Multicenter Osteoarthritis Study
Gait, Activity and Balance Variables Derived from Accelerometry

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Introduction

Gait, Activity and Balance variables were derived in MOST using raw data from movement sensors worn by participants during exams that were part of the 144-month clinic visit. During an in-clinic exam participants wore Opal accelerometers (Opal inertial system (APDM Inc.)) during the 20 Meter Walk test and during the Six Minute Walk test. Following the clinic visit, participants wore Axivity AX3 accelerometers (AX3 Logging Accelerometer, Axivity Ltd, York, UK) during waking hours for up to seven days while engaged in their usual daily activities.

This documentation was provided by Dr. Jeff Hausdorff's laboratory* for the Multicenter Osteoarthritis Study and describes methods used by Dr. Hausdorff's laboratory to derive gait quality, balance and activity measures from the movement sensors worn by MOST participants. The documentation has been edited and expanded by the MOST Coordinating Center. Some of the variables are derived only from the Opal sensor data, some only from the AX3 sensor data, and some are derived from both types of sensor data. This document describes the concepts, definitions and calculation methods for the derived variables, and indicates from which exams and type of sensor data the variables were derived. Protocols for acquisition of the sensor data were acquired and can be found at https://agingresearchbiobank.nia.nih.gov/studies/most/documents/?f=Manual_of_ProceduresSAS dataset and variable names corresponding to the measures described are listed in Appendix I.

IMPORTANT: It is imperative that analysts and investigators also read the Dataset Description and Analyst Notes for both the Opal and the AX3 in order to have a comprehensive understanding of the datasets and variables before attempting to use the data.

*Also referred to in this document as the Accelerometry Reading Center (ARC).

https://www.tasmc.org.il/sites/en/Personnel/Pages/Hausdorff-Jeff.aspx

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Introductory Notes

The variables described in this document are contained in eight separate SAS datasets:

- Opal data 20M Walk Gait (**V7OPAL20MWALK; 1 record per trial)**
- Opal data Six Minute Walk Test Gait Quality (**V7OPAL6MWT)**
- Opal data Six Minute Walk Test Gait Quality Fatigability (**V7OPAL6MWT_FATIFABILITY)**
- Opal data Sway - Standing Balance (**V7OPAL_SWAY; 1 record per trial)**
- AX3 data daily Gait and Activity (**V7AX3_DAYS; 1 record per day)**
- AX3 data Summary of Gait and Activity **(V7AX3_SUMMARY)**

With a few exceptions, all Gait variables derived from Opal sensor data were calculated from data obtained during both the 20 Meter and Six Minute in-clinic walks. A subset of Gait variables were calculated from both Opal sensor data and AX3 sensor data. Activity variables were calculated from AX3 sensor data only. Sway variables were calculated from Opal sensor data only. Gait variables include both gait quantity (e.g. number of steps/strides, number of walking bouts) and gait quality (e.g. asymmetry, entropy).

Even when the same gait variable is calculated using both Opal and AX3 data, they are measuring two different types of walks. One is in the clinic and the other is daily-living. In addition, the Opal exam in clinic used 3 sensors (2 on the legs, one on the lower back) and the AX3 just one on the lower back. The variables that are calculated from each device/type of walk are different and they are looking at different aspects of gait. The same variable root might have different interpretation depending on the type of walk. For example, during a clinic exam when the subject is walking at more or less steady speed, we would expect the stride time CV to be as small as possible. On the other hand, at the daily-living condition a high stride time CV can indicate robustness in the gait speed and adaptability to the conditions around the subject.

Gait and Activity variables, by sensor type and data set, are listed in Appendix I and Sway variables are listed in Appendix III. For information on data set structure, see also the dataset documentation "DatasetDescription_V7OPAL.pdf"; and "DatasetDescription_V7AX3.pdf".

<u>Walking (Gait) bouts</u>

Walking bouts are used in determining the Opal data to be used in calculating Gait variables and the AX3 data used in calculating Gait and Activity variables. A walking bout is an uninterrupted recording of continuous walking that meets specified criteria. Walking bouts are defined differently for the in-clinic walks using Opal data and the daily-living AX3 data.

Gait quality measures (e.g. regularity, symmetry) are usually designed for straight line walks. For the 20 Meter Walk, a bout is defined as the entire straight line 20 Meter walk. The Opal contains a gyroscope which detects turns. For the Six Minute Walk, a bout is defined as the straight line walk before and after each turn, with the turn steps excluded from the bout. For calculation of gait variables during the Six Minute Walk, the data from all of the straight line bouts before and after the turns are stitched together. For Six Minute Walk fatigability measures, the bout data excluding turn steps for each minute is stitched together in order to get the only the straight line walk that the subject performed during that minute. **Note**: There is one type of gait quantity variable from the Six Minute Walk that is calculated with, and without, including the turn steps. These are the variable for number of strides, and the variable name indicates whether the turn steps are included.

The AX3 does not contain a gyroscope and is unable to detect turns, so bouts are determined by duration of detected continuous walking. For the AX3 a "bout" is any period of continuous walking of 3 steps or more. For calculation of AX3 Gait variables, recorded periods of continuous walking were divided into segments of 60s. Only segments (or "bouts") of 60s duration are used in the calculation of the variables, depending on the analysis. If for example a bout is 70s long then it would be used for one 60s segment (the last 10 sec will not be used). The duration of a bout starts with the first step of the 3 step minimum and continues until there is a pause in walking of 1s or more, which defines the end of the bout.

AX3 Gait variables were calculated separately for each walking bout segment. The median, mean, SD, min, max of each measure are reported on a daily level, using all the walking bouts from that day of 60s. AX3 Gait variables are only calculated for a day if there are one or more segments of continuous walking of 60s detected. In contrast, the AX3 Activity variables for walking (walking time, number of steps) are calculated from all periods of continuous walking of 3 steps or more regardless of duration and from the full duration of all of the periods of continuous walking. See Section 12 for the technical details of the detection algorithm for walking from the AX3 data. A different algorithm was used to detect walking in the Opal data.

Trimming steps/gait cycles from the Opal walking bout data

Opal variables for gait quantity from the 20 Meter and Six Minute Walk data, like number of strides/steps and average velocity, use the data from the entire bout (from the first step to the last step in the bout, with turn steps excluded from the bout). Other Opal variables of gait quality are calculated after trimming data from 4 steps at the beginning and 4 steps at the end of the bout, in which the subject is accelerating or decelerating. The rationale for trimming these steps is to only include the stable straight-line walks or gait cycles in the calculations. For example, for the 20 Meter Walk the first 4 steps and last 4 steps of the walk are excluded when calculating gait quality variables, such as Sample Entropy. For the Six Minute Walk, the 4 steps before and after the turns are similarly excluded for gait quality variable calculations. These same variables calculated for each minute of walking in the fatigability dataset are also based on the trimmed bout data.

Fatigability during the Six Minute Walk (see also Appendix II)

In order to investigate the impact of participant fatigability on gait over the course of the Six Minute Walk, a selection of variables was calculated for each minute of the walk, from 1 to 6, to allow examination of changes in gait variables over the course of the walk. These variables are contained in a separate Fatigability data set (see Appendix II). For the variables calculated minute by minute, the overall value of that variable over the entire Six Minute Walk was also calculated. Most of the overall variables in the Fatigability dataset are analogous to the variables in the Six Minute Walk dataset calculated over the entire walk.

Miscellaneous

Multiple references are made in this document to Parkinson's disease, which has been abbreviated to "PD".

Multiple references are made in this document to coefficient of variation which has been abbreviated to "CV".

The unit symbols in this document follow the SI system except for: Seconds is expanded to "sec".

Notation [-] means the measure is unitless
"g" refers to standard gravity instead of grams. g is approximately 9.81 m/s^2.
SAS dataset and variable names corresponding to the measures described are listed in Appendix I.

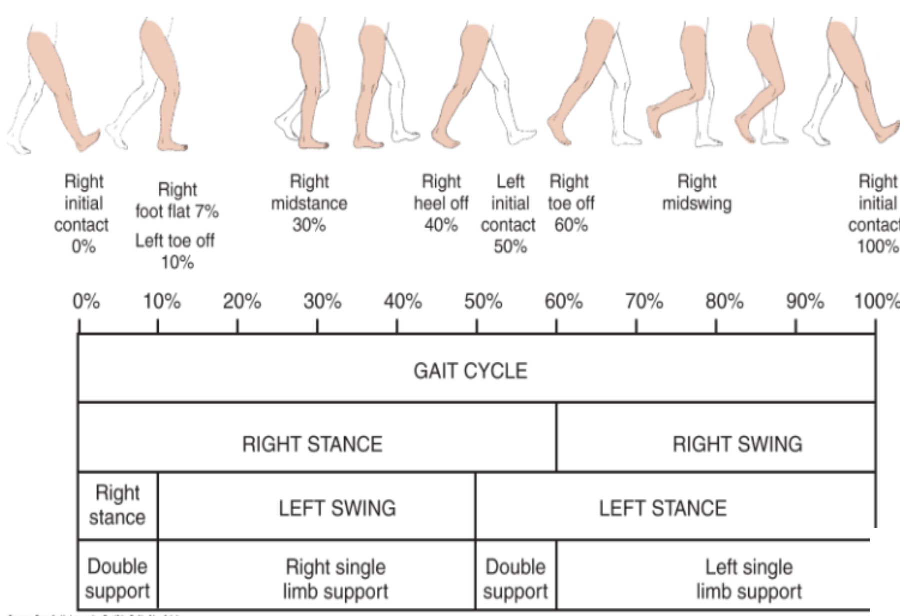
1. Gait variables

1.1 Terminology to describe the events of the gait cycle

Note: There are 28 Opal data variables from the 20 Meter and Six Minute Walks related to the gait cycle in the first Row of Appendix 1.

