Variability in prolonged and fatiguing gait in older persons (PROGOLD)

Applicant: Espen Alexander Fürst Ihlen

Background

A stable walking pattern is crucial for living independently, for interacting with other people and the environment, and for quality of life in general (Brach et. al., 2003; Guralnik et. al., 1992). During aging, multiple factors produce instabilities in the walking pattern. These factors include injuries and diseases but also a gradual decrease in muscle strength (e.g. Lang et. al., 2009). Recently, investigations have focused on the influence of fatigue on the stability of gait in older persons (Helbostad et al. 2007). Elderly were shown to have increased variation in step length and vertical trunk acceleration and decreased variation in mediolateral acceleration after repeated sit and stand movements (Helbostad et al. 2007). Furthermore, variability in gait parameters of prolonged gait trials has been investigated both in younger and older adults and healthy and diseased older persons (Hausdorff et al, 1997, 2007; Jordan et al., 2007, 2009). These studies linked the structure and amplitude of gait variability to the degeneration of the central nervous system with age (Hausdorff et al., 1997; Herman et al., 2005). Despite these results, there have so far been no studies investigating the variability in gait parameters during prolonged and fatiguing gait in older persons. Moreover, variability of gait parameters during prolonged gait in older persons has not been related to muscle strength, muscle cross-sectional area, or force control of muscles of the lower extremities. The maximum capacity of force development in the ankle extensors, knee flexors and hip extensors/adductors and abductors of the older person might be an important parameter in explaining the change in the patterns of variability during prolonged gait (Patrella, et al., 2005; Wolfson, et al., 1995). Furthermore, the ability for older persons to generate specific amounts of force (i.e., force control) during the gait cycle might also be a crucial factor for the amount and structure of variability in their gait pattern (cf. Newell et al. 2009). Both the maximum capacity of force development and force control are related to a decrease in muscle cross-sectional area by reduction of type II motor units and atrophy of type II muscle fibers (Roubenoff et al., 2000; Lang et al., 2009). This condition in older persons is called sarcopenia and is a major risk factor for frailty, disability and mortality (Marzetti & Leeuwenburgh, 2006). The variability in gait parameters will also be compared with the daily activity of older persons. Daily activity is an expression for physical function and mobility of the older person and might be closely related to variability in the gait pattern (Bruin et al., 2008).

Goal

The goal of this project is to investigate how variability in gait parameters changes during prolonged and fatiguing gait in older persons. Furthermore, within-group differences in gait variability will be compared with within-group differences in muscle strength, force control, muscle cross-sectional area, and patterns of daily physical activity. This goal is divided into four specific aims:

Aim 1: Develop a MatLab toolbox of non-conventional analyses of variability. These analyses are wavelet-based multifractal spectrum analysis (Abry et al., 2002; Muzy et al., 1991; Ihlen & Vereijken, in press), multifractal detrended fluctuation analysis (Kantelhardt et al., 2002;

Ihlen, submitted), Hilbert spectrum analysis (Ihlen, 2009), Windowed detrended fluctuation analyses, and local wavelet spectrum analysis (Ihlen, submitted).

Aim 2: Investigate variability of gait parameters during prolonged and fatiguing gait. In addition to conventional parameterizations of variability (standard deviation, interquartile range, coefficient of variance), the toolbox developed in study 1 will be utilized.

Aim 3: Compare the within-group variance in gait variability of healthy older persons in study 2 with the within-group variance in patterns of daily upright activity.

Aim 4: Compare the within-group variance in gait variability of healthy older persons in study 2 with variance in muscular strength, force control, muscle cross-sectional area, and attenuation coefficient.

Methods

***Participants*:** A large convenience sample of 40-60 participants will be recruited within the interquartile range of the fast gait speed of a reference group of 200 older persons (79±5 years, 70% women) drawn from the Folkeregistreret of persons of >70 years of age. A preliminary gait test will be conducted with both preferred and fast gait speed during overground walking to assess the changes in speed since the last measurement in 2007. Only the participants with fast gait speed within the interquartile range of the reference group will be included. The reference group was used in a larger intervention study on cataract surgery at St. Olav hospital where the exclusion criteria were MMS < 20/30, terminal illness at the time of inclusion, suffered stroke, or undergone hip or knee surgery during the last 6 months. An additional exclusion criterion for the present study will be the inability to walk 10 minutes without walking aid.

