

10-7-2021

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Recommended Citation

Rohafza M, Soangra R, Smith JA, Ignasiak NK. Self-paced treadmills do not allow for valid observation of linear and nonlinear gait variability outcomes in patients with Parkinson's disease. *Gait Posture*. 2021;91:35-41. <https://doi.org/10.1016/j.gaitpost.2021.10.008>

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Self-paced Treadmills do not Allow for Valid Observation of Linear and Nonlinear Gait Variability Outcomes in Patients with Parkinson's Disease.

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Abstract

Background

Due to the imposed constant belt speed, motorized treadmills are known to affect linear and nonlinear gait variability outcomes. This is particularly true of patients with Parkinson's Disease where the treadmill can act as an external pacemaker. Self-paced treadmills update the belt speed in response to the subject's walking speed and might, therefore, be a useful tool for measurement of gait variability in this patient population. This study aimed to compare gait variability during walking at self-paced and constant treadmill speeds with overground walking in individuals with PD and individuals with unimpaired gait.

Methods

Thirteen patients with Parkinson's Disease and thirteen healthy controls walked under three conditions: overground, on a treadmill at a constant speed, and using three self-paced treadmill modes. Gait variability was assessed with coefficient of variation (CV), sample entropy (SampEn), and detrended fluctuation analysis (DFA) of stride time and length. Systematic and random error between the conditions was quantified.

Results

For individuals with PD, error in variability measurement was less during self-paced modes compared with constant treadmill speed for stride time but not for stride length. However, there was substantial error for stride time and length variability for all treadmill conditions. For healthy controls the error in measurement associated with treadmill walking was substantially less.

Significance

The large systematic and random errors between overground and treadmill walking prohibit meaningful gait variability observations in patients with Parkinson's Disease using self-paced or constant-speed treadmills.

Introduction

Walking is one of the most common activities of daily living. Walking deteriorates with increasing age and with disease, and unsafe walking patterns are associated with the occurrence of falls. Therefore, characteristics of gait are important clinical outcomes. In particular, measures to quantify variability are increasingly investigated, as they distinguish between diseased and non-diseased populations [1], can evaluate treatment success and might enable prediction of future adverse events such as falling [2].

Gait variability can be quantified by the overall magnitude of spatial and temporal variability in the data [3]. This is commonly done by estimating inter-cycle variations in gait derived outcomes, for example, the standard deviation of multiple stride lengths or stride times. However, this linear statistical approach incorrectly assumes that strides are independent of each other [4]. To overcome this limitation, nonlinear methods have been devised that account for the interdependency of consecutive strides. These measures more accurately quantify the temporal structure of gait variability [4-6]. Two commonly used nonlinear methods to evaluate the regularity and self-similarity in gait time-series data are Sample Entropy (SampEn) and detrended fluctuation analysis (DFA), respectively [7, 8].

Both linear and non-linear methods require recording of a large number of consecutive strides to be measured reliably [9-11]. In a confined laboratory space, consecutive strides can either be recorded using special overground (OG) protocols [9, 12] or on motorized treadmills. However, when using treadmills, the Constant Speed (CS) of the treadmill imposes constraints on gait and thereby reduces the magnitude of movement variability, as well as making the temporal structure of gait variability unrealistically regular compared to OG walking [13-15]. The velocity constraint imposed by the treadmill impedes naturally occurring gait velocity fluctuations, which in return leads to these distinct changes in magnitude and structure of gait variability. For example, in response to a given treadmill velocity, participants are required to modulate their step frequency or step length [16]. Therefore, a general recommendation is to avoid CS treadmills when observing gait variability outcomes.

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4 As an alternative, Self-Paced (SP) treadmills have been developed. SP treadmills continuously update
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6 the belt speed depending on the subject's position on the treadmill and thus match the walking speed of
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8 the participant. This feedback-based corrected belt speed seeks to overcome the major limitation of
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10 traditional CS treadmills and can be implemented with varying degrees of sensitivity. For most non-
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12 variability gait outcomes, SP and CS treadmill results are comparable [17, 18]. SP treadmills, due to their
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14 ability to allow for gait velocity fluctuations, may allow for a more realistic, or OG-like, gait variability
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16 pattern to occur. Therefore, SP treadmills could be a useful tool for data collection of long walking trials
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18 to assess linear and nonlinear gait variability outcomes.
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23 The assessment of gait variability is particularly challenging in individuals with Parkinson's Disease
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25 (PD). The influence of CS treadmills on gait variability may depend on the motor control system's
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27 functioning and, therefore, might be exaggerated in patients with neuromotor deficits like PD. The
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29 typical shuffling and unsteady gait of PD corresponds to generally elevated levels of temporal and spatial
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31 magnitude of gait variability [19]. Furthermore, the temporal structure of gait variability deteriorates in
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33 PD. Long-range correlation across consecutive gait cycles breaks down, and walking performance
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35 becomes more random and less structured [20, 21]. Approaches to manage Parkinsonian gait deficits
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37 include providing individuals with PD with external rhythmic cues to re-gain a rhythmic pattern and,
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39 therefore, normalize the deteriorated gait variability [22, 23]. Interestingly, CS treadmills have been used
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41 similarly to provide an external rhythmic cue and restore inadequate levels of gait variability in PD [24].
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43 Therefore, it is likely that the effect of CS treadmills on gait variability outcomes is larger in individuals
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45 with PD than in healthy individuals, as they provide additional external control for the malfunctioning
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47 nervous system to support walking function.
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53 In light of the lack of information regarding the ability of SP treadmills to allow *natural* gait
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55 variability to occur, this comparative study aimed to investigate variability with respect to overground
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57 walking (ground truth). We examined (i) if spatio-temporal linear and nonlinear gait variability outcomes
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59 collected on SP treadmills are more similar to OG walking compared to data collected on CS treadmills in
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4 individuals with PD, (ii) considering OG walking variability as the ground truth variability of the
5 participant, which SP sensitivity setting might result in the most realistic gait variability patterns in
6 individuals with PD and (iii) if SP treadmills also result in more valid spatio-temporal linear and
7 nonlinear gait variability outcomes compared with CS treadmills in individuals with unimpaired gait.
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10 11 12 13 14 **Methods**

