Title: Interlimb coordination in Parkinson's Disease is affected by a visuospatial dual task

Running title: Interlimb coordination and DT in PD

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Summary statement

A dual-task during gait disrupted attempts to compensate for spatial and temporal coordination deficits on the less affected side in a group of people with mild to moderate Parkinson's disease.

Abstract

Parkinson's disease (PD) leads to reduced spatial and temporal interlimb coordination during gait as well as reduced coordination in the upper or lower limbs. While multi-tasking when walking is common during real world activities, the impact of dual-tasking (DT) on intra and interlimb coordination of both lower and upper limbs when walking in people with PD remains unknown. Seventeen volunteers with mild to moderate PD (11M, 65±8 years, 173±8 cm, 74±20 kg, UPDRS III 10±5) participated in gait trials in an Extended-CAREN system, which includes a treadmill, 12-camera Vicon motion capture system, and a 180° field-of-view virtual reality projection screen. Participants completed a 3 min walking trial, and a 2 min visuospatial word recognition DT trial at their preferred walking pace. Single and DT were compared with a paired t-test. During DT, we found the less affected (LA) shoulder ROM decreased by 1.5°, the LA shoulder peak flexion decreased by 1.1°, the LA hip ROM decreased by 0.99° ($p<.04$, $g_{av}>.12$), and hip ROM asymmetry decreased by 0.96° ($p=.01$, $g_{av}=.24$). Upper and lower intralimb phase variability on the LA side increased 3.8° and 0.94°, respectively, during DT ($p<.03$, $g_{av}>.28$). These results suggest that during normal single-task gait, people with PD use attentional resources to compensate for deficits in spatial and temporal coordination. Furthermore, our results may indicate that compensating for deficits in coordination is a higher priority than minimizing asymmetry in gait.

1 Introduction

Parkinson's disease (PD) is a multisystem neurodegenerative disease characterized by the loss of dopaminergic neurons in the substantia nigra with cascading effects in other regions, including those involved in cholinergic systems (Poewe et al., 2017; Yarnall et al., 2011). The neurodegeneration in PD begins unilaterally and progresses bilaterally, and motor symptoms mirror this unilateral emergence and bilateral progression (Djaldetti et al., 2006). The asymmetric development commonly results in one side being more affected than the other (Djaldetti et al., 2006). PD has three cardinal motor symptoms: bradykinesia, rigidity, and tremor. In addition, people with PD develop further motor deficits—including hypokinesia (reduced movement amplitude), increased movement variability, gait asymmetry, and postural instability—which contribute to or reflect impairments in coordinating the upper and lower limbs to achieve successful locomotion. (Mirelman et al., 2019; Plotnik et al., 2007; van Emmerik and Wagenaar, 1996; Yogev et al., 2007). Work by Marigold and Misiaszek (2009) suggests that interlimb coordination is a factor in maintaining dynamic stability during gait based on the presence of whole body reactions involving both the lower and upper limbs in response to perturbations.

Coordination is defined as the context and phase dependent control of spatial and temporal cyclical relationships between body segments (Krasovsky and Levin, 2010). One prominent feature of normal gait coordination (for gait speeds above 0.8 m/s) is the fixed anti-phase swing (180 deg phase offset) between the arms, legs, and ipsilateral arm-leg pairs, while contralateral arm-leg pairs exhibit fixed in-phase swing (Wagenaar and van Emmerik, 2000). These phase relationships result in gait which is generally symmetric in healthy adults (Killeen et al., 2018; Sadeghi et al., 2000). In contrast, asymmetry in spatial and temporal gait characteristics is recognized as a disruption in the coordination of normal gait, and occurs in several populations with pathological gait, including those with PD (Huang et al., 2012; Park et al., 2016; Yogev et al., 2007).

The phase coordination index (PCI) is a measure of accuracy and consistency in the anti-phase coordination of step timing during gait (Plotnik et al., 2007). Results by Plotnik and collaborators (2007) reported worse coordination, as measured by PCI, in people with PD compared to healthy controls. Additionally, other studies evaluating coordination with PCI showed a reduced ability in people with PD to adapt the coordination of the lower limbs to step lengths and times other than preferred, or to external mechanical constraints, such as walking on split-belt treadmills (Fasano et al., 2016; Williams et al., 2013). However, PCI is only used to assess lower limb coordination.