The gait cycle is a repetitive pattern involving steps (stances) and strides. A step refers to one single step; a stride refers to the whole gait cycle. The step time can be defined as the time from one foot hitting the floor to the other foot hitting the floor (or initial contact to initial contact). Classification of the gait cycle involves two main phases:

- **Stance Phase**, the phase during which the foot remains in contact with the ground. It begins with heel strike and ends with toe off of same foot (typically occupies about 60% of the gait cycle).
  Stance has several phases:
  - Heel strike- It starts when the heel comes in contact with floor, with heel strike body weight begins to shift onto stance limb.
  - Foot flat- the entire foot is in contact with floor.
  - Mid- stance- It is the point at which body passes over the stance limb and where the leg is approaching the vertical position offering single-limb support with other limb freely swinging forward.
  - Heel off- Heel off occurs when heel just begins to lift off floor.
  - Toe off- toes just leave the floor, it is end of stance phase and beginning of swing phase.
- **Swing Phase**, the phase during which the foot is not in contact with the ground. It begins when the foot leaves the floor and ends with heel strike of the same foot (typically occupies about 40% of the gait cycle).



Levangie, Norkin, 1983

Figure 1: Gait cycle terminology during walking

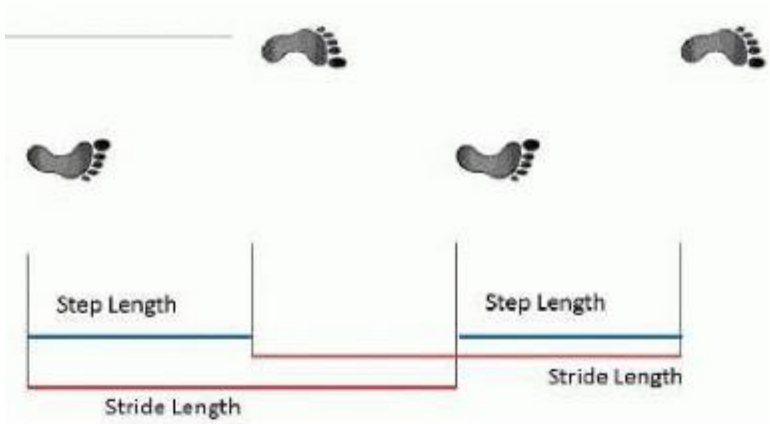


Figure 2: Determination of step length and stride length during walking

Different sub-domains or families of variables can be extracted including pace, rhythm, variability and symmetry, as described further below.

1.2 Fatigability variables

Fatigability during the Six Minute Walk. In order to investigate the impact of participant fatigability over the course of the Six Minute Walk on Gait Quality, a selection of these variables was calculated for each minute of the walk, from 1 to 6, to allow examination of changes in parameter values from minute to minute over the course of the walk. These variables are contained in a separate Fatigability data set (see Appendix II for more details).

2. Pace/Rhythm

2.1 Average step length [m] (Opal 20 Meter and Fatigability measure)

Determined as the total distance walked divided by the number of steps.

Note: We estimated number steps by identifying the toe off phase and the initial contact phase in time domain based on the algorithm that developed by (Trojaniello, Cereatti, 2014). Step length and average speed are calculated only for the 20 Meter Walk using the knowledge that each straight line bout that the subject walked was 20m long. The total number of steps for the 20 Meter Walk is the sum of the variables of number left steps and number of right steps. Distance walked, step length and speed are not calculated for the Six Minute Walk because when the walk ends the subject is usually in the middle of a bout, so these variables are not calculated. For assessment of fatigability, these variables are calculated based on a method for estimating relative average velocity. Calculating the step length directly from the lower back's Ax3 acceleration is not performed by our algorithms.

- For example, shorter steps should be more stable because the COM (center of mass) is closer to the moving BOS (base of support) (Bhatt, Wening, 2005).

2.2 Average velocity [m/sec] (Opal 20m and Fatigability ["Speed"] variable)

Note: Determined as the total distance walked divided by the total walking time. Walking time was implemented for quality check of the data. For Six Minute Walk it should always be 6 min. If the subject walked for a shorter duration (e.g. 3 min) it's possible to exclude that walk from the analysis. Walking time for 20m walk was used in the calculations, but there is no separate variable for this. Walking time can be calculated by dividing 20 meters by "averagevelocity".

For example, slower gaits have been shown to be directly associated with an increased fall risk and are correlated with lower scores on clinical balance scales (Cromwell, Newton, 2004), (Coppin, Shumway-Cook, 2006). Also, reduced gait speed may explain many of the continuous gait disturbances in PD (Hausdorff, 2009).

2.3 Cadence [steps/min] (Opal, Fatigability, AX3 variables)

Note: The calculation of cadence is using the number of steps for each 20 meter bout as an input. For the 20 Meter Walk test, it's the total number of steps, but for the 6MTW the cadence is calculated per each 20 m bout and then averaged.

Walking cadence, number of steps per minute, has been suggested as an approach that may be useful in assessing compliance to current physical activity guidelines, because although it still relies on a step count, it also places emphasis on the speed of the steps, therefore, acting as a method to estimate the intensity (Slaght, Sénéchal, 2017).

Normal range for usual walking: 100-115 [step/min]

- For example, older adults might have a higher walking cadence (Peacock, Hewitt, 2014)

In lab experiments (data record from Opal sensors), we estimated step time by identifying the toe off phase and the initial contact phase in time domain based on the algorithm that developed by (Trojaniello, Cereatti, 2014). For determined cadence, we normalized the average step time to one minutes, multiply it by 60 [sec].

AX3. In daily-living (data recorded from AX3) gait isn't systematic like in lab experiments, so we calculated cadence from the frequency domain (Section 5.4-5.6). We identified the dominant frequency of the signal, Fs, and calculate the inverse value of the dominant frequency, Ts that depict the average step time.

2.4 Mean stride time [sec] (Opal, Fatigability and AX3 variable)

Time of average gait cycle. Cadence and mean stride time are two sides of same coin.

3. Dynamic postural control

3.1 Average double support time as percent of gait cycle [sec] (Fatigability variable)

Average time where both feet are in contact with the floor, within a single gait cycle. We estimated double support period by identifying the time between initial contact phase on one limb and the toe off phase on the other limb based on the algorithm that developed by (Trojaniello, Cereatti, 2014). This variable is hypothesized to be affected by fatigue so was calculated for that dataset.

Note: There are no separate variables for “Average double support time”. The variables included in the fatigability data set are based on the average double support measured as percent of the gait cycle, which is the percentage of the gait cycle that is in double support, on average. (See Appendix II for additional information.)

- For example, increased time with the feet on the ground may explain many of the continuous gait disturbances in PD (Hausdorff, 2009).

3.2 Average swing time [sec] (Opal variable)

Average time for steps when the ipsilateral limb is not in contact with the floor. These variables are calculated separately for the right and left limbs.

We estimated swing period by identifying the time between toe off phase and the initial contact phase for one limb based on the algorithm that developed by (Trojaniello, Cereatti, 2014).

- Patients with PD who were in the early stages of the disease and were not yet treated with any anti-Parkinsonian medications walked more slowly and with reduced swing times while also exhibiting increased left/right swing asymmetry (Hausdorff, 2009).

3.3 Average single support time [sec] (Fatigability variable)

Average time where a single foot is in contact with the floor, within a single gait cycle.   In addition, the percentage of the gait cycle that is in single support on average was calculated. (See Appendix II for additional information.)

4. Symmetry

4.1 Step symmetry [-] (Opal, Fatigability and AX3 variable)

Expresses the symmetry of the acceleration between left and right limbs. Acceleration is the primary type of data collected by the Opal and AX3 sensors and is the basis for most of the calculated gait, activity and sway variables. (See Instrumenting gait with an accelerometer: A system and algorithm examination. http://dx.doi.org/10.1016/j.medengphy.2015.02.003.) Symmetry is the autocorrelation coefficient for neighboring steps divided by the autocorrelation coefficient for neighboring strides. (Nilssen, Helbostad, 2003), (Tura, Raggi, 2010).

Note: Most gait variables from AX3 data are calculated for each of the 3 accelerometer axes (vertical V, medio-lateral ML, anterior-posterior AP).

- A loss of consistency in the ability to produce a steady gait rhythm, resulting in higher stride-to stride variability, is also a characteristic feature of gait in PD (Blin, Ferrandez,1990), (Hausdorff, 2009).

4.2 Phase Coordination Index (Opal and Fatigability variable)

Phase Coordination Index (PCI) is the bilateral coordination of gait and was assessed by quantifying the phase relationship between the step timing of the left and right legs.

The average phase of the stride φ (i) [deg] is first calculated and used in the calculation of the components of the PCI (4.2i – 4.2.iii below). The step time, the time between the start of a gait cycle and the time point when the other leg's heel strike occurs, is used to determine the phase, φ (Fig. 4). Normalizing the step time with respect to the stride time, defines the phase of the stride φ (i) [deg].

$$\varphi_i = 360° \times \frac{t_{Si} - t_{Li}}{t_{L(i+1)} - t_{Li}}$$

Where t_{Li} and t_{Si} denote the time of the heel strike of the legs with the long and short swing times, respectively.

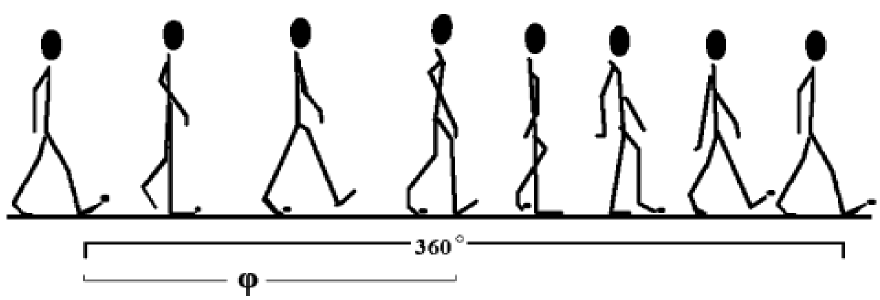


Figure 3: Illustration of phase determination of one leg's stepping with respect to the gait cycle determined by the other leg.

