Assessing the utility of Freezing of Gait Questionnaires in Parkinson's Disease


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A B S T R A C T

There are currently two validated questionnaires, the Freezing of Gait Questionnaire and the New Freezing of Gait Questionnaire, that are intended to assess the degree of freezing of gait in patients with Parkinson’s disease. However, to date no study has attempted to determine whether ratings on these questionnaires accurately reflect the severity (frequency and duration) of actual freezing episodes experienced by patients. We studied twenty-four patients with Parkinson’s disease who self-reported significant freezing while in their practically-defined ‘off’ state. Prior to clinical assessment they completed both freezing of gait questionnaires before being video-recorded while performing a series of timed up-and-go tasks, which incorporated turning, rotating and passing through narrow gaps. The rating of video recordings by two independent observers identified a total of 530 freezing events. The frequency and duration of freezing episodes for each patient were calculated and correlated with questionnaire ratings. Scores on either questionnaire did not correlate with either the frequency or duration of freezing episodes experienced by patients during objective assessment. These results suggest the need to re-evaluate the utility of questionnaires in the assessment of freezing of gait. Furthermore, these results highlight the need for accurate objective methods of identifying freezing events when assessing future clinical interventions aimed at reducing this potentially disabling symptom of Parkinson’s disease.

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1. Introduction

Freezing of Gait (FOG) is a paroxysmal disabling symptom that commonly affects patients with Parkinson’s Disease (PD), particularly in the later stages [1,2]. Patients typically experience abrupt episodes where they are unable to move their feet, leading to an increased incidence of falls and subsequent nursing home placement [3,4]. The pathophysiological mechanisms underlying FOG remain poorly understood (for review see [5]) and response to current treatments is at best limited.

The assessment of FOG is difficult given the paroxysmal nature of this phenomenon. Indeed, patients may appear free of this symptom in the clinical setting, although evaluation during the ‘off’ state can increase the likelihood of recording freezing episodes [6]. In order to allow a more practical symptom appraisal, researchers have previously sought to design questionnaires capable of better characterizing and quantifying FOG.

The first such questionnaire (FOG-Q) comprised six questions (maximum score 24 points) that sought to assess both freezing of gait, as well as global gait disturbance [7]. This tool was validated in a large cohort of advanced PD patients who were participating in ‘LARGO’, a multi-center double-blind, placebo-controlled trial comparing the effects of Rasagiline and Entacapone [8]. The validation study found that a single item on the FOG-Q (question 3 – ‘Do you feel that your feet get glued to the floor while walking, making a turn or when trying to initiate walking (freezing)?’) was able to identify ‘freezers’ at least as well as the specific freezing item on the Unified Parkinson’s Disease Rating Scale (UPDRS question 14), which was previously viewed as the most reliable questionnaire measure of FOG [9]. It was concluded that the FOG-Q was useful both as a screening tool and also as an assessment of treatment intervention given the symptomatic benefits reported in the LARGO trial [8]. The authors of this validation study acknowledged the lack of specificity inherent in the FOG-Q as a subset of questions that were primarily concerned with overall gait dysfunction rather than FOG per se.

To address these concerns, a new questionnaire was developed which sought to introduce questions that were specific to FOG in PD [10]. The New Freezing of Gait Questionnaire (NFOG-Q) is a clinician-administered tool that aims to assess both the clinical aspects of FOG as well as its subsequent impairments on quality of life. In order to increase the likelihood of accurate self-assessment by...
patients, the NFOG-Q incorporates a short focused video that shows a number of FOG examples. The addition of this video appeared to increase the ratings of severity of the condition, however it did not add to the sensitivity or specificity of the tool with regards to identifying FOG. To account for this, the NFOG-Q allocates a single question to act as a screening tool for the presence or absence of FOG. Given the lack of standardized and effective community-based identification of FOG, the NFOG-Q has become a valuable tool for the assessment of freezing.

Clearly, the ability to accurately monitor FOG episodes is of great importance, especially in the evaluation of future therapeutic interventions. For example, the response of FOG symptoms to deep brain stimulation in novel target regions, such as the pedunculo-pontine nuclei [11], will require sensitive and specific outcome measures to determine benefits. However, to date no studies have sought to demonstrate the ability of the NFOG-Q (or the FOG-Q) to reflect actual FOG episodes experienced by patients. This study sought to determine whether scores on these questionnaires correlated with the frequency and/or duration of freezing episodes measured objectively in PD patients reporting FOG.

