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Title: Laboratory-assessed gait cycle entropy for classifying walking limitations among community-dwelling older adults

Year: 2024

Version: Published version

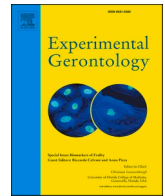
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Please cite the original version:

Mattila, O.-P., Rantanen, T., Rantakokko, M., Karavirta, L., Cronin, N., & Rantalainen, T. (2024). Laboratory-assessed gait cycle entropy for classifying walking limitations among community-dwelling older adults. *Experimental Gerontology*, 188, Article 112381. <https://doi.org/10.1016/j.exger.2024.112381>



Research Paper

Laboratory-assessed gait cycle entropy for classifying walking limitations among community-dwelling older adults

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ARTICLE INFO

Section Editor: Emanuele Marzetti

Keywords:

Gait difficulties

Complexity

Entropy

Accelerometry

ABSTRACT

Among older people, walking difficulty results from actual and perceived declines in physical capacities and environmental requirements for walking. We investigated whether the physiological complexity of the gait cycle covaries with experience of walking difficulty. Walking difficulty, gait speed, and gait cycle complexity were evaluated among 702 community-dwelling older people aged 75, 80, and 85 years who took part in the six-minute walking test in the research laboratory. Walking difficulty for 500 m was self-reported. Complexity was quantified as trunk acceleration multiscale entropy during the gait cycle. Complexity was then compared between those with no reported walking difficulty, walking with modifications but no difficulty, and those reporting walking difficulty. Higher entropy differentiated those reporting no difficulty walking from those reporting walking difficulties, while those reporting having modified their walking, but no difficulty formed an intermediate group that could not be clearly distinguished from the other categories. The higher complexity of the gait cycle is associated with slower gait speed and the presence of self-reported walking difficulty. Among older people, gait cycle complexity which primarily reflects the biomechanical dimensions of gait quality, could be a clinically meaningful measure reflecting specific features of the progression of walking decline. This encourages further investigation of the sensitivity of gait cycle complexity to detect early signs of gait deterioration and to support targeted interventions among older people.

1. Introduction

Reduced walking ability is associated with aging, which often precedes major mobility limitations (Mänty et al., 2007). Modification and experienced difficulty in walking are adaptations to reduced physical capacity and increased subjective demands of the environment (Mänty et al., 2007; Rantakokko et al., 2016b). Among older people, walking slower, using walking aids, and taking breaks during walking may help to sustain community mobility at a previous level despite declining physical capacities (Rantakokko et al., 2017; Rantakokko et al., 2016b; Rantakokko et al., 2016a; Skantz et al., 2021). On the other hand, maladaptive changes of reducing or giving up walking certain distances are associated with loss of activity and full participation in society (Skantz et al., 2020).

Changes in walking ability are monitored using self-assessments or performance measures. Self-assessments are easy to collect; have good validity; and capture the person's immediate experiences of walking in their daily habitat (Fried et al., 2000; Mänty et al., 2007). However, gait performance measures, such as tests on habitual and maximal gait speed, allow comparison between people in standardized conditions (Perera et al., 2006). Self-assessments and gait speed serve as broad indicators of walking ability but lack precision in causal insight. They integrate widely physical, psychological, and behavioral factors influencing gait quality, but do not permit determination of the source for possible defects in gait. Direct or indirect signals from physiological systems measured during gait could provide more understanding of the causes and allow more focused interventions.

The reduced complexity in the dynamics of physiological systems has

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<https://doi.org/10.1016/j.exger.2024.112381>

Received 20 November 2023; Received in revised form 11 February 2024; Accepted 15 February 2024

Available online 22 February 2024

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been associated with aging, disease, and fatigue (Lipsitz and Goldberger, 1992; Pethick et al., 2021; Vaillancourt and Newell, 2002). Complexity is represented in the measurable output from the physiological systems as fluctuating signals with irregular structures and fractal-like behavior (Lipsitz and Goldberger, 1992; Pethick et al., 2021; Vaillancourt and Newell, 2002). Entropy, as a measure of physiological complexity, has been applied in the interpretation of biological signals from the neuromuscular system (Pethick et al., 2021). Lower values of entropy have been observed with older people compared to young in isometric force generation, torque, and EMG (Challis, 2006; Fiogbé et al., 2021; Kang and Dingwell, 2016; Vaillancourt and Newell, 2003). Similarly, lower entropy values in isometric force production are observed in Parkinson's patients, compared to healthy controls (Flood et al., 2019; Vaillancourt et al., 2001). Contrary to the previous, is the finding of higher entropy in older people in a task of generating sinusoidal force pattern with finger abductors, compared to young (Vaillancourt and Newell, 2003). This is hypothesized to be the result of the benefit of less complexity in maintaining optimal output for performing tasks with oscillatory dynamics (Pethick et al., 2021). Gait complexity can distinguish neurological conditions, e.g. patients with Parkinson's disease having higher entropies of body accelerations in laboratory gait than healthy controls (Castiglia et al., 2023). It also differentiates fallers and non-fallers (Ihlen et al., 2018; Ihlen et al., 2016; Riva et al., 2013), but the associations of entropy differences are not conclusive (Bizovska et al., 2017) and vary between methods and measurement environments.

Building on the theoretical base of complexity in biological signals (Lipsitz and Goldberger, 1992; Vaillancourt and Newell, 2002) the intrinsically oscillatory dynamics of gait should display higher entropy for people with more gait difficulty compared to those with less gait difficulty when no environmental and task demand pressures are present (Vaillancourt and Newell, 2002). The theory suggests that the entropy of trunk motion could be more directly linked to the generation of rhythmic and repetitive walking in the nervous system and, therefore, trunk motion entropy could reveal underlying changes in the neuromuscular system when people modify their walking or perceive walking difficulty. If trunk motion entropy were to describe the early changes in the generation of gait, it could provide a valuable tool to identify targets for early interventions and mitigate walking limitations.

We have previously shown that self-reported walking difficulty predicts further disability (Rantakokko et al., 2013; Skantz et al., 2021; Skantz et al., 2020). We hypothesize that the complexity of the gait cycle, assessed with the Refined Composite Multiscale Entropy (RCMSE) (Costa et al., 2003; Wu et al., 2014) from the acceleration signal of the trunk, can be used to describe biomechanical gait quality, which potentially increases with aging. We also postulate that gait complexity measures will enable us to differentiate between older people not experiencing walking difficulty, those reporting walking modifications but no difficulty, and those experiencing walking difficulty.

Therefore, this study aimed to investigate whether gait cycle complexity covaries with perceived walking difficulty and to examine the discriminative capacity. We also wanted to evaluate the associations of gait entropy with other key gait quality metrics, including habitual walking speed (Fried et al., 2000), stride time variability (Hausdorff, 2005), and within-stride step asymmetry (Hodt-Billington et al., 2008) for distinguishing among different categories of walking limitations.

