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Dopamine replacement therapy does not restore the ability of Parkinsonian patients to make rapid adjustments in motor strategies according to changing sensorimotor contexts

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Abstract

The ability of dopamine replacement to restore rapid motor adjustments in Parkinson's disease was investigated. Medicated and non-medicated patients performed finger-to-nose movements while simultaneously bending the trunk forward, without vision. Trunk motion was blocked unexpectedly, necessitating rapid adjustments in arm trajectories. Patients exhibited irregular hand paths, plateaus in hand velocity, and prolonged movement times which were significantly greater in perturbed trials. Medication improved kinematics but perturbation-induced disturbances persisted and did not approximate the levels of non-perturbed trials nor those of controls. Dopaminergic replenishment in Parkinson's disease may therefore have limited restorative benefits for rapid context-specific motor control.

Keywords

Parkinson's disease; adaptive motor control; dopamine medication; basal ganglia

Introduction

Flexible motor control relies on one's ability not only to use sensorimotor information to update subsequent movements on a trial-to-trial basis, but also to use this information to rapidly modify an ongoing movement according to changing external conditions. While the basal ganglia (BG) have traditionally been associated with trial-to-trial learning [1–3], emerging evidence also implicates a critical role for these nuclei in the ability to switch rapidly between different motor strategies depending upon changes in the environment. In the present study, we investigate whether deficits in the rapid and flexible use of multiple movement repertoires in changing environmental circumstances that is inherent in BG pathology can be reduced by pharmacological intervention.

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The motor deficiencies of Parkinson's disease (PD) result primarily from degeneration of the dopamine containing neurons in the basal ganglia, although many other systems are affected in the disease [4]. Dopamine depletion in PD leads to severe disturbances in neural processing within basal ganglia-cortical circuits. It is now recognized that PD leads to impairment in the ability to adapt the ongoing arm trajectory to mechanical perturbations of the trunk [5,6] or even to visual perturbations of target position [7]. Together, these studies suggest that deficient adaptation of the ongoing movement is not specific to a particular effector and results from malfunctioning of different brain structures, including the BG and BG-thalamocortical circuits. Moreover, we have previously shown that this deficit is not reduced by repeated exposure to a given perturbation [5]. These findings rule out the possibility that this deficit is related to impoverished learning, which has sometimes been reported for PD. It seems likely, therefore, that integrity of BG-thalamocortical circuits may be critical for updating an ongoing action. The malfunctioning of these circuits in PD has often been characterized as an inability to 'switch' between context-specific motor patterns [2,5,8]. This inability may potentially arise due to difficulties in coordinating actions in different frames of reference [5,6]. It remains unknown whether such deficits are responsive to dopaminergic treatment in PD.

Pharmacotherapy aimed at replenishing dopamine levels has proven rather successful in reducing the majority of the motor deficits of PD, i.e. akinesia and bradykinesia [9–11], rigidity [12,13], and resting tremor [9,10,14], but has shown modest effects on restoring coordinated movements when demands on precision are high, such as for prehensile actions or reaching/pointing toward a target. For example, dopamine replacement therapy failed to improve some aspects of reach-to-grasp actions [15,16] and reaching movements [17,18], and even led to increased spatial errors [11]. Disruptions in movement amplitude and velocity, which we have termed intensive aspects of movement, may be amendable to dopamine replenishment therapy [15] perhaps due to thalamo-cortical disinhibition resulting in an increase of BG-thalamocortical signals to the primary and supplementary motor areas [19]. Conversely, other coordinative aspects of an action may be resistive to pharmacotherapy since these aspects may not be restored by a simple facilitation of the BG-thalamo-cortical pathways [15].