15 16 17 *Participants*

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20 Thirteen individuals with PD participated in the study (8 females; mean [SD] age, height, and
21 weight: 71.2 [7.3] years, 172.2 [11.4] cm, 70.4 [13.9] kg). They had been diagnosed for mean 6.9 [SD
22 4.9] years and had a median [minimum; maximum] modified Hoehn & Yahr score of 2 [1; 2.5],
23 representing bilateral symptoms without significant balance impairment. Individuals with PD performed
24 the experiment after intake of their regular anti-Parkinson medication (i.e., ON). To assess unimpaired
25 gait, thirteen healthy control (HC) subjects were also recruited (6 females; mean [SD] age, height, and
26 weight: 24.2 [3.9] years, 171.1 [8.5] cm, 71.5 [13.7] kg). Participants provided written informed consent
27 before participation, and the study protocol was approved by the Chapman University institutional review
28 board and conducted in accordance with the declaration of Helsinki.
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41 *Procedure*

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44 Participants performed at least five walking trials, each of 5–8-minute duration, during one
45 session. The first trial was an uninterrupted OG walking trial, conducted outside along a 0.8km long,
46 relatively straight pavement. The remaining four trials were randomized and performed on a self-paced
47 treadmill (GRAIL, Motek Medical, Hocoma, The Netherlands): CS walking (set at the pace determined
48 during the initial OG trial), default SP mode (SP_{default}), maximally low sensitive SP mode (SP_{low}) and
49 maximally high sensitive SP mode (SP_{high}). The self-paced treadmill algorithm, a proportional-derivative
50 controller, aims to keep a subject within the boundaries of a prescribed anterior-posterior 0.95m space
51 around the center of the treadmill. To achieve this, the average trajectory position from four infra-red
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4 markers on the pelvis (right and left ASIS and PSIS) is the central tenet in controlling the treadmill speed
5 relative to the walking speed. The treadmill belt speed is updated proportionally to a change in the
6 subject's position relative to the treadmill's center and while considering the current gait speed. The goal
7 of the self-pace algorithm is to keep the participant at the center of the treadmill. When participants
8 walked faster the treadmill belt moves faster, and when participants slow down then the moving treadmill
9 belt slows down as well. The different sensitivity settings scale the response of the treadmill in terms of
10 stronger (i.e., SP_{high}) or weaker (i.e., SP_{low}) response to a position change and greater (i.e., SP_{high}) or
11 smaller (i.e., SP_{low}) changes in belt speed [18].
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23 Before the treadmill trials, participants got at least five minutes to familiarize themselves with
24 walking in the self-paced mode. During all trials, participants were instructed to maintain their preferred
25 comfortable walking speed. Consecutive Stride Lengths (SL) and Stride Times (ST) from the dominant
26 foot were recorded using a validated inertial-measurement unit system (APDM Mobility lab, USA) [25].
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30 All data can be found in the supplementary material.
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34 To quantify the response stability of the linear and nonlinear gait variability outcomes (and
35 therefore to determine the extent of error associated with the variability measurement rather than due to
36 the treadmill conditions) HC participants additionally performed a second OG walking trial, which was
37 randomized together with the treadmill trials.
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44 *Data analysis*

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47 For each trial, the first and last five strides were removed and all trials for an individual subject
48 were cropped to the shortest trial of the subject in order to ensure the same data length in the subsequent
49 analysis. The stride times and stride lengths time series data were then analyzed for linear gait variability
50 magnitude, regularity and self-similarity by calculating the coefficient of variation (CV), SampEn and
51 DFA, respectively. For SampEn we used a constant vector length (i.e., m) of 2 and similarity threshold
52 (i.e., r) of 0.2 for all trials [8]. In order to investigate the sensitivity of the SampEn estimation to the input
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4 parameters, additional m and r combinations were tested (see supplementary material) [8]. For DFA,
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6 minimum and maximum window length was set at 16 and a ninth of the total data length, respectively
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8 [26]. Computation of DFA and SampEn were done using customized MATLAB (R2020b, The
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10 Mathworks Inc., Natick, MA) programs.