***Protocol*:** The four aims will be pursued by one data collection consisting of four sessions. *Session one* is a medical assessment before inclusion of neurological, cognitive, cardiovascular, auditory and visual function and registration of prescribed medication. Furthermore, the included participants will answer a ten item fear of falling (FES-I) (Tinetti et al., 1990) and Health related quality of life (SF-36) questionnaire (Loge et al., 1998) in this session. After the medical assessment, an ActivPAL® body-worn sensor is attached to the right thigh of the included participants. The sensor will be detached at the beginning of session two a week after session one (battery life time of ActivPAL®).

Session two contains tests of maximal isometric force, maximum rate of force development, and force control. The maximal isometric force and rate of force development (RFD) will be tested for the knee flexors/extensors, ankle extensors and hip abductors/adductors in a Biodex® dynamometer. For each muscle, three bouts of 3 seconds of maximal force/RFD will be conducted on two different joint angles. Between each bout there will be a 1.5-3 minutes break. The joints, joint angles and duration of bouts/breaks to be used will be decided through pilot testing to secure the relevance for the force generation during gait. In addition, the participant will perform an isometric force control task in which they will trace a sinusoid force path shown on a computer screen, with three different frequencies (4, 8 and 12 Hz; cf. Newell, 2009).

Session three is a gait session consisting of three tests. The first test is a pretest in which the participant will perform three trials of 7 meters overground walking at both preferred and fast gait speed. The second test is a prolonged gait test in which the participants will walk for 20 minutes at preferred speed directly followed by 20 minutes of fast and

fatiguing gait speed. The fast gait speed will be set according to a percentage of the interval between the preferred and fastest overground gait speed of the pretest for each participant (Dal et al., 2010). The particular percentage will be decided through pilot testing. The third test is a posttest that replicates the pretest. This test is conducted to determine the influence of the prolonged treadmill test on gait parameters during overground walking.

Session four is a CT scan of the ankle and thigh segments. Two to three cross sections will be taken of each segment relative to bony landmarks (cf. Lang et al., 2009).

Outcome measures: The outcome measures from the Biodex® dynamometer in session two will be the maximal force in each of the three bouts and the maximum rate of force development. In the force control task, the outcome measure is the deviation between the displayed target force trajectory and the generated force trajectory. In the gait session (session three) the Vicon® 3D camera system is used to measure the trajectories of reflex markers placed on predefined landmarks on the lower extremities (modified Helen Hayes's marker placement). Furthermore, a trunk-worn 3D sensor (TRASK) will be used to measure the acceleration of the trunk in the vertical, anterioposterior and mediolateral directions. The heart rate as measured by an electrocardiogram (ECG) and the level of exhaustion measured on a BORG scale (Borg, 1970) will be used as measures of the changes in fatigue towards exhaustion in the prolonged gait test. The duration of the periods in upright activities (standing and walking) will be measured by an ActivPAL® body-worn sensor (Grant et. al., 2008). A CT scan will measure the muscle cross-sectional area and the attenuation coefficient (the ratio of intramuscular fat and muscle tissue) of the muscles in the thigh and ankle segments.

