely affected in OPCA, and the impairment was restricted primarily to longer-term retention in PD. The study suggests that: (1) the ability to acquire movement scaling in a task that requires conscious use of error feedback and no new coordination may depend little on the cerebellum, and (2) the basal ganglia may participate in longer-term storage of scaling information.

## Introduction

For both theoretical and clinical reasons, the neural processes that underlie human motor learning and adaptation have aroused considerable interest, prompting multiple behavioral and imaging motor learning studies of neurologically healthy and impaired subjects. The cerebellum and its inputs from the inferior olive (the climbing fiber system) have traditionally been the focal structures to which motor learning is attributed, but some are questioning the central role of the cerebellum, pointing to other sites, such as the basal ganglia and specific areas of the cerebral cortex (Jueptner and Weiller, 1998; Seidler et al., 2002).

A striking feature of previous work is the variety of definitions accorded the term "motor learning," and, consequently, the wide range of motor tasks used - from classical conditioning of the rabbit's nictitating membrane response to whole body movements in humans. In this paper, we contend that there is a useful distinction to be made between lower level *automatic adaptation* processes (such as those involved in prism adaptation) and higher level learning processes requiring *awareness, attention, and decision-making*. Both are central to skill acquisition, but the first has received greater emphasis. This study examines the relationship between such automatic adaptation and *explicit* motor learning, for, as Eccles points out, in the "learning of much more complex human motor skills ... it is essential to have mental concentration with a planned strategy of action and a subsequent evaluation and correction of errors in successive attempts. Mental activities such as critical evaluation, redesigning the intended movement, a further critical evaluation of the new movement, and so on, is experienced by all who try to learn a new skill or improve on an existing one" (Eccles, 1986).

Support for the cerebellum in motor learning has primarily relied on visuomotor adaptation tasks, requiring altered direction or scaling of movements to visual targets. The cerebellum has been shown to mediate visual-motor adaptation in animals (Gilbert and Thach, 1977; Ito, 1993; Keating and Thach, 1990), with the inferior olive's cerebellar projections specifically implicated (Lisberger, 1988). Indeed, the proposition that cerebellar circuitry functions adaptively in a computational fashion is one of the landmarks of modern neuroscience (Albus, 1971; Marr, 1969). However, the available human studies are more equivocal. While lesions of the cerebellum and/or inferior olive can impair visual-motor adaptation or rate of adaptation (Deuschl et al., 1996; Gauthier et al., 1979; Martin et al., 1996a), a well-controlled PET study of prism adaptation during reaching showed the most significant changes occurred in the parietal cortex (Clower et al. 1996).

Damage to the basal ganglia, as in Parkinson's disease (PD), suggests that movement scaling is impaired (Jackson et al., 2000; Pfann et al., 2001), although changes in scaling with practice have not been examined. Tracking (Frith et al., 1986; Harrington et al., 1990) and mirror tracing tasks (Schnider et al., 1995) indicate that learning is impaired, although others found poorer control but no learning deficit (Hufschmidt and Lucking, 1995). A more robust result is that people with PD rely on external stimuli rather than internally generated memory (Burleigh-Jacobs et al., 1997; Flowers, 1978; Majsak et al., 1998), indicating impaired guidance of movement based on an internal representation.

We sought to explore the contrast between automatic adaptation and explicit motor learning by employing a task that in certain respects resembles automatic visuomotor adaptation, for which the strongest evidence of cerebellar involvement exists, namely, the acquisition of a novel movement scaling. But we placed the task in a "richer" learning and performance context that we anticipated would call on more explicit processes. Subjects were required to: (1) *acquire* an arbitrary scaling, or gain, between a perceptual input and a motor output, using a movement with

no new coordination requirements (thus preventing any learning from being masked by pure control limitations); (2) *retain* this learned scaling for use with no error feedback or knowledge of results (KR), thus meeting the criterion for motor learning in behavioral research, i.e., a relatively permanent improvement in performance resulting from practice in the absence of augmented feedback (Salmoni et al., 1984; Schmidt and Lee, 1998); (3) *extrapolate* the scaling to produce similar movements but of a magnitude not previously practiced, thus assessing the type of ubiquitous schema learning described by Schmidt (1975) and modeled as a regression-like process by Koh and Meyer (1991); and, finally, to (4) *adapt* to a different scaling; and (5) *retain* this newly learned scaling for use when KR was withdrawn.

Thus the current study tested the proposition that the acquisition of movement scaling, normally thought of as an implicit process, will be intact when placed in an explicit context, both in those with damage to the basal ganglia (people with PD), or the cerebellum and the climbing fiber system (people with olivopontocerebellar atrophy, OPCA). Such an outcome would demonstrate that explicit motor learning might not depend on the integrity of these structures. If, on the other hand, all forms of visual-motor adaptation involve these circuits, then OPCA subjects would perform poorly in all phases of the task because of an inability to acquire the correct scaling. PD subjects would be at a disadvantage primarily in the absence of augmented error information (retention and extrapolation phases), because of impaired use of an internal representation, defined as psychological structures and processes that allow us to utilize past experience in improving motor behavior (Ivry, 1996).

## Materials and methods

### Subjects

The local ethics committee approved recruitment and testing of subjects. Nine subjects with diagnosed idiopathic PD (six men and three women) and nine age-matched neurologically healthy controls (five men and four women) participated in this study. Handedness was confirmed using the Crovitz-Zener Handedness Inventory (Crovitz and Zener, 1962). All were right-handed except one, and this person was matched with a left-hand-dominant control. The PD patient population had to meet several criteria: no greater than moderate bradykinesia and/or rigidity, and mild or no tremor. Patients with manifestations of cognitive impairment and with moderate or severe on/off fluctuations were excluded, as were those with a history of drug or alcohol abuse, or neuropathology other than PD. Testing occurred at approximately the same time and at a similar point in their medication cycle across the 2 days in order to limit differences in symptoms. Clinical evaluations were obtained for all PD patients (see Table 1).

In addition, seven subjects with OPCA were studied, and seven age-matched neurologically healthy controls (one man and six women in both groups), one of whom also served as a control for the PD group. The OPCA patients included both sporadic and inherited cases (the latter more recently classified as spinocerebellar atrophy); all showed upper extremity ataxia and gait ataxia. Diagnosis of OPCA was confirmed by MRI, which showed gross atrophy of the cerebellum and pons in all subjects except one (see Table 2.)