11 12 13 14 *Statistical analysis*

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16 The results from the OG trials served as the gold standard. All treadmill conditions were
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18 compared to the OG trial. Data were tested for normality and were log transformed where necessary.
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20 Three distinct but complementary approaches were used to quantify the error associated with variability
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22 measurement during the treadmill walking conditions compared to OG: 1) Method Error; 2) Bland and
23
24 Altman analysis; 3) standard deviation of the residuals. 1) Method Error (ME) provides a measure of the
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26 differences between two conditions. The differences between paired conditions are calculated and the
27
28 standard deviation of those individual differences is expressed as a percentage of the mean of the initial
29
30 data set. Systematic error results in small percentage of ME and random error results in larger percentage
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32 of ME. 2) In Bland and Altman analysis, Bias is the mean difference between two conditions, and the
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34 Limits of Agreement (LoA) are the 95% confidence interval of the difference. Bias and LoA represent
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36 systematic and random error effects between two conditions, respectively and here are expressed as raw
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38 values and as a percentage of the measurement mean. 3) Residual standard deviation (RSD) was used to
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40 explore the extent of difference in variability measured during the treadmill conditions controlling for the
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42 variability in the original OG measurement [27]. The results from each treadmill condition were
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44 regressed on the OG results. The standard deviation of the residuals from the regression analysis provides
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46 a measure of the dispersion of the differences in observed values on the treadmill from the values
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48 predicted by the OG condition (the dispersion of differences from a linear relationship between treadmill
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50 and OG values).

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52 To assess the intrasession response stability of the measures during OG walking, ME, Bias, LoA
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54 and RSD were calculated for the two OG walking trials in the HC group. There is currently no evidence
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4 indicating what constitutes an acceptable difference in gait variability when measured during treadmill
5 walking when compared with gait variability measured during overground walking. For data
6 interpretation therefore the magnitude of error for each variability measurement in each condition was
7 compared with the error calculated from the response stability data. Statistical analyses were conducted
8 using MATLAB (R2020b, The Mathworks Inc., Natick, MA) and IBM® SPSS® Statistics (Version 26,
9 IBM, Armonk, NY).

18 Results

21 Individual data for all outcomes are provided in Appendix A. Bland-Altman plots for all
22 comparisons are provided in Appendix B.

26 *Self-paced treadmill validation for PD*

29 The average OG gait speed of the PD group was 1.2 [SD 0.2] m/s. They performed, on average,
30 263 [SD 87] stride cycles during the OG trial. One outlier in the PD group was removed for the ST-CV
31 and ST-DFA analyses. Log transformation was performed for the following variables: stride time DFA
32 SP_{low} , SampEn CS, and CV OG, CS and $SP_{default}$, stride length DFA CS, CV OG, CS and SP_{high} .

35 Method error, bias, limits of agreement, and standard deviation of residuals for stride time and
36 stride length for all comparisons are shown in Table 1 and group and individual values for each outcome
37 are displayed in Figure 1. For stride time, method error was least during SP_{high} and $SP_{default}$ for all three
38 variability measurements. Systematic error (bias) was least during CS for CV and SampEn, and during
39 SP_{high} for DFA. Random error (limits of agreement) was least during SP_{high} and $SP_{default}$. Standard
40 deviations of the residuals were smallest for the CV measure, indicating that the error of the CV
41 measurement during treadmill walking is more dependent upon level of variability during overground
42 walking than for SampEn or DFA. The error associated with all the treadmill conditions far exceeded the
43 intrasession error of the repeated overground trials for stride time (Table 3). Of the three variability
44 measurements, SampEn had the lowest error across all treadmill conditions.

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4 For stride length, there was no consistent pattern across variability measures for method error.
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6 Systematic error (bias) was least during CS for CV and SampEn, and during SP_{low} for DFA. There was
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8 no consistent pattern across variability measures for random error. The CV measurement again
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10 demonstrated the smallest RSD values. The error associated with all the treadmill conditions far exceeded
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12 the intrasession error of the repeated overground trials for stride length (Table 3).
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16 TABLE 1 HERE
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19 *Self-paced treadmill validation for healthy controls*
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22 The average OG gait speed of the HC group was 1.4 [SD 0.1] m/s. They performed on average
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24 445 [SD 24] stride cycles during the OG trials. Log transformation was performed for the stride length
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26 DFA OG and CV CS variables.
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29 Error values for all comparisons for the HC group are shown in Table 2 and values for each
30
31 outcome are displayed in Figure 1. For stride time, method error was least during CS for SampEn and
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33 DFA, and during SP_{low} for CV. Systematic error (bias) was also least during SP_{default} for SampEn and
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35 DFA, and during SP_{low} for CV. There was no consistent pattern across variability measures for random
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37 error. The RSD values were low for both CV and SampEn, indicating that the extent of error in these
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39 measurements during treadmill walking is more dependent upon level of variability during overground
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41 walking than for DFA. The error associated with all the treadmill conditions exceeded the intrasession
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43 error of the repeated overground trials for stride time but to a much smaller extent than in the PD group
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45 (Table 3).
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50 For stride length in the HC group, method error was least during SP_{high} for CV and SampEn and
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52 during SP_{default} for DFA. Systematic error (bias) was least during SP_{low} for CV and SampEn, and during
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54 SP_{default} for DFA. Random error was also least during SP_{low} for CV and SampEn, and during SP_{default} for
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56 DFA. The RSD values were lowest for the CV measurement. The error associated with all the treadmill
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4 conditions exceeded the intrasession error of the repeated overground trials for stride length but again to a
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6 smaller extent than in the PD group (Table 3).
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10 TABLE 2 HERE
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12 *Benchmark response stability*

