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## Effects of Medication on Turning Deficits in Individuals with Parkinson's Disease

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### Abstract

**Background and Purpose**—People with Parkinson disease (PD) often have difficulty executing turns. To date, most studies of turning have examined subjects ON their anti-Parkinson medications. No studies have examined what specific aspects of turning are modified or remain unchanged when medication is administered. The purpose of this study was to determine how anti-Parkinson medications affect temporal and spatial features of turning performance in individuals with PD.

**Methods**—We examined turning kinematics in 10 people with PD who were assessed both OFF and ON medication. For both conditions, participants were evaluated with the UPDRS motor subscale, rated how well their medication was working on a visual analogue scale (VAS), performed straight-line walking and 180 degree in-place turns. We determined average walking velocity, time and number of steps to execute turns, sequence of yaw rotation onsets of the head, trunk, and pelvis during turns, and amplitudes of yaw rotation of the head, trunk, and pelvis during turns.

**Results**—Medication significantly improved UPDRS scores ( $p = 0.02$ ), VAS ratings ( $p = 0.03$ ), and walking velocity ( $p = 0.02$ ). While improvements in turning were not statistically significant, medication did reduce the time and number of steps required to turn, slightly increased the amplitudes of yaw rotation of the various segments, and increased the rotation of the head relative to the other segments. Medication did not improve the timing of segment rotations, which showed “en bloc” turn initiation in both the OFF and ON medication conditions.

**Discussion and Conclusion**—These results suggest that only certain aspects of turning may be responsive to anti-Parkinson medications. As such, additional rehabilitative approaches to address turning are needed, as turning may not be effectively addressed by pharmacological approaches. These results should be interpreted cautiously given the small sample size.

### Keywords

Parkinson disease; walking; turning

### Background and Purpose

Impaired turning affects a large percentage of people with Parkinson disease (PD) and is often present before other gait abnormalities.<sup>1,2</sup> Turning impairment hinders activities of daily living, is associated with falls, and has a significant effect on quality of life.<sup>1,3–6</sup> Previous studies have

noted several deficits in turning. Individuals with PD have been repeatedly noted to require more steps and more time to complete a turn than age-matched controls.<sup>6-9</sup> Individuals with PD also demonstrate altered timing of turn initiation with near simultaneous onset of rotation of the head, trunk, and pelvis.<sup>2,7,10-12</sup> This pattern of simultaneous rotation onsets together with reduced relative rotations between the segments is commonly referred to as “en bloc” turning.<sup>7</sup> Control subjects turn with a top-down sequence of rotation onsets with the head rotating first followed by the trunk and then the pelvis.<sup>7</sup> In addition to alterations in timing of yaw rotation (a turn about the vertical axis) onsets, reductions in the amount of relative rotation between the body segments and in the peak velocity of yaw rotation during turning have also been reported for those with PD.<sup>7,8,12,13</sup>

To our knowledge, no studies have examined the specific effects of anti-Parkinson medication on turning performance and only a single study has examined turning performance in individuals OFF medication.<sup>7</sup> The purpose of this study was to determine whether and how anti-Parkinson medications alter the temporal and spatial features of turning in a small pilot sample of people with PD. Various hypotheses have been put forth regarding the nature of turning impairment, including the possibility that turning problems are related to axial rigidity, disrupted interlimb coordination, asymmetry of disease effects, and difficulty modifying the ongoing motor program.<sup>6,12,14,15</sup> Information about what aspects of turning difficulties may or may not be effectively targeted by pharmacological interventions could provide insights into the role of the basal ganglia in certain aspects of motor control and help to guide interventions to address problems that remain unresolved with medication. We hypothesized that medication would reduce time to turn and number of steps to turn. We further hypothesized that medication would enhance spatial aspects of turning (i.e., amplitude of segment rotations), more than temporal aspects of turning (i.e. relative timing of segment rotations).

## Methods

### Participants

Ten participants with idiopathic PD diagnosed according to standard clinical criteria<sup>16</sup> participated (see Table 1 for subject demographics). Exclusionary criteria included history/evidence of orthopedic or neurologic condition (other than PD) and presence of dyskinesia. All participants responded positively when asked if they had turning difficulty and all had normal or corrected to normal vision. In addition, each had been noted to turn “en bloc” during evaluations conducted by movement disorders neurologists on routine clinical exam prior to this study and turning difficulty had been noted in each individual's medical record. “En bloc” turning was defined as turning the head, trunk, and pelvis as a unit rather than turning the segments in a top-down sequence as is seen in healthy controls.<sup>7</sup> Participants were tested after overnight withdrawal of anti-Parkinson medications (OFF condition, average off time = 13.7 ± 0.7 hours). After completing the protocol, participants took their medications, waited one hour, and were re-tested (ON condition). Testing first OFF then ON medications was performed to permit all measurements on a single day, as many participants traveled long distances and were unable to come for two visits. All testing was done without shoes on a linoleum floor in a fully illuminated room. Participants provided written informed consent prior to participation and the protocol was approved by the Human Research Protection Office at Washington University School of Medicine.