4.2.i Percentage of the absolute difference from 180 deg [%] (Opal variable)

In order to maintain successful walking, φ should have the value of approximately 180°. Therefore, the level of accuracy in phase generation, i.e., how close are the series of generated phases to the value 180°, was assessed by the mean value of the series of absolute differences between the phase at each stride and 180°, denoted as φ_ABS.

$$\varphi\_\text{ABS} = \overline{|\varphi_i - 180°|}.$$

$$\text{P}\varphi\_\text{ABS} = 100 \times (\varphi\_\text{ABS}/180).$$

4.2.ii Coefficient of variation of the phase [%] (Opal variable)

The coefficient of variation of the mean of φ for each subject depicts the consistency in phase generation. This variable is denoted as φ_{cv} [%].

$$\varphi_{cv} = \frac{SD(\varphi)}{\overline{\varphi}} \ [\%]$$

4.2.iii Phase coordination index (PCI) [%] (Opal and Fatigability variable)

The sum of two percentile values, reflecting both accuracy and consistency of phase generation.

$$PCI = P\varphi_{ABS} + \varphi_{cv}$$

- For example, for patients with PD, PCI values were significantly higher (poorer coordination) during dual-task walking condition compared with usual walking (Plotnik, Giladi, 2008).

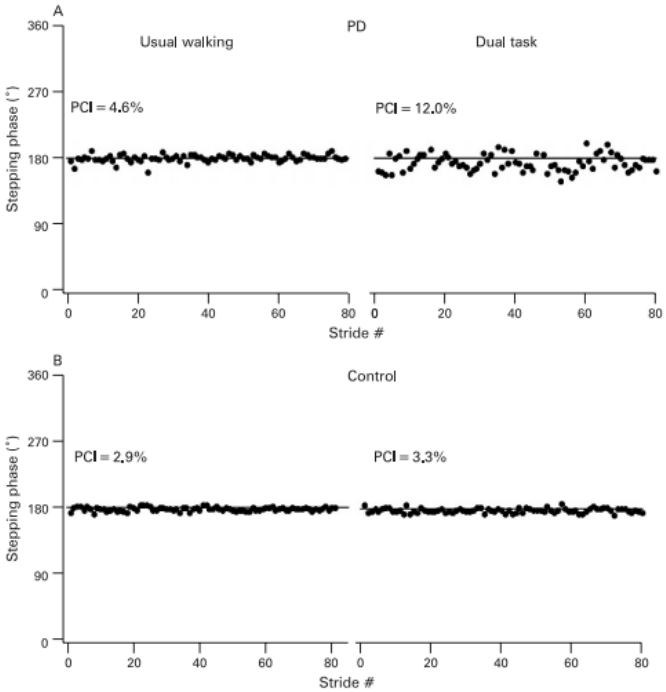


Figure 4: Left–right stepping phase values are plotted for a series of strides. For the patient with Parkinson's disease (A), during dual tasking (DT) (right panel) compared with usual walking (left panel). Data from the control subject showed only minor change in left–right stepping phase pattern in the presence of DT (B).

4.3 Gait Asymmetry [-] (Opal and Fatigability variable)

Swing time ratio that provides a measure of temporal left–right asymmetry. This variable is denoted as GA,

Gait Asymmetry: $100 * \left|\ln\left({}^{Swing_{Time_{Right}}}\big/_{Swing_{Time_{Left}}}\right)\right|$

Values of 0.0 reflect perfect symmetry and higher values reflect greater degrees of asymmetry and the practice values ranging from 0 to 57.

- For example, in a study (Springer, Hausdorff, 2006) for both the PD patients and the elderly fallers GA values were significantly higher during the usual walking condition, as compared with the control group. In addition, for both the PD patients and the elderly fallers, GA significantly increased when they walked and performed a dual task, compared with the usual walking condition.

5. Gait Variability - magnitude

5.1 Stride Time CV [%] (Opal and Fatigability variable)

Stride time CV = 100 * [SD (stride time)]\[Mean(stride time)].

The CV quantifies the magnitude of the stride-to-stride variability but is not sensitive to changes in the ordering of the stride times or the dynamics (Hausdorff, 2009).

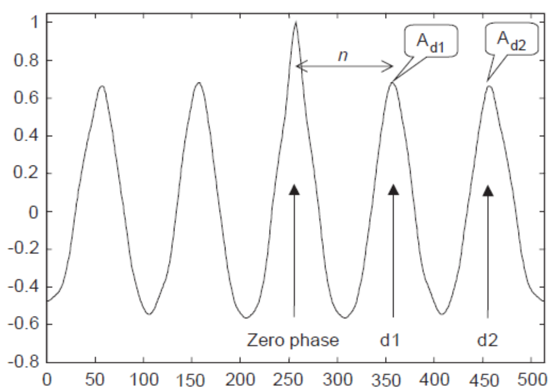
- Stride-time variability reported as the most sensitive gait parameter to distinguish fallers from nonfallers (Moon, Wajda, 2015).

5.2 Step regularity [-] (Opal, Fatigability and AX3 variable)

Expresses the regularity of the acceleration between consecutive steps. Low step regularity indicated that there is a low regularity between steps or a systematic asymmetry between left and right leg. (Nilssen, Helbostad, 2003)

5.3 Stride regularity [-] (Opal, Fatigability and AX3 measures)

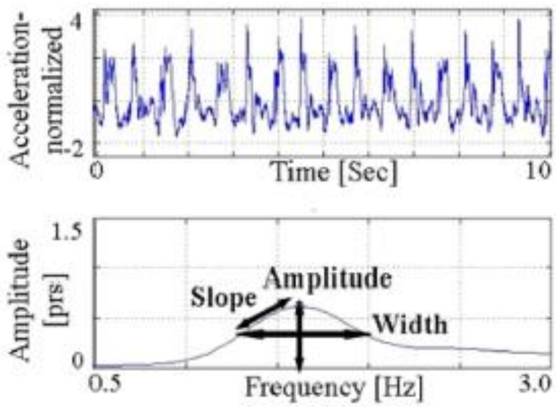
Expresses the regularity of the acceleration between consecutive strides (Nilssen, Helbostad, 2003), (Tura, Raggi, 2010).



(Nilssen, Helbostad, 2003)

Figure 5: Central part of unbiased autocorrelation coefficient sequence from a vertical axis trunk accelerometry time series during walking, including two dominant periods (one stride).d1, 2 is phase lag equivalent to one step and one stride, respectively. Ad1, 2 is autocorrelation coefficient for neighboring steps and stride, respectively.

- For example, older adults displayed significantly less regularity of the anteroposterior accelerations in the AP direction, compared to healthy young adults (Kobsar, Olson, 2013)



(Weiss, Sharifi, 2011)

Figure 6: An acceleration signal on time and frequency domain.

5.4 Dominant frequency of the power spectrum [Hz] (Opal, Fatigability and AX3 variable)

The frequency with the largest amplitude in the signal in a certain band of 0.5-3 [Hz]. For instance, a Fourier transform that decomposes the signal (that is a function of time) into its constituent frequencies, the dominant frequency will simply reflect the average step time that is, approximately 50% of the gait cycle duration. Indeed, lower dominant frequency reflects a higher average stride time.

5.5 Amplitude of the dominant frequency [-] (Opal, Fatigability and AX3 variable)

Depicts the strength of the dominant frequency of the normalized signal. The normalized signal is calculated by removing the signal's mean value and then division of the signal by its standard deviation. The amplitude is obtained by performing Fourier transform on the normalized signal.

- For example, this measure can discriminate between people with Parkinson's disease (PD) and healthy controls in daily life and in lab experiments (Weiss, Sharifi, 2011). It is lower, reflecting a less consistent within bout walking pattern in patients, than in the controls.

5.6 Width of the dominant frequency in the power spectrum [Hz] (Opal, Fatigability and AX3 variable)

The frequency dispersion that expresses the variability of the signal. Whereas average stride time is closely related to the dominant frequency, stride time variability was most closely associated with width.

5.7 Slope of the dominant frequency [1/Hz] (AX3 variable)

Is a combination of the amplitude and the width and reflects both the periodicity and the frequency dispersion.

This measure can discriminate between PD and healthy in daily life and in lab experiments (Weiss, Sharifi, 2011). For example, for PD patients the slope was smaller than the slope of the control group, with a lower slope reflecting greater stride-to-stride variability.

6. Gait Variability - change over time, complexity, dynamics

Above, we described outcome measures of gait variability that reflect the magnitude of the stride-to-stride fluctuations. Here we describe outcome measures that also reflect how gait changes over time, i.e., gait dynamics and complexity.

6.1 Adaptive Fractal Analysis (AFA) (Opal Six Minute Walk variable)

In order to quantify the structure of stride-to-stride variability during the Six Minute Walk, Detrended Fluctuation Analysis (DFA) and Adaptive Fractal Analysis (AFA) can be applied. DFA and AFA are methods that quantify the fractal dynamics or self-similarity of a time series. The method outputs a scaling exponent which can be interpreted in terms of correlations. There are important differences which provide AFA some advantages over DFA. First, AFA can deal with arbitrary, strong non-linear trends, while DFA cannot. Second, AFA presents a more robust method for short time series compared to DFA (Riley, Bonnette, 2012).

The degree of correlation in a time series is indexed by the Hurst exponent, H [-]. Where H = 0.5 indicates a random or short-memory process, $0<H<0.5$ indicates a negatively correlated process, and $0.5<H<1$ indicates a positively correlated long-memory process (Kuznetsov, Bonnette, 2012).

<u>Coordinating Center note</u>: The reading center provides Adaptive Fractal Analysis (AFA) for 3 different fractal scales. The “AFA” variable is quantified over the entire scale of the AFA log-log plot. The “AFA_Short” variable is quantified over the first half of the log-log plot, and the “AFA_Long” variable is quantified over the second half.

In literature, no consistent recommendations are published concerning the minimum number of strides needed to attain accurate results of gait analysis. (Dingwell, Cusumano, 2010) studied the number of strides required, and recommended a minimum of 600 strides, whereas others showed good results of DFA with smaller number of data points (Delignieres, Ramdani, 2006). There is a method of stitching together trials in order to yield longer time series. It's seems to be an appropriate methods in order to distinguish between healthy and pathological gait (Kirchner, Schubert, 2014).