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15 Response stability for stride time variability estimates was slightly better than for stride length, with a
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17 smaller amount of method error and systematic and random error effects (Table 3). SampEn showed the
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19 highest response stability of the three outcome measures.
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23 FIGURE 1 HERE
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26 TABLE 3 HERE
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28 Discussion

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32 This study investigated if self-paced treadmills avoid the limitations imposed by constant speed
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34 treadmills during the assessment of linear and nonlinear gait variability outcomes in individual with PD.
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36 Stride time outcomes in the PD group were most similar to overground walking using the default or high
37
38 sensitivity self-paced modes. For stride length outcomes however, there was no clear advantage of self-
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40 paced treadmill modes over constant speed. In the healthy control group, any advantage of self-paced
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42 modes over constant speed was highly dependent upon the gait variability measure.
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46 The regulatory effect of motorized treadmills, that act as an external pacemaker, on patients with
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48 Parkinson's Disease has been documented before. Similarly to Warlop and colleagues, we find elevated
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50 levels of magnitude of variability in PD during treadmill walking compared with overground walking that
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52 is not evident in healthy controls [28]. The high extent of error in all outcomes in the PD group indicates
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54 that treadmill use is particularly problematic for the assessment in individuals with PD. For example, the
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56 average effect size (Cohen's d) from comparing stride time variability outcomes in PD and HC is about
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58 0.63 and the effect of antiparkinson medication on temporal gait variability measures was found to be
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4 0.66 [19, 29]. In this study, the effect of the treadmill on the CV of stride time of PD in the best condition
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6 (i.e., SP_{low}) was 0.78. For the overall most similar condition (e.g. spatial sample entropy during CS
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8 treadmill walking), the effect size is still 0.3, or about 50% of the disease or medication effect.
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11 The validity of gait variability outcomes derived from treadmill walking depends on the
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13 reliability of the assessment of the outcome under observation as well as the treadmill pacing mode. A
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15 larger number of strides is required for the reliable evaluation of gait variability compared to mean gait
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17 measures. For linear measures (e.g., coefficient of variation), about 50 strides have been found to result in
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19 reliable variability estimates for healthy persons and PD [9, 12]. However, for sample entropy and DFA,
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21 it is recommended to include not less than 200 and 500 samples for reliable estimates, respectively [8, 10,
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23 11]. The number of samples in the present study exceeded the recommended number for CV and SampEn
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25 but not for DFA in both groups.
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30 This study has some limitations. Participants performed a minimum of six walking trials of at
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32 least five minutes duration. This might have caused fatigue, particularly in the PD group. The potential
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34 influence of fatigue was not evaluated and can therefore not be excluded. However, during the
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36 experiment, participants were frequently asked about their fatigue and were offered rest periods whenever
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38 necessary between trials. Secondly, the HC group was not aged-matched to the PD cohort. There is a
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40 known effect of age on gait variability. The aim of the study was not to compare HC and PD walking, but
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42 to contrast the validity of SP treadmills in a cohort that presumably is very little effected by the treadmill
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44 constraints and can adapt easily to the new condition and a group with well-established sensitivity to
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46 external cues, such as treadmill speed. Therefore, the study provides information about the “best” and
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48 “worst case” when using self-paced treadmills to evaluate gait behaviour in a variety of populations.
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53 In conclusion, for patients with Parkinson’s Disease, temporal gait variability outcomes are best
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55 assessed using default or high sensitivity self-paced treadmills, albeit with generally substantial
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57 differences to overground walking. There is no consistent benefit of self-paced modes over constant speed
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for spatial gait variability. For these reasons, using constant or self-paced treadmills for the assessment of gait variability outcomes in individuals with PD is problematic.