### Protocol

The Unified Parkinson Disease Rating Scale (UPDRS) subscale III was administered by a trained physical therapist. Participants rated how well their medication was working using a 10 cm visual analogue scale (VAS). Responses could range from 0 % if they thought medications were not working at all to 100% if they thought they were getting maximum

benefit. We used an eight-camera 3-D motion capture system (Motion Analysis Corporation, Santa Rosa, CA), accurate to within 1mm, that was calibrated before each session. Thirty-three reflective markers were used: four on the head (top of head, left ear, right ear, and a head offset marker placed in an arbitrary position on one side of the head to create an asymmetrical marker set in order to assist with automatic identification of markers via the motion capture software), five on the trunk (left and right acromions, right scapula, 12<sup>th</sup> thoracic vertebra, sternal notch), four on the pelvis (left and right anterior superior iliac spines, left posterior superior iliac spine, sacrum) and ten on each leg (greater trochanter, anterior thigh, femoral condyle, fibular head, middle tibia, lateral malleolus, calcaneus, navicular, 5<sup>th</sup> metatarsal head, great toe). Markers were left in place throughout testing period to minimize shifts in marker position from OFF to ON. There were two components to the study, a walking component and a turning component. For the walking component, participants walked at self-selected pace across a 10 m walkway, three times. For the turning component, all turns were made from quiet stance and were 180 degrees in amplitude. This procedure has been used in previous studies, and was selected for this study because turns of this nature are used in everyday activities and can be consistently elicited without providing an external cue to indicate the desired turn amplitude.<sup>7</sup> Participants were given the instruction “turn and face the wall behind you whenever you are ready”. Each participant performed turns to the left and to the right, completing practice trials in each direction to verify that they understood the instructions. Data were then collected for 10 trials, with each participant turning five times in each direction in random order (determined in advance by random number generator). Order of task performance, walking or turning, was also randomized. Participants were allowed to rest as long as needed between trials.

## Analysis

There were no differences between turns toward and away from the most affected side, so we combined data from the two directions for analysis. Results were averaged across walking trials and across turning trials. Walking velocity was the velocity of the T12 marker across the middle 3m of the walkway. We determined: 1) turn duration, 2) number of steps used to turn, 3) sequence of yaw rotation onsets for the head, trunk, and pelvis at turn initiation, 4) amplitude of angular rotation for each segment in the yaw plane during the first stride of the turn, and 5) amplitude of relative rotation angles between different segments for the first stride of the turn (Kintrak, Motion Analysis Corporation, Santa Rosa, CA). Turn duration was defined as the time from liftoff of the foot used to initiate the turn through touchdown of the foot taking the final step of the turn. These times were clearly identifiable, as turns were made from quiet stance and subjects resumed quiet stance upon completion of each turn. Yaw rotation was defined as rotation in the horizontal plane and in the direction of the turn. Relative rotation angles were defined as the maximum rotation present between two segments and was assessed across the entire period of the first stride. Values for head rotation relative to trunk were obtained by subtracting trunk values from head values, for trunk relative to pelvis were obtained by subtracting pelvis values from trunk values, and for head relative to pelvis were obtained by subtracting pelvis values from head values. Sequence of rotation onsets was determined relative to start of the first step of the turn and expressed as a percentage of the gait cycle for the first stride. The beginning and end of the first step of each turn were identified in Kintrak and visually confirmed. The first stride was defined as the time from first liftoff of the foot used to initiate the turn through the next liftoff of that same foot. Amplitudes of angular rotation of each segment were determined relative to laboratory axes. We compared OFF and ON conditions using paired t-tests, or Wilcoxon tests if data were not normally distributed ( $p \leq 0.05$ , SigmaStat, Systat Software Inc, Richmond, CA). Corrections for multiple t-tests were not used, given the exploratory and pilot nature of this study. Effect sizes were also calculated.