2. Material and methods

2.1. Study participants

The interview and measurements of this study were carried out in the 'Active Ageing—resilience and external support as modifiers of the disablement outcome' (AGNES) observational cross-sectional cohort study in 2017–2018 (Rantanen et al., 2018). The study covered three population-based age cohorts (75, 80, and 85) from the Jyväskylä area in Central Finland, comprising a total of 1021 participants. The inclusion

criteria for the participants were being community-dwelling, having the willingness to participate, and being able to communicate. The exclusion criteria were not willing to participate and inability to communicate in a meaningful way. The study included a home interview on quality of life, physical condition, and life habits; a daily life survey wearing two body-attached accelerometers; and a visit to a laboratory at the University of Jyväskylä. Attrition in the different phases of the AGNES study and the analysis of non-respondents are described in detail elsewhere (Portegijs et al., 2019). 798 participants, wearing an upper trunk mounted accelerometer, participated in the 6-min walking test during laboratory measurements. From these, all relevant data for complexity analysis were available from 702 participants, who form the sample of this study. All participants provided informed consent by the Helsinki Declaration.

2.2. Perceived walking limitations, physical, and cognitive health

The study included a home interview of life circumstances and behavior, together with the Short Physical Performance Battery (SPPB) test (Guralnik et al., 1994) and a laboratory visit with extensive physical examination including lower extremity force testing, and a 6-minute walk test (Lipkin et al., 1986).

2.2.1. Perceived walking limitations

Perceived walking difficulty and walking modifications were evaluated using two questions (Fried et al., 1996; Mänty et al., 2007). The first question was: 'Do you have difficulty walking half a kilometer?' The response options were: (1) able to manage without difficulty, (2) able to manage with some difficulty, (3) able to manage with a great deal of difficulty, (4) able to manage only with the help of another person, and (5) unable to manage even with help. Participants who responded with option (1) indicating no difficulty walking a half kilometer were then asked a follow-up question about possible walking modifications: 'Have you noticed any of the following changes when walking half a kilometer due to your health or physical functioning?' The changes indicated were: (a) having stopped walking this distance, (b) walking slower, (c) resting during walking, (d) using an aid, and (e) reducing the frequency of walking this distance.

Concurring with experience of difficulty walking a half kilometer, identifies those with prominent walking difficulty. Those reporting changes in the walking task in the second question form an intermediate group between the groups of experienced walking difficulty and no perception of difficulty. This intermediate group has been found to have an increased risk of manifesting further mobility limitations (Mänty et al., 2007). Participants who reported no difficulty in walking 500 m were assigned to the category 'intact walking' (intact). Those reporting at least some difficulty walking 500 m were classified as having 'walking difficulty' (difficulty). All others, who reported no difficulty but mentioned at least one modification (a)-(e), were categorized as having 'walking modifications' (modifications).

2.2.2. Participant characteristics

The number of participants in the three walking categories was 460, 139, and 103 for intact, modifications, and difficulties groups, respectively. In addition to age, body height, and mass, cognitive impairment, number of chronic conditions, and years of education are reported from the AGNES-study examinations (Rantanen et al., 2018). Cognitive impairment was assessed using the 19-item Mini-Mental State Examination (MMSE) with a maximum score of 30 (a higher score indicating better functioning) (Folstein et al., 1975; Rantanen et al., 2018). Cognitive decline is related to neurological gait disorders and expressed in gait variability (Hausdorff, 2005; Snijders et al., 2007). As a general descriptor of health status, the number of physician-diagnosed chronic conditions based on a list of diseases was reported by each participant (Rantanen et al., 2018). Years of education were used to describe the socioeconomic status of the participants (Rantanen et al., 2018). Some

participants were missing data for some of the characteristics variables but were included in the analysis if data for complexity analysis was available. The participant characteristics are given in Table 1.

2.2.3. Physical performance tests

A modified Short Physical Performance Battery (SPPB) (Guralnik et al., 1994), carried out during home interviews, was used to characterize balance and lower extremity strength in the participant population. The test includes standing balance, walking speed over a 3-m distance, and the ability to rise from a chair. Participants were scored between 0 and 12 if at least two of the three tests were completed. A higher score indicates better performance.

During the laboratory visit, gait characteristics were derived from the six-minute walk test with habitual walking speed. Participants walked for six minutes on a 20-meter straight flat corridor, and the distance in meters was recorded (Rantanen et al., 2018). Standardized instructions, encouragement, and time left in the test at every minute were provided during the test. Additionally, the maximal isometric knee extension force was measured from the dominant lower limb with a chair dynamometer (Metitur LTD, Jyväskylä, Finland). The highest force from at least three attempts was chosen for analysis (Rantanen et al., 1997).

2.3. Accelerometer recordings

During the walk test, an electrocardiograph (ECG) recorder, used in a daily life survey in AGNES study, that also includes a tri-axial accelerometer (14-bit ±16 g, 100 Hz, eMotion Faros 180, Bittium Corporation, Oulu, Finland) was attached on the sternum, or diagonally on the left side of the chest under the breast, depending on the participant's anatomy, and comfort of the placement. The sensor was covered with a self-

Table 1
Participant characteristics (N = 702) stratified for the three perceived walking limitations groups.

Characteristic	Missing	Intact	Modified	Difficulty	p*
		n = 460 (66 %)	n = 139 (20 %)	n = 103 (15 %)	
Sex	0				0.001
Men		217 (47.2 %)	44 (31.7 %)	36 (35.0 %)	
Women		243 (52.8 %)	95 (68.3 %)	67 (65.0 %)	
Age	0				<0.001
75		266 (57.8 %)	59 (42.4 %)	35 (34.0 %)	
80		132 (28.7 %)	53 (38.1 %)	32 (31.1 %)	
85		62 (13.5 %)	27 (19.4 %)	36 (35.0 %)	
SPPB score	2	10.9 (1.3)	9.9 (1.7)	8.7 (2.3)	<0.001
MMSE score	3	27.6 (2.2)	27.1 (2.6)	27.2 (2.1)	0.040
Chronic cond. (count)	0	2.8 (1.7)	3.5 (1.9)	4.5 (2.1)	<0.001
Education (years)	2	12.0 (4.3)	11.1 (4.1)	10.9 (3.8)	<0.001
					p [†]
Height (cm)	2	165.2 (8.9)	162.7 (8.5)	162.7 (8.9)	0.358
Body mass (kg)	2	72.0 (12.1)	75.9 (11.4) [†]	75.9 (14.1) [†]	<0.001
Knee extension strength (N)	3	368 (112)	313 (105) [†]	290 (110) [†]	<0.001

No differences were found between the Modified and Difficulty groups.

* Kruskal-Wallis test.

† Two-way-ANOVA adjusting for sex.

[†] Difference to Intact group (p < 0.05) after adjusting for sex.

adhesive film. For participants not taking part in the daily life survey the sensor was attached to a chest strap holding a heart rate sensor to be worn during the laboratory visit. The ECG signals were not analyzed in this study.