References

- [1] N. Konig, W.R. Taylor, C.R. Baumann, N. Wenderoth, N.B. Singh, Revealing the quality of movement: A meta-analysis review to quantify the thresholds to pathological variability during standing and walking, *Neurosci Biobehav Rev* 68 (2016) 111-119. <http://www.ncbi.nlm.nih.gov/pubmed/27189783>.
- [2] N. Konig, W.R. Taylor, G. Armbrrecht, R. Dietzel, N.B. Singh, Identification of functional parameters for the classification of older female fallers and prediction of 'first-time' fallers, *Journal of the Royal Society, Interface / the Royal Society* 11(97) (2014) 20140353. <http://www.ncbi.nlm.nih.gov/pubmed/24898021>.
- [3] A. Gabell, U.S. Nayak, The effect of age on variability in gait, *J Gerontol* 39(6) (1984) 662-6. <https://www.ncbi.nlm.nih.gov/pubmed/6491179>.
- [4] J.B. Dingwell, J.P. Cusumano, Nonlinear time series analysis of normal and pathological human walking, *Chaos* 10(4) (2000) 848-863. <https://www.ncbi.nlm.nih.gov/pubmed/12779434>.
- [5] J.M. Hausdorff, Gait dynamics, fractals and falls: finding meaning in the stride-to-stride fluctuations of human walking, *Hum Mov Sci* 26(4) (2007) 555-89. <https://www.ncbi.nlm.nih.gov/pubmed/17618701>.
- [6] N. Stergiou, L.M. Decker, Human movement variability, nonlinear dynamics, and pathology: is there a connection?, *Hum Mov Sci* 30(5) (2011) 869-88. <https://www.ncbi.nlm.nih.gov/pubmed/21802756>.
- [7] J.B. Dingwell, J.P. Cusumano, Re-interpreting detrended fluctuation analyses of stride-to-stride variability in human walking, *Gait Posture* 32(3) (2010) 348-53. <https://www.ncbi.nlm.nih.gov/pubmed/20605097>.
- [8] J.M. Yentes, W. Denton, J. McCamley, P.C. Raffalt, K.K. Schmid, Effect of parameter selection on entropy calculation for long walking trials, *Gait Posture* 60 (2018) 128-134. <https://www.ncbi.nlm.nih.gov/pubmed/29202357>.
- [9] N. Konig, N.B. Singh, J. von Beckerath, L. Janke, W.R. Taylor, Is gait variability reliable? An assessment of spatio-temporal parameters of gait variability during continuous overground walking, *Gait Posture* 39(1) (2014) 615-7. <https://www.ncbi.nlm.nih.gov/pubmed/23838361>.
- [10] V. Marmelat, R.L. Meidinger, Fractal analysis of gait in people with Parkinson's disease: three minutes is not enough, *Gait Posture* 70 (2019) 229-234. <https://www.ncbi.nlm.nih.gov/pubmed/30909002>.
- [11] J.M. Yentes, N. Hunt, K.K. Schmid, J.P. Kaipust, D. McGrath, N. Stergiou, The appropriate use of approximate entropy and sample entropy with short data sets, *Ann Biomed Eng* 41(2) (2013) 349-65. <https://www.ncbi.nlm.nih.gov/pubmed/23064819>.
- [12] B. Galna, S. Lord, L. Rochester, Is gait variability reliable in older adults and Parkinson's disease? Towards an optimal testing protocol, *Gait Posture* 37(4) (2013) 580-5. <https://www.ncbi.nlm.nih.gov/pubmed/23103242>.
- [13] J.B. Dingwell, J.P. Cusumano, P.R. Cavanagh, D. Sternad, Local dynamic stability versus kinematic variability of continuous overground and treadmill walking, *J Biomech Eng* 123(1) (2001) 27-32. <https://www.ncbi.nlm.nih.gov/pubmed/11277298>.
- [14] P. Terrier, O. Deriaz, Kinematic variability, fractal dynamics and local dynamic stability of treadmill walking, *J Neuroeng Rehabil* 8 (2011) 12. <https://www.ncbi.nlm.nih.gov/pubmed/21345241>.
- [15] J.H. Hollman, M.K. Watkins, A.C. Imhoff, C.E. Braun, K.A. Akervik, D.K. Ness, Complexity, fractal dynamics and determinism in treadmill ambulation: Implications for clinical biomechanists, *Clin Biomech (Bristol, Avon)* 37 (2016) 91-97. <https://www.ncbi.nlm.nih.gov/pubmed/27380204>.
- [16] J. Bailey, T. Mata, J.A. Mercer, Is the Relationship Between Stride Length, Frequency, and Velocity Influenced by Running on a Treadmill or Overground?, *Int J Exerc Sci* 10(7) (2017) 1067-1075. <https://www.ncbi.nlm.nih.gov/pubmed/29170707>.