- For example, Kirchner study founded a lower fractal scaling exponents in PD patients compared to control group (Kirchner, Schubert, 2014).

6.2 Harmonic Ratio [-] (OPAL Sway variable, AX3 variable)

The measured accelerations for each stride are analyzed in the frequency domain through a well-established technique of Fourier analysis based on the stride frequency (Bellanca, Lowry, 2013).

Note: The opal system has sensors on the legs from which we derive a different symmetry measures.

The harmonic ratio method can be used to investigate changes in gait patterns. Specifically, step-to-step asymmetry within a stride. In gait research, the harmonic ratio is most commonly extracted from trunk accelerations in the anteroposterior (AP) and mediolateral (ML) directions. In symmetric gait, left and right steps yield equal AP signals but opposite ML signals (Rispens, van Schooten, 2014).

6.3 Lyapunov Exponent [-] (Opal variable)

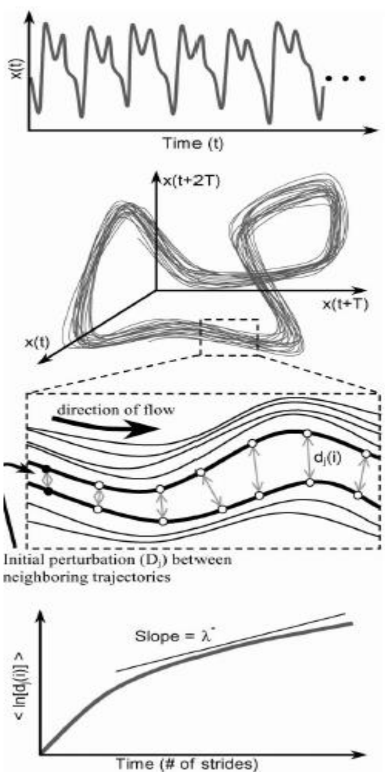
Lyapunov exponent of a dynamic system is quantity the rate of how trajectories separate one from other. In order to understand the stability during walking it is common to use local dynamic stability methods from dynamic system theory. Local dynamic stability is calculated by estimating maximal Lyapunov exponents, which quantify the logarithmic rate of divergence of a system after a small perturbation (Bruijn, Bregman, 2011). The maximum Lyapunov exponent (λ) for a dynamical system can be defined using:

$$d(t) = D\,e^{\lambda_1 t}$$

Where d(t) is the mean displacement between neighboring trajectories in state space at time t, D is the initial separation between neighboring points and λ [-] is the rate of the exponential. λ <0 indicate a stable system while λ >0 indicate an unstable system. λ s and λ L, indicating short and longer term responses, respectively.

It is important to make sure that the data contains the same number of strides for every condition and subject and contain at least 100 strides (Dingwell, Cusumano, 2000)

There is growing evidence that λs, but not λL, may be used to estimate the probability of falling.



(Dingwell, Cusumano, 2000)

Figure 7: Schematic representation of local dynamic stability analysis.

- In-lab gait studies where local dynamic instability was higher in healthy older adults compared with healthy younger adults, and elderly fallers exhibited higher local dynamic instability as compared to elderly non-fallers (Ihlen, 2012; Kang, Dingwell, 2003). These measures also investigate in the daily-life walking of elderly non-fallers, compared with elderly fallers by Ihlen.

6.4 Sample Entropy [-] (Opal and Fatigability measure)

Entropy is a measure that quantifies regularity in time series: the more predictable and less complex a series is, the lower the entropy value (De La Cruz Torres, Sanchez Lopez, 2009).

For a given dimension m, parameter that defining the criterion of similarity r and number of samples N, sample entropy is negative logarithmic of the probability that if two data points with length m have distance <r then data points with length m+1 also have distance<r.

Sample entropy is defined as:

$$\mathrm{SampEn}(m, r, N) = -\log\left(\frac{A(r)}{B(r)}\right)$$

Where, A is the total number of template matches in m dimension; B is the total number of template matches in m+1 dimension (Ramdani, Seigle, 2009).

- For example, it is known that aging reduces entropy and impaired systems exhibit lower entropy than healthy systems (Goldberger, Peng, 2002)

7. Sway

Body sway, a characteristic of standing balance, was assessed in clinic during quiet standing with the Opal sensors worn by participants as they were for the in-clinic walk tests (See Operations Manual chapters 3A and 3N).

7.1 Length

7.1.i Center of pressure (COP) and Center of Mass (COM)

Body sway can be assessed by measuring the deviations in the location of the center of pressure (COP) on the supporting surface by means of a force platform. Movement of the COP is how sway was originally measured and refers to the point at which the pressure of the body over the soles of the feet would be if it were concentrated in one spot (Ruhe, Fejer, 2010; Mancini, Salarian 2012).

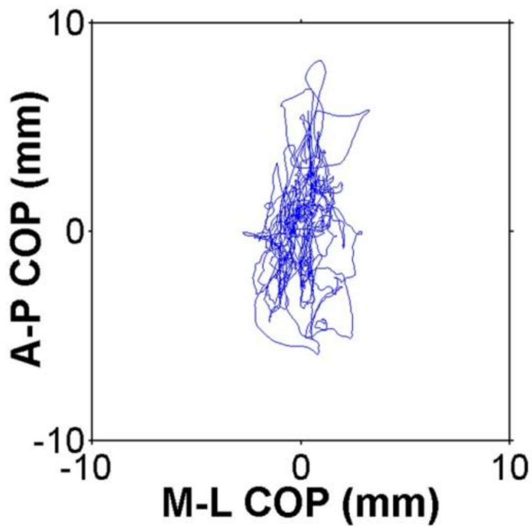


Figure 8: Example sway area plot. COP movement in the mediolateral direction is shown on the X axis, and COP movement in the anteroposterior direction is shown on the Y axis.

Measurement of the COP movements requires force plate which is not always available in the clinical sites. For that reason, a more practical and easy to use method was to estimate the sway using the subject's center of mass, which was obtained with the Opal accelerometer placed on the lower back at the location of the COM.

Note: Sway variables are listed in Appendix III. Measures that contain suffix of AP or ML were calculated from the acceleration signal in the anteroposterior or mediolateral axis of the subject respectively. If there is no suffix then unless stated otherwise the measure was calculated on the magnitude of the acceleration in both directions.

Magnitude(t)=$\sqrt{(Acc\ ML(t))^2 + (Acc\ AP(t))^2}$

7.1.ii Center of mass (COM) displacement path length [m] (Opal Sway variable)

Approximated by twice integrating acceleration signal that obtained from an accelerometer on the lower back (Doheny, Denise, 2012).

7.2 Velocity

7.2.i Center of mass (COM) average velocity [mm/sec] (Opal Sway variable)

Mean velocity has been related to the amount of regulatory activity associated with this level of stability

$$SV\ x = \overline{\frac{|\Delta D\ x|}{\Delta Time}} \quad \ldots x = AP, ML\ or\ hor$$

(Hufschmidt, Dichgans, 1980). Computed by the integration of the AP and ML components of acceleration (Mancini, Horak, 2011).

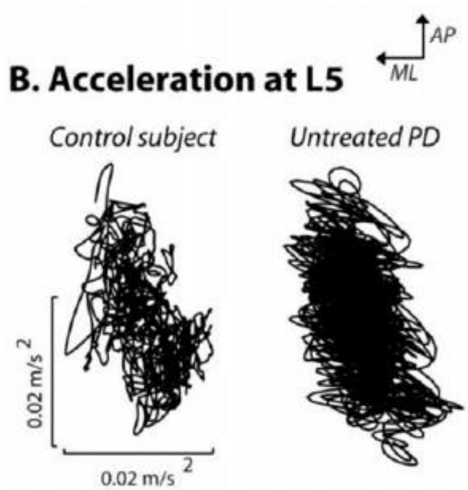
7.2.ii Median absolute deviations (MAD) from center of mass (Opal Sway variable)

Median values of the absolute changes in velocity in the ML and AP axis respectively. From a calculation of the absolute value of the change in velocity, the median value is taken.

$MAD(Velocity) = median(|velocity(t) - median(velocity(t))|)$

7.3 Acceleration

7.3.i Acceleration path length [m/sec^2] (Opal variable)



(Mancini, Horak, 2011)

Figure 9: Acceleration of path length

7.3.ii Root Mean Square Acceleration (RMS) [m/sec^2] (Opal Sway variable)

Quantifies the magnitude of acceleration (Mancini, Horak, 2011). Studies have shown that root mean square (RMS) of the acceleration signal can be sensitive to test conditions (eye closure, standing on one foot), to ageing, and to history of falls (Mancini, Salarian, 2012).

$$RMS = \frac{1}{N}\sqrt{\sum_{t=1}^{N}(Acceleration\ AP(t))^2 + (Acceleration\ ML(t))^2}$$

7.3.iii RMS AP [m/sec^2] and RMS ratio AP [-] (Opal Sway variable)

RMS AP is calculation of RMS on the acceleration in the AP direction.

RMS ratio AP is the ratio between RMS of the acceleration in the AP direction to RMS.

7.3.iv RMS ML [m/sec^2] and RMS ratio ML [-] ((Opal Sway variable)

The same as above, but for the ML axis.

7.4 Frequency

7.4.i Centroidal Frequency [Hz] (Opal Sway variable)

Sway frequency at which the spectral mass is concentrated (Rocchi, Chiari, 2004).

7.4.ii Frequency dispersion [-] (Opal Sway variable)

A unitless measure of variability of the frequency content of the power spectral density (0 for a pure sinusoid, it increases with spectral bandwidth to 1). Quantifies the degree of determinism in the COP or COM displacements.

Frequency dispersion was found to be sensitive to ageing together with mean velocity in the AP direction (Maki, 1990; Prieto, 1996).

