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Quantifying Freezing of Gait in Parkinson's disease during the Instrumented Timed Up and Go test

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Abstract— **Over half of patients with PD eventually develop freezing of gait (FoG), an intermittent failure to initiate or maintain walking that is often associated with trembling of the legs. We tested 21 PD with FoG, 27 PD without FoG, and 21 healthy elderly people in a clinic with the Intrumented Timed Up and Go test (ITUG). FoG was quantified from the power spectral density of the antero-posterior shank acceleration from which a Frequency Ratio was calculated as the square of the total power in the 3-8 Hz band, divided by the square of the total power in the .5-3 Hz band. Spatiotemporal gait parameters calculated from synchronized gyroscopes on the two legs were also measured in these subjects.**
The Frequency Ratio was significantly larger in freezers than in non-freezers or control subjects. It better differentiated gait disorders between PD subjects with and without FoG than traditional gait measures such as stride length, stride velocity and double support time. The Frequency Ratio was validated as significantly correlated with self-perceived severity of gait and balance confidence. This Freezing Ratio will be useful to quantify FoG during a simple ITUG, a popular clinical test of mobility.

I. Introduction

Freezing of Gait (FoG) is one of the most disabling gait symptoms in Parkinson's disease (PD). FoG is defined as "a brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk" [1] and is usually associated by rapid "trembling of the knees" as patients attempt to step [2]. FoG represents a common cause of falls in PD, [3] interferes with daily activities, and significantly impairs quality of life. Over half of patients with PD develop this intermittent failure to initiate or maintain walking, and especially during turning [1].

A recent consensus review of FoG shows a most pressing need to characterize FoG with quantitative, instrumented measures both to understand the pathophysiology and to facilitate clinical trials [1]. Current clinical assessment of FoG is largely based on subjective patient reports, such as the Unified Parkinson's Disease Rating Scale's (UPDRS) Activities of Daily Living Part 15 [4], which rates freezing on a scale from 0 (none) to 4 (frequent falls from freezing) based on patient history. More comprehensive FoG questionnaires were recently validated (FOG-Q [5] and NFOG-Q [6]) but they still rely upon subjective patient recall. Typically, FoG episodes are brief (1 s or less) and are associated with a subjective feeling of "the feet being glued to the floor"[2]. Several laboratory studies have attempted to characterize FoG using electromyographic (EMG) activity and spatiotemporal kinematic parameters of gait such as increased double support time, increased cadence, and decreased stride length, but few have validated their objective FoG measures with a self-perception of freezing or balance [7, 8]. Recent approaches, based on frequency analysis of vertical leg acceleration or leg motion to capture the FoG hallmark "trembling of knees" are promising, with a sensitivity of (75-83%) and specificity of >95% [9-12]. However, most of these approaches are not suitable for clinical trials or clinical practice, since they rely on a Motion Analysis Laboratory. A frequency ratio from vertical acceleration of the shanks has been suggested by Moore, but it is not clear if the vertical acceleration is the best signal to identify FoG [10]. To date, no objective FoG score has been available for both straight-ahead walking, turning, and postural transitions such as sit to stand. We are interested in developing automatic algorithms that quantify FoG objectively for clinical practice, and we hypothesize that FoG could be measured with body-worn accelerometers during a clinically popular mobility test, the Timed Up and Go test.

II. Methods

A. Participants

Twenty-one PD subjects with self-reported FoG, FOG+ (≥1 on Giladi's FoG Questionnaire [5], Items 3-6; "freezers", UPDRS mean 37±12, 63±7.9 years old); 27 PD subjects without self-reported freezing who had similar Motor UPDRS scores, FOG- ("non-freezers", UPDRS mean 39±15), 65 ±10 years old); and 21 healthy control subjects of similar age participated in the study (62±6.9 years old). Subjects did not have any neurological disorders other than PD, or any orthopedic disorders or other impairments that could interfere with gait, and all patients had to be able to walk independently. All participants provided informed consent approved by the Oregon Health & Science University Institutional Review Board.

B. Measurement Protocol

All participants underwent a 1-hour mobility assessment, which included clinical assessments, questionnaires, and quantitative assessments of balance and gait using a clinical user interface and automated algorithms from Mobility Lab,

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by APDM (APDM Inc, USA). Subjects with PD were tested OFF their antiparkinson medication in the morning. All participants performed 3 trials of the extended length Instrumented Timed Up and Go (ITUG) test, which involves standing up from a chair, walking 7 meters, turning around to walk back to the chair, and sitting down [13]. PD patients completed the FoG questionnaire to assess self-perception of freezing and the Activities-Specific Balance Confidence Scale Questionnaire (ABC), to detect loss of balance confidence associated with FoG [14]. Testing was conducted in the Movement Disorders Clinic at Oregon Health and Science University.

