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Clinical assessment of freezing of gait in Parkinson's disease from computer-generated animation

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ABSTRACT

The current 'gold standard' for clinical evaluation of freezing of gait (FOG) in Parkinson's disease (PD) is determination of the number of FOG episodes from video by independent raters. We have previously described a robust technique for objective FOG assessment from lower-limb acceleration. However, there is no existing method for validation of autonomous FOG measures in the absence of video documentation. In this study we compared the results of clinical evaluation of FOG from computer-generated animations (derived from body-mounted inertial sensors) during a timed up and go test with the 'gold standard' of clinical video assessment, utilizing a cohort of 10 experienced raters from four PD centers. Agreement between the 10 clinical observers for scoring of FOG from computer animations was more robust for the relative duration of freeze events (percent time frozen; intraclass correlation coefficient of 0.65) than number of FOG episodes, and was comparable with clinical evaluation of the patient from video (intraclass correlation coefficient 0.73). This result suggests that percent time frozen should be considered (along with number of FOG events) to better convey FOG severity. The ability of clinical observers to quantify FOG from computer-generated animation derived from lower-limb motion data provides a potential approach to validation of accelerometry-based FOG identification outside of the clinic.

1. Introduction

Freezing of gait (FOG), a paroxysmal locomotor block, is a debilitating symptom of Parkinson's disease (PD) associated with an increased risk of falls and early nursing home placement [1]. Clinical management of FOG is limited in large part by the difficult nature of assessing its severity, particularly in a community setting. Current approaches utilize subjective reports from patients or caregivers (either as a simple rating scale or FOG questionnaire), but our recent study of a cohort of PD patients with self-reported FOG symptoms demonstrated that scores from subjective FOG questionnaires did not correlate with actual freeze severity when walking [2]. The *de facto* 'gold standard' of FOG assessment is clinical evaluation (either directly or from video) to determine the number of FOG episodes [5,6], but this subjective approach also has limitations, as evidenced by a moderate inter-rater agreement (intraclass correlation coefficient of 0.6) in our recent study of 10 experienced movement disorder specialists assessing FOG from video [3]. Clinical management of FOG, as well as the evaluation of new targeted interventions, would benefit from the development of objective, standardized FOG measures capable of monitoring this debilitating symptom in a community setting.

We have described an objective technique for robust identification of FOG events from lower limb accelerometry, which has achieved strong agreement with clinical assessment in the laboratory [3,4]. Our ultimate goal is to extend accelerometry-based FOG assessment to community monitoring. However, a critical barrier to validation of such an approach is the current inability to verify FOG in the absence of clinical observation. Although accelerometry has proven viable in a controlled clinical setting [3,4], validation of autonomous FOG monitoring outside of the clinic requires an intermediate step: a means to allow clinical assessment in the absence of video documentation. To this end we developed a technique for visualizing objective lower body motion data of ambulating patients. The aim of this study was to assess the utility of clinical FOG assessment from these 3D computer animations by comparison with the current 'gold standard' of assessment from video of the actual patient. Our hypothesis was

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that computer animation of lower-limb motion generated from body-mounted inertial sensors, in particular the high-frequency (3–8 Hz) 'trembling' associated with FOG [3,4], would provide sufficient information to enable accurate clinical evaluation of freezing. Such a finding would provide a much needed means of validating objective FOG monitoring outside of the clinic, by facilitating a comparison of clinical FOG evaluation from computer-generated animations with accelerometry-based FOG identification [3,4], both derived from ambulatory motion sensors.

2. Methods

2.1. Patients

Ten PD patients (6 male and 4 female) with a clinical history of FOG were recruited from the Parkinson's Disease Research Clinic at the Brain and Mind Research Institute, University of Sydney. Patients were assessed in the practically defined 'off' state following overnight withdrawal of dopaminergic therapy. Two patients were being treated with subthalamic nuclei deep brain stimulation (DBS), which was turned off for 60 min prior to testing. Patient characteristics have been described previously [3], and are summarized here: mean age 67.7 [SD 6.6], disease duration 11.2 years [SD 6.7], Hoehn and Yahr stage 2.5 [SD 0.3], UPDRS – Section III [7] 38.4 [SD 10.7]. None of the patients described any increase in freezing behavior following the administration of their usual dopaminergic therapy.

2.2. Protocol

Subjects were instrumented with seven inertial measurement units (IMUs – Xsens MTx, Enschede, Netherlands) secured to the back (approximately L2), the lateral aspect of each thigh and shank, and the superior aspect of each mid-foot, with elasticized straps. The IMUs were small (38 mm × 53 mm × 21 mm; 30 g) and did not interfere with natural movement. As previously described, patients performed timed up-and-go (TUG) tasks to provoke FOG on a standardized 5-m course, while being recorded on a digital video camera from a consistent vantage point for clinical analysis [2,3]. Fourteen TUG tests were performed with a total duration of 9 min 37 s (four of the ten subjects who performed the TUG task quickly, or who exhibited minimal FOG, were asked to perform a second trial).