2. Methods

2.1. Recruitment

Twenty-four patients who were attending the Parkinson’s Disease Research Clinic at the Brain and Mind Research Institute, University of Sydney were identified for this study by severe self-reported freezing behavior. All patients satisfied UKPDS Brain Bank criteria [12], had a Mini-Mental State Examination (MMSE) [13] score of ≥24 and were deemed unlikely to have dementia or major depression according to DSM-IV criteria by consensus rating of a Neurologist (SJGL) and a Neuropsychologist (SLN). Clinical details are presented in Table 1. The study was approved by the University of Sydney Human Research and Ethics Committee and written informed consent was obtained.

2.2. Clinical evaluation and questionnaires

Patients were assessed in the practically-defined ‘off’ state following overnight withdrawal of dopaminergic therapy. Six patients also had Deep Brain Stimulation (five Subthalamic Nuclei and one Pedunculo-pontine Nuclei), which were turned off for 1 h prior to assessment. They were evaluated on the Movement Disorder Society Unified Parkinson’s Disease Rating Scale – Section III (MDS-UPDRS-III) [14] and Hoehn and Yahr stage score [15]. None of the patients described any increase in freezing behavior following the administration of their usual dopaminergic therapy. Upon arrival at the clinic, patients were administered the FOG-Q and the NFOG-Q. The NFOG-Q was subsequently separated into two parts, Section 1 for screening and Sections 2 and 3 were taken to represent the severity and frequency of FOG [10].

2.3. Timed up-and-go (TUG) tasks

Patients performed a series of timed up-and-go tasks on a standardized course (Fig. 1A) to provoke FOG. All TUG tasks started from a sitting position, from which patients walked along the center of a large open corridor. Five meters (5 m) from the chair was a 0.6 m × 0.6 m target box marked on the floor with yellow tape, in which turning movements were performed. The standard TUG required a 180° turn within the box and a return to the starting chair. Three enhanced TUG assessments were also carried out (Fig. 1B): ‘540°’ TUG in which patients performed two revolutions within the box; ‘walk-around the box’ TUG in which patients were instructed to walk around the outside of the box making tight turns without touching the tape; and ‘narrow gap’ TUG, entailing lateral movement of the chair at the start position (after the patient had begun the TUG) to create a <1 m gap with the wall, alternately to the left or right side, that the patients were required to negotiate on the return journey. All TUG tasks were performed with turns to the patient’s left and right. In addition, dual-tasking (vocalizing the months of the year forwards and backwards whilst walking) was utilized on two trials per patient. The requirements for each TUG task were explained just prior to the trial. If a patient had failed to fully comprehend the requirements of a specific trial it was abandoned and performed again from the start. The beginning of each TUG trial was signaled by a request from the investigator to begin and was completed on return to the seated position.

2.4. Video assessment

All trials were video recorded from a consistent vantage point 3 m from the ‘taped-box’ (STM, TRM and VD; see Fig. 1A). All videos were independently reviewed by two clinicians with an interest in Movement Disorders (JMS and SJGL) for freezing episodes, which were defined as the paroxysmal cessation of a patient’s normal progress through a specific routine, as described elsewhere [16]. The end of each

