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

Minna Hong, PT, PhD, and Gammon M. Earhart, PT, PhD

Background and Purpose: People with Parkinson's disease 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 Parkinson's disease.

Methods: We examined turning kinematics in 10 people with Parkinson's disease who were assessed both OFF and ON medication. For both conditions, participants were evaluated with the Unified Parkinson's Disease Rating Scale motor subscale, rated how well their medication was working on a visual analog scale, and performed straight-line walking and 180-degree in-place turns. We determined the 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 the Unified Parkinson's Disease Rating Scale scores ($P = 0.02$), visual analog scale ratings ($P = 0.03$), and walking velocity ($P = 0.02$). Although 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 because turning may not be effectively addressed by pharmacologic approaches. These results should be interpreted cautiously given the small sample size.

Program in Physical Therapy and Departments of Neurology and Anatomy and Neurobiology (G.M.E.), Washington University School of Medicine, St. Louis, Missouri Spinal Cord Injury Center (M.H.), VA Palo Alto Health Care System, Palo Alto, CA.

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Address correspondence to: Gammon M. Earhart, E-mail: earhartg@wusm.wustl.edu

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INTRODUCTION

Impaired turning affects a large percentage of people with Parkinson disease (PD) and is often present before the onset of other gait abnormalities.[1,2] Turning impairment hinders activities of daily living, is associated with falls, and has a significant effect on the quality of life.[1,3–6] 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 compared with age-matched controls.[6–9] Individuals with PD also demonstrate altered timing of turn initiation with near simultaneous onset of rotation of the head, trunk, and pelvis.[2,7,10–12] This pattern of simultaneous rotation onsets together with reduced relative rotations between the segments is commonly referred to as en bloc turning.[7] Control subjects turn with a top-down sequence of rotation onsets, with the head rotating first followed by the trunk and then the pelvis.[7] 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.[7,8,12,13]

To our knowledge, no studies have examined the specific effects of anti-Parkinson medication on turning performance, and only a single study examined turning performance in individuals OFF medication.[7] 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.[6,12,14,15] Information about what aspects of turning difficulties may or may not be effectively targeted by pharmacologic 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 the time to turn and number of steps to turn. We further hypothesized that medication would enhance spatial aspects of turning (ie, amplitude of segment rotations), more than temporal aspects of turning (ie, relative timing of segment rotations).

TABLE 1. Subject Demographics

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

Abbreviations: PD, Parkinson disease; sinemet, Carbidopa-Levodopa; requip, ropinirole; UPDRS, Unified Parkinson's Disease Rating Scale; tab, tablet; qid, four times daily; tid, three times daily; qhs, every night.

METHODS

Participants

Ten participants with idiopathic PD diagnosed according to standard clinical criteria[16] participated (see Table 1 for subject demographics). Exclusionary criteria included history or evidence of orthopedic or neurologic condition (other than PD) and presence of dyskinesia. All participants responded positively when asked whether they had turning difficulty, and all had normal vision 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 examination before 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.[7] 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 retested (ON condition). Testing first OFF and then ON medications was performed to permit all measurements on a single day because many participants traveled long distances and were unable to come for two visits. All testing was performed without shoes on a linoleum floor in a fully illuminated room. Participants provided written informed consent before participation, and the protocol was approved by the Human Research Protection Office at Washington University School of Medicine.

Protocol

The Unified Parkinson's 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 analog scale. 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 three-dimensional motion capture system (Motion Analysis Corp., Santa Rosa, CA), accurate to within 1 mm, 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 to assist with automatic identification of markers using the motion capture software), five on the trunk (left and right acromions, right scapula, 12th thoracic vertebra, and sternal notch), four on the pelvis (left and right anterior superior iliac spines, left posterior superior iliac spine, and sacrum), and 10 on each leg (greater trochanter, anterior thigh, femoral condyle, fibular head, middle tibia, lateral malleolus, calcaneus, navicular, fifth metatarsal head, and 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.[7] 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; thus, 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

3 m 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 Corp.). Turn duration was defined as the time from liftoff of the foot used to initiate the turn to touchdown of the foot taking the final step of the turn. These times were clearly identifiable because turns were made from quiet stance, and subjects resumed quiet stance on 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 were assessed across the entire period of the first stride. Values for head rotation relative to the trunk were obtained by subtracting trunk values from head values, for the trunk relative to pelvis were obtained by subtracting pelvis values from trunk values, and for the head relative to pelvis were obtained by subtracting pelvis values from head values. The 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 to 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 (ie, 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.[7] Participants reported significantly greater benefit from medication in the ON compared with the OFF medication condition (Table 2) as noted by the visual analog scale. 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 (Fig. 1). The relative timing between segments was not altered by medication, and PD subjects showed nearly 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 (Fig. 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 versus long course of disease or lower versus 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. Although turning performance was not significantly altered, there was evidence of 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 <0.15). Our results suggest that only certain features of impaired turning may be respon-