Continuous relative phase (CRP) is a technique which has been previously used to measure the accuracy and stability of coordination between limb or joint pairs, including upper and lower limbs (Schmidt et al., 1993). Previous studies have found that compared to healthy peers, people with PD have reduced coordination accuracy and stability (measured with CRP) for upper and lower interlimb coordination during gait and bimanual coordination tasks (Almeida and Brown, 2013; van Emmerik and Wagenaar, 1996). Similarly, CRP can be used to measure coordination stability within individual limbs (i.e. intralimb coordination), but we are not aware of previous studies having studied this in people with PD (Barela et al., 2000; Byrne et al., 2002).

Other measures of coordination (cross-correlation techniques, arm swing asymmetry, and intracycle phase variability) have been used to detect reduced coordination between the upper limbs in people with PD compared to healthy controls (Huang et al., 2012; Sterling et al., 2015). Furthermore, investigations of ipsilateral and contralateral arm-leg coordination have found reduced coupling (measured by cross-correlation) (Roemmich et al., 2013) and a larger phase offset between the more affected shoulder and hip (Nanhoe-Mahabier et al., 2011) in people with PD compared to healthy controls.

Performing a secondary task during gait adds an attentional stressor that can reveal the loss of automaticity for some aspects of gait (e.g. gait speed, gait variability, etc.) (Yogev-Seligmann et al., 2008). In addition, gait while dual tasking may be more similar to gait in the real world than typical laboratory recordings of steady state gait (Hillel et al., 2019). Although bilateral coordination has been found to be sensitive to dual tasks in healthy young and old adults and people with PD (Yogev-Seligmann et al., 2008), few studies have directly investigated coordination of gait in people with PD while dual tasking. Among those studies, people with PD show a larger decline in lower limb coordination measured by PCI during a dual task compared to healthy controls, and PCI in PD fallers and freezers is more affected by a dual task than PD non-fallers and freezers (Plotnik and Hausdorff, 2008; Plotnik et al., 2009; Plotnik et al., 2011). In addition, studies have found reduced arm swing during gait in people with PD during a dual task compared to single task gait (Baron et al., 2018; Mirelman et al., 2016). However, no previous studies have explored coordination of both upper and lower limbs during gait, including intra and interlimb coordination, in people with PD while dual tasking. The purpose of this study is to investigate spatial and temporal coordination within and between the upper and lower limbs during single and dual task gait in people with PD. We hypothesize that a visuospatial dual task will decrease coordination and increase asymmetry.

2 Methods

2.1 Participants

Volunteers with mild to moderate PD (between I-III Hoehn & Yahr) were recruited from the Ottawa-Gatineau area. Exclusion criteria included any additional neurological impairment, a recent orthopedic injury or surgery that could interfere with gait, the use of a walking aid, or any discomfort with using a projected virtual reality system. Participant characteristics for sex, age, height, weight, handedness, Unified Parkinson’s Disease Rating Scale (UPDRS) motor section (III), freezing and falling status, and interval since diagnosis of PD were recorded (Table 1). The more affected (MA) side was defined as the side where PD motor symptoms first occurred, as reported by participants. Participants were tested while optimally medicated. All participants provided written informed consent, and the study was approved by local ethics review boards.

2.2 Protocol

Data was collected using the CAREN system (CAREN-Extended, Motekforce Link, Amsterdam, NL). The CAREN system consists of an instrumented split-belt treadmill (Bertec Corp., Columbus. OH) embedded in a six degree-of-freedom motion platform, a 12-camera motion capture system (Vicon, Oxford, UK), and a 180 deg field of view projection screen. A safety harness attached to an overhead frame on the motion platform prevents participants from falling without restricting movement.