We seek to determine whether dopamine replenishment in Parkinson's patients can restore control of ongoing movements in the face of motor perturbations. To this end, medicated and unmedicated PD patients were required without visual feedback to move the hand to the nose while simultaneously leaning the trunk forward [5]. This task challenged subjects' ability to rapidly adjust an ongoing movement [simultaneous trunk flexion and finger-to-nose movement) to a new movement (finger-to-nose movement only) on a minority of randomly selected trials in which the trunk motion was blocked. We hypothesize that medication may restore the intensive components of the movement, such as velocity, but would have a modest effect in improving patients' ability to make rapid, context-dependent, movement adjustments in response to the trunk perturbation.

Methods

Subjects

Nine right-handed [20], non-depressed and non-demented (assessed with the Beck Depression Inventory and the Mini-Mental Examination, respectively), patients with idiopathic Parkinson's disease (PD patients) participated after signing informed consent documents approved by the human subjects ethics committee at the Rehabilitation Institute of Montreal. Table 1 presents the clinical characteristics of the patients. Each PD patient was tested in the morning a) before taking the first dose of antiparkinsonian medication of the day, being off medication for at least 12 hours after their dose of the previous night (OFF), and b) 1–2 hours after taking the first dose of antiparkinsonian medication of the day (ON). The OFF medication state assured that the majority of the beneficial effects of dopamine replacement therapy were

ameliorated [21]. Each PD patient was tested twice, on separate mornings, with the order of ON and OFF sessions counterbalanced across patients. Immediately prior to each testing session, a trained individual administered the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS) to each patient to provide a clinical measure of disease severity. The UPDRS is perhaps the most commonly used Parkinson's disease severity rating tool, is found to have a stable factor structure as well as a high internal consistency when administered to medicated and unmedicated patients and has proved to be more reliable than any other available clinical rating scale for PD [22–27]. Patient data were compared with the data of six right-handed, age-matched, healthy subjects who were tested on the identical task in a previous study [5]. Though any potential inter-session confounds were controlled for by counterbalancing the order of PD patients' ON-OFF sessions, two additional age-matched healthy subjects were tested over two separate sessions to further rule out any confounds potentially arising from repeated testing.

Setup and procedure

The set up and procedure were identical to those used by [5] and is depicted in Fig. 1. In response to an auditory go signal (a beep), seated subjects performed a finger-to-nose movement while simultaneously moving the nose to the finger by bending the trunk forward from the hip. Vision was occluded during each trial via liquid crystal glasses (Translucent Technologies, Inc.) that became opaque upon an electric signal that was synchronized with the go signal. Subjects wore a vest harnessing a metal plate on the back which, between trials, was locked to an electromagnet (Warner Electric, Inc.) fixed to a wall behind the subject. On 60% of randomly selected trials (54 trials), unrestrained trunk motion was allowed by deactivating the electromagnet at the time of the go signal (free-trunk condition). On the remaining trials (36 trials), trunk motion was blocked (blocked-trunk condition) by keeping the electromagnet activated during the trial. Before the experiment, subjects were trained on 10 free-trunk trials. For the experiment, subjects were instructed to try to perform arm and trunk motions simultaneously, but that the goal of the task was to get the finger to touch the nose; this goal remained unchanged whether or not their trunk motion was blocked. Subjects reported no discomfort from these procedures.

Data Acquisition

Arm–trunk kinematics were derived from the recorded 3D positions of seven infrared emitting diodes (IRED) attached to the following locations: between the lenses of the glasses, the bony landmarks of the lower sternum (trunk), acromion processes of both scapulae (shoulders), lateral epicondyle of the elbow, wrist styloid, and index fingertip. Each IRED's position was captured by optoelectronic cameras (Optotrak 3010, Northern Digital, sampling rate 100 Hz). The Optotrak 3D measuring system has outstanding precision and excellent reliability [28]. Offline, missing samples were interpolated using a five-point algorithm and the data were low-pass filtered at 8 Hz.

