Brain and Cognition 87 (2014) 76–85

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Motor planning in Parkinson's disease patients experiencing freezing of gait: The influence of cognitive load when approaching obstacles

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ARTICLE INFO

Article history:
Accepted 13 March 2014
Available online 12 April 2014

Keywords:
Freezing of gait
Gait with obstacle
Motor planning
Cognitive load
Dual task
Parkinson's disease

ABSTRACT

Freezing of gait (FOG) in Parkinson's disease (PD) is typically assumed to be a pure motor deficit, although it is important to consider how an abrupt loss of gait automaticity might be associated with an overloaded central resource capacity. If resource capacity limits are a factor underlying FOG, then obstacle crossing may be particularly sensitive to dual task effects in eliciting FOG. Participants performed a dual task (auditory digit monitoring) in order to increase cognitive load during obstacle crossing. Forty-two non-demented participants (14 PD patients with FOG, 13 PD who do not freeze, and 14 age-matched healthy control participants) were required to walk and step over a horizontal obstacle set at 15% of the participants' height. Kinematic data were split into two phases of their approach: early (farthest away from the obstacle), and late (just prior to the obstacle). Interestingly, step length variability and step time variability increased when PD patients with FOG performed the dual task, but only in the late phase prior to the obstacle (i.e. when closest to the obstacle). Additionally, immediately after crossing, freezers landed the lead foot abnormally close to the obstacle regardless of dual task condition, and also contacted the obstacle more frequently (planning errors). Strength of the dual task effect was associated with low general cognitive status, declined executive function, and inappropriate spatial planning, but only in the PD-FOG group. This study is the first to demonstrate that cognitive load differentially impacts planning of the final steps needed to avoid an obstacle in PD patients with freezing, but not non-freezers or healthy controls, suggesting specific neural networks associated with FOG behaviours.

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1. Introduction

Parkinson's disease is a movement disorder that is characterized by marked gait impairments, including freezing of gait (FOG) which occurs in approximately 30% of people with Parkinson's disease (PD) (Giladi et al., 2001). FOG episodes have been associated with other gait deficits such as increased gait variability, increased gait asymmetry, slower gait velocity, and shorter steps (Cowie, Limousin, Peters, & Day, 2010; Hausdorff, Schaafsma, et al., 2003; Nanhoe-Mahabier et al., 2011; Plotnik, Giladi, Balash, Peretz, & Hausdorff, 2005). Interestingly, these gait abnormalities and FOG episodes tend to occur more commonly during goal-oriented gait tasks that require a greater level of planning (i.e., increased level of conscious control), such as turning (Spildooren et al., 2010), passing through small apertures (Almeida & Lebold, 2010), avoiding a sudden obstacle (Snijders et al., 2008). Since these situations involve a greater level of conscious control, it may be suggestive of a limited central resource capacity in those PD patients who experience FOG (PD-FOG). Furthermore, it might be expected that areas of the brain that are known to be involved with attention and planning, such as the prefrontal cortex (Pochon et al., 2001), contribute to the impairments seen in FOG. Given this potential limited capacity, PD FOG might be hypothesized to be more susceptible to the influence of a secondary cognitive task, while attempting to step over an obstacle. While it has been well documented that in dual task situations PD often walk slower and with greater step to step variability (Hausdorff, Balash, & Giladi, 2003; Yogev et al., 2005), it is important to evaluate the interaction between cognitive load and motor planning in PD-FOG.

Recent research has demonstrated that increased planning demand during a locomotor task has a direct influence on movement control in PD-FOG only (Knobl, Kielstra, & Almeida, 2011). PD-FOG have also been shown to have a greater percentage of FOG episodes in situations where participants have more time available to plan for an unexpected obstacle (compared to less time available to plan

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http://dx.doi.org/10.1016/j.bandc.2014.03.005
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a step over) (Snijders et al., 2010). Thus, both of these studies seem to suggest that goal-directed planning during gait may serve as a dual task, thereby imposing increased load on those who experience FOG, hence the resultant FOG behaviour. Recent research (Moreau et al., 2008) has suggested that so called "modulated gait", is controlled through a specific pathway involving prefrontal cortex projections through the subthalamic nucleus and downstream to the locomotor centres of the brainstem, and this is only employed during gait tasks that require a higher level of processing (i.e. no longer automatic gait).

Recent imaging work has associated FOG with problems processing complex visual information, with the notion that PD FOG may have an impaired ability to recruit cortical and sub cortical areas in such complex tasks (Lewis & Barker, 2009; Naismith, Shine, & Lewis, 2010; Shine, Matar, Ward, Botilho, Gilat, et al., 2013; Shine, Matar, Ward, Botilho, Pearson, et al., 2013). These studies point to a direct link between the limited cognitive resources and impaired step generation, where the dorsolateral prefrontal cortex specifically is overactive during freezing behaviours. Interestingly, Almeida, Wishart, and Lee (2003) showed that shifting motor plans from a more automatic to a more consciously controlled form of interlimb coordination may overload attentional resources mediated by the dorsolateral prefrontal cortex of PD patients, thus causing motor blocks and other motor control abnormalities. Thus, it seems possible that the increased demands associated with complex gait tasks may limit the resources available for other secondary tasks in PD-FOG. Arguably, obstacle crossing could be considered a secondary task in itself, since shifting from a more automatic gait (during the early stages of approach toward an obstacle) to a more consciously controlled gait pattern (to plan for safe clearance over an obstacle), becomes necessary as one approaches an obstacle. Thus, studying this behaviour allows us to evaluate the contributions of the prefrontal cortex–basal ganglia network to freezing behaviour. While it has been well documented that in dual task situations, PD often prioritize a secondary task over gait control (Bloem, Grimbergen, van Dijk, & Munneke, 2006), leading to increased gait variability (Hausdorff, Balash, et al., 2003) and decreased gait speed (Yogev et al., 2005), it is important to evaluate how cognitive load might influence motor planning in PD-FOG during complex gait tasks, such as obstacle crossing. Perhaps more importantly, evaluating when cognitive overload may influence gait control during the approach to an upcoming obstacle, might yield important insight into the underlying mechanisms of basal ganglia dysfunction. Specifically, the current study sought to investigate if (and when) the transition from a more automatic to a less automatic control of gait might be a primary contributing factor in FOG behaviours, and if this could be systematically associated with the depletion of resources mediated by prefrontal areas of the brain in PD-FOG.

