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Effects of dopamine replacement therapy on lower extremity kinetics and kinematics during a rapid force production task in persons with Parkinson disease

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Abstract

Postural instability appears to be a dopamine resistance motor deficit in persons with Parkinson disease (PD); however, little is known about the effects of dopamine replacement on the relative biomechanical contributions of individual lower extremity joints during postural control tasks. To gain insight, we examined persons with PD using both clinical and laboratory measures. For a clinical measure of motor severity we utilized the Unified Parkinson Disease Rating Scale motor subsection during both OFF and ON medication conditions. For the laboratory measure we utilized data gathered during a rapid lower extremity force production task. Kinematic and kinetic variables at the hip, knee, and ankle were gathered during a counter movement jump during both OFF and ON medication conditions. Sixteen persons with PD with a median Hoehn and Yahr severity of 2.5 completed the study. Medication resulted in significant improvements of angular displacement for the hip, knee, and ankle. Furthermore, significant improvements were revealed only at the hip for peak net moments and average angular velocity compared to the OFF medication condition. These results suggest that dopamine replacement medication result in decreased clinical motor disease severity and have a greater influence on kinetics and kinematics proximally. This proximally focused improvement may be due to active recruitment of muscle force and reductions in passive restraint during lower extremity rapid force production.

Keywords

Parkinson disease; Balance; Counter movement jump

1. Introduction

While dopamine replacement medication improves rigidity and bradykinesia in persons with Parkinson disease (PD) [1], its effect on postural instability is limited suggesting that postural instability is a dopamine resistant motor deficit [1,2]. While the limited dopamine effect on the overall outcome of reactive and anticipatory postural control responses is a consistent finding, little is known about the effects of dopamine replacement on the relative contributions of individual lower extremity joints during postural control tasks that require rapid force production. Therefore, to gain insight into a potentially differential effect of

dopamine replacement medication on proximal versus distal lower extremity (LE) joints, this study examined the kinetics and kinematics of a rapid LE force production task during OFF and ON dopamine replacement medication conditions. Based on previous research [3], we hypothesized that dopamine replacement medications would increase peak joint extension moments, angular displacements, and average angular velocities of the LE joints during a countermovement jump (CMJ).

2. Clinical significance

Cardinal signs of PD include bradykinesia, hypokinesia, tremor, postural instability and rigidity [4]. Medical management with dopamine replacement is a ubiquitous treatment for persons with moderate PD, however it may be ineffective at improving postural instability and decreasing falls. Any countermeasure targeted at improving rapid force production during postural tasks, should address the shortcomings of dopamine replacement treatments. This IRB approved study sought to clarify the limitations in the effects of medication on lower extremity kinetics and kinematics in order to provide intervention targets to improve rapid force production capacity.

3. Methods

Potential participants were a sample of convenience recruited through referral from local neurologists or through response to advertisement in a PD support group newsletter. Inclusion criteria were a neurologist confirmed diagnosis of idiopathic PD, current management with dopamine replacement medications, and clinical signs of hypokinesia during gait and balance tasks. Exclusion criteria were uncontrolled motor fluctuations, uncontrolled dyskinesias, or previous surgical management of their PD. Clinical motor severity testing was accomplished using the motor subsection of the Unified Parkinson Disease Rating Scale (UPDRS) [5]. In addition, the sum of rigidity items (UPDRS motor subsection item 22) was recorded for both ON and OFF medication conditions. Higher scores on both the overall motor UPDRS and for the rigidity item indicate worse motor deficits. The lower extremity with the higher motor UPDRS score was defined as the more affected extremity. For the laboratory testing, participants were instrumented with the full body Plug-In-Gait marker set (Vicon Motion Systems, Oxford, UK) and performed 5 CMJs during OFF and ON medication conditions. The clinically defined OFF medication condition was induced by having the participant refrain from taking their dopamine replacement medications for at least 12 h prior to testing. After completing OFF medication testing, participants took their medication and rested for 1–1.5 h and were re-tested in a clinically defined ON medication condition [6]. Data was acquired using 2 AMTI-OR6 force platforms (AMTI; Watertown, MA) at 250 Hz and an 8-camera Vicon motion analysis system (Vicon Motion Systems; Oxford, UK) at 250 Hz. Data were recorded and synchronized using Vicon Nexus (Vicon Motion Systems; Oxford, UK) and post-processing using Visual3D (C-Motion, Germantown, MD). Marker and force platform data were filtered using a low pass Butterworth filter at 6 Hz and 15 Hz, respectively.

In order to prevent losses of balance or falls, postural control responses require rapid LE force production to move the limbs and center of mass quickly. Because we were interested in capturing data during a postural task that would be internally valid and repeatable yet required rapid LE force production, we constrained our focus on kinetic and kinematic variables during the explosive phase of the CMJ. During the CMJ, participants were asked to keep their arms slightly away from their sides in order to avoid blocking or knocking off reflective markers but arm movement was not restricted during the CMJ [7,8]. The explosive phase was defined as the time from when the subject's center of mass was at its lowest point to the time that the ground reaction force reached zero (when both feet had left the force

platforms). Each subject's first three satisfactory trials were averaged and the data from both lower extremities was tested for normality. A satisfactory trial was defined as any trial in which the subject's feet cleared the force platforms and all markers remained visible. Outcome variables were generated for both the more affected and less affected lower extremities and compared using interval estimators and statistical tests for differences [9]. If their 95% confidence intervals overlapped and there was no significant difference, the limbs were considered equivalent and the data for angular displacement and average angular velocity was averaged and the peak net extensor moments extracted. OFF and ON medication condition variables were examined using paired sample *t*-tests (significance *p* 0.05). A Wilcoxon matched pairs test was run for the differences between rigidity items on the motor UPDRS. Between medication condition effect sizes were calculated to examine differences in the magnitude of effect between joints [10].