Subjects participated in a battery of tests to ascertain their overall emotional, cognitive and motor status (see Table 3). Both patient groups were more depressed than their controls as measured by the Beck Depression Inventory (Beck and Steer, 1987). The depression scores were similar for the two patient groups, as previously reported for PD and multiple system atrophy (Pilo et al., 1996), of which OPCA is generally considered a major subset (Wenning et al., 1996). Cognitive status was evaluated through the Shipley Institute of Living Scale (Zachary, 1986), which includes a vocabulary test and an abstract thinking test, the Symbol Digit Modalities Test (Smith, 1982), which provides a measure of efficiency of processing and matching numbers with visual symbols, and the Object-Retention Test, which was designed to test spatial memory (two to four objects placed on a grid, viewed for 10 s, removed by the experimenter and then replaced by the subject).

Both patient groups exhibited a lower IQ than their respective controls, but the average of all groups was above 100. Only the OPCA group exhibited poorer performance on the Symbol Digit test (visual matches between numbers and symbols), partially explained by impaired eye control as indicated by poorer visual functioning on the Talland Line Tracing task (Pilo et al., 1996). There were no differences in spatial memory based on the Object-Retention Test.

Motor performance was assessed through the Purdue Pegboard test (Lafayette Instruments) and the Reciprocal Tapping task, in which subjects were to make as many movements as possible back and forth across a 20-cm area marked on a board in 30 s. Both hands were tested. Both patient groups performed significantly worse than controls in speed of manual and finger dexterity as measured by all four parts of the Purdue Pegboard test, as well as in reciprocal tapping. Thus, the expected differences in motor function, a prime characteristic of each disease, were evident.

## **Apparatus**

The linear slide consisted of a vertical handle connected to ball bushings mounted on two parallel steel rods. This allowed the handle to move freely along the horizontal axis for a maximum of 67 cm. All movements began with the handle in contact with a rigid stop at the left end of the slide. A lightweight, non-extensible, steel-braided chain was attached to the base of the handle, and ran over a sprocket mounted on the shaft of a precision ten-turn ball-bearing mounted potentiometer. This allowed computer recording (12-bit analog-to digital conversion) of handle position at 4-ms intervals with a precision of less than 1 mm. Kinematic data were then filtered (10-Hz cutoff dual-pass Butterworth digital filter). A screen was mounted horizontally above the slide so subjects could not see any part of the moving limb. Thus no cues provided by the movement or apparatus could guide subjects to the correct position. A flat-tension monitor with high contrast was situated at eye level about 55 cm in front of the subject, and was used to present both target bars and error information (Figure 1).

## **Procedures**

Testing occurred across two consecutive 2-h morning sessions, including breaks, beginning and ending with several of the neuropsychological tests (described above). The primary movement task was initiated after a sufficient rest break.

This learning task required subjects to make linear arm movements of a distance indicated by a visual display, using augmented error feedback (KR) to learn the correct scaling. The task had five distinct phases, described below. The basic movement was a rightward, linear arm movement from a common starting position, with the right hand holding the slide handle.

Subjects were required to move briskly to the desired position, reversing direction without any attempt to make corrections, so as to return at least halfway to the start within 3 s of the target's presentation. The distance moved was the furthest point from the start, i.e., the reversal point.

The visual display was a rectangular bar projecting horizontally from the left edge of the screen. The length of the bar represented the required movement distance, but the scaling (the relationship of the visual target length to the required linear arm movement distance) was initially unknown to the subject. The target bar remained visible until the subject completed the movement. In the two acquisition phases, KR was provided. This took the form of a rectangular bar projecting from a vertical white line in the center of the screen either to the left (representing an undershoot) or the right (overshoot). The length of the bar indicated the size of the error, using the same scaling as that for the target bar display. Summary KR after every 12 trials was given in the form of a histogram (average error of each preceding set of 12 trials represented by successive red bars, with the last (blue) bar showing the set of 12 just completed), which showed subjects their progress. Testing involved five different phases: acquisition, retention (immediate, delayed, 24-h), extrapolation, gain change acquisition and immediate retention of gain change.

## **Acquisition phase**

This phase consisted of 144 trials, with targets corresponding to 12-, 16-, 20- or 24-cm movements (48 trials each). Every set of six consecutive trials was to the same target. All four targets were presented before any were repeated, so that sets of 24 consecutive trials each consisted of six repetitions of the four targets (one block). The order of target presentation within the 24 trials varied from one set to the next. During this phase, KR was provided after every second trial.

### **Retention phase**

This was the same as the acquisition phase only no KR was given. "Immediate retention" (48 trials) occurred without a break. After a 6-min break (about 18 min following acquisition) subjects completed another 96 trials ("delayed retention"). On the following day subjects performed an additional 24 trials before receiving any KR ("24-h retention").

### **Extrapolation phase**

Subjects were then given 48 trials as in the acquisition phase (i.e., six trials of the four distances with KR), so as to remind them of the original scaling. Following this, they were informed that they would see a new set of target bars, longer than those originally practiced, and therefore requiring longer movements but using the same scaling, i.e., the *relationship* between the length of the bar and that of the required movement was the same. These new target bars corresponded to movements of 28, 32, 36 and 40 cm; the shortest of these was 4 cm longer than the longest of the previously practiced movements. There were 48 extrapolation trials, all without KR, again with six consecutive trials to the same target.

### **Gain change acquisition phase**

After extrapolation, subjects executed another 144 trials with KR (conducted in exactly the same manner as the original acquisition phase) using the same set of target bars as in the original acquisition phase. The only difference was that the correct movements were *50% longer* than those for the original gain, i.e., movements of 18, 24, 30 and 36 cm. This required subjects to abandon the scaling they had originally learned and acquire a new one. They were informed that the scaling had changed and that the movements would be longer, but they did not know by how much.

### **Gain change retention phase**

Finally, 48 immediate retention trials were administered, again requiring reliance on retained information about the new scaling.

### **Data reduction and analysis**

The task was to learn to scale the movement accurately. This was assessed by analysis of the slopes, intercepts and correlations from a linear regression of *distance actually moved* against *required movement distance*. A perfect performer who moved the required distance on all trials would generate data having a slope of one, an intercept of zero and a correlation coefficient of one. In addition, variable error (VB) was obtained: the standard deviation of the signed error measuring the variability shown by the subject. All variables were calculated separately for each subject and target within each block of trials, and then averaged across subjects to obtain group scores. All trials were analyzed; all subjects complied with task requirements on all trials, so there were no error trials.

A mixed model ANOVA with Group as a between-subjects factor and Trial and Block as repeated measure factors were used to analyze the data. Fischer's LSD test was used to compare pairs of means where appropriate. When correlation coefficients were analyzed Fisher's  $r$  to  $z$  transformation was performed.

## Results

### Acquisition

The acquisition (and retention) performance of all four groups is shown in Figs. 2, 3 and 4. Figures 2 and 4 show the overall movement scaling for each group, and Figure 3 depicts the VE over the six blocks of acquisition trials (and retention phases).