For the gait characteristics and entropy calculated from vertical acceleration, the vertical acceleration was recomputed to compensate for the different alignments of the sensors, using the method presented by Vähä-Ypyä et al. (2018). All original sensor axis values were filtered with 2nd order Butterworth low-pass filter with 0.5 Hz cutoff frequency. Then vertical acceleration component was computed using,

$$a_v = \frac{x_i x_F + y_i y_F + z_i z_F}{\sqrt{x_F^2 + y_F^2 + z_F^2}}$$

where x_i, y_i and z_i are the measured acceleration components in the sensor frame and x_F, y_F and z_F are the low-pass-filtered values at the same moment. All gait characteristics were calculated only for the straight sections of the six-minute walk. The first two steps were removed before and after each turn from the time series to exclude acceleration and deceleration phases before turns. The anteroposterior acceleration was filtered with a moving mean and negative peaks in the acceleration used to identify the turning points. The data series were visually checked and missing turning points were manually added if needed. Using the detection of initial contacts (IC) the first two steps before and after the turn were removed from the analysis.

2.4. Gait characteristics

Gait speed was estimated from the distance covered during the 6-min walk test. The ICs of the gait cycle (McCamley et al., 2012), spatio-temporal gait parameters of cadence and stride time variability (Godfrey et al., 2015; Zijlstra and Hof, 2003), and trunk movement regularity during step, and stride and gait symmetry (Sym_{gait}) (Hodt-Billington et al., 2008; Moe-Nilssen and Helbostad, 2004) were computed with scikit-digital-health (SKDH, ver. 0.12.0), an open-source software package for Python (Adamowicz et al., 2022). The procedures are briefly described below.

2.4.1. Initial contacts and stride time variability

For the computation of the initial contacts, the vertical acceleration signal was first integrated and then differentiated with a Gaussian filter. The ICs were determined as the times of the minima of the smoothed signal (McCamley et al., 2012). The ICs were used to determine the cadence, defined as the average of 60s/step time (the time between two consecutive ICs), used in the normalization of acceleration time-series between subjects (see Section 2.4.3), and stride times, i.e. time passed between three consecutive ICs, and the stride time variability taken as the standard deviation (SD) of all recorded strides (Stride t SD).

2.4.2. Gait symmetry

Trunk movement regularity during step and stride was calculated as the first and second dominant period of the autocorrelation of the acceleration signal, with values close to 1.0 indicating regularity and much <1.0 indicating irregularity. Trunk movement symmetry (Sym_{gait}) was defined as,

$$Sym_{gait} = A_{d2} - |A_{d1}|,$$

where A_{d1} and A_{d2} are the first and second dominant peaks of the autocorrelation of the acceleration signal. Sym_{gait} close to zero represents symmetry between sides, and values away from zero indicate asymmetry (Hodt-Billington et al., 2008; Moe-Nilssen and Helbostad, 2004).

2.4.3. Entropy

To describe the gait complexity, we used refined composite multi-scale entropy (RCMSE) for vertical and horizontal acceleration. The

RCMSE algorithm is based on sample entropy (Richman and Moorman, 2000). SE is calculated by creating template vectors with a length of m from the time-series x_i ,

$$x_i^m = \{x_i, x_{i+1}, x_{i+2}, \dots, x_{i+m-1}\},$$

and counting the matches between template vectors with a distance smaller than tolerance r ,

$$n_{k,m}^r = \frac{1}{N-m} \sum_{j=1}^{N-m} n_{k,m,j}^r,$$

where the distance between two vectors is defined as the maximum norm of the difference between two vectors (d_{ij}),

$$d_{ij}^m = \max(\|x_i^m - x_j^m\|),$$

and counting the number of matches, n . The SE is defined as the natural logarithm of the ratio between the number of matches for template vectors $m+1$ and m ,

$$SE(x, m, r) = -\ln \frac{n^{m+1}}{n^m},$$

Multiscale entropy (MSE) (Costa et al., 2002) adds a scale dimension to SE. The original time series is coarse-grained by averaging non-overlapping segments of length τ , and SE is calculated for each coarse-graining scale. Refined composite multiscale entropy (RCMSE) (Wu et al., 2014) repeats the MSE for all possible coarse-graining segmentations for scale τ (from 1 to τ). The entropy is obtained from the SE of the ratio of the mean number of matches for m and $m+1$ with scale τ ,

$$RCMSE(x, \tau, m, r) = -\ln \left(\frac{\sum_{k=1}^{\tau} n_{k,\tau}^{m+1}}{\sum_{k=1}^{\tau} n_{k,\tau}^m} \right),$$

The RCMSE method is more robust for short time series, producing fewer cases of zero matches that could lead to undefined entropy values (Wu et al., 2014). The implementation was ported from Matlab to Python using the code from previously published supplementary material (Ihlen et al., 2016).

The sample entropy (SE) decreases with increasing sampling frequency when applied to cyclical patterns (McCamley et al., 2018). Therefore, to examine the entropy of the gait cycle, there needs to be an equal number of samples per step for each participant. We normalized the number of samples per step by downsampling the data series of each participant with a ratio of the subject's cadence (c_i) to the highest cadence ($c_{high} = 136.2$ steps/min) among the participants. The downsampling frequency for each participant, calculated from the cadence ratio, was,

$$f_{cr} = \frac{c_i}{c_{high}} f_n,$$

where f_n (= 100 Hz) is the nominal sampling frequency of the accelerometer.

The vertical (a_v , see Section 2.3) and resultant horizontal acceleration (a_h) were used in the entropy calculations due to the varying placement of the acceleration sensor between subjects, making the data unsuitable for analyzing the anterior-posterior and medial-lateral directions separately in the horizontal plane. The horizontal acceleration was calculated from the overall resultant from measured accelerations (a_x, a_y, a_z),

$$a_R = \sqrt{a_x^2 + a_y^2 + a_z^2},$$

and further, the horizontal resultant acceleration from,

$$a_h = \sqrt{a_R^2 - a_v^2},$$

RCMSE was calculated for the vertical and resultant horizontal from the normalized acceleration signals (see above) from each straight-walking segment, and the segments were averaged for the final entropy value. We used template vector lengths (m) of 2, 3, 4, 5, 6, and 8 and similarity threshold (r) of 0.2, 0.25, 0.3, 0.35, and 0.4 times the standard deviation of vertical and horizontal accelerations (SD_v and SD_h), and coarse-graining scales (τ) ranging from 1 to 20 (the mean of τ samples). The results for multiple scales are reported with $m = 2-5$ and $r = 0.3 * SD_{[v, h]}$. All parameter combinations are provided in the Appendix A, including all similarity thresholds and $m = 6$ and 8. With a coarse-graining scale τ ranging from 1 to 20, and with the resampling for equalizing the data series between participants to 44.1 samples per step, the combination of coarse-graining and the template vector length covers segment lengths ($m * \tau$) corresponding from 2.2 % of the gait cycle ($m = 2, \tau = 1$) to approximately 1.12 gait cycles (112 %, $m = 5, \tau = 20$). With the resampling for normalization mentioned above, and gait speeds of participants being below 1.8 m/s, this created an acceleration time series with over 1000 samples for each 20 m stretch, a number well within the recommended range of samples (200–2000) for reliable entropy estimates (Delgado-Bonal and Marshak, 2019; Yentes et al., 2013; Yentes and Raffalt, 2021). Additionally, the use of RCMSE provides further confidence in the entropy values (Wu et al., 2014).