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2
3
4 [17] L.H. Sloom, J. Harlaar, M.M. van der Krogt, Self-paced versus fixed speed walking and the effect of
5 virtual reality in children with cerebral palsy, *Gait Posture* 42(4) (2015) 498-504.
6 <https://www.ncbi.nlm.nih.gov/pubmed/26338532>.
7
8 [18] L.H. Sloom, M.M. van der Krogt, J. Harlaar, Self-paced versus fixed speed treadmill walking, *Gait*
9 *Posture* 39(1) (2014) 478-84. <https://www.ncbi.nlm.nih.gov/pubmed/24055003>.
10
11 [19] N. Konig, N.B. Singh, C.R. Baumann, W.R. Taylor, Can Gait Signatures Provide Quantitative Measures
12 for Aiding Clinical Decision-Making? A Systematic Meta-Analysis of Gait Variability Behavior in Patients
13 with Parkinson's Disease, *Front Hum Neurosci* 10 (2016) 319.
14 <https://www.ncbi.nlm.nih.gov/pubmed/27445759>.
15
16 [20] J.M. Hausdorff, Gait dynamics in Parkinson's disease: common and distinct behavior among stride
17 length, gait variability, and fractal-like scaling, *Chaos* 19(2) (2009) 026113.
18 <https://www.ncbi.nlm.nih.gov/pubmed/19566273>.
19
20 [21] T. Warlop, C. Detrembleur, B. Bollens, G. Stoquart, F. Crevecoeur, A. Jeanjean, et al., Temporal
21 organization of stride duration variability as a marker of gait instability in Parkinson's disease, *J Rehabil*
22 *Med* 48(10) (2016) 865-871. <https://www.ncbi.nlm.nih.gov/pubmed/27735982>.
23
24 [22] T.C. Rubinstein, N. Giladi, J.M. Hausdorff, The power of cueing to circumvent dopamine deficits: a
25 review of physical therapy treatment of gait disturbances in Parkinson's disease, *Mov Disord* 17(6)
26 (2002) 1148-60. <https://www.ncbi.nlm.nih.gov/pubmed/12465051>.
27
28 [23] I. Lim, E. van Wegen, C. de Goede, M. Deutekom, A. Nieuwboer, A. Willems, et al., Effects of
29 external rhythmical cueing on gait in patients with Parkinson's disease: a systematic review, *Clin Rehabil*
30 19(7) (2005) 695-713. <https://www.ncbi.nlm.nih.gov/pubmed/16250189>.
31
32 [24] S. Frenkel-Toledo, N. Giladi, C. Peretz, T. Herman, L. Gruendlinger, J.M. Hausdorff, Treadmill walking
33 as an external pacemaker to improve gait rhythm and stability in Parkinson's disease, *Mov Disord* 20(9)
34 (2005) 1109-14. <https://www.ncbi.nlm.nih.gov/pubmed/15929090>.
35
36 [25] R. Morris, S. Stuart, G. McBarron, P.C. Fino, M. Mancini, C. Curtze, Validity of Mobility Lab (version
37 2) for gait assessment in young adults, older adults and Parkinson's disease, *Physiol Meas* 40(9) (2019)
38 095003. <https://www.ncbi.nlm.nih.gov/pubmed/31470423>.
39
40 [26] S. Damouras, M.D. Chang, E. Sejdic, T. Chau, An empirical examination of detrended fluctuation
41 analysis for gait data, *Gait Posture* 31(3) (2010) 336-40.
42 <https://www.ncbi.nlm.nih.gov/pubmed/20060298>.
43
44 [27] C.L. Howard, C. Wallace, J. Abbas, D.S. Stokic, Residual standard deviation: Validation of a new
45 measure of dual-task cost in below-knee prosthesis users, *Gait Posture* 51 (2017) 91-96.
46 <https://www.ncbi.nlm.nih.gov/pubmed/27728877>.
47
48 [28] T. Warlop, C. Detrembleur, G. Stoquart, T. Lejeune, A. Jeanjean, Gait Complexity and Regularity Are
49 Differently Modulated by Treadmill Walking in Parkinson's Disease and Healthy Population, *Front Physiol*
50 9 (2018) 68. <https://www.ncbi.nlm.nih.gov/pubmed/29467673>.
51
52 [29] M.S. Bryant, D.H. Rintala, J.G. Hou, R.L. Collins, E.J. Protas, Gait variability in Parkinson's disease:
53 levodopa and walking direction, *Acta Neurol Scand* 134(1) (2016) 83-6.
54 <https://www.ncbi.nlm.nih.gov/pubmed/26399376>.

Acknowledgements

55 The authors would like to thank the study participants for their time and effort, as well as Kaitlyn
56 Raymundo and Courtney Justus for their assistance during the conduct of the measurements.
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Author contribution

All authors have approved the submitted version of the manuscript. Individual contributions were: MR: Data acquisition, analysis, manuscript preparation; RS: Design, data analysis, manuscript preparation; JAS: data analysis, interpretation, manuscript preparation; NKI: Conception, design, acquisition, analysis, interpretation, manuscript preparation.

Additional information

The authors declare no competing interests. All stride time and stride length data used in this study, as well as the comparison of different input parameter choices during the SampEn analysis can be found at: <https://doi.org/10.36837/chapman.000126>

Figure legends

Figure 1: a) Individual data, and b) Group results for three variability measures (Coefficient of variation (CV), Sample Entropy (SampEn), Detrended Fluctuation Analysis (DFA)) across five walking conditions (Overground (OG), Constant Speed (CS), Default (Self-paced mode), High (high sensitivity self-paced mode), Low (low sensitivity self-paced mode)) for healthy control subjects and Patients with Parkinson's Disease. Error bars are standard errors.