### **PD**

There were no major kinematic differences between PD and control groups: movement time (983 vs. 879 ms), peak velocity (35 vs. 40 cm/s), time-to-peak velocity (477 vs. 460 ms) and time-from-peak velocity (506 vs. 419 ms, PD vs. Control groups, respectively). Although the velocity profiles differed in a typical fashion between groups (a smooth increase to peak velocity for subjects in the control group vs. a discontinuous increase for the PD group), PD subjects scaled their velocity based on movement distance in a manner similar to the control group. Note that in order to reduce control difficulties that may obscure learning processes, the goal was not a speeded movement - subjects were allowed to make the out-and-back movement within 3 s.

Figure 2 shows that the PD group was initially poorer in movement scaling compared to the control group, but by block 3 (after 48 trials) improved to normal levels with practice (a significant Group by Block interaction for slope,  $F(5,80)=2.52, p<0.05$ ). Specifically, the PD group did not move far enough in block one for the longer targets, as shown by the lower slope. Post-hoc analyses showed the PD slope to be lower than controls only in the first block ( $p<0.0005$ ). A similar outcome was evident for the intercepts of the actual distance/target distance regression, i.e., the actual movement value predicted by the best-fitting line for this function for a nominal required distance of 0 cm. The PD group intercept was significantly higher on block one only ( $p<0.05$ ). Intercept values otherwise seldom differed, and since the correlation values remained high, we used the slope values as the primary index of scaling hereafter because they index the increment in distance moved per unit increment in target distance. Again in the first block only, the PD group tended to move distances that were less well correlated with the required distances ( $r=0.76$  vs.  $0.88$ , PD and control group, respectively), but this difference did not attain significance. For the remaining five blocks, these correlations averaged between 0.95 and 1.0 for both groups, indicating highly linear scaling.

Figure 3A shows that the VE scores for the two groups were quite similar, especially at the end of practice. Both PD and control groups similarly reduced variability over these 144 acquisition trials,  $F(5,80)=5.86, p<0.001$ .

### **OPCA**

Kinematic measures did not differ between OPCA and control groups. Mean movement time was 807 vs. 767 ms for the OPCA and control groups, respectively. Peak velocity (40 vs. 43 cm/s), time-to-peak velocity (510 vs. 419 ms) and time-from-peak velocity (379 vs. 347 ms) were also not significantly different (in all cases OPCA mean first, then Control).

The only group differences were in the first block. OPCA movement scaling was initially poorer, but improved with practice to the point of being indistinguishable from the control group (see blocks 3-6, Figure 4). The change in slope with practice was different for the two groups,  $F(5,60)=2.73, p<0.05$  for Group x Block. Post hoc analysis revealed that the OPCA group had a lower slope than controls only in the initial block ( $p<0.003$ ). The only other group difference that attained statistical significance was that the correlation between actual and required movement



distances increased with practice. It approached 1.0 more closely over blocks,  $F(5,60)=11.97$ ,  $p<0.001$ , but there was no difference between groups in this improvement.

As depicted in Figure 3B, VE showed a decline with practice, with a main effect of Block,  $F(5,60)=3.53$ ,  $p<0.005$ , but no interaction between Group and Block. The overall level of variability was similar for the groups.

Both the PD and OPCA patients showed a substantial initial deficit in movement scaling, but overcame this rapidly. Any deficit entirely disappeared by the third block. Moreover, neither clinical group showed significantly heightened variability or any failure to decrease variability with practice.

### **Retention phase**

#### **PD**

Following withdrawal of KR there was an initial performance disruption; both groups exhibited a lower slope in the immediate retention phase, but there were no group differences. There was, however, a deficit in the delayed retention for the PD group and at the 24-h retention test (see lower three panels of Figure 2). The PD group's movements were shorter than required (hypometric), especially for the longer movements. Overall there was only a trend towards a group difference in slopes across the three retention intervals ( $F(1,16)=2.63$ ,  $p=0.1$ ), but PD slopes were significantly lower and intercepts significantly higher for the delayed and 24-h retention intervals (slopes: delayed retention,  $p<0.003$ ; 24-h retention,  $p<0.001$ ; intercepts:  $p<0.05$  for both intervals based on post-hoc tests). The PD group was not significantly more variable during any of the retention phases (see Figure 3A).

#### **OPCA**

Figure 4 (last three panels) shows that in the immediate retention phase, the OPCA group's slope was too steep (1.32) and the control group's slope was not steep enough (0.74). The delayed and 24-h retention tests did not show this slope difference, however. The Group x Interval effect was significant,  $F(2,24)=15.37$ ,  $p<0.0005$ . Post-hoc analysis confirmed that the slope difference was confined to the immediate retention phase. In addition, the OPCA intercept was significantly higher on immediate retention ( $p<0.001$ ). Figure 3B shows that the OPCA group was also significantly more variable than controls in immediate retention, but the reverse was true in the delayed retention interval as shown by a Group x Interval interaction,  $F(2,24)=31.57$ ,  $p<0.0001$ . Post-hoc analysis confirmed these differences for the first two retention phases only ( $p<0.0005$  in both cases).

There is no obvious explanation for these transient effects involving the first two retention phases. We note, however, that the size of the slope *error* (difference from 1) was very similar for the two groups on immediate retention (approximately 30%). Further, and unlike the results for PD, the OPCA group showed no retention deficit relative to the controls after 24 h in the slope, correlation, or VE. Indeed, the only measure by which the OPCA group differed significantly was the intercept, which was *smaller* than that of controls, i.e., closer to the ideal of zero ( $p<0.05$ ), thus exhibiting *better* performance than the control group.

## **Extrapolation phase**

### **PD**

Both groups successfully applied the learned scaling to novel targets, even without KR. During this phase even the shortest targets required movements longer than any of those previously practiced. Thus, if subjects failed to extrapolate, they would respond with large undershoots averaging about 10 cm (the difference between the longest of the practiced and the average of the novel targets). This was not the case. As Figure 5A shows, both groups tended to undershoot (PD = -5.7 cm; Control = -1.7 cm), but they nevertheless increased their movement distances, and did so with slopes that did not differ significantly (PD = 0.61; Control = 0.74). In this phase there was no group difference in VE (PD = 2.21 cm; Control = 2.08 cm). Nor were intercepts different (PD = 7.4 cm, Control = 7.3 cm). Of course, if any two lines with different, but not *significantly* different slopes sharing a common intercept are extended sufficiently far, the *actual values* of those lines may differ. Even by this conservative measure, however, the somewhat larger actual PD undershoots shown in Figure 5A did not differ significantly from control values.