***Data analysis and statistics*:** The torque/force measures from the Biodex® are preprocessed by a low pass 4th order recursive Butterworth filter with a 25 Hz cut-off frequency while the the position data from the Vicon® 3D data are preprocessed with 10 Hz cut off frequency. The filter position signal of the markers will then be used to calculate the joint angles. The difference between the local maxima and minima within each gait cycle for the ankle, knee and hip joint angles defines the range of motion (ROM). Furthermore, the position and velocity of the heel marker in the vertical, anterioposterior and vertical directions will be used to identify the step/stride length, width and time. The ROM, step/stride length, width and time can be plotted against the stride number for the prolonged gait test to depict the fluctuation/variability of these parameters. Furthermore, the medial, vertical and mediolateral accelerations will also contain stride-dependent variability. Next, the fluctuations in ROM, stride/step length, width and time, and acceleration in the vertical, mediolateral and anterioposterior directions will be parameterized by both conventional and non-conventional statistical analyses. The amount or magnitude of the fluctuations will be assessed by conventional parameters like root-mean-square. The average structure of the variability (i.e., long-range autocorrelation) will be computed by the linear least square slope of the log-power spectrum computed through a discrete Fourier transform (Eke et al., 2002) and log-scaling spectrum computed by a detrended fluctuation analysis (DFA) (Peng et al., 1993). Furthermore, the intermittent structure of variability will be parameterized by wavelet-based multifractal analysis (Ihlen, submitted) and multifractal detrended fluctuation analysis (Kantelhardt et al., 2002). All these analyses will be programmed in Matlab R2009a. All algorithms not represented in the literature will be tested on statistical models with known parameters (Ihlen, in prep) (aim 1).

To pursue aim 2, the parameters of variability in the stride/step length, time and width and the anterioposterior, mediolateral and vertical trunk accelerations will be correlated (statistical method) with the absolute change in heart rate and reported level of exhaustion on

a BORG scale during the prolonged gait test. Furthermore, a windowed extension of the variability analyses above will be used to visually compare the temporal change in the amplitude, correlation and intermittency of the variability in ROM, stride/step length, width, time, mediolateral, anterioposterior and vertical trunk accelerations with changes in heart rate and on the Borg scale.

To pursue aims 3 and 4, the magnitude, long-range correlation, and intermittency in the variability in the ROM, stride/step length, width, time and mediolateral, vertical and anterior posterior trunk accelerations will be dependent variables in a multivariate regression analysis with muscle cross-sectional area, attenuation coefficient, the maximal force and rate of force development as independent variables. In addition, the amplitude, autocorrelation and intermittency of the force deviation from a target force trajectory and the duration of periods in physical activity will be used as independent variables.

Ethical considerations

All studies will be conducted in compliance with the Declaration of Helsinki. Study descriptions and test protocols will be sent to the Regional Ethical Committee (REK) for approval and registered at the Norwegian Social science Data service (NSD).

Work progression schedule and dissemination of results

1st term *Aim 1*: Programming of algorithms for variability analyses in Matlab
2nd term *Aim 1*: Manuscript preparation and pilot measurements studies 2 and 3
3rd term *Aim 2 and 3*: Data collection
4th term *Aim 2 and 3*: Analysis and manuscript preparation
5th term *Aim 2 and 3*: Analysis and manuscript preparation + pilot measurements study 4
6th term *Aim 4*: Data collection
7th term *Aim 4*: Analysis and manuscript preparation
8th term *Aim 4*: Enclosing *Studies 1-4* into the Ph.D. thesis

Obligatory work and PhD courses will be distributed over the 4-year period. The results of all studies (four papers) will be disseminated in recognized, international peer-reviewed scientific journals in medical engineering, geriatrics and human movement science and communicated through presentations at national and international conferences and professional meetings.

Research group

This project is conducted within the multidisciplinary research network HMC (Human Motor Control). The overall scientific goal of HMC is to become the nationally leading and an internationally significant research network on motor control by developing and applying clinically useful instruments, tests, and analyses regarding human movement. This project will be embedded in three strong research groups at NTNU, consisting of scientists from the Research Group on Geriatrics, Department of Neuroscience (DMF), the Human Movement Science Programme (SVT) and the Department of Engineering Cybernetics (IME), all collaborating within the HMC network.

Data collections will mainly be conducted in the laboratories at the Department of Neuroscience under the supervision of Jorunn Helbostad (*main supervisor*) and professor

Olav Sletvold (*additional supervisor*). In addition, there will be collaboration with Human Movement Science Programme under the supervision of Beatrix Vereijken (*additional supervisor*).

Finally, the present project will be conducted in collaboration with professor Jaap van Dieën (*external collaborator*) and assistant professor Miriam Pijnappels at the Faculty of Human Movement Sciences at the Free University of Amsterdam, the Netherlands.

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