Behavioural Brain Research 268 (2014) 31–39

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Effects of dopaminergic therapy on locomotor adaptation and adaptive learning in persons with Parkinson's disease

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HIGHLIGHTS

- Persons with Parkinson's disease walked on a split-belt treadmill.
- Dopaminergic medication did not affect the ability to adapt locomotion.
- Aftereffects were reduced when the participants were withdrawn from medication.
- Savings of the adapted gait pattern were apparent in both medicated states.

ARTICLE INFO

Article history:
Received 18 December 2013
Received in revised form 28 February 2014
Accepted 24 March 2014
Available online 31 March 2014

Keywords:
Parkinson's disease
Adaptation
Split-belt treadmill
Dopamine
Motor learning

ABSTRACT

Persons with Parkinson's disease (PD) are characterized by multifactorial gait deficits, though the factors which influence the abilities of persons with PD to adapt and store new gait patterns are unclear. The purpose of this study was to investigate the effects of dopaminergic therapy on the abilities of persons with PD to adapt and store gait parameters during split-belt treadmill (SBT) walking.

Ten participants with idiopathic PD who were being treated with stable doses of orally-administered dopaminergic therapy participated. All participants performed two randomized testing sessions on separate days: once while optimally-medicated (ON meds) and once after 12-h withdrawal from dopaminergic medication (OFF meds). During each session, locomotor adaptation was investigated as the participants walked on a SBT for 10 min while the belts moved at a 2:1 speed ratio. We assessed locomotor adaptive learning by quantifying: (1) aftereffects during de-adaptation (once the belts returned to tied speeds immediately following SBT walking) and (2) savings during re-adaptation (as the participants repeated the same SBT walking task after washout of aftereffects following the initial SBT task).

The withholding of dopaminergic medication diminished step length aftereffects significantly during de-adaptation. However, both locomotor adaptation and savings were unaffected by levodopa. These findings suggest that dopaminergic pathways influence aftereffect storage but do not influence locomotor adaptation or savings within a single session of SBT walking. It appears important that persons with PD should be optimally-medicated if walking on the SBT as gait rehabilitation.

1. Introduction

Persons with Parkinson's disease (PD) can exhibit a variety of locomotor deficits, including gait slowness [1], increased risk of falling during transitional periods [2], and the presence of gait asymmetry [3]. While some treatments induce modest gait improvement, no interventions exist which wholly restore gait performance in PD. Recent research has investigated locomotor adaptation and adaptive learning processes within the context of gait rehabilitation for populations characterized by gait

Abbreviations: PD, Parkinson's disease; SBT, split-belt treadmill; UPDRS, Unified Parkinson's Disease Rating Scale; AP-GRF, anterior–posterior ground reaction force.

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http://dx.doi.org/10.1016/j.bbr.2014.03.041
0166-4328/

asymmetry, including persons post-stroke [4,5] and with PD [6–8]. Certainly, developing a better understanding of the abilities of persons with PD to adapt and store gait patterns could have significant impact on the design of gait rehabilitation paradigms and further insight into the neural substrates facilitating these processes.

Motor adaptation and adaptive learning processes have been studied across a variety of experimental conditions, including eye movements [9], upper extremity motor tasks [10–12], and locomotion [13]. Adaptation has been defined as a short-term process of adjusting a movement to new task demands through trial-and-error practice [14]. Adaptive learning is a longer-term process representing the stored ability after practice to predict new demands and accordingly adjust movement parameters [15]. Motor adaptation is commonly studied by inducing an unfamiliar perturbation into an otherwise familiar task. The motor response (i.e., adaptation) to the perturbation is characterized by large initial errors which are eventually reduced toward a baseline asymptote given repeated exposure to the perturbation [16]. Adaptive learning is assessed during ensuing de-adaptation and re-adaptation phases. Following adaptation, de-adaptation occurs when the perturbation is removed and conditions return to baseline. Large errors (commonly termed aftereffects) are initially present in the direction opposite those observed during initial adaptation and wash out over time as performance returns to baseline. Re-adaptation is studied during a second exposure to the perturbation following washout of the first. The phenomenon of savings is apparent if some memory of the first adaptation task is evident such that initial errors during re-adaptation are diminished and the rate of adaptation increases [17,18].