### **OPCA**

The OPCA group was just as proficient as controls in the extrapolation phase based on remembered scaling. The absence of any significant difference in slope is readily seen in the very similar group values in Figure 5B (OPCA = 0.95; Control = 0.90). Therefore, even with no concurrent information about error, OPCA patients showed very accurate extrapolation, like their control counterparts. Moreover, both OPCA and control subjects were very close to slopes of 1. There was no group difference in absolute slope values and movement distance in VE (OPCA = 2.07 cm; Control = 2.77 cm).

## **Gain change acquisition**

### **PD**

PD subjects began this phase with better scaling than they did in the initial acquisition phase (compare block 1 in Figure 2 with block 1 in Figure 6). In addition, they rapidly improved their scaling with practice of this new gain to an accurate level, as indicated in Figure 6. Had they used the originally learned scaling (i.e., failed to adapt), markedly shorter movements would have been made. The initial slope for the PD group was 0.73 and attained a level of 0.89 by block 6. The comparable values for controls were 0.89 and 0.94. The Block effect was significant,  $F(5,80)=2.71, p<0.05$ , but there was no Group x Block interaction. The large difference between the groups that was apparent in initial acquisition was much reduced in size with the new gain.

Analysis for VE (see Figure 7A) showed a substantial overall decline in variability across blocks,  $F(5,80)=5.5, p<0.0005$ , but no group difference and no Group x Block interaction.

### **OPCA**

Both OPCA and control subjects rapidly adapted to the new gain; slopes even in the initial block were equal to 0.85 for both groups (see Figure 8). Performance was very stable over blocks as seen by no Block main effect. There was neither a difference between the slopes of the two groups nor an interaction between Group and Block.

Similarly, both groups reduced variability over blocks,  $F(5,55)=2.87$ ,  $p<0.05$ , but there was no difference between the groups overall nor was there an interaction between Block and Group (see Figure 7B). (Note that data for one OPCA control subject were lost for the final two of the six gain change acquisition blocks. Thus, this subject's data were excluded from the analysis of both the gain change acquisition and retention phases.)

### **Gain change retention**

#### **PD**

Without the aid of KR, the slopes of both groups declined slightly from the final acquisition block (PD = 0.75; Control = 0.85, Figure 6, last panel). However, the group slopes did not differ significantly, as was true for the immediate retention of the initial gain shown in Figure 2. With VE means of 2.1 cm (PD) and 2.0 cm (controls), there was no Group difference in variability during retention of the new gain (see Figure 7A).

#### **OPCA**

Immediate retention for the OPCA group was almost identical to that of the controls, with no difference between slopes (Figure 8, last panel). In addition, the OPCA and control groups had similar VE means of 2.15 cm and 2.84 cm, respectively (see Figure 7B).

## Discussion

Movement scaling is central to many goal-directed movements. In this study the acquisition of movement scaling was assessed in people with OPCA and PD through retention of a scaling relationship in a visuomotor task, extrapolation to novel targets, and relearning the scaling relationship after a gain change, i.e., "schema" learning (Schmidt, 1975; Koh and Meyer, 1991).

### Parkinson's disease

The PD group's performance, acquisition and extrapolation of this task were generally similar to that of controls. Others have also reported normal motor learning, adaptation and transfer in PD (Agostino et al., 1996; Hufschmidt and Lucking, 1995; Jordon and Sagar, 1994; Swinnen et al., 2000; Dominey et al., 1997). For the first time, however, we show that PD patients can extrapolate movement scaling without KR to conditions outside the practiced range.

There were two deficits, however. First, the PD group's initial performance was significantly poorer. Since they successfully made much longer movements in later phases, simple hypometria is an unsatisfactory explanation. Our results are consistent with previous reports of a slower learning rate in PD, especially early in learning (Krebs et al., 2001; Postle et al., 1997). That gain change acquisition was similar to controls is also consistent with slower early learning in PD; they had only to acquire a new gain in an otherwise familiar task.

The second and more noteworthy deficit was the PD group's poorer *retention* of the scaling relationship. The loss was progressive; poorer retention was not evident on the immediate test, but was quite apparent approximately 18 min later, and even more pronounced on the following day. Indeed, after 24 h, the PD slopes had returned to the level of block one acquisition. By contrast, controls were able to maintain quite accurate movement scaling even after 24 h. This observed deficit is consistent with other empirical results (Platz et al., 1998; Smiley-Oyen et al., 2002) and with Mishkin's concept of the basal ganglia as the storage system for motor and non-motor "habits" (Mishkin and Petri, 1984), but is in contrast to a report of only minor deterioration after 48 h of sequential rapid aiming in PD (Behrman et al., 2000).

Why could the PD group utilize an internal representation to accurately extrapolate to new targets, but not retain the relationship? We suggest that the time interval from the last KR trial is a likely explanation. Both the immediate retention and extrapolation phases were completed within approximately 12 min of the final KR trial, but PD subjects could not sustain an accurate representation beyond this time, in agreement with other findings (Verschuere et al., 1997). It is possible that the learning of movement scaling depends on cortical processes that induce plastic changes in basal ganglia circuitry (Calabresi et al., 1992). Damage to these inputs may prevent short-term cortical adaptation from becoming a habitual, automatic response embodied in the basal ganglia.

We also note that it is common practice in behavioral motor learning studies to employ 'no-feedback' (KR withdrawal) retention tests (Salmoni et al., 1984; Schmidt, 1988) since these can yield outcomes diametrically opposed to those seen at the end of acquisition, e.g., contextual interference (Shea and Morgan, 1979) and reduced frequency of KR (Winstein and Schmidt, 1990). Here, such retention tests showed a PD deficit that was not apparent during acquisition. Thus, we suggest that these procedures are essential to prevent inaccurate inferences about the role of the nervous system in motor learning.

## **Olivopontocerebellar atrophy**

The OPCA group learned, extrapolated and retained the scaling as well as their controls, and quickly acquired a new gain, in spite of their clearly uncoordinated limb movements and significantly poorer scores on reciprocal tapping and the Purdue Pegboard. Only in the first of the six acquisition blocks did the OPCA group have significantly lower slope values than controls. The groups' performances were indistinguishable thereafter. Despite much literature to the contrary, this absence of a cerebellar learning deficit is consistent with the observation of a patient whose episodic ataxia clearly impaired motor performance but did not affect adaptation and motor learning, as assessed by prism adaptation and ideogram drawing (Miall and Silburn, 1997) and in other tasks in which the cerebellum was involved in changes in performance but not in learning (Friston et al., 1992; Jueptner and Weiller, 1998; Seidler et al., 2002). The ability of the OPCA group to extrapolate to novel target distances is in agreement with Timmann et al., (1996), who found that cerebellar patients could learn a two-dimensional pattern and redraw it in a new orientation from memory.