Kinematic Variables

Using customized Matlab software (Mathworks, Woburn, MA) movement onset was defined as the time at which the tangential hand velocity first exceeded 5% of the peak tangential hand velocity of that trial (measured in an absolute, laboratory frame of reference). Movement offset was defined as the time when finger-to-nose contact occurred (the time at which 3D distance between the finger and nose did not change by more than 5% for at least 100 ms). Four dependent measures were computed: 1) Hand *movement time* (MT) defined as the time interval between the onset and offset, 2) Peak tangential *hand velocity* (PV), 3) *Normalized integrated jerk* (NIJ, an indicator of hand movement smoothness) defined as $NIJ = \sqrt{(T^5/2L^2) \int J^2 dt}$, where J is the third time derivative of hand position, sqrt is square root, T is movement duration,

L is hand path length, and the limits of integration are (0,T). This measure is relatively independent of movement duration and amplitude [29–31], and 4) *Movement Tardiness Index* [5]. Mostly in PD patients, the trunk arrest influenced the hand movement by slowing it, and on rare occasions even completely stopping it. In the latter case, the hand movement was reinitiated after some period of time. In the former case, the hand velocity, although decreased, remained above zero and could fluctuate about an almost constant level for a given period of time. A tardiness in the movement was therefore defined as a >50 ms interval of time during which the fluctuations in hand velocity did not exceed 3% of the peak hand peak velocity. This period of time was considered as a velocity plateau. The total duration of these plateaus in each trial of each subject was computed and will be referred to as the movement tardiness index. The use of velocity threshold in the measurement of the tardiness index assured that the index value was not confounded by changing in movement latency that could result from bradykinesia.

Statistics

Each variable was analyzed using a repeated measures analysis of variance (ANOVA) within the PD group (within-group factors [levels]: medication [ON, OFF], movement condition [free-trunk, blocked-trunk]) to test for the effects of dopamine replacement therapy on rapid adjustments to movement perturbation. Additionally, the PD-OFF and PD-ON medication conditions were analyzed using between-group ANOVAs for comparisons with healthy subjects. Post-hoc analysis of significant interactions was performed with the Student–Newman–Keuls test. To determine any changes in performance in the BLOCKED condition as a function of time, a multiple regression analysis was performed between each subject's tardiness index and trial number. A paired t-test was used to compare OFF- with ON-medicated UPDRS scores (overall score and postural stability score). Effects on a given measure were considered to be significant if $p < 0.05$.

Results

The left panels in Figure 2 show strobe plots of a representative trial from a typical healthy subject performing the finger-to-nose task in the free-trunk (top left) and the blocked-trunk (middle left) conditions. In these plots, successive positions of the arm and nose are shown at 30 ms intervals. The location at which the finger and the nose come in contact with each other is indicated for both conditions by a dashed circle. Note that the hand trajectory (H) toward the nose (N) remained smooth irrespective of whether the trunk motion was unrestrained (allowing full movement of the trunk-nose unit) or blocked unexpectedly (keeping the trunk-nose unit at approximately its starting location). Healthy subject's hand velocity profiles (Fig. 2, bottom left) likewise remained smooth and bell-shaped for the free- and blocked-trunk conditions.

Like controls, PD patients were able to successfully execute the goal of the task – to make contact between the fingertip and the nose. Fig. 2 (top center and right) shows a representative PD subject performing a trial in the trunk-free condition. The strobe plot illustrates that in this condition, the PD subjects' hand traveled toward the nose in a relatively smooth, albeit slower (see also velocity profiles in lower panels), manner compared to the control trajectory shown in the left panel. However, in the trials on which trunk motion was unexpectedly blocked (middle row, center and right panels), PD subjects' hand movements showed spatiotemporal disturbances. A typical disturbance, shown in Fig. 2, was characterized by a slowing of the hand movement (seen as a closer spacing between strobe lines in the trajectory) and an irregular hand path in external space (arrow). This disturbance is also clearly characterized by the double peak velocity profile (Fig. 2, lower center and right panels).