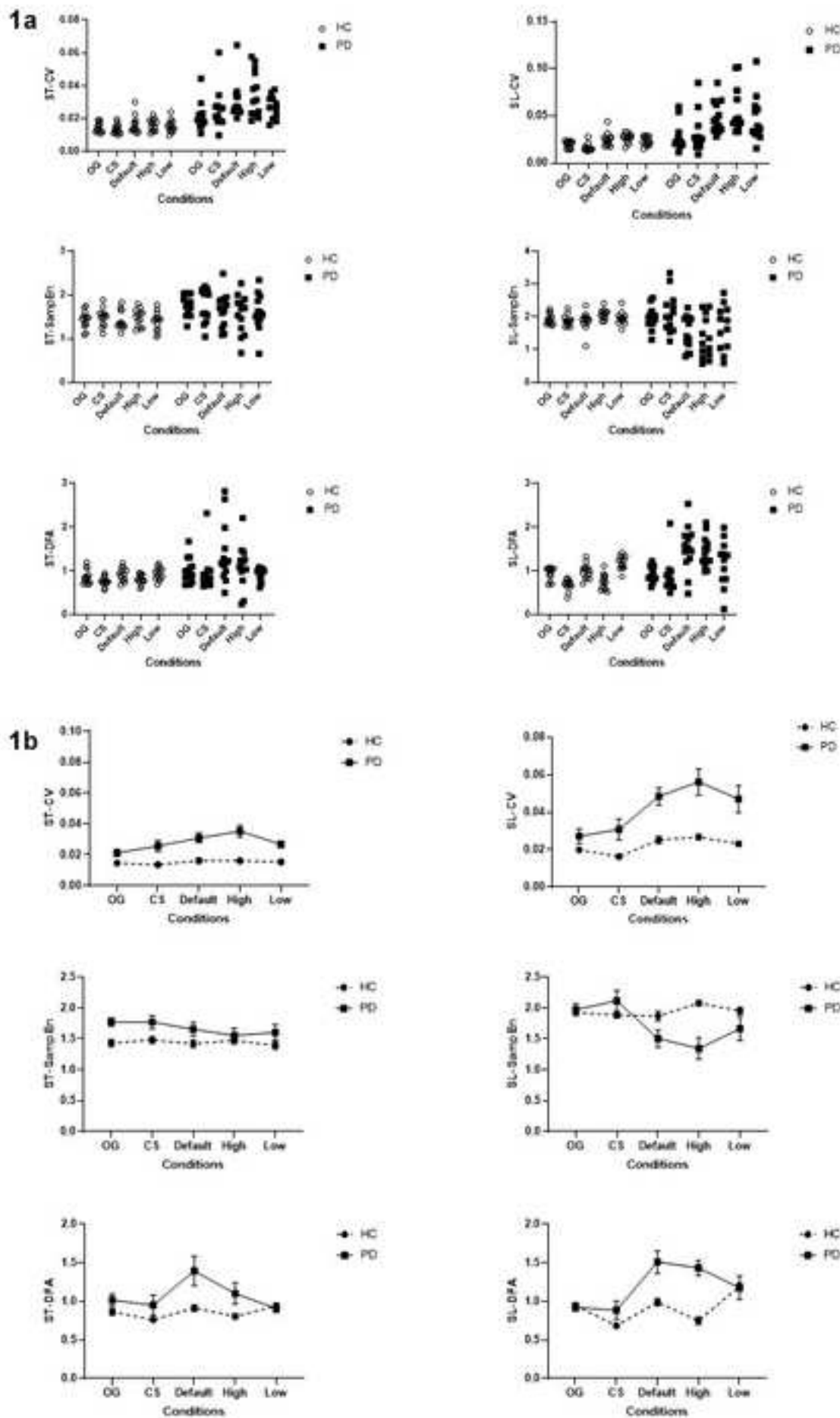


Table 1: Statistical comparison of overground and treadmill trials for the Parkinson's Disease (PD) group. The three variability measures for temporal and spatial outcomes are coefficient of variation (CV), Sample Entropy (SampEn) and Detrended Fluctuation Analysis (DFA).

			RSD¹	ME [95% CI]²	Bias (%)³	LoA (%)⁴
Stride time	CV	OG – CS	0.216	56 [40; 92]	-0.008 (35)	0.040 (155)
		OG – SP _{default}	0.126	40 [29; 67]	-0.009 (37)	0.029 (112)
		OG – SP _{high}	0.014	36 [26; 60]	-0.014 (50)	0.029 (101)
		OG – SP _{low}	0.007	40 [28; 68]	-0.011 (42)	0.029 (111)
	SampEn	OG – CS	0.102	17 [12; 28]	-0.000 (<1)	0.829 (47)
		OG – SP _{default}	0.368	16 [11; 26]	0.115 (7)	0.747 (44)
		OG – SP _{high}	0.381	16 [12; 27]	0.219 (13)	0.747 (45)
		OG – SP _{low}	0.408	18 [13; 30]	0.146 (9)	0.822 (49)
	DFA	OG – CS	1.266	142 [101; 234]	0.468 (60)	3.074 (394)
		OG – SP _{default}	0.531	33 [23; 54]	-0.378 (31)	1.085 (90)
		OG – SP _{high}	0.480	34 [24; 55]	-0.084 (8)	0.982 (93)
		OG – SP _{low}	1.265	78 [55; 132]	0.389 (47)	1.785 (215)
Stride length	CV	OG – CS	0.193	39 [28; 64]	-0.004 (12)	0.031 (108)
		OG – SP _{default}	0.016	34 [24; 56]	-0.021 (56)	0.036 (95)
		OG – SP _{high}	0.239	78 [56; 128]	-0.042 (87)	0.103 (215)
		OG – SP _{low}	0.020	35 [24; 59]	-0.020 (55)	0.035 (96)
	SampEn	OG – CS	0.395	14 [10; 24]	-0.141 (7)	0.808 (40)
		OG – SP _{default}	0.464	20 [14; 33]	0.470 (27)	0.950 (55)
		OG – SP _{high}	0.613	33 [24; 54]	0.631 (38)	1.509 (91)
		OG – SP _{low}	0.537	21 [15; 36]	0.266 (15)	1.057 (59)
	DFA	OG – CS	0.154	83 [59; 137]	0.240 (30)	1.835 (229)
		OG – SP _{default}	0.495	29 [21; 48]	-0.588 (48)	0.971 (80)

OG – SP _{high}	0.331	20 [15; 33]	-0.512 (44)	0.660 (56)
OG – SP _{low}	0.451	31 [22; 53]	-0.247 (24)	0.904 (86)

¹Residual Standard Deviation (RSD)

²Method Error (ME) - % error relative to the mean [95% confidence interval of the % error]

³Bias - mean difference between conditions (difference expressed as % of the mean)

⁴Limits of Agreement (LoA) – 95% confidence interval of the mean difference (confidence interval expressed as % of the mean)

Table 2: Statistical comparison of overground and treadmill trials for the Healthy Control (HC) group. The three variability measures for temporal and spatial outcomes are coefficient of variation (CV), Sample Entropy (SampEn) and Detrended Fluctuation Analysis (DFA).