7.5 Variability - change over time, complexity, dynamics

7.5.i Adaptive Fractal Analysis (AFA) [-] (Opal Sway variable)

AFA quantifies the structure the fractal dynamics or self-similarity of a time series. It is used for gait to quantify the structure of stride-to-stride variability. The output of the AFA analysis is the Hurst exponent H [-]. Value of 0.5 indicates a random or short-memory process. Previous studies found that patients with PD had a lower fractal scaling exponent than the control group (Kirchner, Schubert, 2014).

7.5.ii Lyapunov Exponent [-] (Opal Sway variable)

A system's sensitivity to initial conditions can be quantified by computing its Lyapunov characteristic exponents (Collins, De Luca, 1994).

The largest Lyapunov exponent provides a measure of the local stability of a dynamical system (Abarbanel , 1996), the system’s sensitivity to initial conditions or its resistance to small internal perturbations, such as the natural fluctuations that occur while maintaining an upright stance (Donker, Roerdink, 2007). For more information see Lyapunov exponent as mention in the gait section.

7.5.iii Sample Entropy [-] (Opal Sway variable)

A method to quantify the regularity of time-series is the sample entropy analysis. A decrease in sample entropy (more regular sway fluctuations) interpreted as a decrease in the effectiveness of postural control.

- For example, COP trajectories were more regular (as indexed by reduced sample entropy) in stroke patients than in healthy older adults and became less regular when performing a secondary cognitive task while standing (Donker, Roerdink, 2007).

7.5.iv Square Mean Jerk [m^2/sec^5] (Opal Sway variable)

The time derivative of acceleration. Commonly viewed as an index of smoothness, the relative smoothness of postural sway can be interpreted as a measure of dynamic stability, reflecting the amount of active postural corrections (Mancini, Salarian, 2012).

$$JERK = \frac{1}{2}\int_0^t \left(\frac{dACCL_{AP}}{dt}\right)^2 + \left(\frac{dACCL_{ML}}{dt}\right)^2$$

- The JERK of sway acceleration was found to be the most sensitive measure to discriminate untreated PD and control subjects (Mancini, Horak, 2011).

Square mean jerk AP and Square mean jerk ML are calculated by the applying the same formula as above only on the AP or ML axis respectively.

7.5.v 95% Ellipse Area [m^2/sec^4] (Opal Sway variable)

Area of the 95% bivariate confidence ellipse, which is expected to enclose approximately 95% of the points on the COM path (Prieto, Myklebust, 1996).

The area of the confidence ellipse is used as a measure of energetic expenditure of the subject to maintain his balance (Rocchi, Sist, 2005).

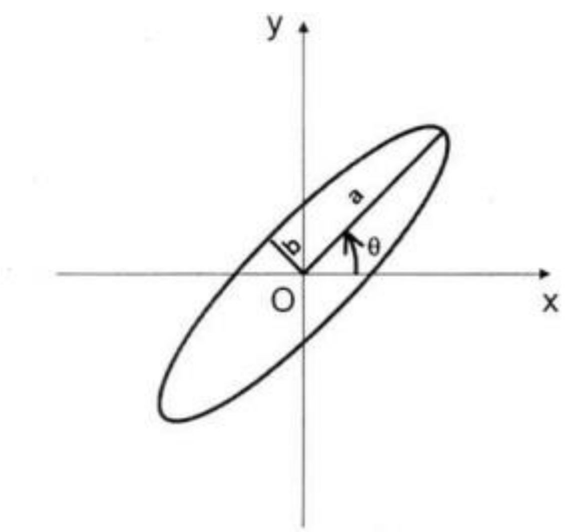


Figure 10: Definition of parameters of ellipse centered at origin (o). x, ML component of COM. y, AP component of COP. ϑ, direction of ellipse with respect to the ML axis. a, the major and b is the minor radii of the 95% confidence ellipse.

- For example, for subjects with Parkinson's disease, ellipse area was larger than normal owing to an increase of sway mostly in the anteroposterior direction.

7.5.vi 95% Ellipse Major & Minor Axes [m/sec^2] (Opal Sway variable)

Length of major and minor axes of the 95% bivariate confidence ellipse. The major axis is shown as “a” and the minor axis is shown as “b” in Figure 10 above.

7.5.vii 95% Ellipse Major Axis Rotation [degrees] (Opal Sway variable)

The angle of rotation from the ML component of the COM to the major axis of the 95% bivariate confidence ellipse. This corresponds to θ, or the angle between the x-axis and “a”, in Figure 10.

7.5.viii Skewness of acceleration in the ML direction [-] (Opal Sway variable)

Measures asymmetry of probability distribution of acceleration. Negative skew indicate that the mass of the distribution is concentrated on the right, and positive skew indicate that the mass of the distribution is concentrated on the left.

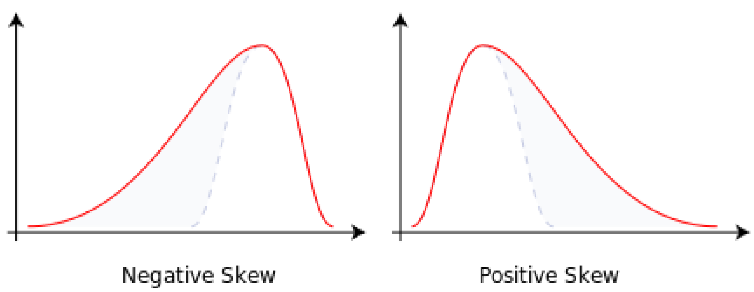


Figure 11: Negative and positive skewness function

ML direction was chosen to be analyzed for two reasons. The first is because in ML direction of movement, the desired signal has lower amplitude than in the AP direction, therefore, the signal-to-noise ratio is lower. The second reason is that measures related to the control of ML stability have been proven of clinical value in assessing fall risk (Palmerini, Rocchi, 2014).

8. AX3 Long-term recordings during daily-living

8.1 AX3 Variables Overview

The variables derived from the AX3 recordings can broadly be divided into two families of metrics, Gait Quality and Activity.

1) Gait quality (the quality of the walking pattern). These variables are calculated using data from walking bouts, defined as detected continuous walking of a minimum duration (See Introductory Notes for definitions of bouts and section 12 for the algorithm for detection of walking bouts). Walking bouts are divided into 30s and 60s segments. AX3 Gait variables are calculated separately for each 30s and each 60s walking bout segment. The median, mean, SD, min, max of each measure are reported on a daily level, using all the walking bouts from that day. AX3 gait variables are only calculated for each day (1 to 7) if there are one or more segments of continuous walking of 30s, or 60s, depending the analysis, for that day.

Gait quality measures can be further subdivided into several subdomains:

a) Pace: e.g., gait speed and step length (will only be provided if the subject's height available).
b) Rhythm, e.g., step time, stride time, cadence, dominant frequency
c) Symmetry, e.g., step regularity, step symmetry, harmonic ratio
d) Variability, e.g., stride regularity, amplitude, width and slope of the peak in the frequency domain.
e) Measurements that reflect the amplitude of the acceleration, e.g, acceleration root mean square, range

Some Gait measures are determined for each of the 3 accelerometer axes (vertical V, medio-lateral ML, anterior-posterior AP). The gait and activity measures are described in further detail below.

See (I Galperin. 2019) for additional description of the process.

2) Activity (e.g., total daily-living physical activity, step counts). Activity measures are calculated using AX3 data from each day (1 to 7) only during periods of AX3 wear time. Activity variables for walking (walking time, number of steps) are calculated from all periods of continuous walking of 3 steps or more (i.e. bouts) regardless of duration and from the full duration of all of the periods of continuous walking.

More information on Activity variables is in Section 10. See Section 12 for detection of wear time.

Note: AX3 Gait and Activity variables in the dataset **V7AX3_DAYS** are calculated for days 1 through 7 only, which are the days for AX3 data collection specified in the study protocol. AX3 Activity variables in the dataset **V7AX3_SUMMARY** are also, with a few exceptions, restricted to using data from days 1 though 7. These variables have the prefix "CC_", and are recommended for use in all analyses. The exceptions are variables with the prefix "ARC_" which may include data from day 0 and day 8. Analyst should calculate additional summary variables from raw days data of interest.

9. AX3 Gait Quality Variables

9.1 Rhythm variables

9.1.i stepTime - Mean step time [sec] (AX3 variable) See further information in section 2.3.

9.1.ii strideTime - Mean stride time [sec] (AX3 variable) See further information in section 2.4.

9.1.iii Dominant frequency of the power spectrum [Hz] (AX3 variable) See further information in section 5.4.

9.1.iv Cadence [steps/min] (AX3 variable)

Cadence (time domain) – $number\ of\ steps * \frac{60\ [sec]}{total\ bout\ length\ [sec]}$

Cadence (frequency domain) – $frq * 60\ [sec]$

See further information in section 2.3.

9.2 Symmetry Variables

9.2.i Step regularity [-] (AX3 variable) See further information in section 5.2.

9.2.ii Step Asymmetry [-] (AX3 variable)

$$\text{step symmetry} = \frac{step\ Regularity}{stride\ Regularity}$$

Closer step symmetry to 1 the more symmetric walk it is. Thus,

$$\text{stepAsym} = |1 - \text{step symmetry}|$$

9.2.iii HR- Harmonic Ratio [-] (AX3 variable) See further information in section 6.2.

9.3 Variability Variables

9.3.i Stride regularity [-] (AX3 variable) See further information in section 5.2.

9.3.ii Width of the dominant frequency in the power spectrum [Hz] (AX3 variable) See further information in section 5.6.

9.3.iii Amplitude of the dominant frequency [g^2/Hz] (AX3 variable) See further information in section 5.5.

9.3.iv Slope of the dominant frequency [g^2/Hz^2] (AX3 variable) See further information in section 5.7.

