Letter to the Editor

Attentional set-shifting deficits correlate with the severity of freezing of gait in Parkinson’s disease

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1. Introduction

Freezing of gait (FOG) is a poorly understood symptom of Parkinson’s disease (PD) during which a patient suffers an abrupt cessation of walking [1]. Whilst little consensus exists regarding the mechanisms underlying FOG [2], there is considerable evidence that additional cognitive demand whilst walking represents a significant trigger in the pathophysiology of FOG [2]. In addition, the severity of self-reported FOG has been correlated with a selective deficit in attentional set-shifting [3]. Taken together, these findings suggest a degree of commonality between corticostriatal networks serving attention and the pathophysiology of FOG. However, no study has directly linked clinical measures of FOG severity during walking with diminished executive function, in particular the ability to rapidly switch between tasks. In this study we hypothesized that impaired behavioral performance on cognitive testing should correlate with objective measures of actual freezing events whilst walking.

2. Methods

2.1. Participants

Twenty-six PD patients with self-reported FOG were recruited from the Parkinson’s Disease Research Clinic at the Brain and Mind Research Institute (Table 1). The study was approved by The University of Sydney Human Research and Ethics Committee and written informed consent was obtained. Patients satisfied UKPDS Brain Bank criteria and were deemed unlikely to have dementia or major depression according to DSM-IV criteria. They were also assessed on the new Movement Disorders Society Unified Parkinson’s Disease Rating Scale (UPDRS-III). Patients were screened for the study by answering positively to item three of the Freezing of Gait Questionnaire (FOG-Q3 – “Do you feel that your feet get glued to the floor while walking, making a turn or when trying to initiate walking (freezing)?”) [4]. Patients were assessed in their ‘on’ state following overnight withdrawal of dopaminergic therapy.

2.2. Timed up-and-Go tasks

Patients performed a series of standardized timed up-and-go (TUG) tasks [5], which started in the sitting position from which patients walked 5 m at their preferred pace toward a 0.6 m² target box marked on the floor, where participants made a 180° or 540° turn (counterbalanced left and right) on two occasions before returning to sit in the chair. No dual-tasking was performed.

Similar to a previous study [5], freezing episodes were defined as the paroxysmal absence of forward progression of the feet despite the intention to walk. TUG trials were video-recorded for post hoc analysis by two experienced clinical raters (intraclass correlation coefficient [ICC] for number of FOG = 0.82; percent time frozen ICC = 0.99) [5]. Where agreement could not be reached the data were not included for further analysis (n = 15/336 episodes). Following rating, we calculated the total number of FOG events as well as the ‘percent time frozen’ (time spent frozen as a proportion of total time spent walking). Although 5 of the 26 patients (19%) did not suffer from a freezing episode during the TUG assessment, they were included in the final analysis so as to appropriately model the spectrum of freezing behavior.

2.3. Neuropsychological assessment

Patients performed the Trail Making Test part A (TMTA – drawing a line linking consecutive numbers from 1 to 25) and part B (TMTB – drawing a line connecting alternating numbers and letters in sequence; e.g. 1 – A – 2 – B – 3 – C). As has been described previously, the difference in time to completion between TMTB and TMTA (TMTB–A) measured the patient’s ability to rapidly ‘set-shift’ [3].

2.4. Statistical analysis

Bivariate Spearman’s rank–order correlations were calculated between TMTB–A and percent time frozen and the number of freezing episodes using the SPSS software package (Version 19.0). All tests were two-tailed with an alpha of 0.05.
Once the TUG tasks were successful in eliciting FOG in 21 of the 26 patients (81%) with a total of 321 events, averaging 12.3 (SD 11.2) per patient (median 11; range 0–78). The mean percent time frozen was 30.9% (SD 30.1; median 29.0; range 0.0–78.0).

TMT-B A was significantly correlated with both percent time frozen (Fig. 1A; Spearman’s rho = 0.530; p = 0.005) and the number of freezing episodes (Fig. 1B; rho = 0.420; p = 0.033). Both of the correlations remained significant after performing a partial correlation with the total UPDRS score (percent time frozen: rho = 0.540; p = 0.004; number of episodes: rho = 0.463; p = 0.017). In addition, motor severity (UPDRS-III) was not significantly correlated with TMT-B A (rho = 0.261; p = 0.190) or either measure of FOG (percent: rho = 0.038; p = 0.841; number: rho = −0.090; p = 0.624).

### 3. Results

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### 4. Discussion

While a relationship between FOG and cognitive dysfunction has long been recognized in PD patients [2,3], this is the first study to show a significant correlation between impaired performance on a specific neuropsychological test of set-shifting and objective clinical measures of FOG severity. These results extend previous work linking attentional set-shifting impairment with self-reported FOG symptoms [3].

We did not find any evidence for a significant correlation between attentional set-shifting and the severity of Parkinsonian symptoms, suggesting that the attentional set-shifting impairments seen in FOG were not simply due to worse PD severity. In addition, the results of the study could not confirm any correlation between the severity of self-reported symptoms and the amount of actual FOG observed in the ‘Off’ state. This finding is consistent with a recent study that demonstrated that ratings on such self-report questionnaires may not correlate with the actual severity of freezing during clinical assessment [5]. Previously, ratings on the FOG-Q have been correlated with performance on the TMT-B A [3], a finding that was not confirmed here. However, this earlier study was conducted in a larger group of patients containing both freezers and non-freezers, suggesting that TMT-B A impairment may exist along a spectrum in PD.

The correlation between impaired set-shifting and FOG severity observed in this study supports the hypothesis that an inability to shift between competing attentional demands may form part of the pathophysiological mechanisms underlying FOG [2]. A more profound understanding of these processes may have significant implications for future clinical management. For instance, whilst current therapies offer only limited symptom amelioration, it is possible that targeted cognitive training therapies may prove beneficial without adding to an already complicated medication regimen.

### Author roles

JM Shine – Conception and organization of the research project; execution and review of the statistical analysis; writing of the first draft and review of the manuscript. ST Moore – Conception of the research project; execution and review of the statistical analysis; review of the manuscript. NC Palavra – Execution of the research project; review of the statistical analysis; review of the manuscript. V Dilda – Execution of the research project; review of the statistical analysis; review of the manuscript. TR Morris – Execution of the research project; review of the statistical analysis; review of the manuscript. SL Naismith – Conception and organization of the research project; design and review of the statistical analysis; review of the manuscript. SJG Lewis – Conception of the research project; design and review of the statistical analysis; review of the manuscript.

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References


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