The disturbances observed in the PD subjects' hand movements were quantified. Relative to healthy subjects, PD patients tested in the non-medicated state exhibited significantly slower tangential hand velocity (group main: $F_{(1,13)}=105.9$, $p<0.0001$), increased movement time (group main effect: $F_{(1,13)}=19.9$, $p<0.001$), less smooth movement (NIJ group main effect: $F_{(1,13)}=7.6$, $p=0.016$), and increased tardiness index (see Methods) ($F_{(1,13)}=15.1$, $p=0.002$). Additionally, significant group x trunk motion interactions were noted for movement time ($F_{(1,13)}=11.5$, $p=0.005$) and the tardiness index ($F_{(1,13)}=12.5$, $p=0.004$). Post-hoc comparisons indicated that these interactions were driven by significant differences between the free- and blocked-trunk conditions for movement time (Cohen's d (effect size)=1.3) and the tardiness index ($d=1.2$). These results confirm a task-specific impairment in the PD-OFF group wherein their ability to generate a rapid adjustment of the hand to the trunk perturbation was dramatically impoverished (see Fig. 2).

Expectedly, dopamine repletion had beneficial effects on the clinical deficits associated with Parkinson's disease. A significant, 32.7%, reduction in the UPDRS scores was noted from the OFF (mean score $\pm$ std, 26.6 ± 6.5) to the ON (17.9 ± 5.0) medication state indicating that subjects' motor symptoms were responsive to the pharmacologic therapy. Moreover, substantial improvements were noted not only on the arm and leg components of the UPDRS motor scale, but also a significant improvement was noted on the postural stability component ($t=2.828$, $p=0.022$) (Table 2), indicating that dopaminergic replenishment had a global benefit to the patients.

Dopamine administration also improved movement kinematics (Fig. 3). First, medication administration led to a 51% reduction in movement jerkiness in the free-trunk condition, and a 57% reduction in the blocked-trunk condition, though the medication main effect only approached significance ($p=0.064$). Second, medication administration led to a 24% increase in the peak hand velocity in the free-trunk condition and a 21% increase in the blocked-trunk condition. Third, medication led to an 11.9% decrease in movement time in the free-trunk condition and a 23% decrease in the blocked-trunk condition. A significant medication x trunk motion interaction for movement time ($F_{(1,8)}=6.9$, $p=0.03$) indicated that this medication-induced benefit was predominantly in the blocked-trunk condition (Fig. 3), though post-hoc comparisons did not yield significant effects.

Notably, medication administration led to a 30% reduction in the tardiness index in the free-trunk condition and a 46% reduction in the blocked-trunk condition, although the medication main effect did not reach significance ($p=0.053$). A significant medication x trunk motion interaction ($F_{(1,8)}=6.7$, $p=0.03$) and subsequent post-hoc statistics ($d=1.2$) confirmed that the medication-induced benefit was significant in the blocked-trunk but not in the free-trunk condition. It is noteworthy here that the more pronounced reduction in movement time in the blocked-trunk condition was mostly attributed to the reduction in the tardiness index (for which a significant interaction was noted) as opposed to the increase in peak hand velocity (for which no interaction was observed).

Because procedural, trial-to-trial, learning is known to be impaired in Parkinson's disease [1, 2], it is possible that the medication-induced benefit in the tardiness index resulted from a more effective learning process over the course of ON, relative to OFF, trials. To test for this, we correlated the tardiness index in the blocked-trunk condition with the trial number, on a subject-by-subject basis. In the OFF medication condition, two of the nine PD patients (s1: $r^2=0.212$, $p=0.031$; s9: $r^2=0.78$, $p<0.001$; all others: $r^2<0.37$, $p>0.05$) showed a significant, positive, correlation between movement tardiness and trial number. In the ON medication condition, two of the nine PD patients (s4: $r^2=0.43$, $p=0.016$; s9: $r^2=0.34$, $p=0.02$) showed a significant positive correlation and one (s8: $r^2=0.34$, $p=0.02$) showed a significant negative correlation (all others: $r^2<0.32$, $p>0.05$). In other words, the majority of the subjects did not show any signs