9.4 Variables that reflect the amplitude of the acceleration during walking

9.4.i Acceleration Range (Rng) [m/sec^2] (AX3 variable)

$$\text{Rng} = \max(\text{acc}) - \min(\text{acc})$$

9.4.ii Root Mean Square Acceleration [m/sec^2] (AX3 variable)

Quantifies the magnitude of acceleration (Mancini, Horak, 2011). Studies have shown that root mean square (RMS) of the acceleration signal can be sensitive to test conditions (eye closure, standing on one foot), to ageing, and to history of falls (Mancini, Salarian, 2012).

$$\mathrm{RMS} = \mathrm{sqrt}(\mathrm{mean}(\mathrm{acc.}^2))$$

9.4.iii Activity Level

Mean RMS of acceleration. This is a gait variable that reflects the amount of energy during walking.

$$\text{Activity level} = \mathrm{mean}(\mathrm{sqrt}(\mathrm{mean}(\mathrm{acc.}^2)))$$

10. AX3 Activity Variables

10.1 Full day variables and variables conditioned on wear time

Activity variables were calculated using data collected during AX3 wear time over a full day (24 hours), periods of non-wear were not included for activity variable calculations. See Section 12 for notes on definitions and algorithms for detection of AX3 wear time, non wear time, upside down wear, wear while lying down and walking.

Summary variables. Calculated variables providing summaries of the activity measures over days 1 to 7 are also available for some measures. In addition, some of the summary Activity variables only use data from days that meet the minimum requirements of 6 hours and 10 hours of wear time. Since recorded wear time on some days can be minimal, the 6 hour and 10 hour wear time variables will give a better representation of a participant's daily activity. Summary variables with the prefix "CC_" are calculated using Day 1 to Day 7. Summary variables with the prefix "ARC_" may include data from day 0 and day 8 (days not included in the study protocol), and for that reason in some cases only the CC variables are provided.

*Additional information on calculated Activity variables may be found in the document MOST DatasetDescription_V7AX3.pdf

10.2 Walking Time [min] and Percent Walking [%] (AX3 variable)

Walking between 00:00-24:00 in each calendar date is calculated using all continuous walks of 3 steps or more.

Percent walking calculated according to the formula

$$Percent\ Walking = 100 \cdot \frac{Walking\ Time\ between\ 00{:}00 - 24{:}00}{Minutes\ Wear\ Time\ between\ 00{:}00 - 24{:}00}$$

10.3 Lying Time [min] and Percent Lying [%] (AX3 variable)

Lying between 00:00-24:00 in each calendar date (only during wear time).

Percent walking calculated according to the formula

$$Percent\ Lying = 100 \cdot \frac{Lying\ Time\ between\ 00:00 - 24:00}{Minutes\ Wear\ Time\ between\ 00:00 - 24:00}$$

10.4 Sitting/Standing Time [Min] and Percent Sitting/Standing Quietly (AX3 variable)

Sitting/standing time between 00:00-24:00 in each calendar date (only during wear time).

Percent Sitting/Standing Quietly calculated according to the formula

$$Percent\ Sitting/Standing = 100 \cdot \frac{Sitting/Standing\ Time\ between\ 00:00 - 24:00}{Minutes\ Wear\ Time\ between\ 00:00 - 24:00}$$

10.5 Other Time [min] and Percent Other time [%](AX3 variable)

Other activities (Not walking, not lying, not sitting/standing quietly) time 00:00-24:00 in each calendar date (only during wear time).

Percent Other time calculated according to the formula

$$Percent\ Other = 100 \cdot \frac{Other\ activities\ Time\ between\ 00:00 - 24:00}{Minutes\ Wear\ Time\ between\ 00:00 - 24:00}$$

Note: The sum of percent walking, lying, sitting/standing quietly and other is 100%.

10.6 Sedentary Time [min] and Percent Sedentary time [%] (AX3 variable)

Sum of Lying and Sitting / Standing between 00:00-24:00 in each calendar date (only during wear time).

Percent Sedentary or - sum of Lying and Sitting / Standing – time calculated according to the formula

$$Percent\ Sedentary = 100 \cdot \frac{Sedentary\ Time\ between\ 00:00 - 24:00}{Minutes\ Wear\ Time\ between\ 00:00 - 24:00}$$

Sections 10.7 to 10.9 describe measures of overall daily-living physical activity calculated for each day.

10.7 Sum SVM Day [mg] (AX3 variable)

Sum of signal vector magnitude of the measured acceleration signal from three axes, normalized by wear time between 00:00-24:00.

SVM= $\sqrt{V^2 + ML^2 + AP^2}$

10.8 Mean SVM Day [mg] (AX3 variable)

Mean of signal vector magnitude, averaged from all 15-second epochs, of the measured acceleration signal from three axes, normalized by wear time between 00:00-24:00.

10.9 Percent Active Day [%] (AX3 variable)

A threshold for activity was defined as the mean value between walking and lying epochs, then the percent activity epochs for each calendar date between 00:00-24:00, was calculated.

10.10 Step Count (AX3 variable)

Sum of steps per calendar date (only during wear time), calculated from all periods of continuous walking of 3 steps or more during time range 00:00-24:00.

11. AX3 Metadata Descriptive Variables

11.1 Day Number (AX3 variable)

A numeric integer identifying the day of an activity measure trial; day number 1 represents the first day of the activity measure trial and subsequent integers up to 7 represent the subsequent days, chronologically.

Note: Day number 1 is defined as the first full day in which participants were instructed to wear the activity monitors. The monitors were not programmed to cease recording until after day number 7. Data may or may not be recorded preceding day 1 (i.e. day 0) and after day 7 (i.e. day 8). The data from day 0 and day 8 recordings are excluded from calculations of summary variables with the prefix "CC_".

Time Start (No variable in data set; for information only)

The starting date and time for which recorded activity data is assessed for activity measures, for a particular day. The time may be limited by the actual data recording, the threshold limits of the variable (i.e. 00:00).

Time End (No variable in data set; for information only)

The ending date and time for which recorded activity data is assessed for activity measures, for a particular day. The time may be limited by the actual data recording, the threshold limits of the variable (i.e. 11:59:59).

11.2 Minutes Recorded (AX3 variable)

The minutes of recorded data, for a given day and for the summary variable for days 1 to 7, between the Time Start and Time End variables.

11.3 Minutes Wear Time (AX3 variable)

The minutes of wear time detected using the reading center algorithm described in section 12.1, for a given day and for the summary variable for days 1 to 7, between the Time Start and Time End variables. Wear time calculated by the Accelerometry Reading Center (ARC) was used in all calculations of variables that depend on the amount of wear time recorded.

11.4 Minutes Non-Wear Time (AX3 variable)

The minutes of recording without any wear time detected, for a given day and for the summary variable for days 1 to 7, between the Time Start and Time End variables. The wear time detection algorithm used by ARC is described in Section 12. The sum of Minutes Wear Time and Minutes Non-Wear Time are equal to Minutes Recorded.

11.5 Minutes Upside-Down Wear (AX3 variable)

The minutes of wear time in which the AX3 monitor was worn upside down are categorized as upside-down wear, for a given day and for the summary variable for days 1 to 7, between the Time Start and Time End variables. The upside-down detection algorithm is described in Section 12. A correction based on flipping the AP and ML axes of acceleration was made for upside-down wear when appropriate.

11.6 Number Of Days (AX3 variable)

The number of calendar days recorded in the time data, for a given participant. Each participant typically has 7 days of activity data recorded regardless of whether any wear time was detected during a calendar day.

11.7 Valid Days 6 Hour (AX3 variable)

Days with at least 6 hours of wear time detected, for a given day and for the summary variable for days 1 to 7, for a given participant.

11.8 Valid Days 10 Hour (AX3 variable)

Days with at least 6 hours of wear time detected, for a given day and for the summary variable for days 1 to 7, for a given participant.

11.9 Number of Walking Bouts (AX3 variable)

The total number of walking bouts, or segments, of 60 seconds detected each day, and that were used in the calculation of gait variables using these respective thresholds for walking bout duration.

Note: If a period of continuous walking was longer than 60s and shorter than 120s, it was trimmed to one 60s bout. Further, periods of continuous walking of 120s or longer were divided into 60s segments (with no overlap) and the excess time that did not last at least 60s was discarded.

12. Notes on Detection Algorithms for AX3 Activity Variables

12.1 Wear Time/Non-Wear Time Detection

Wear time is used in the calculation of AX3 activity variables and to determine valid days (see 11.7 and 11.8).

The Accelerometry Reading Center (ARC) algorithm for wear time uses the acceleration and temperature signals to detect non wear times. Basically, it searches for 10 minutes periods with no movement (std<threshold) and then it's verified if it's a non-wear time by thresholding the change from the average temperature. A period of non wear time ends when movement lasting >1s is detected. All periods during the specified recording intervals (24 hours) that were not classified as non wear were classified as wear time.

The Coordinating Center created a separate algorithm that uses movement, but not temperature, to detect non wear time. This was used as a check on the ARC wear time detection.

12.2 Up Side Down Detection

The algorithm checks whether the sensor is upside down using a threshold on the vertical axis. Then we search for walking segments, there we know how the AP axis should look like if the sensor is positioned correctly and flip the AP or ML acceleration axes accordingly.

12.3 Gait (Walking) Detection

Gait events were estimated from a continuous wavelet transform (CWT, using the cwt MATLAB function) of the vertical acceleration signal which was first filtered, using 4th order Butterworth filter between 0.15 and 4 Hz. The wavelet transform decomposes signals over scaled and translated version of mother wavelet function, in our case Morlet wavelet. After the wavelet transform, all coefficients were summed and the envelope was calculated. A threshold on the summed coefficient signal was then applied to discriminate between gait events and non-gait events.

Note: Walking detection is also applied to the in-clinic walks Opal data to detect walking inside the entire data recording. This uses a different algorithm than the one used for the AX3 daily living data for two reason: the in-clinic walks contain basically three types of data: walks, turns and standing still whereas the daily-living data are much more challenging. The second reason is that the in-clinic walks also include Opal sensors on the lags which are used combined with the sensor on the lower back to detect walking and assess gait.

12.3 Lying Detection

The vertical acceleration axis was divided into sliding windows (window size = 1 sec with overlap of 0.5 sec) from which the mean magnitude values were extracted. If the mean value is under a threshold, the window was determined to be lying position. Lying Time less than 5 minutes was discarded.