## Results

In the medicated state, participants had significantly lower (i.e., better), UPDRS-III scores (Table 2). Participants also walked significantly faster when ON medication, although their walking velocity remained well below that reported previously for age-matched controls.<sup>7</sup> Participants reported significantly greater benefit from medication in the ON as compared to the OFF medication condition (Table 2) as noted by the VAS. The number of steps to turn and time to turn also improved with medication, although not significantly (Table 2). With medication the timing of yaw rotation onsets of the various segments relative to liftoff of the first foot occurred earlier in time, and further from control values (Figure 1). The relative timing between segments was not altered by medication and PD subjects showed near simultaneous onset of head, trunk, and pelvis rotation in both the OFF and ON medication conditions (Table 2). The amplitudes of absolute rotation of the head, trunk and pelvis all increased slightly, although not significantly, and remained well below values previously reported for age-matched controls (Figure 2). The relative rotation between the head, trunk, and pelvis increased with medication, although not significantly (Table 2). There was no evidence of systematic differences in responses of individuals with short vs. long disease duration or lower vs. higher UPDRS scores.

## Discussion

This study is, to our knowledge, the first to examine the effects of anti-Parkinson medications on specific aspects of turning in people with PD. Medication had a statistically significant impact on UPDRS scores and walking velocities, demonstrating that participants did generally have an overall benefit from medication. While turning performance was not significantly altered, there was evidence for improvements particularly with respect to the amplitudes of relative rotation between segment rotations, with effect sizes ranging from 0.42 to 0.70. In contrast, there was no improvement in the timing of rotation onsets of the different segments relative to one another (effect sizes all lower than 0.15). Our results suggest that only certain features of impaired turning may be responsive to anti-Parkinson medication. Future work with larger sample sizes is needed to confirm or refute this speculation. We acknowledge that the present study is limited by the small sample size, high variability, and lack of correction for multiple tests given the pilot nature of the work. In addition, the differences between subjects in terms of dosage and frequency of medication across participants could have contributed to the lack of differences observed. Despite these limitations, turning has been shown by others to be less responsive than other behaviors to intervention in PD. Turning deficits do not improve with auditory cues known to enhance straight walking.<sup>17</sup> This line of evidence also highlights a potential difference in responsiveness of turning versus straight walking to interventions. At present it is unclear why interventions, such as cues, that enhance straight walking may not similarly enhance turning or why certain aspects of turn performance may respond to medication while others do not.

While the mechanisms underlying turning difficulty remain unclear, it is apparent that individuals with PD have difficulty turning and that, like other axial symptoms of PD including postural stability and freezing of gait, turning may not be adequately addressed by medication alone. The improvements noted in amplitudes of rotation without improvements in timing of rotation onsets are in keeping with other studies showing that medication can improve movement velocity without improving timing of muscle activity. Robichaud et al.<sup>18</sup> noted improvements in elbow flexion velocity and in the amplitude of muscle activity with medication, but noted no improvements in timing of muscle activity. Despite the improvements observed in velocity and amplitudes during turning, these parameters were generally still quite different from those of age-matched controls as previously reported.<sup>7</sup> Similar medication effects on arm and leg movements have been reported. Vaillancourt et al.<sup>19,20</sup> reported

improvements in movement velocity and amplitude but failure of medication to fully normalize these features, as deficits in amplitude scaling and temporal patterns remained even after administration of medication. Finally, O'Sullivan et al.<sup>21</sup> noted that medication improved gait velocity and stride length without concomitant improvements in cadence. This again suggests the potentially greater effectiveness of levodopa in improving velocity and amplitude as compared to timing of movements.

Individuals with PD who have difficulty turning are likely to have difficulty with many everyday activities.<sup>6</sup> Although we did not note any directional asymmetry in turning in the present study, this has been recently reported in other work.<sup>6</sup> This discrepancy may be due to our smaller sample size or to differences in level of PD symptom asymmetry between the samples of the two studies. Other than this discrepancy, our findings are in keeping with those of prior studies with respect to time to turn, number of steps, reduced amplitudes of yaw rotation, and both spatial and temporal alterations in intersegmental rotations.

## Limitations

The results of this study must be considered in light of a small sample size and lack of statistical correction for multiple tests. Between-subject differences in medication dosage and frequency could have been a factor in the high variability we observed in the measures, and this may have contributed to an inability to detect differences.

## Conclusions

Turning impairments associated with PD are not be fully addressed by medication. In particular, medication may enhance spatial features of turning to a greater extent than temporal features. This is in keeping with other work noting improvements in amplitude but not timing of arm and leg movements. Given the lack of improvement in temporal aspects of turning, additional non-pharmacological approaches to address turning difficulty are needed, as impaired turning can interfere with activities of daily living and can place individuals with PD at risk for falls during turning.