These phenomena have recently been investigated within locomotor paradigms using a split-belt treadmill (SBT): a treadmill consisting of one independently-controlled belt under each limb [13]. These treadmills allow for creation of walking tasks during which the limbs walk at different speeds or directions simultaneously. Previous research on SBT walking in healthy adults demonstrated that step lengths are asymmetric during initial adaptation (as the limb walking on the slow belt takes a longer step than the limb walking on the fast belt), gradually adapt toward baseline over time, and exhibit aftereffects and savings during de-adaptation and re-adaptation, respectively [13,19]. Therefore, step length is a reliable spatiotemporal measure upon which to study the response of the nervous system to errors in the gait pattern. However, during conventional gait, it has been well-established that stance phase kinetics (specifically, ankle power production during late stance) have a profound effect on step length [20]. Kinetic changes during SBT adaptation have only recently been studied [21–23] and little is known about kinetic aftereffects and savings during locomotion. A more thorough investigation of the kinetics during late stance could indicate whether kinetic changes drive the kinematic changes occurring during adaptation and adaptive learning (as during conventional walking) or whether they are differentially controlled.

Previous work on SBT walking in PD showed that optimally medicated persons with PD adapted step lengths toward an asymmetric asymptote which paralleled their baseline asymmetry while age-matched controls adapted to a relatively symmetric state [8]. Impairments in the storage of aftereffects or savings were not observed. However, these findings were in contrast to several previous studies of upper extremity motor adaptation tasks which noted disruptions in these phenomena in PD [24–29]. A key difference is that many of these studies investigated persons with PD after levodopa withdrawal. Thus, a comparison of locomotor adaptation and adaptive learning in persons with PD on and off dopaminergic medication could provide insight into the influence of dopaminergic pathways on these processes.

The purpose of this study was to investigate the effects of dopaminergic therapy on the abilities of persons with PD to adapt and store kinetic and spatiotemporal gait parameters during SBT walking. We hypothesized that, in accordance with previous research on upper extremity motor adaptation in PD, storage of locomotor aftereffects and savings would be diminished when the participants were withdrawn from their medication, though adaptation would be unaffected. We suggest that these findings could have significant impact with regard to both gait rehabilitation in persons with PD as well as the understanding of neural and biomechanical mechanisms which contribute to locomotor adaptation and adaptive learning.

2. Methods

2.1. Participants

Ten persons with PD were recruited for the study (mean ± SD: height 172.5 ± 9.7 cm, body mass 75.8 ± 9.1 kg; Table 1). Diagnosis of idiopathic PD was confirmed by a movement disorders specialist at the University's Center for Movement Disorders and Neurorestoration. Participants had neither walked on a SBT nor experienced any lower-extremity orthopedic injury for at least one year prior to participation. All were being treated with stable doses of orally-administered levodopa therapy. Four participants were also taking a dopamine agonist in addition to levodopa. All participants provided written informed consent before participating in the study as approved by the University Institutional Review Board.

Table 1
Participant characteristics and demographic information.

ID	Sex	Age (yrs)	Disease duration (yrs)	OFF meds UPDRS	ON meds UPDRS	OFF meds H&Y	ON meds H&Y	OFF meds gait speed (m/s)	ON meds gait speed (m/s)	LEDD (mg/day)	TD/PIGD
1	M	65	5	40	38	2.5	2.5	0.99	1.29	1100	PIGD
2	F	71	1	46	41	3	3	0.95	1.12	375	PIGD
3	M	69	6	39	42	2.5	2.5	0.94	1.14	825	TD
4	M	76	N/A	58	46	3	3	1.31	1.35	1250	TD
5	M	65	4	40	39	2.5	2	1.07	1.22	413	PIGD
6	M	66	5	45	39	2.5	2	0.82	1.3	750	PIGD
7	F	49	5	24	23	2	2	1.16	1.17	N/A	PIGD
8	M	72	10	41	37	2.5	2.5	1.02	1.35	642	PIGD
9	M	70	9	32	34	3	2.5	1.00	1.02	N/A	PIGD
10	M	65	4	31	28	2.5	2.5	0.98	1.03	488	PIGD
Mean		66.8	5.4	39.6	36.7	2.6	2.5	1.03	1.20	730.4	
SD		7.3	2.7	9.3	6.8	0.3	0.4	0.14	0.12	318.4	

ID – participant ID, disease duration – time since initial diagnosis, UPDRS – Unified Parkinson's Disease Rating Scale Motor Score (Section III), H&Y – Hoehn & Yahr stage, gait speed – self-selected overground gait speed, LEDD – levodopa equivalent daily dose, TD/PIGD – tremor-dominant/postural instability and gait disorder subtype [45], N/A – data not available.