Appendix I – Translational Table

	SAS Datasets				
	OPAL			AX3	
	V7OPAL20MWALK	**V7OPAL6MWT**	**V7OPAL6MWT_ Fatigability** (1)	**V7AX3_DAYS**	**V7AX3_SUMMARY**
(See sections referenced below for calculation methods for each variable.)	**Variable Names**			**Variable Names**	
Variables related to Gait Cycle (Section 1.1) For variables not described in the text, contact Dr. Hausdorf's lab for explanation.	StridesNumber, NumberLeftLegSteps, LeftLegMeanTime, LeftLegTimeCV, NumberRightLegSteps, RightLegMeanTime, RightLegTimeCV, StanceRightLegTime, StanceRightLegPercent StanceLeftLegTime, StanceLeftLegPercent	WalkTime, NumberGaitBouts, StridesNumber, StridesNumberWOturns, LeftLegMeanTime, LeftLegTimeCV, RightLegMeanTime, RightLegTimeCV, StanceRightLegTime, StanceRightLegPercent, StanceLeftLegTime, StanceLeftLegPercent	Walk_Time, Number_of_Bouts, Number_of_Bouts_N (1), NumStridesWOturns, NumStridesWOturns_N,	NA/NP^	NA/NP
Average step length [m] (Section 2.1)	AverageStepLength	NA/NP	Step_Length, Step_Length_N	NA/NP	NA/NP
Average velocity [m/sec] (Section 2.2)	AverageVelocity	NA/NP	Speed, Speed_N	NA/NP	NA/NP
Cadence [steps/min] (Section 2.3, 8.1, 9.1.i, 9.1.iv)	Cadence	Cadence	Cadence, Cadence_N	Cadence_timeDomain_<suffix> (2) Cadence_freqencyDomain_<suffix>	
Mean step time [sec] (Section 9.1.i)				stepTime_<suffix>	stepTime_med_Mean (The CC calculated this as a QA check.)
Mean stride time [sec] (Section 2.4, 9.1.ii)	StrideMeanTime	StrideMeanTime	StrideMeanTime, StrideMeanTime_N	strideTime_<suffix>	NA/NP
Average turn duration [sec] (Appendix II)	NA/NP	NA/NP	TurnDurationAvg, TurnDurationAvg_N	NA/NP	NA/NP
Angular velocity maximum peak [deg/sec] (Appendix II)	NA/NP	NA/NP	AngularVelocityMaxPeak AngularVelocityMaxPeak_N	NA/NP	NA/NP
Average double support time [sec] (Section 3.1)	NA/NP	NA/NP	NA/NP	NA/NP	NA/NP
Average double support measured as % from gait cycle (Section 3.1, Appendix II)	NA/NP	NA/NP	DoubleSupport_percent DoubleSupport_percent_N DoubleSupport_percent_CV,	NA/NP	NA/NP

	SAS Datasets				
	OPAL			AX3	
	V7OPAL20MWALK	**V7OPAL6MWT**	**V7OPAL6MWT_ Fatigability (1)**	**V7AX3_DAYS**	**V7AX3_SUMMARY**
(See sections referenced below for calculation methods for each variable.)	**Variable Names**			**Variable Names**	
			DoubleSupport_percent_CV_N		
Average single support time [sec] (Section 3.3, Appendix II)	NA/NP	NA/NP	SingleSupport, SingleSupport_N SingleSupport_CV, SingleSupport_CV_N	NA/NP	NA/NP
Average single support measured as % from gait cycle Section (Section 3.3, Appendix II)	NA/NP	NA/NP	SingleSupport_percent SingleSupport_percent_N SingleSupport_percent_CV, SingleSupport_percent_CV_N	NA/NP	NA/NP
Average swing time [sec] (Section 3.2)	SwingRightLegTime, SwingRightLegPercent, SwingLeftLegTime, SwingLeftLegPercent	SwingRightLegTime, SwingRightLegPercent, SwingLeftLegTime, SwingLeftLegPercent	NA/NP	NA/NP	NA/NP
Step symmetry / assymmetry (Section 4.1, 8.1, 9.2.ii)	StepSymmetry	StepSymmetry	StepSymmetry, StepSymmetry_N	stepAsymV_<suffix>, stepAsymML_<suffix>, stepAsymAP_<suffix>	NA/NP
Percentage of the absolute difference from 180 deg [%] (Section 4.2.i)	Pph_ABS	Pph_ABS	NA/NP	NA/NP	NA/NP
Coefficient of variation of the phase [%] (Section 4.2.ii)	ph_cv	ph_cv	NA/NP	NA/NP	NA/NP
Phase coordination index (PCI) [%] (Section 4.2.iii)	PCI	PCI	PCI, PCI_N	NA/NP	NA/NP
Gait asymmetry (Section 4.3)	GaitAsymmetry	GaitAsymmetry	GaitAsymmetry, GaitAsymmetry_N	NA/NP	NA/NP
Stride time CV [%] (Section 5.1)	StrideTimeCV	StrideTimeCV	StrideTimeCV, StrideTimeCV_N	NA/NP	NA/NP
Step regularity (Section 5.2, 8.1, 9.2.i)	StepRegularity	StepRegularity	StepRegularity, StepRegularity_N	stpRegV_<suffix>, stpRegML_<suffix>, stpRegAP_<suffix>	NA/NP
Stride regularity (Section 5.3, 8.1, 9.3.i)	StrideRegularity	StrideRegularity	StrideRegularity, StrideRegularity_N	strRegV_<suffix>, strRegML_<suffix>, strRegAP_<suffix>	NA/NP

	SAS Datasets				
	OPAL			AX3	
	V7OPAL20MWALK	**V7OPAL6MWT**	**V7OPAL6MWT_ Fatigability** (1)	**V7AX3_DAYS**	**V7AX3_SUMMARY**
(See sections referenced below for calculation methods for each variable.)	**Variable Names**			**Variable Names**	
Dominant frequency of the power spectrum [Hz] (Section 5.4, 8.1, 9.3.ii)	DominantFrequency	DominantFrequency	DominantFrequency, DominantFrequency_N	frqV_<suffix>, frqML_<suffix>, frqAP_<suffix>	NA/NP
Amplitude of the dominant frequency [g^2/Hz] (Section 5.5, 8.1, 9.3.iii)	AmplitudeDominantFrequency	AmplitudeDominantFrequency	AmplitudeDominantFrequency, AmplitudeDominantFrequency_N	ampV_<suffix>, ampML_<suffix>, ampAP_<suffix>	NA/NP
Width of the dominant frequency [Hz] (Section 5.6, 8.1, 9.3.ii)	WidthDominantFrequency	WidthDominantFrequency	WidthDominantFrequency, WidthDominantFrequency_N	wdV_<suffix>, wdML_<suffix>, wdAP_<suffix>	NA/NP
Slope of the dominant frequency [g^2/Hz^2] (Section 5.7, 8.1, 9.3.iv)	NA/NP	NA/NP	NA/NP	slpV_<suffix>, slpML_<suffix>, slpAP_<suffix>	NA/NP
Adaptive fractal analysis (AFA) (Section 6.1)	NA/NP	AFA, AFA_Short, AFA_Long	NA/NP	NA/NP	NA/NP
Harmonic ratio (Section 6.2, 8.1, 9.2.iii)	NA/NP	NA/NP	NA/NP	HRv_<suffix>, HRml_<suffix>, HRap_<suffix>s	NA/NP
Lyapunov exponent (Section 6.3)	LyapunovExponentShortDivergan	LyapunovExponentShortDivergan	NA/NP	NA/NP	NA/NP
Sample entropy (Section 6.4)	SampleEntropy	SampleEntropy	SampleEntropy, SampleEntropy_N	NA/NP	NA/NP
AX3 Gait and Activity variables					
Acceleration range [m/sec^2] (Section 8.1, 9.4.i)	NA/NP	NA/NP	NA/NP	rngV_<suffix>, rngML_<suffix>, rngAP_<suffix>	NA/NP
Root mean square acceleration [m/sec^2] (Section 8.1, 9.4.ii)	NA/NP	NA/NP	NA/NP	rmsV_<suffix>, rmsML_<suffix>, rmsAP_<suffix>	NA/NP
Activity level [m/sec^2] (Section 8.1, 9.4.iii)	NA/NP	NA/NP	NA/NP	ActivityLevel_<suffix>	NA/NP

	SAS Datasets				
	OPAL			AX3	
	V7OPAL20MWALK	**V7OPAL6MWT**	**V7OPAL6MWT_ Fatigability** (1)	**V7AX3_DAYS**	**V7AX3_SUMMARY**
(See sections referenced below for calculation methods for each variable.)	**Variable Names**			**Variable Names**	
Walking time [min] (Section 10.2)	NA/NP	NA/NP	NA/NP	WalkingTime	NA/NP
Lying time [min] (Section 10.3)	NA/NP	NA/NP	NA/NP	LyingTime	NA/NP
Sitting/standing time [min] (Section 10.4)	NA/NP	NA/NP	NA/NP	SittingStandingTime	NA/NP
Other time [min] (Section 10.5)	NA/NP	NA/NP	NA/NP	OtherTime,	NA/NP
Sedentary time [min] (Section 10.6)	NA/NP	NA/NP	NA/NP	SedentaryTime	NA/NP
Percent walking [%] (Section 10.2) **Note**: Summary Activity variables do not include data from Day 0 and Day 8. See Section 10.1.	NA/NP	NA/NP	NA/NP	PercentWalking	CC_PercentWalking, CC_PercWalking6hr, CC_PercWalking10hr, CC_PercWalkingMean6hr, CC_PercWalkingMean10hr
Percent lying [%] (Section 10.3)	NA/NP	NA/NP	NA/NP	PercentLying	CC_PercentLying, CC_PercLying6hr, CC_PercLying10hr, CC_PercLyingMean6hr, CC_PercLyingMean10hr
Percent sitting/standing [%] (Section 10.4)	NA/NP	NA/NP	NA/NP	PercentSittingStanding	CC_PercentSitStand, CC_PercSitStand6hr, CC_PercSitStand10hr, CC_PercSitStandMean6hr, CC_PercSitStandMean10hr
Percent other [%] (Section 10.5)	NA/NP	NA/NP	NA/NP	PercentOther,	CC_PercentOther, CC_PercOther6hr, CC_PercOther10hr, CC_PercOtherMean6hr, CC_PercOtherMean10hr
Percent sedentary [%] (Section 10.6)	NA/NP	NA/NP	NA/NP	PercentSedentary	NA/NP
Sum SVM day [mg]	NA/NP	NA/NP	NA/NP	SumSVMperHr_Day	NA/NP