Participants were allowed an initial familiarization period with the CAREN system; the familiarization period was also used to determine their preferred walking speed for the gait trials. The single task trial was 3 min long, while the dual task trial was 2 min long. The dual task consisted of a visuospatial word recognition and acknowledgement task where a word was shown at eye level at a random position between 20-70 deg to the left or right of center. Twelve words were randomly drawn from a standard list of 16 possible words in the native language of the participant (English or French). The dual task began 20 s into the trial, and a new word was shown for 3 s every 2-4 s for 80 s. The dual task was designed to be an ecologically valid recreation of common daily life situations (e.g. public transportation terminal, etc.) requiring perception and comprehension of visual cues (Ahmadi et al., 2021; Siragy and Nantel, 2020). Participants were allowed to rest between trials when requested.

2.3 Data reduction

A set of 57 markers (Wilken et al., 2012) was used to capture full-body kinematics at 100 Hz; marker data was then filtered using a 4th order dual-pass Butterworth low-pass filter with a cutoff frequency of 12 Hz. Low pass filter cutoff frequency was chosen based on a residual frequency analysis of marker data using an RMS noise of 0.5 mm measured from static markers fixed to the motion platform (Winter, 2009). Gait events were calculated using an algorithm based on the local extrema of the vertical position and velocity of the heel marker (Roerdink et al., 2008). OpenSim was used with the Rajagopal et al. (2016) model to perform inverse kinematics to extract bilateral knee, elbow, and shoulder and hip flexion/extension angles (Delp et al., 2007). The wrist pronation/supination range of motion of the model was expanded from 90 deg to 160 deg to better match normative characteristics (Shaaban et al., 2008).

Spatial coordination was assessed as the bilateral peak flexion and average range of motion (ROM) for the shoulder and hip joints and asymmetry therein. Asymmetry was calculated as the difference between MA and less affected (LA) sides, $MA - LA$, as previously recommended (Hill and Nantel, 2022a). Temporal coordination was assessed using CRP (Lamb and Stöckl, 2014) to measure average phase offset and average intercycle phase variability between interlimb (homologous, ipsilateral, and contralateral shoulder and hip) and intralimb (shoulder and elbow, hip and knee) joint pairs. Continuous phase was calculated as the angle of the complex analytic signal produced by the Hilbert transform after centering the original signal (Lamb and Stöckl, 2014). Relative phase was calculated as $\theta_{MA} - \theta_{LA}$ for bilateral joint pairs, $\theta_{shoulder} - \theta_{hip}$ for ipsilateral shoulder-hip pairs, and $\theta_{proximal} - \theta_{distal}$ for intralimb joint pairs. Furthermore, asymmetry was measured for intralimb and ipsilateral phase variability, and PCI was used as an additional measure of temporal coordination (Plotnik et al., 2007).

2.4 Statistics

Paired t-tests with a critical alpha of 0.05 were used for all variables. Two-tailed p-values were used to test for changes in average phase offsets and asymmetry; one-tailed p-values were used to test for decreases in peak flexion and ROM, and for increases in phase variability and PCI. Effect sizes were reported using Cohen's d_{av} with a Hedges g correction, noted as g_{av} (Cumming, 2011; Lakens, 2013). A sensitivity power analysis was conducted in G*Power (Faul et al., 2007) to find that the minimum detectable effect size is $d_z = 0.63$ and $d_z = 0.72$ for one and two-tailed t-tests, respectively, when $\alpha = .05$, $\beta = 0.8$, and the sample size is 17. Arm swing for a given shoulder was treated as functionally absent when ROM was less than 5 deg. No meaningful coordination was expected between any joint and a shoulder with functionally absent arm swing; therefore, the inter- and intralimb CRP variables for affected subjects/shoulders were removed as outliers—3 subjects at most, depending on the variable. Circular statistics (circular mean and standard deviations) were used for all variables, which were in angular units (Fisher, 1993). All data reduction and statistical analyses were performed with the Julia language using open-source libraries and code (Bezanson et al., 2017; Hill and Nantel, 2022b).

3 Results

Participant demographics are reported in Table 1. Twenty subjects who met the inclusion criteria were recruited. Two participants with severe dyskinesia were excluded from this study, and a third participant was excluded for talking with their hands during a significant portion of a trial; both behaviors produce movements (Jankovic, 2005) which are disruptive to the normal coordination patterns of steady state gait. Subjects were diagnosed with PD an average of 7.4 ± 4.5 years prior to study participation.