### **Why was acquisition not affected in either population?**

If these two subcortical structures are indispensable to motor learning, then why were the two groups with clear-cut motor control symptoms so successful in acquiring the movement scaling? Our explanation focuses on the task and the type of error feedback.

Firstly, this task did not require a *new coordination pattern*. Secondly, we deliberately allowed the subjects to move at a submaximal rate. *Motor control* limitations would be far more evident when subjects move at the extreme of their speed-accuracy function, and could be wrongly interpreted as a general learning impairment (e.g., Topka et al., 1998).

Thirdly, the *type of error feedback* we used required comprehension of the error and deliberate changes to the ensuing movements. These *explicit error correction* processes are excluded in some previous adaptation studies, such as dart-throwing (Martin et al. 1996a, 1996b), in which subjects were required to proceed without making conscious changes to the movement. In addition, our subjects could not view their limbs, again, unlike previous studies (Gauthier et al., 1979; Weiner et al., 1983). In fact, when monkeys learned a novel gain under such conditions, complex spike activity was more clearly related to velocity control than to long-term learning processes (Ojakangas and Ebner, 1992). We suggest that conscious feedback use - a major ingredient of human skill acquisition - is a cortically mediated process that can bypass automatic adaptation, and is therefore still functional when the structures that undertake automatic adaptation are damaged.

One alternative explanation is that real differences exist but were not seen because of low power. This is improbable because there were clear and significant differences between the clinical and control groups in initial acquisition, the Purdue Pegboard and reciprocal tapping tests. Neither is it plausible that the motor symptoms were too mild for performance differences to be assessable. The effect of the disease on movement *control* was fully apparent, but this did not extend to a general motor learning impairment when motor control limitations were lifted.

A limitation to any inferences about the roles of damaged structures is that sufficient connections might survive to permit substantial residual function, or that different unaffected brain regions may acquire those functions. For the present study, however, one must assume that motor control functions of the basal ganglia and cerebellar circuits, manifestly impaired in both the PD and OPCA subjects, were much more susceptible to disruption than were the learning functions of these areas or, alternatively, that they were much less readily transferred to other regions.

## **Conclusions**

Overall, the relative normality in the acquisition of this task in the clinical groups was unexpected and striking, especially in the case of OPCA, given the pivotal role ascribed to the climbing fiber system (Gauthier et al., 1979; Martin et al., 1996a; Sanes et al., 1990; Weiner et al., 1983). Coupled with evidence for the participation of other brain structures in visual-motor adaptation (Clower et al., 1996) and difficulties in the interpretation of some animal studies (Bloedel et al., 1991), these results highlight the need to continue careful evaluation of the cerebellum's role in motor learning. In common with Thach and coworkers (Thach et al., 1992; Martin et al., 1996a), we suggest that the cerebellar role is restricted primarily to learning new forms of coordination, and for adapting and combining simple responses in a relatively automatic way, or with processing of sensory information (Jueptner and Weiller, 1998), with other facets of motor skill acquisition unaffected. Our data also suggest that basal ganglia damage only minimally disrupts acquisition of movement scaling when augmented feedback is available to guide learning, but does impair long-term retention when that feedback ceases to be available.

Motor learning is not a single uniform process. In our view, it is completely consistent for the cerebellum to undertake adaptation of scaling when this is "automatic," and for non-cerebellar structures to do so when conscious use of feedback is necessary. The latter is more likely to occur in humans than in animals, more with delayed than with concurrent feedback, and when such feedback is representational and not inherent to the task. These are frequently the unique attributes of distinctly human skills.

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PD: ID	Age (years)	Right limb bradykinesia	Right limb resting tremor	Right limb rigidity	Other comments	Medication dosage/day
01	69	Moderate	Minimal	Moderate	Moderate on/off fluctuations; mild dyskinesia	Carbidopa/levodopa 25/100/12x
02	74	Mild	Moderate	Mild	-	Carbidopa/levodopa 25/100/3x Selegiline 40 mg/2x
03	56	None <sup>a</sup>	None	Minimal	Left side more affected	Selegiline
04	56	None <sup>b</sup>	None	None	Left side more affected	Selegiline 5 mg Carbidopa/levodopa 25/250/2x Selegiline 5 mg/2x
05	60	Minimal	None	None	Moderate dyskinesia	Carbidopa/levodopa 5/100/8x Bromocriptine 2.5 mg/8x Selegiline 5 mg/2x
06	55	Mild	None	Mild	Left side more affected	Carbidopa 25 mg/3x Carbidopa/levodopa 25/100/4.5x Carbidopa/levodopa 25/100/3.5x
07	69	Moderate	Mild	Moderate	-	Benzotropine 2 mg Selegiline 5 mg/2x
08	48	None <sup>c</sup>	None	Moderate	-	Carbidopa/levodopa 25/100/3x
09	65	Minimal	None	Minimal	Left side more affected	Carbidopa/levodopa 25/100/3x Selegiline/3x Bromocriptine 2.5 mg/8x

<sup>a,b,c</sup>Bradykinesia was not clinically apparent in the right limb, but was apparent in the reciprocal tapping task, which is a task that is sensitive to bradykinesia. The following are scores for the right hand of the patient vs. right hand control group mean:

<sup>a</sup>03 vs. control group mean (dominant hand): 99 vs. 136 taps/30 s

<sup>b</sup>04 vs. control group mean (non-dominant hand): 93 vs. 116 taps/30 s

<sup>c</sup>08 vs. control group mean (dominant hand): 87 vs. 136 taps/30 s

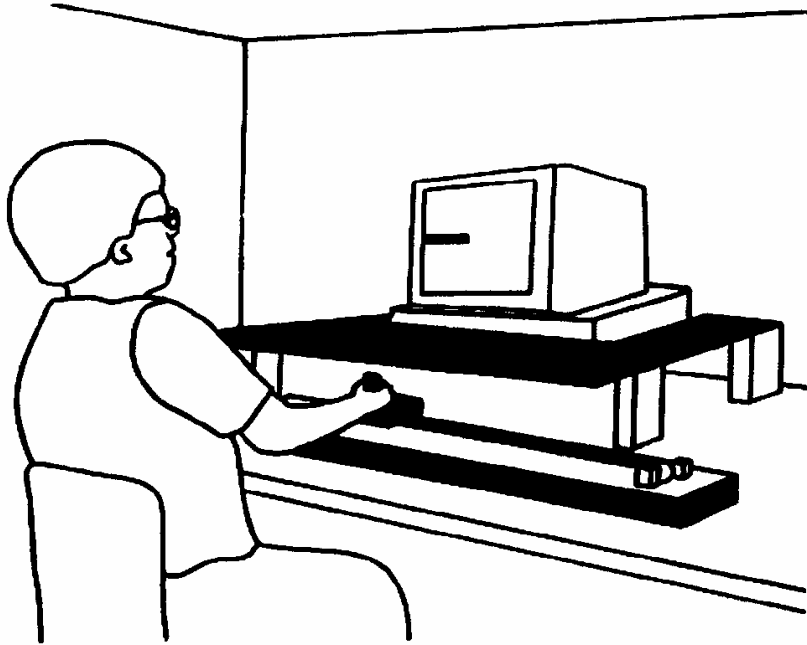
**Table 1. Symptoms/medications for PD patients.**