of accommodation, or learning-related effects, to the perturbation either in the OFF- or ON-medicated states, and, the couple of cases who did, actually showed a positive correlation, i.e. a deterioration effect. The same analysis performed on a subject-by-subject basis on the healthy subjects also did not reveal any learning effects (for all subjects, both conditions: $r^2 < 0.5$, $p > 0.1$). Moreover, the healthy subjects tested on two separate sessions did not show any change in performance across the sessions (i.e. tardiness index between session 1 and session 2 for blocked or free conditions: $p > 0.16$).

Despite any of the medication-induced benefits, none of the dependent measures even came close to the levels observed in the healthy group (PD-ON vs. healthy group main effects for tardiness: $p < 0.002$; for PV: $p < 0.0001$; for MT $p < 0.0007$; for NIJ $p < 0.017$), suggesting that dopamine replacement was not sufficient to fully restore normative adjustments to motor perturbation.

Discussion

Basic findings

The purpose of the present experiment was to understand whether dopamine replacement therapy remediates deficits in rapid adjustments of ongoing movements in the face of motor perturbations. To this end, medicated and non-medicated PD patients performed a task previously shown to elicit robust disruptions in such rapid movement adjustments in non-medicated PD patients [5]. Consistent with our previous study, adjustment of ongoing movements (measured with the tardiness index) was markedly disrupted in the blocked-trunk trials of non-medicated PD patients. Administration of dopaminergic medication, in addition to significantly improving the UPDRS motor scores and improving movement velocity, movement time, and smoothness, also improved rapid adjustments in ongoing movements – evidenced by a reduced tardiness index. However, even in the PD-ON group, the tardiness index remained significantly greater in the blocked-trunk than the free-trunk condition and significantly greater than that of the healthy subjects.

The tardiness index represents the amount of time that the hand movement spends in a paused state during the movement and is therefore particularly sensitive to trunk-perturbation induced disturbances in the hand path. In order to rapidly reconfigure arm trajectories without vision of the arm when the trunk motion is unexpectedly blocked, subjects must precisely integrate in real time, proprioception from the moving arm with that of the suddenly blocked trunk to modify the movement of the appropriate body segments. It has recently become clear that cells in basal ganglia, thalamic, and cortical motor areas show a lack of specificity in responding to limb proprioception in primate models of PD [32–34], and that PD patients show deficits in processing proprioceptive signals [35–37]. Thus, PD patients may have lost the precision in proprioceptive processing required to rapidly reconfigure their arm trajectories under conditions of motor perturbations. The pauses in the arm movements of the PD patients when the trunk motion was blocked may reflect this imprecision in processing and integrating of proprioceptive signals. Our study demonstrates that PD subjects' performance, and in particular the tardiness index, improved but did not normalize when patients were in the medicated state, despite the significant effect that medication had in lowering the scores on standard clinical motor scale (the UPDRS). These results not only confirm previous data implicating the basal ganglia's role in coordinating rapid adjustment of motor behavior, but suggest that this function may remain partially resistant to L-dopa therapy.

Rapid adjustments of ongoing movements and cortico-striatal circuits

Two noteworthy findings emerged from this experiment. First, dopamine replenishment led to a general enhancement of performance in both free- and blocked-trunk conditions. In the case

of the tardiness index and movement time measures, this improvement was significantly greater in the blocked-trunk condition. The second, and perhaps more interesting finding, is the lack of normalization of ongoing movement adjustments (between the free- and blocked-trunk conditions) in the medicated PD subjects. We propose that the divergence between these two main findings can be explained by a differential effect of dopamine on the cortico-striatal circuits that mediate such ongoing movement adjustments to changing external conditions. This is discussed below.