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic, neurological, cognitive and freezing characteristics of the sample.</th>
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<tbody>
<tr>
<td></td>
<td>Range</td>
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<tr>
<td>N = 24</td>
<td></td>
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<tr>
<td>Age, years</td>
<td>56–84</td>
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<tr>
<td>Hoehn and Yahr</td>
<td>2–4</td>
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<tr>
<td>UPDRS III</td>
<td>10–65</td>
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<tr>
<td>Mini-Mental State Examination</td>
<td>24–30</td>
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<tr>
<td>Freezing questionnaires</td>
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<tr>
<td>FOG-Q total</td>
<td>10–22</td>
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<tr>
<td>NFOG-Q; 2 and 3</td>
<td>0–25</td>
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<tr>
<td>Clinical Assessment</td>
<td></td>
</tr>
<tr>
<td>Frequency of freezing episodes</td>
<td>1–63</td>
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<tr>
<td>Percentage of time freezing</td>
<td>0.3–75.7</td>
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</tbody>
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FOG episode was defined as the ability of the patient to perform an effective step with gait-parameters similar to their normal stride. The presence of ‘trembling in place’ was not used as an identification criteria. Freezing episodes were logged according to their time of onset and offset. The frequency and duration of episodes were determined for each patient utilizing a video FOG tagging program developed by the investigators (TRM and STM). Each video observer was instructed to tag the onset of a freeze by pressing the “T” key and holding down the key throughout the duration of the event. Video editing tools enabled the observers to drag the ends of a horizontal bar representing the duration of the tagged freeze (which also moved backwards or forwards through the video by a corresponding amount of time) to accurately log the onset and offset of each FOG event. To facilitate accurate assessment of freeze duration, the raters were instructed to repeatedly view the video footage and adjust onset/offset points until entirely satisfied. An intra-class correlation analysis (ICC) established the reliability (ICC = 0.9) of the video FOG scores from the two raters for both frequency and duration of freezing episodes. The total duration of all trials was calculated as the sum total of the time taken from the beginning to the completion of each individual trial. Percentage time spent freezing was defined as the total duration of FOG episodes (regardless of type of freezing) over the total test duration.

In accordance with previous research [16], we also distinguished a number of sub-types of FOG relating to the clinical situation in which they occurred, and calculated the relative frequency of each sub-type.

(i) Turn hesitations, in which one of the patient’s legs failed to complete the normal turning circle or a tight turn during any of the routines;
(ii) Runway freezes, which were defined as FOG episodes occurring in the absence of turns, targets or gaps;
(iii) Freezing during narrow gaps, defined as freezing occurring during the navigation of a narrow portion of the routine;
(iv) Target hesitations, which occurred upon the arrival (within 2 m) to a defined target, such as a line of tape on the ground;
(v) Start hesitations, where patients had difficulty initiating gait at the start of a TUG task in any of the routines.

2.5. Statistical analysis

Results from the questionnaires were tabulated and compared statistically with the output measures of the video assessments. The data were analyzed through pairwise parametric correlations using Statistical Package for the Social Sciences software (SPSS Inc., Chicago IL).

3. Results

The TUG tasks were highly successful in eliciting FOG. The total number of FOG events was 530, averaging 21.7 (SD 17.6) per subject (range 1–63). This is consistent with a recent study [17] in which the mean number of FOG events was 23.7 (SD 20.7), ranging from 0 to 66 episodes per subject. The mean percentage of time freezing was 23.7% (SD 23.0), ranging from 0.3 to 75.7%. There was a large variability in the frequency and duration of FOG episodes across subjects, which allowed for a robust correlation analysis with the rating scales.

The proportion of the sub-types of FOG (Fig. 2) was generally similar to those previously reported [16]. Patients were most likely to freeze during turns (299 FOG events; 56.4% of total) and 22 of the 24 patients (92%) suffered a freeze during a turn, making it the most sensitive measure for eliciting a freezing episode. There were a substantial number of runway freezes (141 events; 26.6% of total; 58% of patients), however the vast majority (120 events) occurred in only 4 patients, with the balance (21) occurring infrequently in the rest of the cohort. We also observed freezing during narrow gaps (56 events; 10.6% of total; 42% of patients) as well as target (22 events; 4.2% of total; 38% of patients) and start hesitations (12 events; 2.3% of total; 33% of patients). Marked ‘trembling in place’ was observed on a number of trials, however the presence or absence of this feature was not analyzed in this study.

The correlations between the percentage of time spent ‘frozen’ during the TUG tasks and ratings on the FOG-Q (r = 0.11, p = 0.613) and NFOG-Q (r = 0.30, p = 0.150) were not significant (Fig. 3A). The correlation was even weaker (Fig. 3B) between the number of FOG events per subject and ratings on the FOG-Q (r = 0.11, p = 0.613) and NFOG-Q (r = 0.30, p = 0.150). There was a trend for a single question on the FOG-Q (question 3 — Do you feel that your feet get glued to the floor while walking, making a turn or when trying to initiate walking (freezing)?) to be associated with frequency of freezing episodes (r = 0.40, p = 0.052) but not with the percentage of total time spent frozen (r = 0.29, p = 0.178). However, this data was poorly distributed for a correlation analysis with only one subject scoring less than 2 on FOG-Q question 3.