2.3. Animations

During testing each IMU acquired triaxial linear acceleration, angular velocity and readings of the Earth's magnetic field; transmitted wirelessly to a computer at a sample rate of 50 Hz. Synchronization of video and accelerometer recordings was performed prior to data collection by alignment of the video camera and data-acquisition computer clocks. Data was processed *post hoc* to determine the orientation of each sensor array in space using a commercial sensor fusion algorithm (MT Manager, Xsens, Enschede, Netherlands). IMUs do not provide absolute position data. Therefore, to generate an animation of patient gait during the TUG task we created a virtual humanoid lower body with two robotic chains (right and left leg) based on the 'Nancy' model [8] using the LabVIEW Robotics Module (National Instruments, Austin, TX) (Fig. 1). Each IMU generated a matrix representing the orientation of the sensor (and associated limb segment) in 3D space, which was referenced to a neutral (upright) position determined from a pre-TUG calibration (320 ms during quiet stance):

$$M_i = m_i \times N_i^{-1} \tag{1}$$

where N_i is the orientation matrix representing the neutral position for sensor i, m_i is the original (uncalibrated) orientation matrix representing the current orientation of the IMU in space, and M_i represents the orientation of this body segment with respect to the neutral position N_i. After aligning all sensor orientations with respect to neutral, joint angles (J) for the left and right leg were calculated [9] in a downward cascade from the orientation of the distal sensor with respect to the proximal sensor for the hip (thigh relative to back), knee (shank relative to thigh) and ankle (shank relative to foot) (Fig. 2).

$$J_{hip} = M_{thigh} \times M_{back}^{-1} \tag{2}$$

$$J_{knee} = M_{shank} \times M_{thigh}^{-1} \tag{3}$$

$$J_{ankle} = M_{foot} \times M_{shank}^{-1} \tag{4}$$

The yaw orientation of the back sensor determined heading (the direction in which the patient's avatar was facing; Fig. 1). The resultant joint angles, limited to the range of the biomechanically possible (hip 121° flexion to −20° extension; knee −143° flexion to 5° extension; ankle 13° flexion to −56° extension [10]), were used to drive the robotic chains of the humanoid model, and an animation was created from each image at a rate of 50 frames per second (Fig. 1 and supplementary video).

2.4. Clinical assessment of FOG

Clinicians experienced in evaluation of freezing (n = 10) were recruited from four Parkinson's disease centers (Mount Sinai, the Bronx VA, and Beth Israel in New York City; the University of Sydney) to independently assess the videos and animations for FOG (the results for rater agreement from video have been presented previously [3]). Each rater reviewed a total of 32 videos, which comprised 14 unique videos of ambulating patients and 14 corresponding animations, and 4 repeated video/animation pairs to assess intra-rater (within each observer) reliability. The 32 videos/animations were presented in a random order (with no two observers having the same sequence) such that clinicians were blinded as to which video a particular animation was associated with. Raters were not informed that some patients had more than one video/animation trial or that four of the video/animation pairs were presented twice (all observers viewed the same four repeat trials). The avatars were identical for each animated trial; therefore observers had no visual cue as to patient identification apart from lower-body motion. The frequency and relative duration of freezing episodes for each video and animation were quantified with a FOG tagging program [2,3]. Each rater used their best clinical judgment to identify FOG episodes, tagging the onset of a freeze by pressing the 'T' key and holding down the key for the duration of each event. The program saved the clinical ratings as a binary signal with a baseline of zero (no freeze) and a value of 1 indicating a freeze event, from which the *number of FOG events* and *percent time frozen* (the cumulative duration of all FOG episodes divided by the total duration of the walking task) were calculated [2,3].

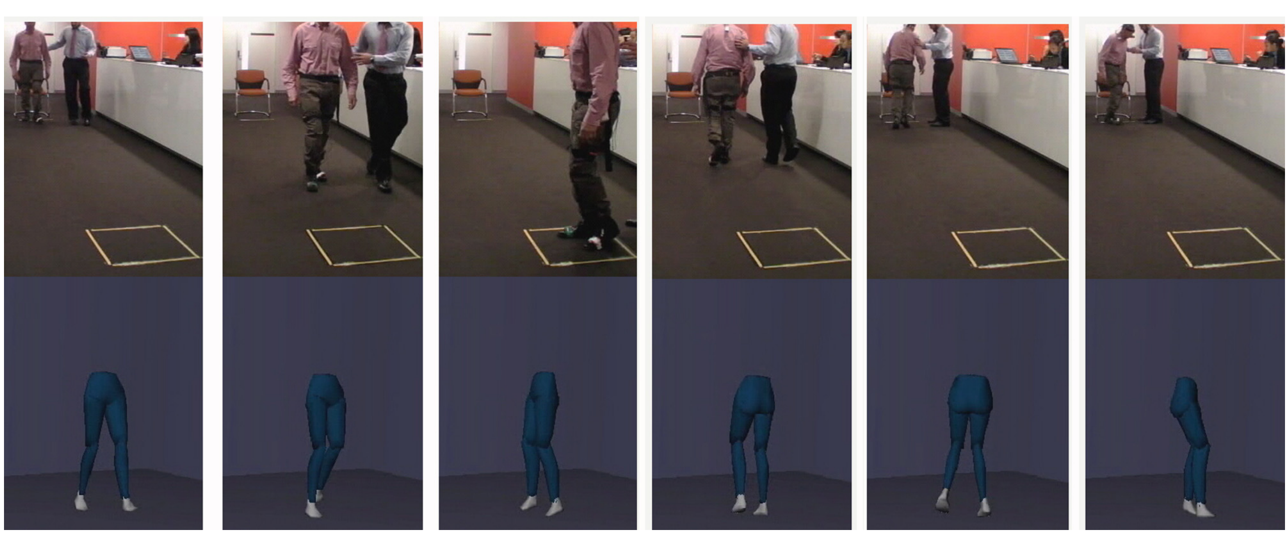

Fig. 1. A sequence of video frames from a patient performing the TUG task and the corresponding computer-generated animation (see also supplementary video).