I. Deficits in ongoing movement adjustments that may be responsive to dopamine replenishment—What may have been the underlying factor that led to the medication-induced benefit across the free- and blocked-trunk conditions? One possibility is that in the OFF state, PD subjects insufficiently learned the task, a procedural learning deficit that may have been ameliorated by dopamine replenishment. However, trial-to-trial performance did not change in the healthy subjects, or in a majority of the PD-ON and PD-OFF subjects - and the few PD subjects who did show a change, actually showed a slight deterioration, rather than an enhancement, of performance. Overall, however, performance remained relatively consistent across the testing session, making a trial-to-trial learning confound an unlikely explanation for any medication-induced benefit.

What is more probable, instead, is that dopamine replenishment acted to directly improve some aspects of motor control, perhaps via disinhibition of BG-thalamocortical regions (motor and premotor). Neuroimaging studies [19,38,39] and electroencephalographic recordings [40] have demonstrated that neural activation within these regions normalizes after dopamine administration. This enhancement is thought to underlie the improvement in intensive motor deficits, such as reduced movement amplitude or velocity, present in the off-medicated state (see Introduction). Thus, improvements in velocity and movement time were likely a direct result of this medication induced benefit. It is noteworthy, however, that though the dependent measures in the PD-ON group were improved, they did not normalize to the level of controls. Moreover, Figure 2 (right panel) shows clearly that the spatio-temporal hesitations persisted in the PD-ON group for the blocked-trunk trials, indicating that ongoing movement adjustments to the perturbation had a considerable non-responsive component to the medication.

II. Deficits in ongoing movement adjustments that may not be responsive to dopamine replenishment—Despite an overall medication-induced benefit to movement (revealed by the general improvement in the kinematic measures and in the significant improvement in the scores on the motor section of the UPDRS), the dependent measures, in particular the tardiness index, did not normalize in the blocked-trunk condition to the levels observed in the free-trunk condition, nor to the levels observed in the healthy group. It should be noted that although UPDRS scores did not completely normalize after medication, they nevertheless improved significantly from the OFF state. In contrast, although movement performance measures improved after medication, this improvement did not significantly interact with the trunk perturbation condition. For this reason, we feel that it is unlikely that “incomplete” effects of medication underlay the inability of PD subjects to make proper motor adjustments even in the medicated state. Neither is it likely that the deficit in rapid adjustment of ongoing movements is attributable to any postural disturbances elicited by the trunk perturbation. First, subjects were securely seated without any threat of falling. Second, a significant 41.4% improvement in postural stability was noted on the UPDRS scale in the medicated state, suggesting that that postural stability was actually quite responsive to the medication.

Instead, it is more likely that the impaired ability to modify the movement pattern according to contextual demands is more directly attributed to impaired BG function. This finding

suggests at least two interpretations. One possibility is that cortical sensorimotor regions known to be the targets of BG outflow, but those that do not show positive responses to dopamine replenishment may be suspect in mediating context dependent movement modification. A second possibility is that the increase in dopaminergic drive due to medication may not be sufficient to restore the proper fine-grained processing of neural information within the basal ganglia itself and in related brain structures. Numerous studies have found premotor cells to respond to various perturbations [41] as well as have some temporal covariation in firing activity with the putamen [42,43]. Therefore, it is likely the BG-premotor and possibly even the newly-recognized BG-parietal circuits [44] are contributing to aspects of rapid adjustments of ongoing movements in changing environmental conditions. Experiments directly aimed at differentiating the specific involvement in each of these circuits should become an important focus of future research. Another possibility is that while dopaminergic medication may carry beneficial effects on improving signal output from the basal ganglia, it may have null or even deleterious effects on the noise of the signal within these neural circuits. Deep brain stimulation, which is used to induce a virtual lesion in the subthalamic nucleus and perhaps reduce noisy (or incorrect) information, may offer a window to understanding this possibility. This hypothesis remains to be tested.