TABLE 2. Effects of Medication

Variable	OFF Medication	ON Medication	Effect Size[a]	*P*
UPDRS subscale III motor rating[b,c]	35.14 ± 3.23	29.95 ± 3.51	0.58	0.02
Medication VAS[b,c]	25.09 ± 7.16	56.18 ± 7.83	1.31	0.03
Straight walking velocity (m/s)[b,c]	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 (degree)	11.83 ± 1.95	15.67 ± 2.49	0.53	0.08
Trunk re: pelvis rotation amplitude (degree)	4.19 ± 0.37	5.45 ± 0.67	0.70	0.07
Head re: pelvis rotation amplitude (degree)	13.52 ± 2.08	16.51 ± 2.38	0.42	0.09

Values are mean ± standard error.
[a] Negative effect sizes denote changes in a direction away from control values, whereas positive effect sizes denote changes that are considered improvements (ie, toward control values).
[b] Significant difference OFF versus ON.
[c] Mann-Whitney *U* test.
Abbreviations: UPDRS, Unified Parkinson's Disease Rating Scale; VAS, visual analog scale; re, relative to.

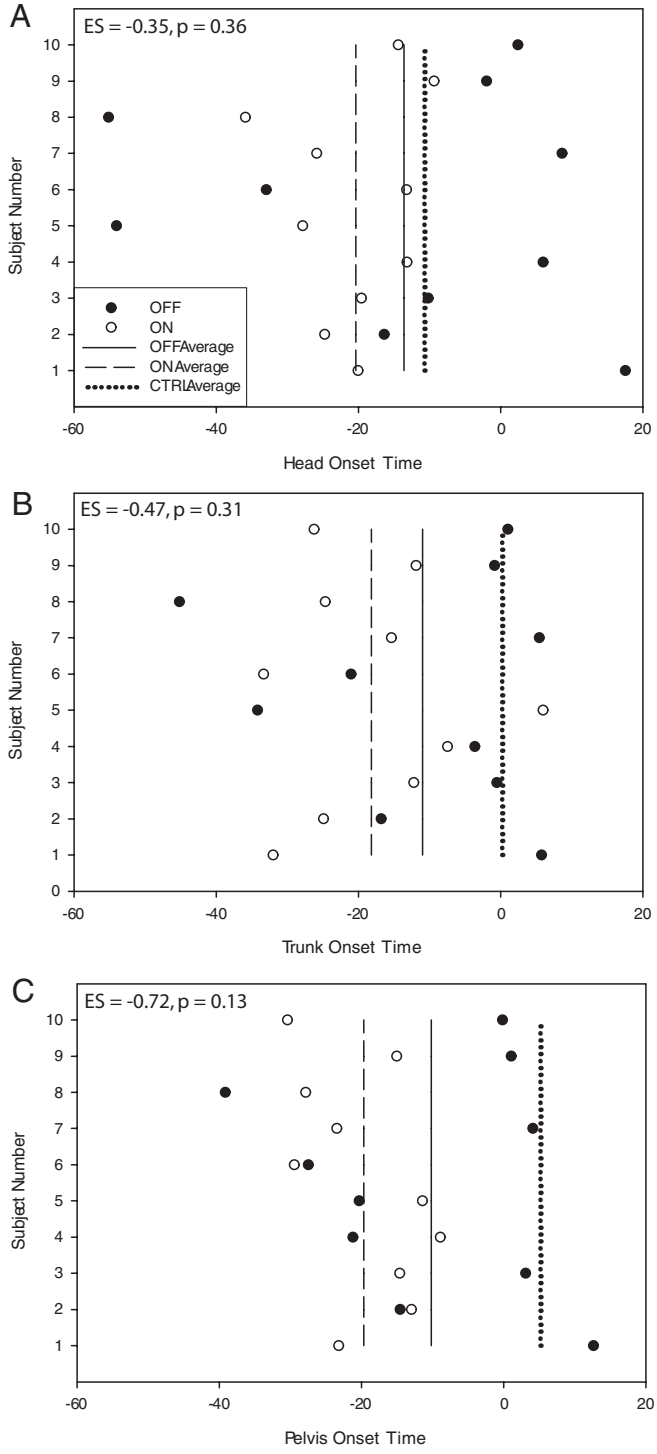

FIGURE 1. Onsets of yaw rotation for the head (A), trunk (B), and pelvis (C) for each individual. Onset times are expressed as percentage of the gait cycle, with 0% representing the time of liftoff for the first step of the turn. Filled circles show values when OFF medication and open circles are ON 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 controls.[7] ES = effect size. *P* values are for paired *t* tests comparing ON with OFF.