4. Results

Sixteen participants with idiopathic PD (11 M, 5 F; median age 67, range 51–82; median years with disease 5.5, range 1–11) with a median Hoehn and Yahr score of 2.5 (range = 1–3) were tested. All participants were taking dopamine replacement medications, while eight of the 16 were taking dopamine agonist medications, and four were taking acetylcholinesterase inhibitors. According to the results of the UPDRS (motor subsection), during the ON medication condition, clinical motor disease severity was significantly lower (12.29 (7.19)) compared to the OFF medication condition (23.07 (11.00); *p* = 0.0005, *t* = 4.63). Rigidity also declined as a result of dopamine replacement (ON meds median rigidity = 0 (0.99); OFF meds median rigidity = 2.00 (1.45); *p* = 0.003, *z* = 2.95).

For both ON and OFF medication conditions, the interval estimators and the statistical tests for differences revealed that the more affected and less affected extremities were equivalent in 18 out of the 18 variable comparisons (nine comparisons for ON medication and nine comparisons for OFF medication conditions). For this reason, the ON and OFF medication comparisons were performed on the averaged angular displacement and average angular velocity as well as the net moment values from both lower extremities.

For the laboratory testing, the averaged angular displacement of the bilateral hip, knee and ankle were significantly greater in the ON medication condition when compared to the OFF medication condition. Regarding average angular velocity and peak net joint moments, the hip was the only joint that was significantly greater in the ON medication condition when compared to the OFF medication condition (Table 1 and Fig. 1). For all variables, the magnitude of effect size measures indicated a more robust effect on the hip in comparison to the knee and ankle [10].

5. Discussion

Our results demonstrate that dopamine replacement medication overall resulted in a decrease in motor disease severity and had a greater influence on kinetics and kinematics proximally (hip) than distally (knee and ankle). Despite the proximal effect, when compared to previously published results of healthy young, our cohort of subjects produced 18–60% smaller moments at the hip, knee, and ankle during the CMJ [8]. Furthermore, our findings of ON medication increases in hip extensor torque expands on the previous observations that demonstrated dopamine replacement mediated increases in the proximal upper extremity [11]. Robichaud and colleagues [8,9] have demonstrated what appears to be a differential effect of PD on the extensor musculature and limitations of dopamine replacement on EMG patterns of the proximal UE. However due a lack of research in this area, to our knowledge, a unifying explanation of how dopamine replacement might affect proximal versus distal

components of the lower extremity is not present. The increase in hip moments could be due to increases in muscle force (an active parameter) [11] or the reduction of rigidity (a passive parameter) [1,12]. The decreases in UPDRS measured rigidity in this study may have reduced the passive resistance to movement during the postural task. Such reductions during postural tasks have previously been reported [1]. If present, decreased rigidity may allow increased joint range of motion and as a result, changed the moments acting on the joint.

Although clarification of the active versus passive contributions to the proximal focused effect requires more study, these results do provide additional evidence regarding the limitations of dopamine replacement in postural tasks. If dopamine replacement medication is limited to proximal specific effects, other interventions may be needed to complement this effect. Further research is needed to determine if interventions such as surgery or lower extremity resistance training affect knee and ankle extensor contributions to rapid force production during postural tasks.

Although these results suggest a proximal biased effect of dopamine replacement during a rapid LE force production task, they should be interpreted with caution. Limitations of this study include the small sample size and the fact that OFF and ON conditions were always performed in the same order therefore an order effect cannot be discounted. In addition, a family wise error risk correction was not performed. We felt it would be overly conservative based on our analysis that included the comparison of three variables for three joints (nine comparisons). Future research with larger samples is needed to gain insight into differential effects of medication on lower extremity kinetics and kinematics of rapid force production during postural tasks.

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Fig. 1.
Magnitude of medication induced extensor moment changes.

Table 1

Lower extremity kinematics and kinetics.

	Peak extensor moments (Nm/kg)			Angular displacement (°)			Avg. angular velocity (°/s)		
	Mean (SD)		ES	Mean (SD)		ES	Mean (SD)		ES
	OFF	ON		OFF	ON		OFF	ON	
Hip	1.09 (0.49)	1.24 (0.50) *	0.30	30.62 (9.35)	35.89 (10.22) *	0.54	129.63 (30.17)	147.53 (37.11) *	0.53
Knee	1.80 (0.48)	1.82 (0.50)	0.04	50.18 (13.88)	52.96 (13.09) *	0.21	212.38 (43.90)	217.78 (46.57)	0.12
Ankle	2.29 (0.45)	2.38 (0.41)	0.21	46.46 (11.57)	49.71 (10.32) *	0.30	199.72 (47.89)	207.96 (47.37)	0.17

ES = effect size; SD = standard deviation; LE = lower extremity.

* $p < 0.05$.