<b>OPCA: ID</b>	<b>Age (years)</b>	<b>Form of OPCA</b>	<b>Upper extremity ataxia</b>	<b>Gait ataxia</b>
101	32	Hereditary	Mild	Moderate
102	50	Hereditary	Mild	Moderate
103	61	Sporadic	Moderate	Moderate
104	47	Sporadic	Severe	Severe
105	33	Hereditary	Moderate	Moderate
106	67	Unclear	Mild	Mild
107	42	Hereditary	Moderate	Moderate

**Table 2. Symptoms for OPCA patients.**

	<b>PD</b>	<b>PD control</b>	<b>OPCA</b>	<b>OPCA control</b>
	<b>Mean (SD)</b>	<b>Mean (SD)</b>	<b>Mean (SD)</b>	<b>Mean (SD)</b>
Age (years)	61.3 (8.40)	64.8 (7.3)	47.4 (13.2)	50.9 (15.6)
Education (years)	16.2 (2.40)	15.6 (2.4)	14.1* (2.2)	16.0 (2.1)
Beck Depression Scale (Beck and Steer 1987)	9.89* (8.07)	3.3 (3.12)	9.60* (3.30)	3.29 (2.14)
Shipley IQ (Zachary 1986)	109.8* (10.50)	115.4 (8.8)	103.7* (10.0)	109.0 (11.7)
Symbol Digit Modality (Smith 1982)	51.2 (9.80)	49.7 (6.5)	42.1* (7.7)	58.1 (11.8)
Object Retention	60.4 (6.60)	61.6 (7.2)	66.1 (3.6)	66.0 (3.4)
Talland Line Tracing (Pilo et al. 1996)	5.0 (0)	5.0 (0)	4.1* (1.1)	5.0 (0)
Purdue Pegboard (dominant hand)	10.1* (2)	12.4 (2.3)	7.6* (4.0)	14.4 (1.7)
Purdue Pegboard (non-dominant hand)	10.6 (2.4)	12.1 (2.3)	6.1* (3.6)	14.4 (1.1)
Purdue Pegboard (both hands)	6.6* (2.8)	9.9 (1.9)	5.0* (2.3)	11.7 (1.7)
Purdue Pegboard (assembly)	20.7* (6.1)	29.0 (3.8)	15.3* (8.6)	36.6 (4.5)
Reciprocal Tapping (dominant hand)	92.0* (11.9)	136.1 (18.6)	74.4* (19.8)	146.0 (13.4)
Reciprocal Tapping (non-dominant hand)	86.3* (17.2)	115.9 (17.7)	70.7* (16.7)	128.0 (13.7)

**Table 3. Results of the battery of emotional, cognitive and motor function tests.**



**Figure 1. Experimental apparatus. Movement is from left to right. A target bar is shown on the monitor. The cover for the arm is cut away to better show the apparatus and arm.**

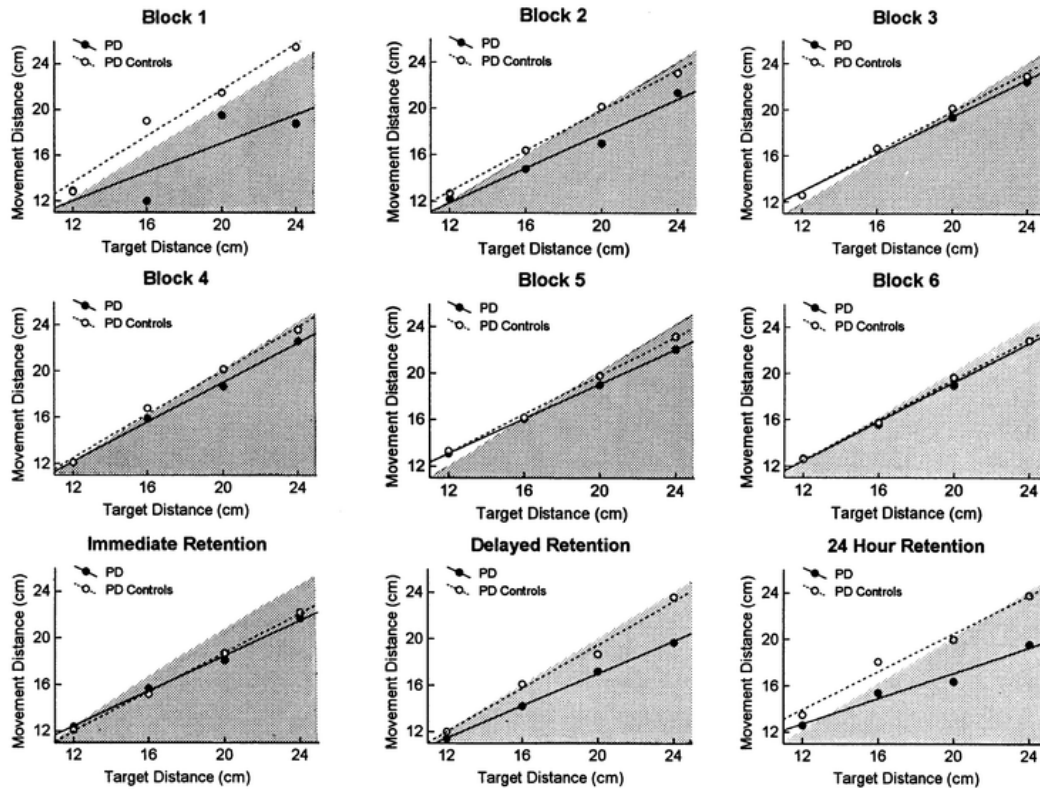
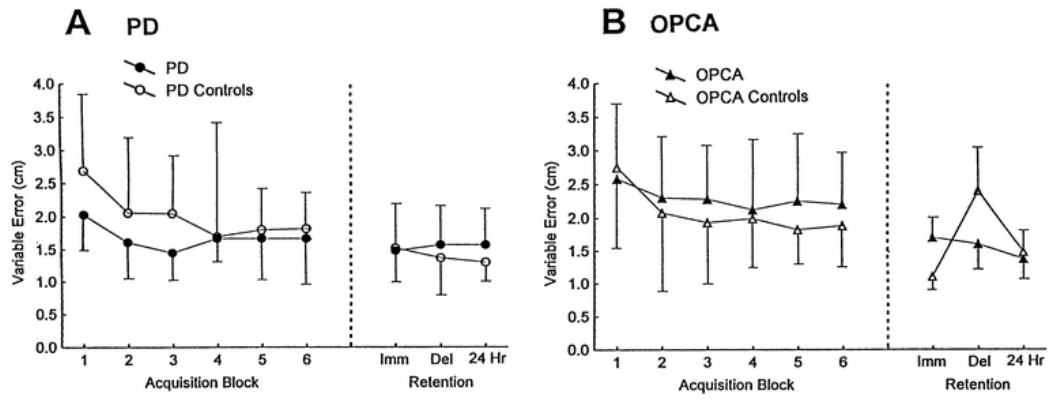