C. Measurement System

Subjects wore a portable data receiver (X-Bus) connected to 3 MTX Xsens sensors (Xsens, Enschede, the Netherlands) composed of 3-D accelerometers (±1.7g range) and 3-D gyroscopes (±300°/s range). The sensors were positioned with Velcro belts on the posterior trunk, near the body center of mass and on the anterior shank of each leg. The data receiver wirelessly streamed the sensor data to a laptop at 128 Hz.

D. Data Analysis

An automated analysis algorithm identified the sit-to-stand, gait, turning and turn-to-sit components of the TUG and provided 52 spatial-temporal metrics [13]. From this automatic analysis, we reported the following measures: Stride length, Stride Velocity and Double Support Time.

We examined the 3-D accelerations and angular rate signals of the shanks offline and found the clearest freezing ratio from the power spectral density (PSD) of antero-posterior, and not vertical (as previously reported-Moore [10]), shank accelerations. A Frequency Ratio was calculated as the square of the total power in the 3-8 Hz band (freeze band), divided by the square of the total power in the 0.5-3 Hz band (locomotor band) [10]. The PSD was calculated for each trial using a 4-s Hanning window with 50% overlap (using the Welch method). The total power was then normalized to the area under the PSD curve for each subject, as shown in Figure 1 from representative subjects. Matlab R2009b (The MathWorks, Inc) was used for the offline frequency analysis of the acceleration signals.

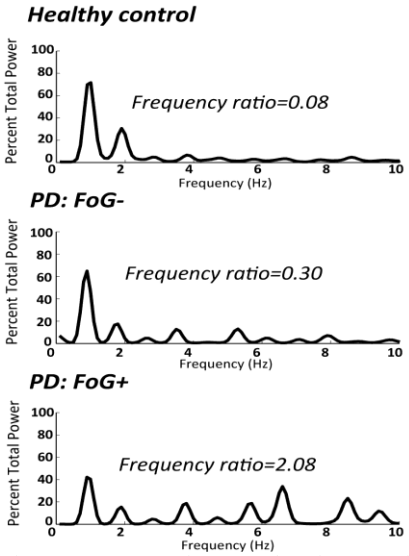

Figure 1: Representative examples of PSDs and Frequency Ratios in a healthy control subject, PD non-freezer and freezer during the ITUG test.

A non-parametric Kruskal-Wallis test was used to determine whether differences existed among the 3 groups on each measure (Chi-square and - values are reported). When a significant difference was found, a post-hoc analysis was performed using Bonferroni adjustment ($p < 0.0083$ for 3 pair-wise comparisons) to test which group (control, FOG+, FOG-) differed from each other.

Spearman rank correlation (ρ) was used to evaluate the association between subjects' perception of FoG and instrumented scores. The statistical analyses were performed using NCSS Software (Kaysville, Utah).

III. Results

The Frequency Ratio was significantly different among groups ($\chi 2 = 28 \leq .09$, p=0.0007). Post-hoc testing revealed a significantly larger Frequency Ratio in PD FOG+ compared to PD FOG- (p=0.001), and in PD FOG- versus controls (p=0.007). Subjects with the largest Frequency Ratios showed obvious FoG only during turning and turn to sit in the videos of their performance.

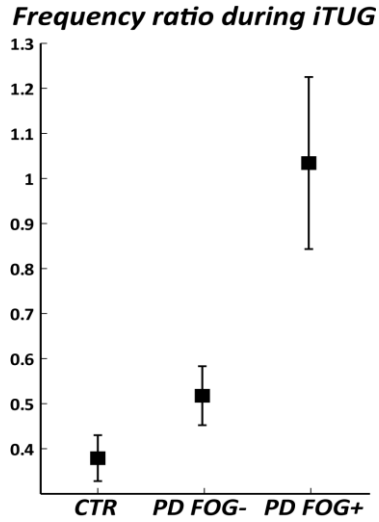

Figure 2. Mean Frequency Ratio in controls, non-freezers and freezers during the ITUG test.