To produce a single entropy value that incorporates information from different scales of RCMSE, we used the first principal component from Maximum Variation Principal Component Analysis (PCA) over all the calculated scales to quantify vertical and horizontal entropies (Pitulainen et al., 2021), referred to as RCMSE-V-PC1 and RCMSE-H-PC1 from here on. The PCA analysis was done from RCMSE analysis with $m = 4, r = 0.3 * SD_{[v, h]}$, and $\tau = 1-20$, following the parameterization of Ihlen et al. (2016). These were used in the Receiver Operating Characteristic (ROC) analysis of the gait characteristics.

2.5. Statistics and software

The AGNES -study was estimated, a priori, for 80 % power to observe 5 % differences in the mean of the continuous variables between cohorts with a sample size of 650 when the standard deviation was approximated to be a third of the mean (Rantanen et al., 2018).

Descriptive characteristics of the participants and their gait, grouped by perceived walking limitations, are presented as percentages for categorical variables and as means with standard deviations (SD) for continuous variables. The continuous variables were tested for normality using the Shapiro-Wilks test and by visualizing the distributions with quantile-quantile plots. Perceived walking limitation groups were compared with Two-way-ANOVA or Kruskal-Wallis tests, and pairwise comparisons with Tukey's test or Pairwise Wilcoxon signed-rank test. Partial Spearman correlations, controlling for sex, were calculated to examine relationships between gait speed and entropies with other key gait characteristics (Stride t SD, Sym_{gait}). Spearman correlation between cadence and entropies was calculated to evaluate the influence of the normalization procedure. The entropy values for each combination of m and τ are reported here (and in the Appendix A) with the mean and confidence intervals at a 95 % level.

Univariate ROC analysis was conducted for the selected gait characteristics, along with associated ROC curves for those with intact walking, walking modifications, and walking difficulty. The three-class classification was done with the macro-averaged One-vs-One (OvO) strategy, where each class is compared to the other with each class getting equal weight. The class comparisons are assigned with binary classifier (0 vs. 1) as follows: Intact vs. modifications, intact vs. difficulties, and modifications vs. difficulties. The area-under-curve AUC, describing the overall performance of the classifier, accuracy, and the cutoff points based on the closest-to-(0,1) criterion (Perkins and

Schisterman, 2006) are reported from the ROC analysis.

Preprocessing, gait characteristics, and RCMSE computations were carried out with Python 3.10 (Van Rossum and Drake, 2009) using the numpy (1.26.2) package (Harris et al., 2020). All statistical analyses and PCA were performed using R 4.3.1. (R Core Team, 2023), and main results were produced with rstatix (0.7.2) (Kassambara, 2023), and ROCR (1.0.11) (Sing et al., 2005) packages.

3. Results

Table 1 provides an overview of the general characteristics of the participants. The maximum isometric knee extension force and SPPB scores are highest, and the number of chronic conditions is lowest among those with intact walking, and intermediate among those with walking modifications while those with walking difficulty have the highest number of chronic conditions and lowest knee extension force and SPPB scores. The MMSE scores do not differ between the walking

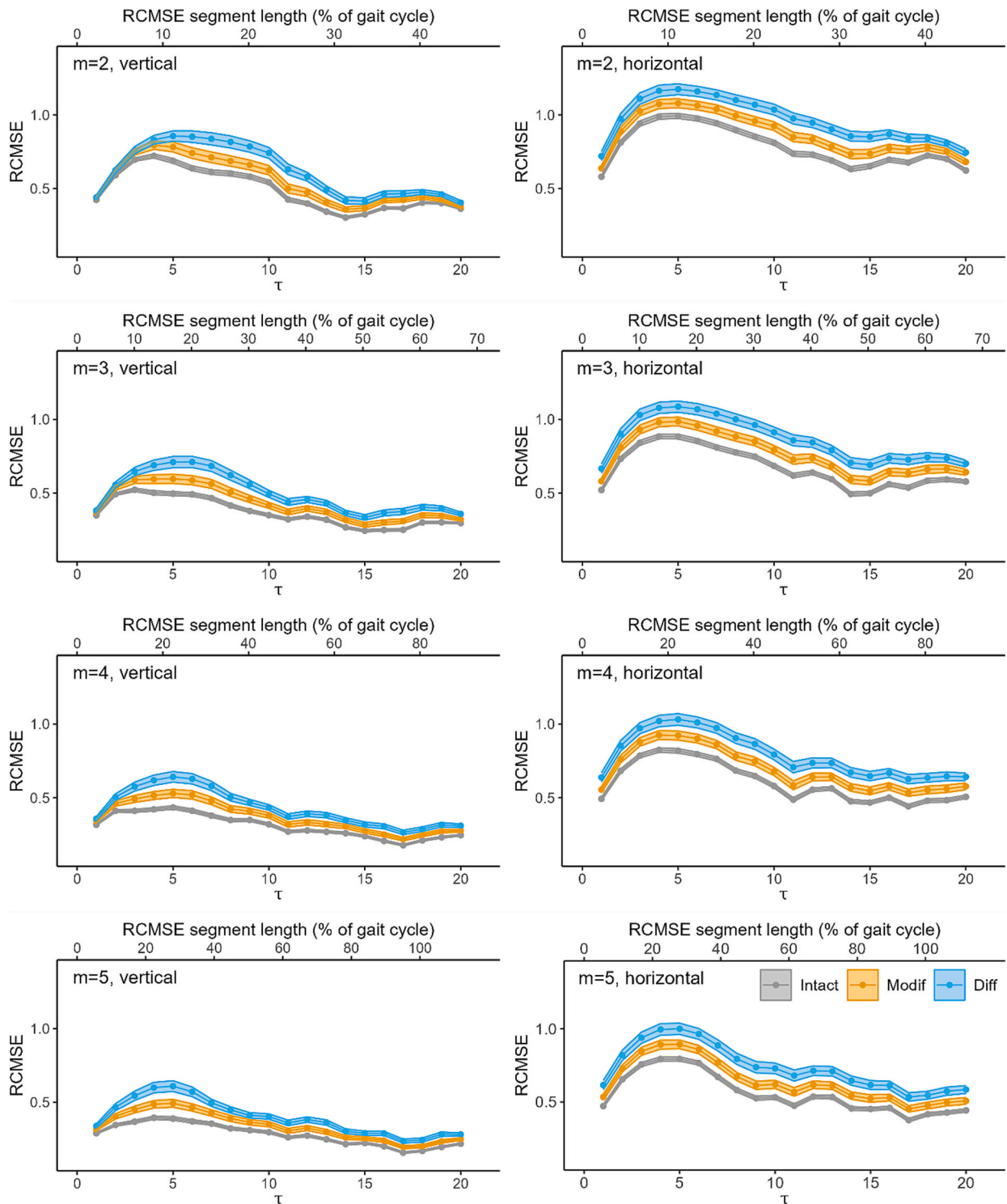


Fig. 1. The mean and 95 % confidence intervals of RCMSE values for intact, modified, and difficulty groups, of vertical (left) and horizontal (right) trunk accelerations for $m = [2, 3, 4, 5]$ and coarse-graining parameters $\tau = 1-20$ and similarity threshold $r = 0.3 \cdot SD_{[v, h]}$.

limitation classes.