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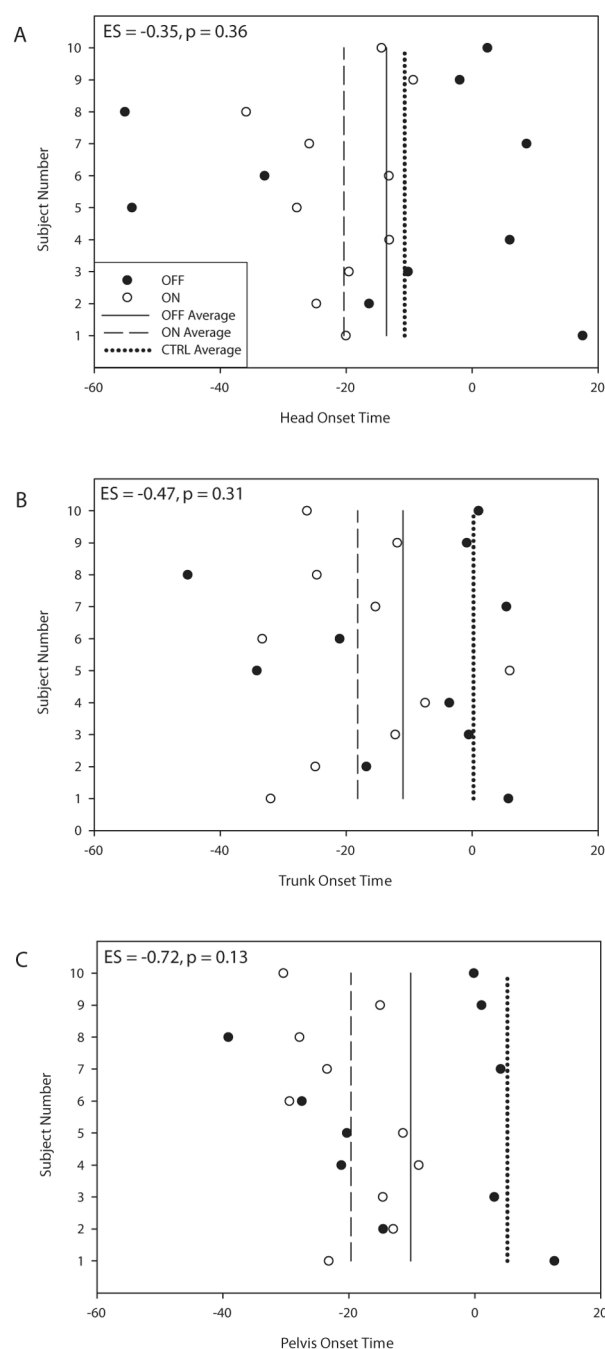
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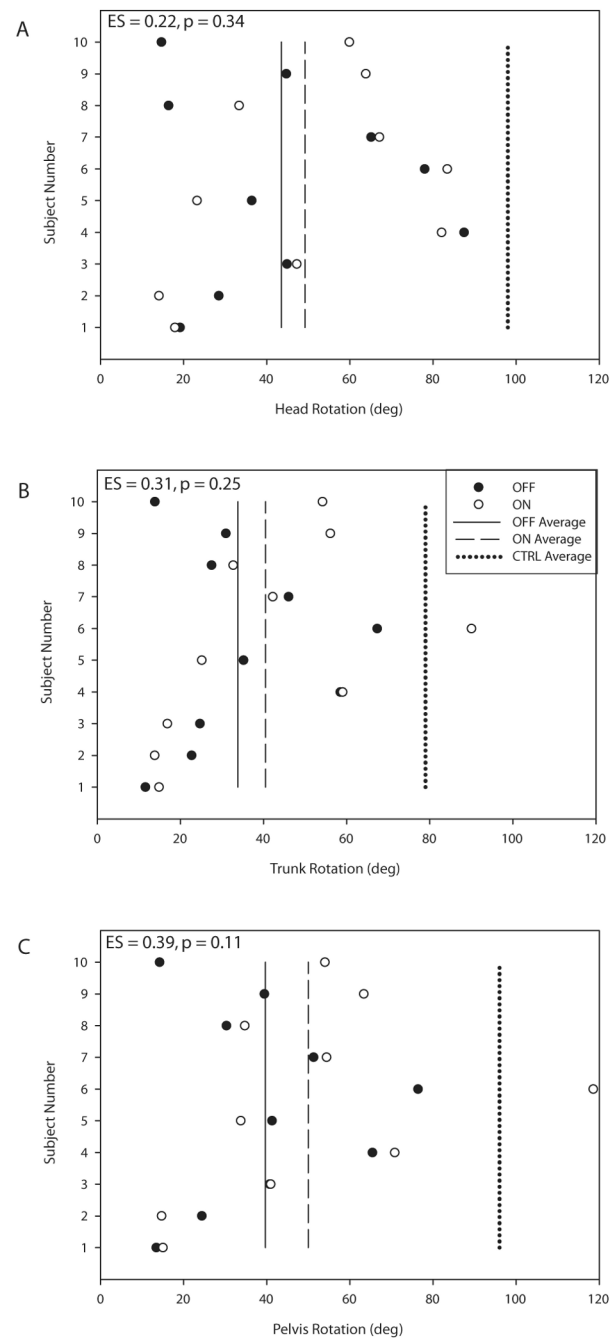
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**Figure 1.**