			RSD¹	ME [95% CI]²	Bias (%)³	LoA (%)⁴	
Stride time	CV	OG – CS	0.003	18 [13; 30]	0.001 (8)	0.007 (50)	
		OG – SP _{default}	0.004	17 [13; 29]	-0.002 (10)	0.008 (49)	
		OG – SP _{high}	0.003	16 [11; 26]	-0.002 (9)	0.007 (43)	
		OG – SP _{low}	0.003	14 [11; 24]	-0.001 (4)	0.006 (41)	
	SampEn	OG – CS	0.049	8 [6; 14]	-0.005 (3)	0.344 (24)	
		OG – SP _{default}	0.043	8 [5; 12]	0.010 (1)	0.297 (21)	
		OG – SP _{high}	0.149	8 [6; 13]	-0.042 (3)	0.321 (22)	
		OG – SP _{low}	0.058	10 [7; 16]	0.039 (3)	0.381 (27)	
	DFA	OG – CS	0.092	12 [9; 21]	0.102 (13)	0.281 (35)	
		OG – SP _{default}	0.152	18 [13; 30]	-0.051 (6)	0.452 (51)	
		OG – SP _{high}	0.098	13 [9; 21]	0.057 (7)	0.294 (35)	
		OG – SP _{low}	0.139	16 [11; 26]	-0.075 (8)	0.392 (44)	
	Stride length	CV	OG – CS	0.087	24 [17; 39]	0.003 (20)	0.012 (66)
			OG – SP _{default}	0.007	22 [15; 36]	-0.005 (23)	0.013 (60)
			OG – SP _{high}	0.004	13 [10; 22]	-0.007 (29)	0.009 (37)
			OG – SP _{low}	0.004	16 [12; 27]	-0.003 (15)	0.010 (45)
SampEn		OG – CS	0.155	7 [5; 11]	0.045 (2)	0.364 (19)	
		OG – SP _{default}	0.279	12 [9; 20]	0.057 (3)	0.647 (34)	
		OG – SP _{high}	0.130	6 [4; 9]	-0.150 (7)	0.310 (15)	
		OG – SP _{low}	0.177	7 [5; 12]	-0.028 (1)	0.390 (20)	
DFA		OG – CS	0.113	20 [14; 33]	0.260 (32)	0.448 (55)	
		OG – SP _{default}	0.167	14 [10; 24]	-0.045 (5)	0.387 (40)	

OG – SP _{high}	0.174	18 [13; 29]	0.196 (23)	0.411 (49)
OG – SP _{low}	0.152	15 [11; 24]	-0.248 (23)	0.436 (41)

¹Residual Standard Deviation (RSD)

²Method Error (ME) - % error relative to the mean [95% confidence interval of the % error]

³Bias - mean difference between conditions (difference expressed as % of the mean)

⁴Limits of Agreement (LoA) – 95% confidence interval of the mean difference (confidence interval expressed as % of the mean)

Table 3: Intrasession response stability for the Healthy Control (HC) group who performed two Over Ground (OG) walking trials during the same day. The three variability measures for temporal and spatial outcomes are coefficient of variation (CV), Sample Entropy (SampEn) and Detrended Fluctuation Analysis (DFA).

		RSD¹	ME [95% CI]²	Bias (%)³	LoA (%)⁴
Stride time	CV	0.002	9 [7; 16]	0.0001 (<1)	0.004 (26)
	SampEn	0.079	6 [4; 9]	0.0109 (<1)	0.221 (16)
	DFA	0.087	8 [6; 13]	-0.0139 (2)	0.189 (22)
Stride length	CV	0.002	10 [7; 16]	0.0006 (3)	0.005 (28)
	SampEn	0.096	4 [3; 7]	-0.0253 (1)	0.235 (12)
	DFA	0.096	10 [7; 17]	0.0592 (6)	0.263 (29)

¹Residual Standard Deviation (RSD)

²Method Error (ME) - % error relative to the mean [95% confidence interval of the % error]

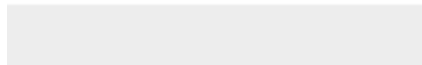
³Bias - mean difference between conditions (difference expressed as % of the mean)

⁴Limits of Agreement (LoA) – 95% confidence interval of the mean difference (confidence interval expressed as % of the mean)

DECLARATION OF INTEREST: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.



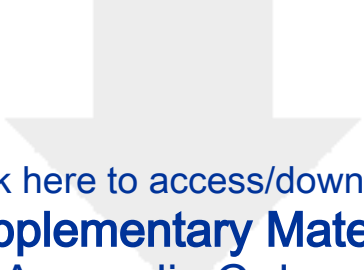
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