Fig. 1 displays the entropies for each combination of m (2, 3, 4, and 5), $r = 0.3 \cdot SD_{[v, h]}$ (vertical/horizontal), and τ (1–20) along with the respective proportion of the gait cycle, and with 95 % confidence intervals. The highest values of RCMSE are in the segment lengths of 10–30 % of the full gait cycle, irrespective of embedding vector length m . The RCMSE-H-PC1 is higher than RCMSE-V-PC1 throughout the gait cycle and displays leveling of the values later than RCMSE-V-PC1.

Fig. 2 shows the box plots and group differences for the gait variables. All parameters were able to differentiate between the walking limitation groups ($p < 0.05$). RCMSE-V-PC1, $StrideT_{var}$, and Sym_{gait} show higher values for those with walking modification and even higher for those with walking difficulties when compared to the intact group. The values of the first principal component of PCA from the horizontal trunk acceleration displayed similar distributions with the vertical acceleration within the walking limitation groups. Differences between the groups were all significant with $p < 0.05$.

Fig. 3 shows the RCMSE-V-PC1 for the three age cohorts (75, 80, and

85 years) and for the walking limitation groups split between men and women. RCMSE-V-PC1 is higher for those with more walking difficulties and increases with age. Within sexes, the group differences in walking limitations and age cohorts remain. Between sexes, the women display higher entropy in all age cohorts, and in walking limitation groups except for those experiencing walking difficulties, where there was no significant difference between the sexes.

The OvO ROC analysis results are presented in Table 2. The classification accuracy varies between 0.57 and 0.88 for intact vs. difficulty. Gait speed has the highest AUC of 0.88. AUC for RCMSE-V-PC1 and RCMSE-H-PC1 have an AUC of 0.83 and 0.81, respectively. For the classification Intact vs. modifications only gait speed displays a high AUC of 0.70, while other gait parameters show values between 0.51 and 0.64. Similarly, for classification modifications vs. difficulties, gait speed shows an AUC of 0.74 and other parameter values between 0.66 and 0.68. The ROC curves of gait speed, RCMSE-V-PC1, RCMSE-H-PC1, $Stride t SD$, and Sym_{gait} for classifications against intact class are shown in Fig. 4.

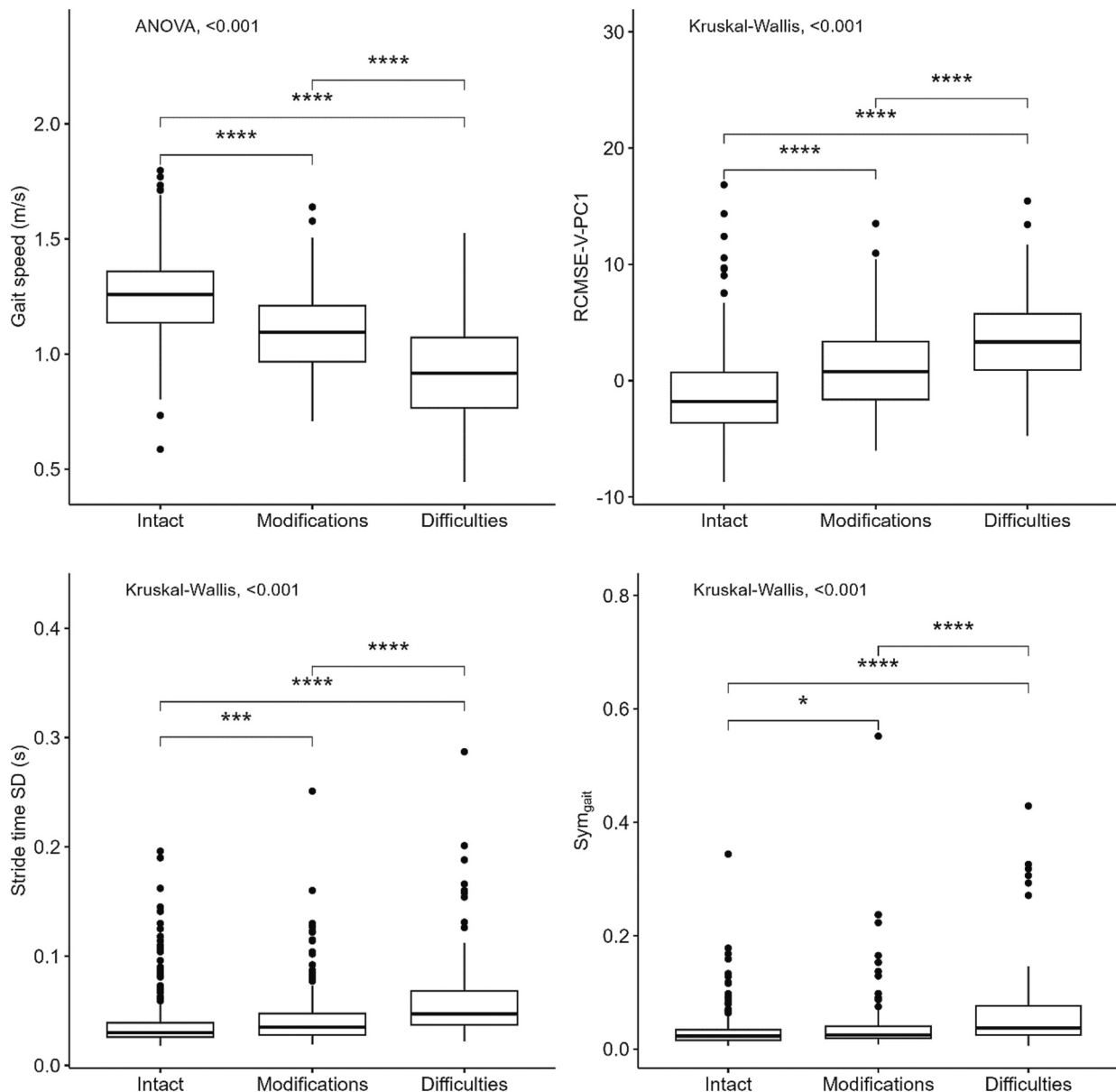


Fig. 2. Distributions of gait speed, RCMSE-V-PC1, $Stride t SD$, and Sym_{gait} , the statistical significance of differences between groups (Kruskal-Wallis), and pairwise comparison (Wilcoxon). * ($p < 0.05$) ** ($p < 0.01$) *** ($p < 0.001$) **** ($p < 0.0001$).