4. Discussion

The major finding of this study was that the FOG-Q and the NFOG-Q rating scores did not correlate with actual clinical measures of FOG severity (frequency and duration of freezing episodes) in a cohort of PD patients with established FOG while in the clinical ‘off’ state. A single item on the FOG-Q (namely, the third question) trended towards significance when correlated with the total frequency of freezing episodes experienced by patients. This study also confirmed the utility of the TUG task as a reliable method for provoking FOG in the clinical environment, particularly in the ‘off’ state [17,18]. The use of the TUG and associated turning and obstacle avoidance tasks proved useful in demonstrating the different sub-types of FOG, dominated by freezing episodes (over half of 530 FOG events), then (in decreasing order of frequency) runway, narrow gaps, target and start hesitations. The similarity in relative proportions of freeze sub-types with those previously reported [16] suggests that the clinical tasks conducted in this experiment were consistent with those utilized to study FOG across different clinical centers.

FOG-Q and NFOG-Q have been validated in large cohorts of PD patients [9,10]. However, this validation did not utilize objective clinimetric tools that can distinguish specific freezing episodes in a clinical environment, but relied purely on subjective patient and carer responses to the questions, as well as self-reporting and clinician-mediated questionnaires for the comparative analysis. The lack of any correlation between FOG-Q and NFOG-Q scores and actual freezing in PD patients suggests that such subjective ‘validation’ techniques are inadequate and may not in fact validate rating scales in an objective or clinical sense. Although our findings do not undermine the validity of the FOG questionnaires to act as screening tool for the presence of FOG in a sample of patients with PD, our results suggest that a single question (FOG-Q question 3) may be sufficient for this task. The ability to accurately...
assess FOG severity is fundamental to the future evaluation of interventions aimed at decreasing the frequency and duration of FOG events. The results of our study suggest that existing FOG questionnaires are unsuited to this task and may in fact provide an inaccurate estimate of FOG severity, which may be exacerbated in patients with more advanced disease who spend longer periods in the ‘off’ state [1].

One interpretation of the findings in this study is that the questionnaires are probing a more general freezing phenomenon, rather than freezing confined to the domain of gait [19,20]. In keeping with this viewpoint, a number of studies have shown that scores on these questionnaires correlate with specific impairments in cognition [21,22], particularly under temporal pressure [23,24]. Other research has shown specific links between self-reported freezing and panic attacks in patients with PD [25]. This explanation suggests that the pathophysiological mechanism of FOG may not operate independently in one specific domain, such as motor function. As such, neural regions responsible for domain-general functions, such as the subcortical nuclei and brainstem structures, may be responsible for these clinical correlations. If correct, this would suggest that freezing behavior occurring across walking, handwriting or even thinking may be due to an underlying and unifying mechanism [26].

Given the potential limitations of questionnaire ratings there is a pressing need for the development of novel tools that can be used to objectively assess FOG. Members of our research team have previously developed and validated an ambulatory objective technique for identifying the presence and duration of a FOG event based on a frequency analysis of the vertical acceleration of the leg [27], and other groups have further validated this freeze detection algorithm [28]. FOG is identified with an accuracy of 80–90% based on the appearance of high-frequency ‘trembling’ in a 3–8 Hz ‘freeze’ band and a corresponding decrease in power in the locomotor (0–3 Hz) band [27]. This technique is also capable of identifying FOG sub-types (start hesitation, turning, runway freeze) based on context (i.e., did the FOG event occur after a period of standing or sitting still, in conjunction with angular velocity indicating a turn, or whilst walking). The high-frequency lower limb oscillations, known clinically as ‘trembling in place’, are often (but not always) visible to the naked eye [27]. Ambulatory monitoring of FOG with inertial sensor arrays will likely prove more accurate than clinical observation and allows the possibility to extend objective monitoring from the clinic to the community. However, further work is required to validate objective freeze monitoring, particularly in the absence of simultaneous clinical observation.

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References