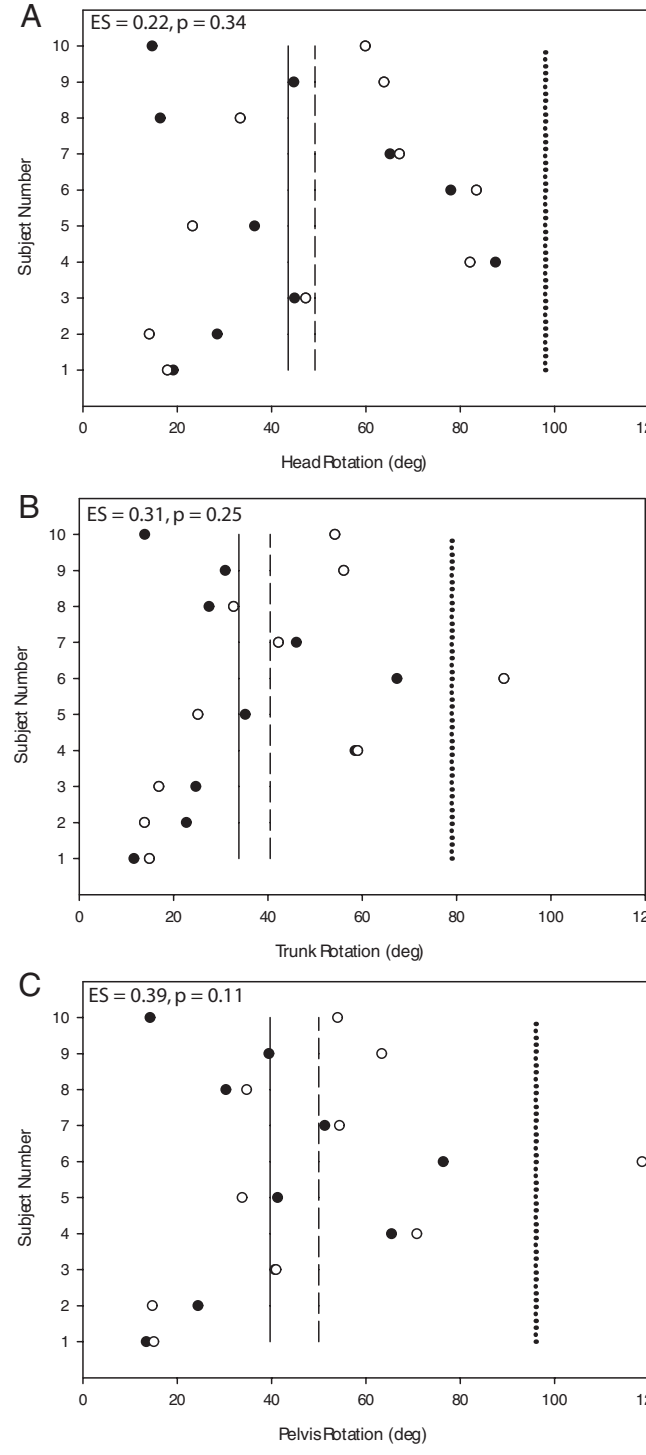

FIGURE 2. Amplitudes of absolute rotation of the head (A), trunk (B), and pelvis (C) during the first stride of the turn for each individual. Filled circles show values when OFF medication and open circles are ON medication. The group average OFF medication is shown with the solid vertical line and ON medication with the dashed vertical line. The dotted vertical line shows normative values previously reported for age-matched controls.[7] ES = effect size. *P* values are for paired *t* tests comparing ON with OFF.

sive to anti-Parkinson medication. Future work with larger sample sizes is needed to confirm or refute this speculation. We acknowledge that this 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 dose 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.[17] 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, which enhance straight walking may not similarly enhance turning or why certain aspects of turn performance may respond to medication, and others do not.

Although 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[18] 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.[7] Similar medication effects on arm and leg movements have been reported. Vaillancourt et al[19,20] reported improvements in movement velocity and amplitude and failure of medication to fully normalize these features because deficits in amplitude scaling and temporal patterns remained even after administration of medication. O'Sullivan et al[21] 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 with timing of movements.

Individuals with PD who have difficulty turning are likely to have difficulty with many everyday activities.[6] Although we did not note any directional asymmetry in turning in this study, this has been recently reported in other work.[6] This discrepancy may be due to our smaller sample size or 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 previous 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 the small sample size and lack of statistical correction for multiple tests. Between-subject differences in medication dose and frequency could have been a factor in the high variability that we observed in the measures, and this may have contributed to an inability to detect differences.

CONCLUSIONS

Turning impairments associated with PD are not being 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 the timing of arm and leg movements.[18–21] Given the lack of improvement in temporal aspects of turning, additional nonpharmacologic approaches to address turning difficulty are needed because impaired turning can interfere with activities of daily living and can place individuals with PD at risk of falls during turning.

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