Table 1 Participant demographics

Characteristic	Mean ± SD	Range
Sex (n)	11 M, 6 F	
Age (years)	64.8 ± 7.7	48-79
Height (cm)	173.3 ± 7.6	165-188
Weight (kg)	74.2 ± 19.9	52-128
Handedness	14 R, 3 L	
More affected side	9 R, 8 L	
UPDRS III	10.2 ± 5.3	0-20
Freezers (n)	5	
Fallers (n, <1yr)	10	

Single and dual task results were calculated using an average of 139 ± 19 and 74 ± 6 steps, respectively (dual task trial length was shorter than the single task trial). Preferred gait speed was 1.0 ± 0.2 m/s among subjects. Spatial coordination results are reported in Table 2. The LA shoulder ROM and peak flexion decreased by 1.5 deg and 1.1 deg, respectively, during dual task compared to single task walking. The LA hip ROM decreased by 0.99 deg during the dual task, and hip ROM asymmetry decreased by 0.97 deg during the dual task. Temporal coordination results are reported in Table 3. Intralimb phase variability on the LA side increased by 3.8 deg and 0.94 deg in the upper and lower limbs, respectively, during the dual task. The phase offset between MA hip and knee decreased by 1.7 deg during the dual task.

Table 2 Spatial coordination and asymmetry between the more and less affected sides during single and dual task

Variable		Single task	Dual task	*t*-test	p-value	g_{av}
Shoulder ROM (deg)	Asym	-3.4 ± 9.5	-0.3 ± 13.9	t(16)=1.25	0.228	0.27
	LA	20.9 ± 12.8	19.5 ± 11.9	t(16)=-2.51	**0.012**	-0.12
	MA	17.5 ± 12.1	19.2 ± 14.3	t(16)=0.66	0.742	0.12
Shoulder peak flexion (deg)	Asym	-2.2 ± 8.6	-0.4 ± 11.6	t(16)=1.14	0.272	0.18
	LA	15.0 ± 8.5	13.9 ± 8.1	t(16)=-2.44	**0.013**	-0.14
	MA	12.8 ± 7.8	13.5 ± 9.5	t(16)=0.46	0.676	0.08
Hip ROM (deg)	Asym	-1.5 ± 3.9	-0.6 ± 3.9	t(16)=2.84	**0.012**	0.24
	LA	38.8 ± 4.0	37.9 ± 3.9	t(16)=-1.89	**0.038**	-0.25
	MA	37.3 ± 5.0	37.3 ± 5.2	t(16)=-0.05	0.480	0
Hip peak flexion (deg)	Asym	-2.3 ± 3.2	-2.1 ± 3.0	t(16)=0.71	0.487	0.08

	LA	25.2 ± 6.5	25.0 ± 6.9	t(16)=-0.92	0.186	-0.04
	MA	22.9 ± 7.9	22.9 ± 7.7	t(16)=0.09	0.534	0

ROM stands for range of motion. LA/MA stands for less/more affected side. Asym is an abbreviation for asymmetry. g_{av} is the Cohen's d_{av} effect size corrected with Hedge's g.

Table 3 Temporal coordination and asymmetry between the more and less affected during single and dual task