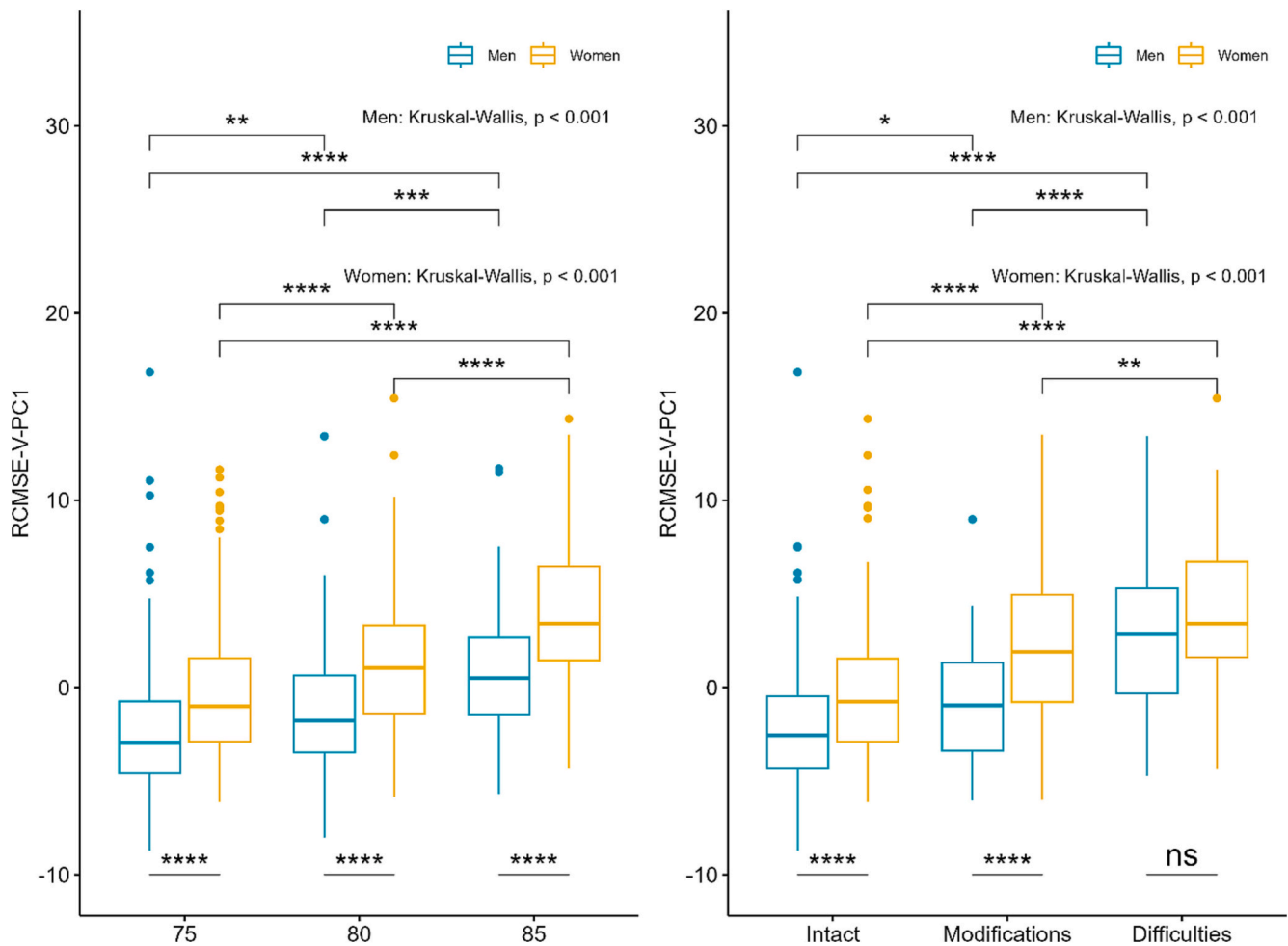


Fig. 3. Distributions of RCMSE-V-PC1 for men and women grouped with age cohort (left) and with walking limitation class (right). Statistical significance of differences between groups (Wilcoxon) is marked with non-significant (ns) ($p > 0.05$) * ($p < 0.05$) ** ($p < 0.01$) *** ($p < 0.001$) **** ($p < 0.0001$).

Table 2

AUC with 95 % confidence intervals, accuracy, and cutoff value based on closest-to-(0,1) criterion for three-class OvO ROC analysis of gait speed, RCMSE-V-PC1 and RCMSE-H-PC1 ($m = 4$, $r = 0.3 * SD_{[v, h]}$, $\tau = 1-20$), Stride t SD and Sym_{gait} between perceived walking limitation classes of intact walking, walking modifications and walking difficulties.

	Intact vs. difficulties			Intact vs. modified			Modified vs. difficulties		
	AUC AUC [95 % CI]	Acc	Cutoff	AUC AUC [95 % CI]	Acc	Cutoff	AUC AUC [95 % CI]	Acc	Cutoff
Gait speed (m/s)	0.88 [0.84,0.93]	0.83	1.09	0.74 [0.69,0.79]	0.69	1.16	0.74 [0.68,0.81]	0.67	1.03
RCMSE-V-PC1	0.83 [0.78,0.88]	0.80	1.45	0.67 [0.62,0.73]	0.61	-0.90	0.68 [0.61,0.74]	0.65	2.57
RCMSE-H-PC1	0.81 [0.75,0.86]	0.75	1.04	0.67 [0.61,0.73]	0.64	-0.34	0.67 [0.60,0.74]	0.64	2.67
Stride t SD (s)	0.76 [0.71,0.80]	0.72	0.04	0.61 [0.55,0.66]	0.63	0.04	0.66 [0.59,0.73]	0.67	0.04
Sym_{gait}	0.57 [0.66,0.77]	0.65	0.03	0.57 [0.51,0.62]	0.51	0.02	0.66 [0.59,0.70]	0.65	0.03

Controlling for sex the Spearman rank correlations between gait speed and the other gait characteristics show correlations ($p < 0.05$) with RCMSE-V-PC1: gait speed -0.59 and -0.69 , RCMSE-H-PC1 0.66 and 0.62 , Stride t SD 0.57 and 0.62 , and $Sym_{gait} - 0.56$ and -0.56 , for men and women, respectively. Similarly, the correlations of gait speed were: RCMSE-H-PC1 -0.59 and -0.59 , Stride t SD -0.38 and -0.42 , and $Sym_{gait} 0.42$ and 0.50 . The correlation between cadence and entropies was: RCMSE-V-PC1 -0.36 and RCMSE-H-PC1 -0.35 .

4. Discussion

We found that perceived difficulty walking and slow walking speed are associated with more complex trunk motion patterns during the gait cycle. Additionally, our research suggests that gait cycle entropy is more strongly correlated with stride time variability and gait symmetry compared to habitual gait speed, pointing towards a potential neuromuscular origin. To our knowledge, this is the first study to examine the associations between the entropy of body acceleration patterns of the