Figure 2. Acquisition and Retention for PD and control groups, movement distance plotted against target distance. The top six panels represent the six blocks of acquisition trials (six trials for each of the distances per block). The final three are retention trials: immediate, delayed (approximately 18 min after acquisition) and 24 h. Best fitting lines are shown for each group (PD: solid; controls: dashed). The boundary between the shaded and white areas is a line showing perfect performance. Note that the origin of the plots is not 0,0 so the slope of the lines must be extended for the intercept.



**Figure 3. A** Variable error for the PD and control groups during initial Acquisition and Retention phases. Error bars represent between subject standard deviation for each group. **B** Similar plot for OPCA and control groups.



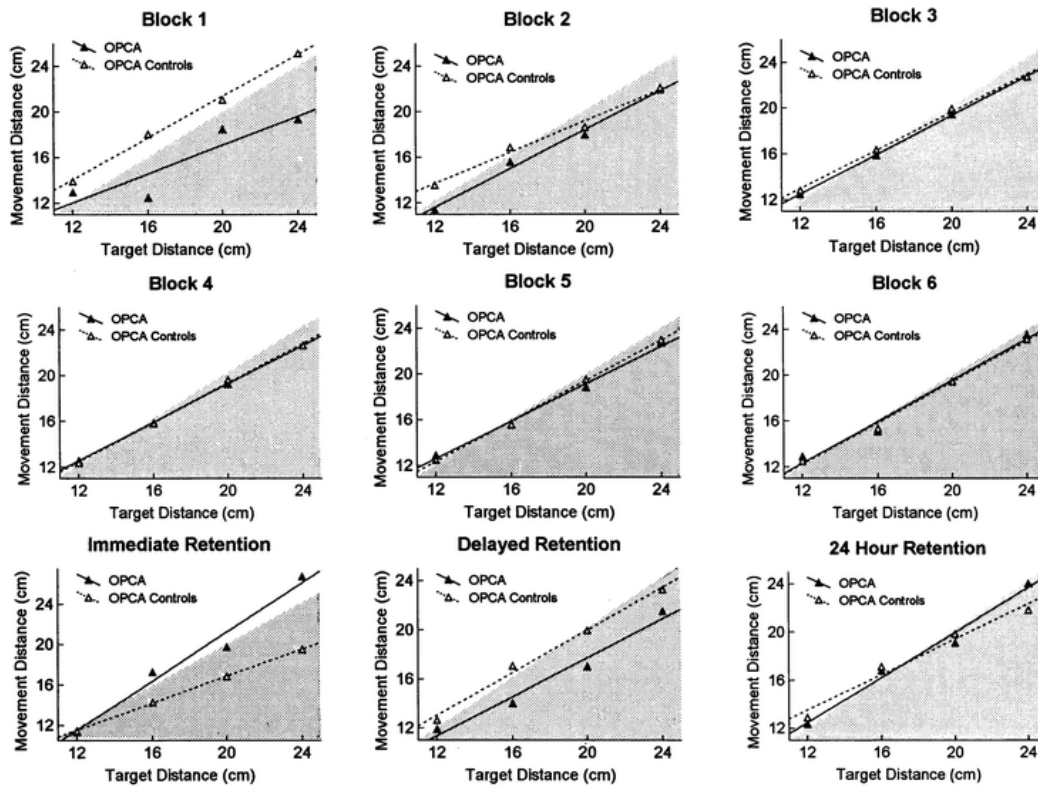


Figure 4. Acquisition and Retention for OPCA and control groups, plotted as in Figure 2.

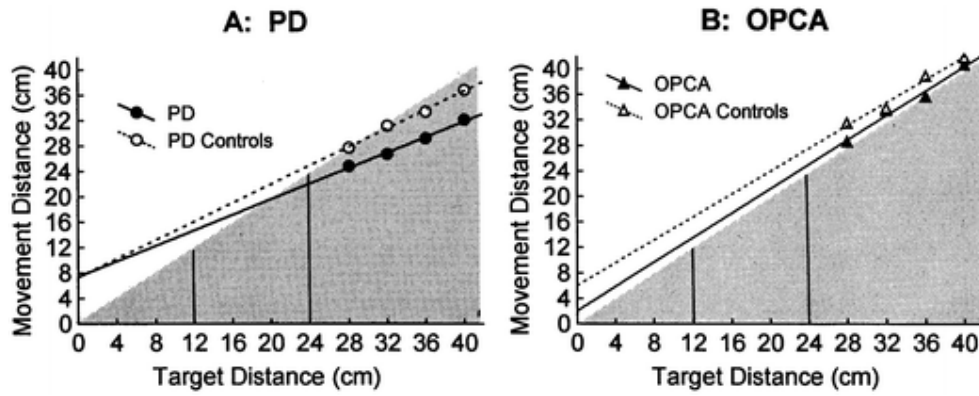


Figure 5. A: Extrapolation for PD and control groups (no KR provided), movement distance plotted against target distance as in Figure 2. Note that Acquisition target distances were between 12 and 24 cm. B: Similar plot for OPCA and control groups.