Variable		**Single task**	**Dual task**	***t*-test**	**p-value**	**g_{av}**
PCI (deg)		6.6 ± 3.1	7.5 ± 4.0	t(16)=1.71	0.053	0.26
Shoulder interlimb (deg)	θ_{avg}	-178.9 ± 15.2	177.1 ± 21.4	t(13)=1.38	0.120	-0.22
	$\theta_{\mu sd}$	20.0 ± 10.0	21.5 ± 14.1	t(13)=0.51	0.312	0.11
Hip interlimb (deg)	θ_{avg}	178.9 ± 6.8	179.4 ± 8.0	t(16)=1.50	0.605	0.06
	$\theta_{\mu sd}$	6.5 ± 2.0	6.8 ± 2.8	t(16)=0.69	0.252	-0.06
Ipsilateral shoulder-hip (deg)	$\theta_{avg,LA}$	179.9 ± 23.8	178.9 ± 28.1	t(15)=1.29	0.614	-0.04
	$\theta_{avg,MA}$	179.5 ± 20.2	173.7 ± 27.0	t(13)=1.17	0.099	-0.26
	Asym $\theta_{\mu sd}$	1.7 ± 9.5	-4.2 ± 14.5	t(13)=-1.56	0.143	-0.50
	$\theta_{\mu sd,LA}$	17.7 ± 15.6	21.9 ± 17.5	t(15)=1.56	0.070	0.24
	$\theta_{\mu sd,MA}$	16.5 ± 9.1	14.9 ± 6.2	t(13)=-0.26	0.599	-0.13
Contralateral shoulder-hip (deg)*	$\theta_{avg,LA}$	1.5 ± 25.4	0.1 ± 30.2	t(15)=-0.73	0.477	-0.06
	$\theta_{avg,MA}$	-1.4 ± 19.7	-7.4 ± 23.6	t(13)=-1.91	0.077	-0.24
	$\theta_{\mu sd,LA}$	17.6 ± 15.7	22.0 ± 17.6	t(15)=1.63	0.062	0.25
	$\theta_{\mu sd,MA}$	16.0 ± 9.0	14.0 ± 6.2	t(13)=-0.45	0.670	-0.19
Upper intralimb (deg)	$\theta_{avg,LA}$	9.5 ± 13.1	12.3 ± 15.2	t(15)=1.70	0.104	0.21
	$\theta_{avg,MA}$	8.5 ± 35.6	12.1 ± 18.4	t(13)=0.25	0.815	0.08
	Asym $\theta_{\mu sd}$	8.8 ± 21.1	4.1 ± 13.7	t(13)=-0.89	0.390	-0.28
	$\theta_{\mu sd,LA}$	22.0 ± 10.2	25.8 ± 16.0	t(15)=2.02	**0.031**	0.28
	$\theta_{\mu sd,MA}$	31.0 ± 21.5	26.5 ± 13.2	t(13)=-0.53	0.699	-0.16
Lower intralimb (deg)	$\theta_{avg,LA}$	-84.4 ± 9.8	-84.7 ± 9.6	t(16)=-0.49	0.633	-0.03
	$\theta_{avg,MA}$	-84.8 ± 8.9	-83.1 ± 9.1	t(16)=2.26	**0.040**	0.19
	Asym $\theta_{\mu sd}$	0.5 ± 1.3	-0.0 ± 1.1	t(16)=-2.09	0.053	-0.45
	$\theta_{\mu sd,LA}$	6.2 ± 1.5	7.2 ± 2.7	t(16)=2.40	**0.014**	0.29
	$\theta_{\mu sd,MA}$	6.7 ± 1.6	7.1 ± 2.2	t(16)=1.54	0.071	0.06

ROM stands for range of motion. LA/MA stands for less/more affected side. Asym is an abbreviation for asymmetry. g_{av} is the Cohen's d_{av} effect size corrected with Hedge's g. *LA/MA refers to the shoulder of the contralateral shoulder-hip pair. µSD is average intercycle phase variability. Arm swing for three subjects was treated as functionally absent in one or both shoulders, which reduced the degrees of freedom for the t-tests of some variables.

4 Discussion

In this study, we determined that some aspects of coordination are affected by a visuospatial dual task in a cohort of mild to moderate PD. While dual tasking, compared to single task gait, the LA shoulder ROM and peak flexion decreased, and the LA hip ROM decreased leading to reduced hip ROM asymmetry (Table 2). Intralimb phase variability increased in the upper and lower limbs on the LA side during the dual task, and the lag between MA hip and knee decreased during the dual task (Table 3). The changes in LA intralimb coordination may be linked to the decreases in LA shoulder and hip ROM during the dual task, however, more investigation is needed to confirm or refute such a relationship. Our hypothesis of worsened coordination during a dual task is partially supported by these results.

Previous studies show that due to gait asymmetry present in people with PD, the LA side typically exhibits ROM and coordination that are more similar to—but not always matching—healthy peers, while the MA side is less similar to healthy peers (Roemmich et al., 2013; Roggendorf et al., 2012). The single task shoulder ROM in our data showed that the arm swing was fairly symmetric, with shoulder ROM on the LA side slightly larger than the MA side (Table 2), and the shoulder ROM on both sides is slightly reduced compared to normative arm swing data for healthy older adults at similar gait speeds (Killeen et al., 2018; Plate et al., 2015). Similarly, the single task hip ROM and asymmetry (Table 2) match previous results in mild to moderate PD, where the LA hip ROM was slightly larger and more similar to healthy elderly controls, but asymmetry was generally small (Roemmich et al., 2013).