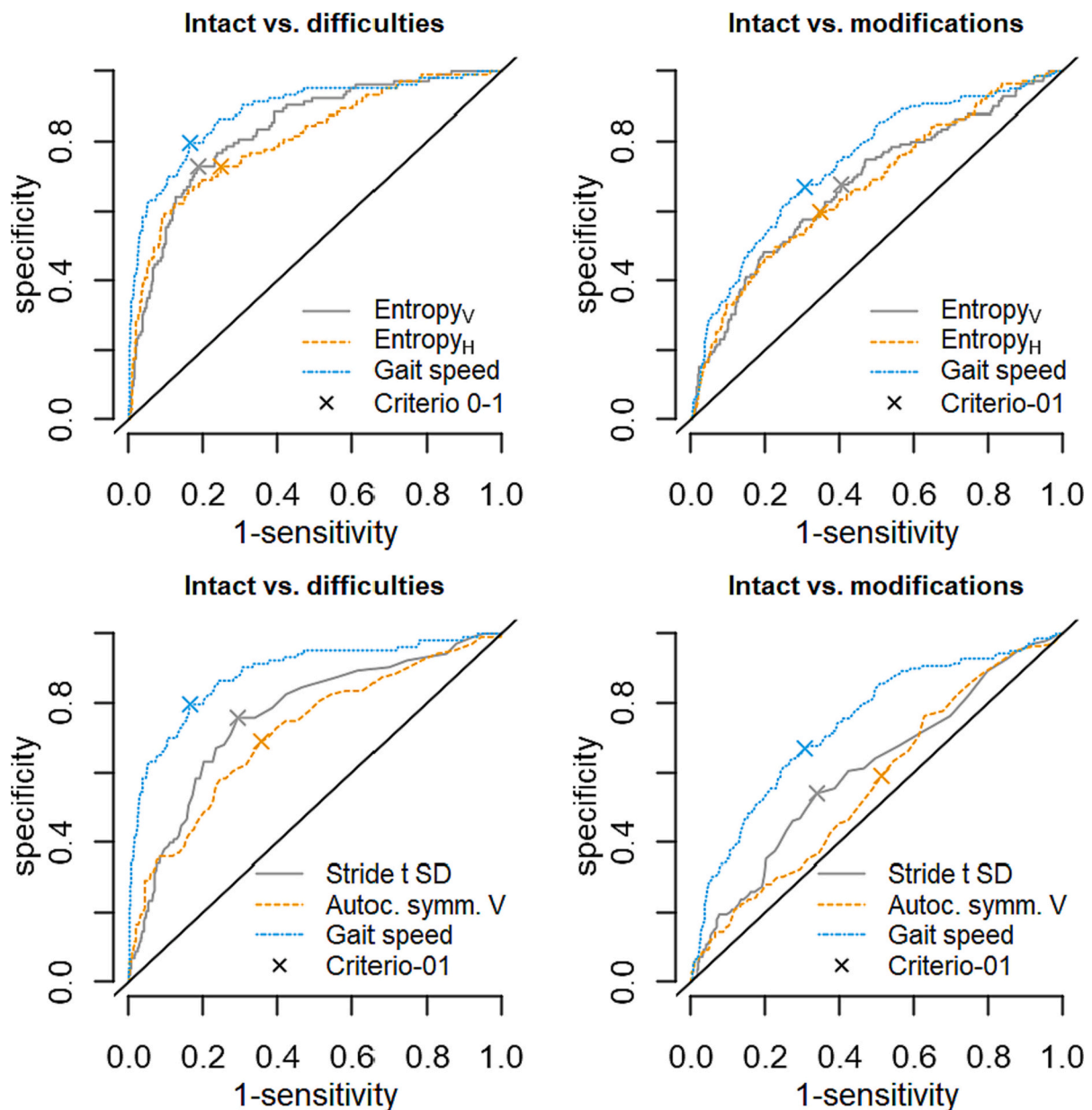


Fig. 4. ROC curves of gait speed, RCMSE-V-PC1, RCMSE-H-PC1, Stride t SD, and Sym_{gait} from vertical acceleration for binary classifiers between Intact vs. difficulties and intact vs. modifications.

gait cycle and perceived walking difficulty.

Our results are in line with the hypothesis of increased complexity in oscillatory tasks related to the degradation of the physiological system (Vaillancourt and Newell, 2003; Vaillancourt and Newell, 2002), in the absence of additional task demands. In level overground walking in a laboratory environment, we observed higher entropy values in vertical trunk accelerations during the gait cycle for those modifying their walking and further those experiencing walking difficulties, compared to those experiencing no changes or difficulties. The overlapping distributions of gait cycle entropy between walking difficulty groups show that irrespective of the gait complexity, or gait speed, a person can feel that there are no limitations in their walking ability, at least over specific distances. For example, the group not reporting difficulty but modifying their walking formed an intermediate group, between groups of no limitations and those experiencing walking difficulties. For this group, the ROC analysis, using the univariate model with RCMSE-V-PC1, is only marginally better than a random model. Behavioral and psychological factors (Simonsick et al., 1999) may play a role in the disparities

observed within groups regarding self-reported walking difficulties and objective measures of gait quality, such as gait speed and gait cycle entropy. It is crucial to identify the underlying causal factors contributing to the perception of walking difficulties in terms of preserving walking ability. Here, gait cycle entropy has the potential to serve as an objective indicator of neuromuscular deterioration.

As the number of conditions influencing the generation of the gait cycle increases with advancing age, the entropy of the gait cycle should also be higher. We observed this in our study population where the gait cycle entropy increased with age from 75 to 85 years. Interestingly, we found that women with no difficulty walking or with walking modification displayed higher gait cycle complexity than men in the respective categories, while no sex differences in gait complexity were observed among those reporting difficulty. This needs further study but may suggest that there are gender differences in how gait complexity characteristics are subjectively translated into perceived difficulty walking. It is worth keeping in mind, that people evaluate their walking difficulty concerning specific distances about their actual walking environment

(Rantakokko et al., 2016b). Our gait assessments took place in a laboratory, which could provide a safer environment and mitigate the effects of a cautious gait (Alexander, 1996). This calls for further investigation of the gait cycle complexity in daily life conditions.

We assessed the discriminative capability of gait cycle entropy in comparison to other commonly observed gait characteristics for aging and disease, namely stride time variability, gait symmetry, and gait speed. Gait speed had the highest AUC in the ROC analysis of the walking limitation groups, indicating the integration of all factors both physical and psychological. While stride time variability and gait symmetry did not produce predictive power, gait complexity displayed the ability to discriminate between the intact and walking difficulties groups. Although gait cycle entropy was not as strong a predictor for self-assessed walking difficulty as gait speed, it could have more relevance in monitoring the progression of gait limitation than gait speed, especially from the perspective of neuromuscular function. We noted a moderate correlation between gait speed and gait complexity. Moreover, there was a stronger correlation between gait complexity and both stride time variability and gait asymmetry compared to its correlation with gait speed. This suggests that complexity may not encompass all aspects related to gait speed but could be more specifically related to neuromuscular function. Our finding is supported by the study of Huijben et al. (2018), who showed that the complexity of trunk acceleration in the vertical and horizontal directions, represented with SE ($m = 5$, $r = 0.3$), is only weakly or not affected, respectively, by gait speed in treadmill walking (Huijben et al., 2018).