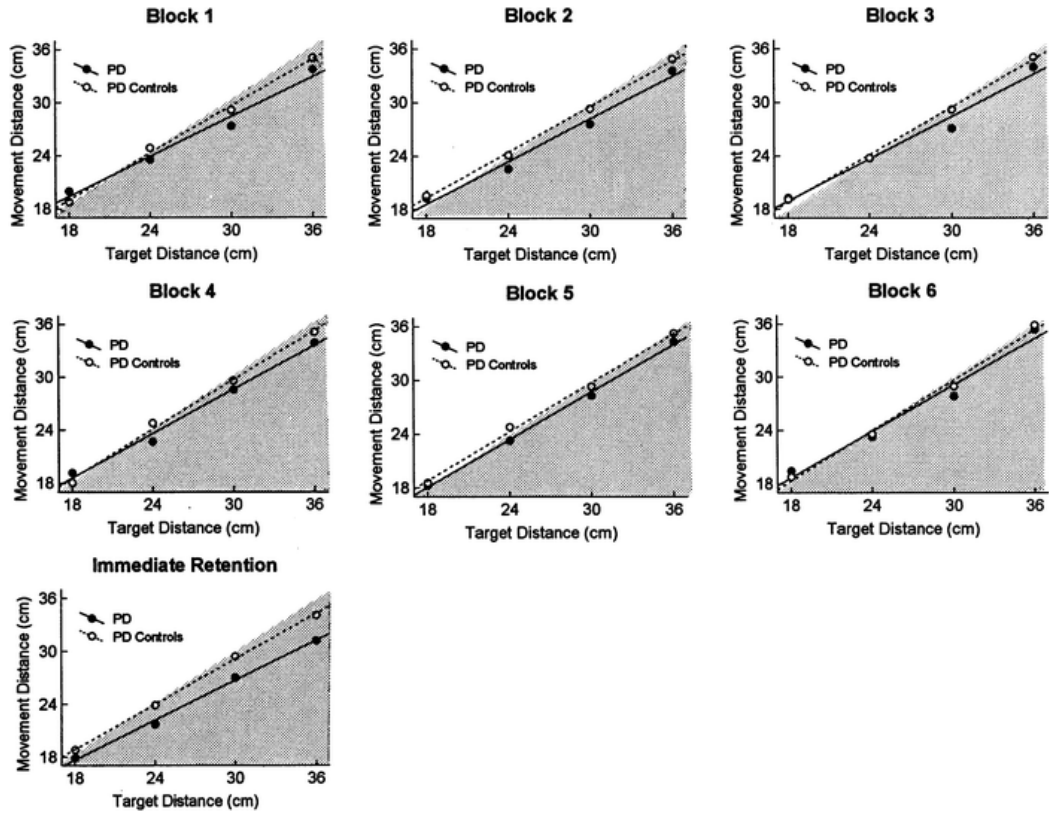
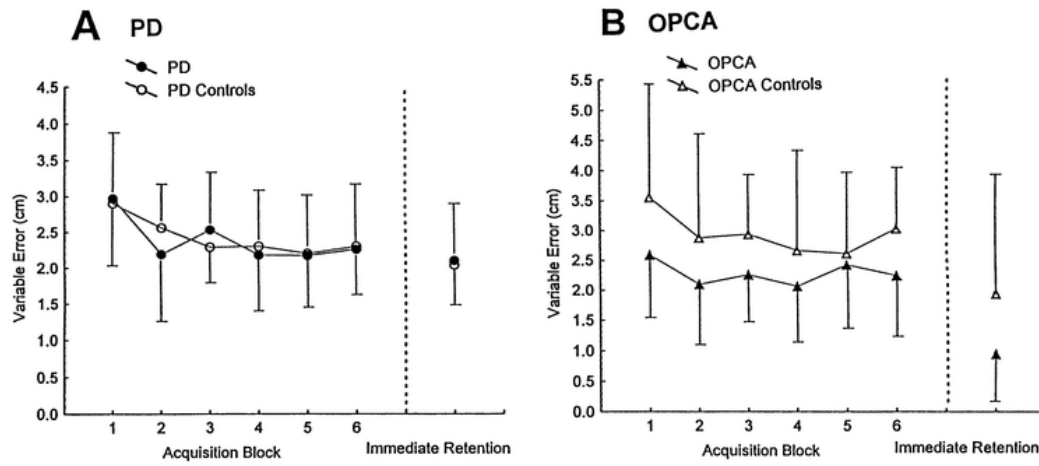


Figure 6. Gain Change Acquisition and Retention for PD and control groups, plotted as in Figure 2.



**Figure 7A, B. Variable error for PD and controls during Gain Change Acquisition and Retention phases. Error bars represent between subject standard deviation for each group.**

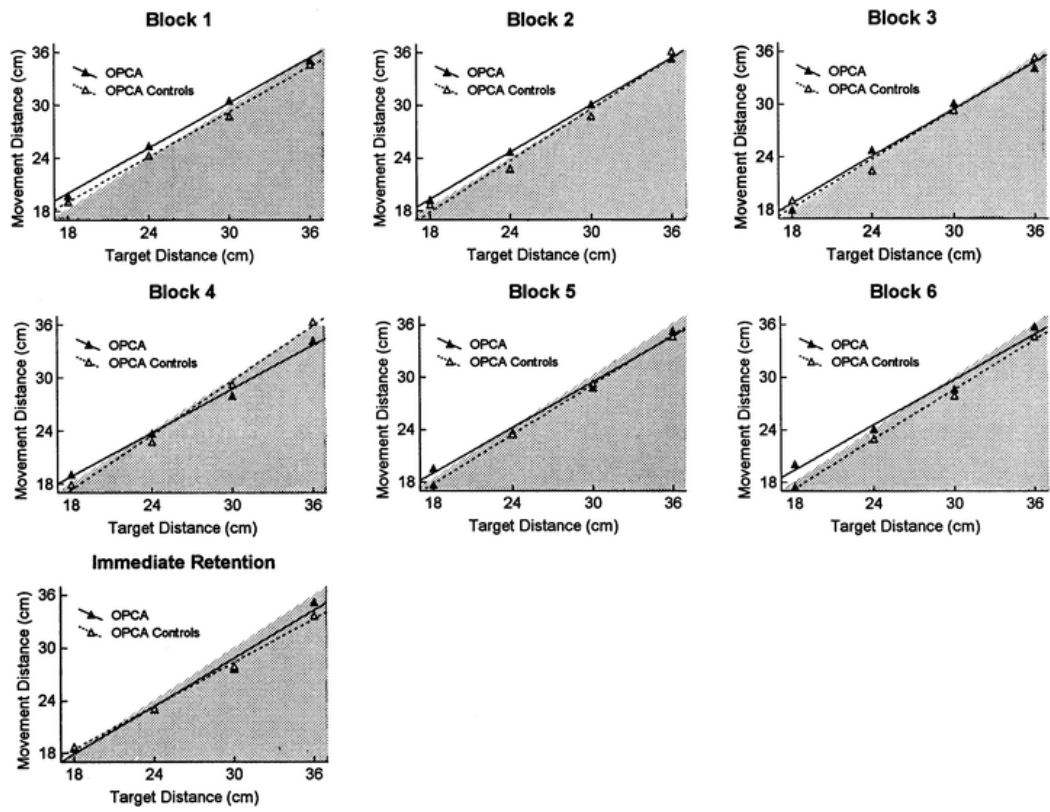


Figure 8. Gain Change Acquisition and Retention for OPCA and control groups, plotted as in Figure 2.