Study limitations

While we made every effort to control for potential confounds, several factors warrant some degree of caution when interpreting these data. For example, examiners administering the UPDRS to the PD patients were not blinded to the medication state of the subjects. While the potential for score bias exists, the UPDRS was performed by a consistent, experienced, examiner ruling out the possibility of inter-rater variance. Another potential limitation is the fact that the PD subjects were predominantly male (6 males and 3 females). Due to the small sample size, we were unable to test for gender effects, and the study was not powered to test for small behavioral differences. In spite of these limitations, the within-subject design of this study provides compelling evidence regarding the effect of pharmacotherapy on a specific, emergent role of basal ganglia-thalamo-cortical circuits in the flexible control of motor behavior.

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Figure 1.
The experimental setup and task conditions.

Figure 2.

Representative arm and nose trajectory profiles for a typical healthy subject (left column), PD subject tested OFF (center column) and ON (right column) medication. Upper and middle rows show strobe trajectories of the arm and nose in the free-trunk condition (top row) and blocked-trunk condition (middle row). Dotted circles demark the points of contact between the finger and the nose. Interval between strobe lines, 30 ms. Arrows show typical spatiotemporal irregularities in hand movement observed in the PD subjects. The bottom row shows tangential hand velocity profiles.

Figure 3.

The mean $\pm$ standard deviation of the dependent measures for the FREE-trunk (light gray) and BLOCKED-trunk (dark gray) conditions. Note that the y-axis scale is different for the PD and control subjects.

Table 1

Clinical Characteristics of PD patients.

Subject	Sex	Age	Motor UPDRS OFF	ON	PD duration (yrs)	Medication
PD1	M	80	33	16	4.5	S _{CR}
PD2	F	69	19	9	6	S, A
PD3	M	72	37	28	6	S, A, Ev
PD4	M	69	29	19	14	S _{CR} , C
PD5	F	56	16	15.5	9	S, M, A
PD6	F	56	28	16	9	S, P
PD7	M	64	24	19	4	S, Mp, Se
PD8	M	75	25	19	8	S _{CR}
PD9	M	53	28.5	20	3	R, Ad
PD mean $\pm$ SD	-	66 $\pm$ 9.4	26.6 $\pm$ 6.5	17.9 $\pm$ 5.0	7.1 $\pm$ 3.4	-
Control mean $\pm$ SD	-	69 $\pm$ 14.0	-	-	-	-

SD, standard deviation; S_{CR}, Sinemet CR; S, Sinemet; M, Mirapex; A, Amantadine; P, Paxil; Mp, Minapril; Se, Selegiline; C, Comtan; Ev, Elavil; R, Requip; Ad, Adomin.

Table 2

Mean group scores for each item on the UPDRS motor section conducted on patients in the OFF and ON states and the percent change in the score.

	OFF	ON	% change
speech	1.13	0.72	35.80
facial expression	0.94	0.78	17.04
tremor face/lips/chin	0.25	0.11	55.56
tremor hands L	0.44	0.17	61.90
tremor hands R	0.38	0.56	-48.15
tremor feet R	0.13	0.00	100.00
tremor feet L	0.50	0.11	77.78
action tremor R	0.88	0.67	23.81
action tremor L	0.69	0.89	-29.29
rigidity neck	0.25	0.33	-33.33
rigidity UE R	1.25	0.83	33.33
rigidity UE L	1.44	0.78	45.89
rigidity LE R	1.56	1.33	14.67
rigidity LE L	1.75	1.00	42.86
finger taps R	2.00	1.11	44.44
finger taps L	2.14	1.00	53.33
hand grips R	1.57	0.78	50.51
hand grips L	1.71	0.94	44.91
hand pro-supination R	1.36	0.89	34.50
hand pro-supination L	1.79	1.11	37.78
leg agility R	1.29	0.61	52.47
leg agility L	1.14	1.11	2.78
rise from chair	0.14	0.00	100.00
posture	0.64	0.61	4.94
postural stability	1.61	0.94	41.38
gait	0.71	0.39	45.56
body bradykinesia	0.50	0.17	66.67