Onsets of yaw rotation for the head (A), trunk (B), and pelvis (C) for each individual. Onset times are expressed as a percentage of the gait cycle, with 0% representing the time of liftoff for the first step of the turn. Filled circles show values when OFF medication and open circles are ON medication. The group average OFF medication is shown with the solid vertical line and ON medication with the dashed vertical line. The dotted vertical line shows normative values previously reported for age-matched control subjects.<sup>7</sup> ES = effect size, p-values are for paired t-tests comparing ON to OFF

**Figure 2.**

Amplitudes of absolute rotation of the head (A), trunk (B), and pelvis (C) during the first stride of the turn for each individual. Filled circles show values when OFF medication and open circles are ON medication. The group average OFF medication is shown with the solid vertical line and ON medication with the dashed vertical line. The dotted vertical line shows normative values previously reported for age-matched control subjects.<sup>7</sup> ES = effect size,  $p$ -values are for paired  $t$ -tests comparing ON to OFF



**Table 1**

Subject	Age	Gender	Time Since PD Diagnosis (years)	UPDRS OffMeds	Anti-Parkinson Medication
1	76	M	8	47	sinemet 10/100mg (2 tab qid), amantadine 100mg (1 tab tid), pramipexole 1mg (.5 tab tid)
2	78	M	2	22	sinemet 25/100 (3 tab qid), requip 3mg (2 tab qhs)
3	60	M	8	22	sinemet 25/100mg (2 tab tid), amantadine 100mg (1 tap tid), pramipexole 0.25mg (0.5 tab tid)
4	68	F	3	26	sinemet 25/250 (2.75 tab qid), tolcapone 200mg (1 tab tid)
5	66	M	8	32	sinemet 25/100mg (1.5 tab tid)
6	74	M	6	39	sinemet 25/100mg (1 tab tid), sinemet CR 50/200 (1 tab tid)
7	57	M	8	31	sinemet 25/100mg (3 tab 6x/day)
8	63	M	21	37	sinemet 25/100mg (1.25 tab 6x/day)
9	71	F	10	48	sinemet 25/10mg (2 tab 7x/day)
10	58	M	6	31	sinemet 25/100mg (1.5 tab 7x/day), pramipexole 1mg (1 tab qid)

**Table 2**

## Effects of Medication

Variable	Off Medication	On Medication	Effect Size	P values
UPDRS subscale III motor rating <sup>*†</sup>	35.14 ± 3.23	29.95 ± 3.51	0.58	0.02
Medication VAS <sup>*†</sup>	25.09 ± 7.16	56.18 ± 7.83	1.31	0.03
Straight walking velocity (m/s) <sup>*†</sup>	0.63 ± 0.11	0.82 ± 0.10	0.58	0.02
Time to turn (sec)	7.45 ± 1.38	7.18 ± 1.50	0.31	0.32
Steps to turn	13.30 ± 3.14	11.15 ± 1.99	0.25	0.28
Head re: trunk rotation onset time (% gait cycle)	-3.41 ± 5.03	-0.69 ± 3.46	-0.09	0.60
Trunk re: pelvis rotation onset time (% gait cycle)	-2.61 ± 3.17	-2.20 ± 4.85	-0.02	0.93
Head re: pelvis rotation onset time (% gait cycle)	-0.79 ± 2.67	1.51 ± 2.64	-0.13	0.60
Head re: trunk rotation amplitude (deg)	11.83 ± 1.95	15.67 ± 2.49	0.53	0.08
Trunk re: pelvis rotation amplitude (deg)	4.19 ± 0.37	5.45 ± 0.67	0.70	0.07
Head re: pelvis rotation amplitude (deg)	13.52 ± 2.08	16.51 ± 2.38	0.42	0.09

Values are means ± SEs.

\* Significant difference OFF vs. ON,

<sup>†</sup> = Mann Whitney U

Negative effect sizes denote changes in a direction away from control values, while positive effect sizes denote changes that are considered improvements (i.e. toward control values).