Table 1

Freezing Ratio and Spatio-Temporal Gait Parameters during iTUG				
	Controls	*FOG-*	*FOG+*	*χ2, p*
Stride length (%stature)	87.9(4.2)	78.3(7.4)	73(7.3)	29.0, p<0.001
Stride Velocity (%stature/s)	85.4(6.6)	72.51(10.6)	65.9(8.5)	27.7, p<0.001
Double Support Time (% Gait Cycle)	21.1(3.7)	21.1(3.7)	24.2(3.1)	7.8, p=0.01
Freezing Ratio (AD)	0.37(0.05)	0.52(0.08)	1.02(0.2)	28.09, p<0.001

Interestingly, we found no differences in Stride Length or Stride Velocity between freezers and non-freezers (only between controls and PD), whereas Double Support Time was longer in freezers compared to non-freezers (p=0.007), although similar between non-freezers and controls (Table 1).

As a test of clinical validity, Frequency Ratios were significantly related to scores on the FoG questionnaire (ρ =0.6, p=0.002) and on the Activity-specific Balance Confidence (ABC) clinical scale (ρ =-0.47, p=0.02) as shown in Figure 3.

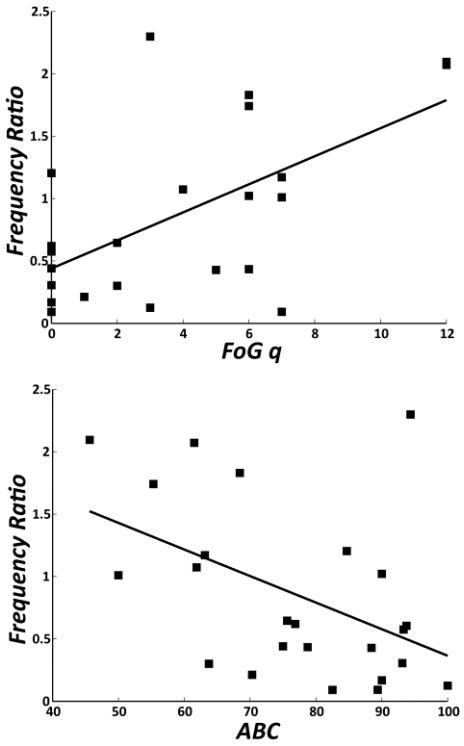

Figure 3. Correlations between the Frequency Ratio and the Freezing of Gait questionnaire (FoG q) and between the Frequency Ratio and the Activities of Balance Confidence scale (ABC).

IV. Conclusion and Future Work

Our Frequency Ratio differentiates between control subjects and PD subjects as well as between PD subjects with and without freezing of gait during a well-known clinical test, of mobility, the TUG. In addition, this Frequency Ratio exhibited good clinical validity as a strong correlation with patients' perception of FoG and balance confidence.

We found the clearest Freezing Ratio from the antero-posterior shank acceleration signals and not from the vertical shank acceleration, as previously reported [10]. This difference may be due more severely affected subjects in the previous study, with frank festination episodes (eg; rapid, small steps while falling forward). Our subjects had very mild FoG and video recordings verified that none experienced festinating gait. Perhaps, a high-frequency, antero-posterior oscillation is more related to a subtle trembling leg motion that occurs when PD patients attempt to turn and initiate gait to overcome the FoG episode. We previously showed that these rapid leg oscillations are associated with repetitive anticipatory postural adjustments with delayed onset of stepping [15].

Previous studies have found an association between FoG and reduced step length [7, 16] suggesting that FoG maybe caused by inability to generate and maintain an adequate stride length. In contrast, in the present study, we found that freezers had similar step length compared to non-freezers. This discrepancy may be due to the fact that the episodes of FoG seen during the ITUG occurred only during the turning or turn-to-sit phase of the task and not during straight-ahead walking.

Consistent with previous studies, we did find an increase in power in the 'freeze' band of 3-8Hz from the shanks, consistent with a higher-frequency harmonic than the stepping motion in freezers, despite the presence of freezing episodes, or failure to maintain forward walking motion [10-12].

Limitations of the present study include lack of validation with movement disorder's expert opinions and that we didn't try to identify subject-specific thresholds that may increase detection of subtle FoG.

Future studies will validate this method with clinical judgment, include other mobility tasks, compare signals from sensors on other body parts and explore other frequency analysis methods to count the number of FoG episodes in a trial.

A "freezing index" that assesses severity of FoG will be useful in clinical studies for evaluation of new therapies or to assess the effect of rehabilitation intervention for FoG, particularly if it is practical for clinical environments. In conclusion, a Frequency Ratio that compares the power of leg accelerations at higher versus at stepping frequencies can be used to quantify severity of FoG during a simple Timed Up and Go test, which is already used by many clinicians to evaluate mobility disability.

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