During the dual task condition, we observed significant changes in spatial and temporal coordination predominantly on the LA side (Table 2-3). In our cohort, changes in spatial coordination (reduced shoulder and hip ROM and increased hip ROM asymmetry) trended away from behavior of healthy peers and trended towards the characteristics of the MA side. Similarly, increased intralimb phase variability in the upper and lower LA limbs and a trend towards increased PCI (p=.053, g_{av}=0.26) suggests a reduced coordinative stability originating from the LA side (Amazeen et al., 1998; Plotnik et al., 2007). These changes suggest that during normal, single task gait, participants used attentional resources to compensate for hypokinesia and other coordination deficits on the LA side, while compensation on the MA side was less effective (so as to produce an effect too small to be detected) or not attempted.

Previous studies of gait symmetry often assume that gait with minimal levels of asymmetry is natural in healthy adults, which was confirmed for many aspects of gait, according to a review by Sadeghi et al. (2000). In addition, healthy adults have been shown to quickly adapt their gait on split-belt treadmills to minimize spatial and temporal asymmetry, and people with PD demonstrate similar, albeit slower, gait adaptations (Malone et al., 2012; Roemmich et al., 2014). However, even some aspects of gait in PD that show adaptation to split-belt walking (e.g. step length) appear to maintain a consistently larger asymmetry than controls before, during, and after adaptation (Roemmich et al., 2014). The consistent asymmetry in PD throughout and post-adaptation may indicate the prioritization of other movement characteristics, such as compensation for motor and coordination deficits, at the expense of minimizing gait asymmetry.

In our results, we found greater asymmetry and larger differences between MA and LA sides during single task gait, when participant's compensation for motor and coordination deficits were not disrupted by a dual task. Therefore, although previous results indicate that symmetric gait is a movement goal in healthy adults and in people with PD (Malone et al., 2012; Roemmich et al., 2014), our results suggest that people with PD may prioritize compensation for motor deficits (e.g. impaired coordination) higher than they prioritize symmetric gait. This theory is supported by previous results from our group and others, which indicate that during single task gait, compensation for motor deficits on the LA side produces step times (Siragy and Nantel, 2020) and arm swing ROM (Mirelman et al., 2016) that are more similar to those of healthy peers, but when compensation is disrupted during dual task gait, the LA side becomes more similar to the performance of the MA side during normal gait. However, more research is needed to confirm the prioritization of compensating for deficits at the expense of increased asymmetry, and whether this strategy is optimal, in terms of dynamic stability.

4.1 Limitations

The participants in this study had generally mild PD, and the arm swing ROM and ROM asymmetry within our cohort is markedly different compared to previously reported PD cohorts (Isaias et al., 2012; Mirelman et al., 2016; Roggendorf et al., 2012; Sterling et al., 2015); it is unclear how coordination would respond in people with similarly mild PD—but with larger levels of arm swing asymmetry, or in people with more severe PD—which have more symmetric arm swing but reduced ROM (Roggendorf et al., 2012).

Additionally, different tasks are known to have unique and specific effects on different aspects of gait which may limit the generalizability of our results (Al-Yahya et al., 2011; Rochester et al., 2014), and the visuospatial dual task in this study was simple (12/17 participants demonstrated perfect performance, and the remaining 5 participants responded to

10 ± 1.5 words out of 12). However, Baron et al. (2018) found that arm swing kinematics were sensitive to multiple common dual tasks.

5 Conclusion

Our results show that a visuospatial dual task during gait contributes to decreased spatial and temporal coordination on the LA side in a group of mild PD. The effect of a dual task on coordination suggests that people with PD use attentional resources to compensate for motor deficits. Additionally, the changes in the LA, but not MA, side may suggest that compensation for motor deficits during normal, single task gait is a higher priority than minimizing gait asymmetry.

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