The aim of current study was to manipulate cognitive load during the approach and crossing phases, when PD patients with and without FOG, were asked to step over an obstacle. Furthermore, by comparing the results of neuropsychological tests of spatial working memory, cognitive flexibility and general cognitive status across our groups, we also aimed to address whether a specific cognitive issue (related to the neuroanatomical correlates described above) might explain FOG behaviours.

2. Material and methods

2.1. Subjects

Twenty-seven PD patients were recruited for the current study: 14 with FOG and 13 without FOG, who were matched for disease severity, duration (Table 1), and severity of asymmetry in lower limbs (Table 2). All patients were tested while "on" regular anti-Parkinsonian medication. Patients were excluded from the sample if they could not independently walk, or had musculoskeletal problems, uncorrected visual problems or other neurological or cardiac diseases. Motor symptom severity and FOG episodes were assessed prior to data collection. In order to assess the frequency of FOG episodes outside of our laboratory all patients answered with at least a score of 2 on question number 3 of the FOG questionnaire (Giladi et al., 2009), as well as a number of clinical tests previously described in (Almeida et al., 2010) to confirm the presence of FOG episodes. A sample of 14 healthy age-matched participants was also evaluated to compare with PD patients' behaviour. The study was approved by the research ethics board at Wilfrid Laurier University, and written informed consent was obtained from all subjects prior to the experiment according to the Declaration of Helsinki.

Table 1
Demographics and neuropsychological measures.

	PD-FOG	PD-nonFOG	Controls	Group effect
Sex	14M	10M/3F	8M/6F	*p* Value
Age (years)	73.6(7.7)	69.6(6.1)	74.7(8.2)	.202
UPDRS-III (total)	37.3(5.1)	33.1(10.7)	NA	.236
Years with PD	8.3(5.0)	7.6(4.6)	0	.879
Height (m)	1.77(.08)	1.76(.09)	1.70(.11)	.141
FOG-Q (item 3)	3.2(0.8)^{a}	0.38(0.7)	0	.0001
Years of educ.	12.9(4.2)	13.6(4.4)	14.5(5.2)	.675
3MS	92.6(6.7)	90.7(14.0)	95.9(3.9)	.340
TMT A(s)	61.6(40.9)	44(29.3)	40.1(21.2)	.177
TMT B(s)	329.5(62.2)^{a,b}	163.7(35.1)	106.9(15.4)	.002
TMT B–A(s)	267.8(53.9)^{a,b}	119.7(30.5)^{c}	66.8(11.9)	.001
Corsi block test	4.0(1)	4.2(1.2)	4.4(1.4)	.573

Means (standard deviation) describing demographics, clinical and cognitive characteristics of our sample. Letters in superscript indicate statistical differences ($p < .05$) identified by Tukey's post hoc analysis in the ANOVA one-way analysis: (a) PD-FOG × Controls; (b) PD-FOG × PD-Non-FOG; (c) PD-Non-FOG × Controls. M = Male/F = Female. NA = Not available. TMT A, B or B–A = Trail Making Test part A, part B or part B–part A; UPDRS = Unifying Parkinson's Disease Rating Scale; 3MS = Mini-Mental state exam 3MS; FOG-Q = Freezing of gait questionnaire item 3; NA = data not available.

2.2. Data collection and procedures

All participants completed three blocks of five trials for a total of 15 trials. The order of blocks was randomized between participants. Participants performed six practice trials without performing the dual task before the actual trials began. These practice trials were not included in the analysis. During the experimental trials, participants were free to choose the foot that would lead the crossing over the obstacle. Participants were required to walk at a comfortable pace on a dark-grey hard floor and to step over a non-solid obstacle. The obstacle was a bar made of white foam covered with a thick white paper (70 cm wide × 4 cm high × 1.5 cm depth; weight = 50 g) and suspended by two lateral plastic poles that were 30 cm in height (similar to high jump hurdles), and was set at 15% of the participant's height (Hahn & Chou, 2004), and positioned ~6.5 m from the starting point. The start position was set depending on the number of steps each participant required to step over the obstacle. Participants made at least eight steps from the starting point to the obstacle; however, because the initial two steps were outside the capture area only six steps prior to the obstacle were analysed. The mental task involved attending to an audio track while walking. This secondary task was chosen because there was no motor component involved thus allowing us to exclude the possibility that the secondary task caused motor interference on the gait task. Participants were instructed to mentally count the number of times they heard a digit spoken by a female voice in the audio track. The numbers participants heard

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