	SAS Datasets				
	OPAL			AX3	
	V7OPAL20MWALK	V7OPAL6MWT	V7OPAL6MWT_ Fatigability (1)	V7AX3_DAYS	V7AX3_SUMMARY
(See sections referenced below for calculation methods for each variable.)	Variable Names			Variable Names	
(Section 10.7)					
Mean SVM day [mg] (Section 10.8)	NA/NP	NA/NP	NA/NP	MeanSVMperHr_Day	NA/NP
Percent active day [%] (Section 10.9)	NA/NP	NA/NP	NA/NP	PrcActive_Day	NA/NP
Step count (Section 10.10)	NA/NP	NA/NP	NA/NP	StepCount	StepCount_Mean,
AX3 Descriptive Meta-data Variables					
Day number (Section 11.1)	NA/NP	NA/NP	NA/NP	DayNumber	ARC_NumberofDays
Minutes recorded (Section 11.2)	NA/NP	NA/NP	NA/NP	ARC_MinutesRecorded	CC_MinRecorded_Summary, CC_MinRecorded6hr_Summary, CC_MinRecorded10hr_Summary
Minutes wear time (Section 11.3,12)	NA/NP	NA/NP	NA/NP	ARC_MinutesWearTime	CC_MinWearTime_Summary, CC_MinWearTime6hr_Summary, CC_MinWearTime10hr_Summary
Minutes non-wear time (Section 11.4,12)	NA/NP	NA/NP	NA/NP	ARC_MinutesNonWear, ARC_NumberNonWearBlocks	CC_MinNonWear_Summary, CC_MinNonWear6hr_Summary, CC_MinNonWear10hr_Summary, ARC_NonWearDetected, NumberNonwearBlocks_Mean
Minutes upside-down wear (Section 11.5,12)	NA/NP	NA/NP	NA/NP	ARC_MinutesUpsideDownwear, ARC_NumberUpsideDownBlocks	ARC_UpsideDownDetected, NumberUpsideDownBlocks_Mean
Number of days (Section 11.6)	NA/NP	NA/NP	NA/NP	NA/NP	ARC_NumberofDays
Number of valid days 6 hr (Section 11.7)	NA/NP	NA/NP	NA/NP	CC_valid6hr	ARC_validDays6HR
Number of valid days 10 hr (Section 11.8)	NA/NP	NA/NP	NA/NP	CC_valid10hr	ARC_validDays10HR
Number of walking bouts (either 30s or 60s segments) (Section 11.9, 12)	NA/NP	NA/NP	NA/NP	NumberofWalkingBouts	NumberofWalkingBouts_Mean

(1) V7OPAL6MWT_Fatigability dataset contains each parameter processed over the entire 6MWT and for each minute, indicated by suffix _N: _1, _2, _3, _4, _5, _6.

(2) <suffix> is indication of characteristic provided such as med, mean, SD, min and max

(3) NA/NP indicates the measure is not available or not provided for that particular dataset.

Appendix II. Fatigability Variables

Fatigability during the Six Minute Walk. In order to investigate participant fatigability over the course of the Six Minute Walk, a selection of variables was calculated for each minute of the walk, from 1 to 6, to allow examination of changes in parameter values over the course of the walk. These variables are contained in a separate Fatigability data set (**V7OPAL6MWT_Fatigability**). For the variables calculated minute by minute, the overall value of that variable over the entire Six Minute walk was also calculated. Most of the overall variables in the Fatigability dataset are analogous to the Six Minute Walk measures calculated over the entire walk. Although the source examination data is identical, the results for the analogous variables in the Fatigability and Six Minute Walk datasets may differ due to changes in calculation required for fatigability analysis. Specifically, analyses of Six Minute Walk exams were performed by calculating parameters per each 20m straight-line-walking bout and then averaged for an overall value for the entire walk. The analysis for fatigability variables was performed with the turns trimmed from the data and bouts then stitched to get continuous data that represents each minute (from 1 to 6). These are different approaches that will produce small differences in the results for overall parameters and it is expected.

Walk Time (sec)

The minimal criteria for analyzing the 6-minute walk exam for fatigability was at least 420 seconds of data (counted from the beginning of the walk). This inclusion criteria resulted in 89 Opal Six Minute Walk records that were not processed: dataset V7OPAL6MWT, N=2437 ppts vs dataset V7OPAL6MWT_Fatigability, N=2348 ppts. Steps that exceed 6 minutes of walk time were removed from the analysis. Pauses are not removed since they are part of the way the subject is performing the test. The pauses would be reflected in some of the measures like the number of strides and the number of bouts that the subject performed at each min. Stride mean time for example would be less affected by pauses since it is calculated only from the strides while the subject was walking.

Number of Walking Bouts Overall and in Each Minute

The fatigability variables combine data from multiple consecutive walking bouts from the Six Minute Walk exam into one minute segments. To account for bouts that start in one minute and end in the next, the percentage of how much each part of the bout was in each minute is relative to the total time of that bout. As a result, bouts numbers per minute are reported with decimal point (non-integer). In addition, the difference between the total number of bouts and the sum of all the bouts per minute always equal 2.5 (as expected).

Number of Strides Not Including Turns

Strides that start in one minute and end in the next are presented as a half stride. This may result in a small discrepancy between the total number of strides and the sum of all the strides per minute.

Average Turn Duration

Turn duration time is provided only as a fatigability measure. It is a measure of the time during the turns in the 6-minute walk exam.

Angular Velocity Max Peak

The max peak of angular velocity is provided only as a fatigability measure. It is a measure of the angular velocity of the turns in the 6-minute walk exam.

Single and Double Support time

Single and Double Support and time measures are provided only as fatigability variables. Single support time is the average time where a single foot is in contact with the floor, within a single gait cycle. The provided measure (variable SingleSupport) is the absolute number of seconds of the gait cycle that is in single support on average. In addition, the variable (SingleSupport_percent) is the percentage of the gait cycle that is in single support on average. Similarly, a variable for the percentage of the gait cycle that is in double support (DoubleSupport_percent), on average, was calculated. Double support time is the average time where both feet are in contact with the floor within a single gait cycle. There is no separate variable for average double support time.

Appendix III. Sway Variables

Variable name	Variable label [units]	Section
RMS	Root Mean Square Acceleration [m/sec^2]	section 7.3.ii
RMS_AP	Root Mean Square Acceleration AP [m/sec^2]	section 7.3.ii
RMS_ML	Root Mean Square Acceleration ML [m/sec^2]	section 7.3.ii
RMS_ratio_AP	RMS ratio AP [-]	section 7.3.iii
RMS_ratio_ML	RMS ratio ML [-]	section 7.3.iii
Square_mean_jerk	Square mean jerk [m^2/sec^5]	section 7.5.iv
Square_mean_jerk_AP	Square mean jerk AP [m^2/sec^5]	section 7.5.iv
Square_mean_jerk_ML	Square mean jerk ML [m^2/sec^5]	section 7.5.iv
Acceleration_path_length	Acceleration path length [m/sec^2]	section 7.3.i
Acceleration_path_length_AP	Acceleration path length AP [m/sec^2]	section 7.3.i
Acceleration_path_length_ML	Acceleration path length ML [m/sec^2]	section 7.3.i
Displacement_path_length	Displacement path length [m]	section 7.1.ii
Displacement_path_length_AP	Displacement path length AP [m]	section 7.1.ii
Displacement_path_length_ML	Displacement path length ML [m]	section 7.1.ii
CenterMassAvg_velocity	Center of mass average velocity [mm/sec]	section 7.2.i
CenterMassAvg_velocity_AP	Center of mass average velocity AP [mm/sec]	section 7.2.i
CenterMassAvg_velocity_ML	Center of mass average velocity ML [mm/sec]	section 7.2.i
Centroidal_freq_power_AP	Centroidal frequency of the power spectrum AP [Hz]	section 7.4.i
Centroidal_freq_power_ML	Centroidal frequency of the power spectrum ML [Hz]	section 7.4.i
Frequency_dispersion_AP	Frequency dispersion AP [-]	section 7.4.ii
Frequency_dispersion_ML	Frequency dispersion ML [-]	section 7.4.ii
Skewness_ML	Skewness ML [-]	section 7.5.viii
Ellipse_area_95	Ellipse area 95 [m^2/sec^4]	section 7.5.v
Ellipse_rotation_95	Ellipse rotation 95 [degrees]	section 7.5.vii
Ellipse_major_axis_length_95	Ellipse major axis length 95 [m/sec^2]	section 7.5.vi
Ellipse_minor_axis_length_95	Ellipse minor axis length 95 [m/sec^2]	section 7.5.vi
Median_abs_deviation_MAD_ML	Median absolute deviation MAD ML [mm/sec]	section 7.2.ii
Median_abs_deviation_MAD_AP	Median absolute deviation MAD AP [mm/sec]	section 7.2.ii
LyapunovExp_ShortDivergance_AP	Lyapunov exponent short divergance AP [-]	section 7.5.ii
LyapunovExp_LongDivergance_AP	Lyapunov exponent long divergance AP [-]	section 7.5.ii
LyapunovExp_ShortDivergance_ML	Lyapunov exponent short divergance ML [-]	section 7.5.ii
LyapunovExp_LongDivergance_ML	Lyapunov exponent long divergance ML [-]	section 7.5.ii
Sample_entropy_AP	Sample entropy AP [-]	section 7.5.iii
Sample_entropy_ML	Sample entropy ML [-]	section 7.5.iii
AFA_AP	AFA AP [-]	section 7.5.i
AFA_ML	AFA ML [-]	section 7.5.i

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