Walking modifications and difficulties in distances of 500 m, employed in this study, indicate notable alterations in independent mobility. Facing difficulties even in covering a distance of 2 km elevates the risk of falls, especially for individuals with a history of falls (Mänty et al., 2010). Although there is a lack of prior research on the correlation between gait complexity and walking difficulties, we can draw comparisons with earlier studies that explored the link between gait complexity and falls in older individuals. Older individuals with a history of falls, compared to those with no fall history, exhibit higher gait complexity in treadmill walking (Riva et al., 2013), but lower in daily life measurements (Ihlen et al., 2016). The differences could be attributed to increased caution in daily life mobility among older people who have experienced falls, and the fact that treadmill walking has higher entropy compared to level walking with the same preferred speed (Bizovska et al., 2018; Row Lazzarini and Kataras, 2016). It is important to note that in these studies, entropy was directly computed from filtered acceleration signals without adjusting for cadence. Furthermore, progressive neurological diseases have also been reported to be associated with increased lower-trunk acceleration complexity (Castiglia et al., 2023; Shema-Shiratzky et al., 2019). The above results suggest that gait complexity is a meaningful indicator of deteriorating movement control and gait cycle generation during aging and in clinical conditions. Further research is needed to better understand the changes in gait complexity with age and diseases with high prevalence in older age. Changes in complexity concerning self-assessments in longitudinal studies need exploring, and clinical populations studied separately.

Comparing absolute entropy values between studies becomes challenging due to variations in data pre-processing techniques, sensor placement, type of entropy measure, time-series length, measurement frequency, and parameters, all of which significantly influence the final entropy values (Ahmadi et al., 2018; Delgado-Bonal and Marshak, 2019; McCamley et al., 2018; Yentes and Raffalt, 2021). Notably, entropy measures have been applied to discretized data, favored for its robustness to parameters of SE compared to continuous data. However, it is essential to acknowledge that the entropy of discretized data fails to capture the within-step (or stride) variation (McCamley et al., 2018), a crucial aspect directly reflecting the neuromuscular generation of motion. The use of similar parameter values in MSE and RCMSE to estimate complexity is common across complexity studies of human movement, even with very different datasets and applications. Using template

vector length, $m = 2$, has been one of the more noticeable “fixed” parameters since the introduction of approximate entropy for heart rate variability (Pincus, 1991). However, there is no reason to assume that the entropy measures would provide the best result with this template length. On the contrary, the use of different parameter values should be investigated further, as suggested by McCamley et al. (2018) and Delgado-Bonal and Marshak (2019). In this study, we provide the entropy estimates with m ranging from 2 to 5 (and additionally 6 and 8 in the Appendix A). Patterns with different values of template vector m , all show the increased entropy with time series segment lengths of 10–30 % of the gait cycle, after which there is a slow decrease towards longer patterns. These results are in line with (Govindan et al., 2007), who point out that SE of periodic signals reach values close to zero, but with oversampled signals further convergence is reached only with longer template vector lengths of $m > 5$. Whether the entropy values and patterns in the scale over a single step length are meaningful would need further investigation. It is important that, in addition to parameters of entropy calculations, and the measurement frequency, the vector length used is reported in absolute or relative terms depending on the observed phenomena when using continuous over discretized data series. When interpreting and comparing entropy outcomes across studies, careful consideration of methodological factors is imperative to ensure meaningful and accurate conclusions. However, before we have a better understanding of the linkages between trunk acceleration complexity and gait quality, and the pros and cons of different entropy measures are known, the comparisons between studies should be done based on the main findings rather than the absolute values.

There are strengths and weaknesses in this study. First of all, the measurements of Stride t SD and Sym_{gait} , in which an increase in the variables has been associated with neurological disorders (Moon et al., 2016; Snijders et al., 2007), indicate that the study cohort was not biased by neurological conditions or pathologies. Entropy measures are sensitive to parameter selection, including sampling frequency. Our normalization of entropy measures between participants was not biased by the resampling, indicated by a weak correlation between cadence and the entropies (RCMSE-V-PC1 -0.36, RCMSE-H-PC1 -0.35). We also acknowledge that the participation of older people in measurements requiring more effort and commitment seems to favor those in good health (Portegijs et al., 2019). This was also the case in our study as indicated by the high scores in SPPB and MMSE. A higher-functioning study sample potentially leads to an underestimation of the strength of associations as those approaching critical levels are missing. Additionally, our assessment is laboratory-based and the results are, therefore, not transferable to daily life conditions. On the other hand, this creates baseline data, which can be used for prospective studies assessing the development of walking difficulties. Furthermore, our sensor placement for the study of trunk motion during gait was not optimal. For an overall biomechanical view, the placement at the L4–5 vertebrae is the obvious choice due to its proximity to the center of mass. In our study, the type of sensor and the comfort of the study participants determined the placement of the accelerometer on the upper trunk with the participants. With some of the sensors placed on the side of the upper body, the computation of acceleration in all anatomic axes was not available. However, vertical and resultant horizontal accelerations and their entropies can be robustly determined from the accelerometer data with the method used in this study (Rantalainen et al., 2020). Looking at the RCMSEs calculated with the different template vector lengths and thresholds (Fig. 1 and Appendix A), instead of the PCA components, the larger values of horizontal trunk acceleration entropy compared to the vertical are likely due to larger entropy in the mediolateral direction (Bisi and Stagni, 2016; Ihlen et al., 2016). This shows that using the method of deriving vertical acceleration with formulation reported in Vähä-Ypyä et al. (2018), provides meaningful data irrespective of the alignment of the sensor. The method provides freedom for the sensor placement but also allows removal and reattachment of the sensor during daily-life studies.

5. Conclusion

The complexity of the gait cycle, determined as the entropy of trunk acceleration during gait, increases with increasing gait limitations. With gait cycle complexity, it is possible to separate those perceiving walking difficulties from those with intact walking. Those who report modifying their walking form an intermediate group which encompasses the progression of walking limitations, but also the mitigation of limitations and retainment of self-efficacy, which cannot be reliably separated from the intact walking and walking difficulty group only with gait cycle complexity. Self-assessment and gait speed measurements effectively capture this preclinical state of disablement in walking (Mänty et al., 2007) but they do not lend themselves to comparison between subjects or give an indication of the underlying causes.

The trunk acceleration complexity is a more focused measure of the biomechanical factors of gait quality than gait speed, which also incorporates personal preference and behavior, other aspects of physical functioning, and diseases than those related to neuromuscular function. Trunk acceleration complexity during walking gait is also coherent with the theory of complexity of physiological systems, where aging brings increasing complexity to intrinsically oscillatory dynamics, such as in the gait cycle.

Further prospective research on older people is needed to see if gait complexity could provide early information on the biomechanical deterioration of physical functioning. With numerous entropy measures available, the link between physiological functioning and entropy should be better understood before consolidating the entropy measures for each purpose and permitting clinical use.

Appendix A

Funding

The AGNES project is financially supported by grants from the European Research Council (grant no. 693045 to Ta. R.) and the Academy of Finland (grant no. 310526 to Ta. R. and grant no. 321336 and 328818 to Ti. R.).

CRediT authorship contribution statement

Olli-Pekka Mattila: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Taina Rantanen:** Writing – review & editing, Supervision, Investigation, Funding acquisition, Data curation, Conceptualization. **Merja Rantakokko:** Writing – review & editing, Conceptualization. **Laura Karavirta:** Writing – review & editing, Investigation, Funding acquisition, Data curation. **Neil Cronin:** Writing – review & editing. **Timo Rantalainen:** Writing – review & editing, Software, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Acknowledgments

We thank the whole AGNES research team for their work in the data collection. We thank all participants of the AGNES study for their time and effort. The Gerontology Research Center is a joint effort between the University of Jyväskylä and the University of Tampere.

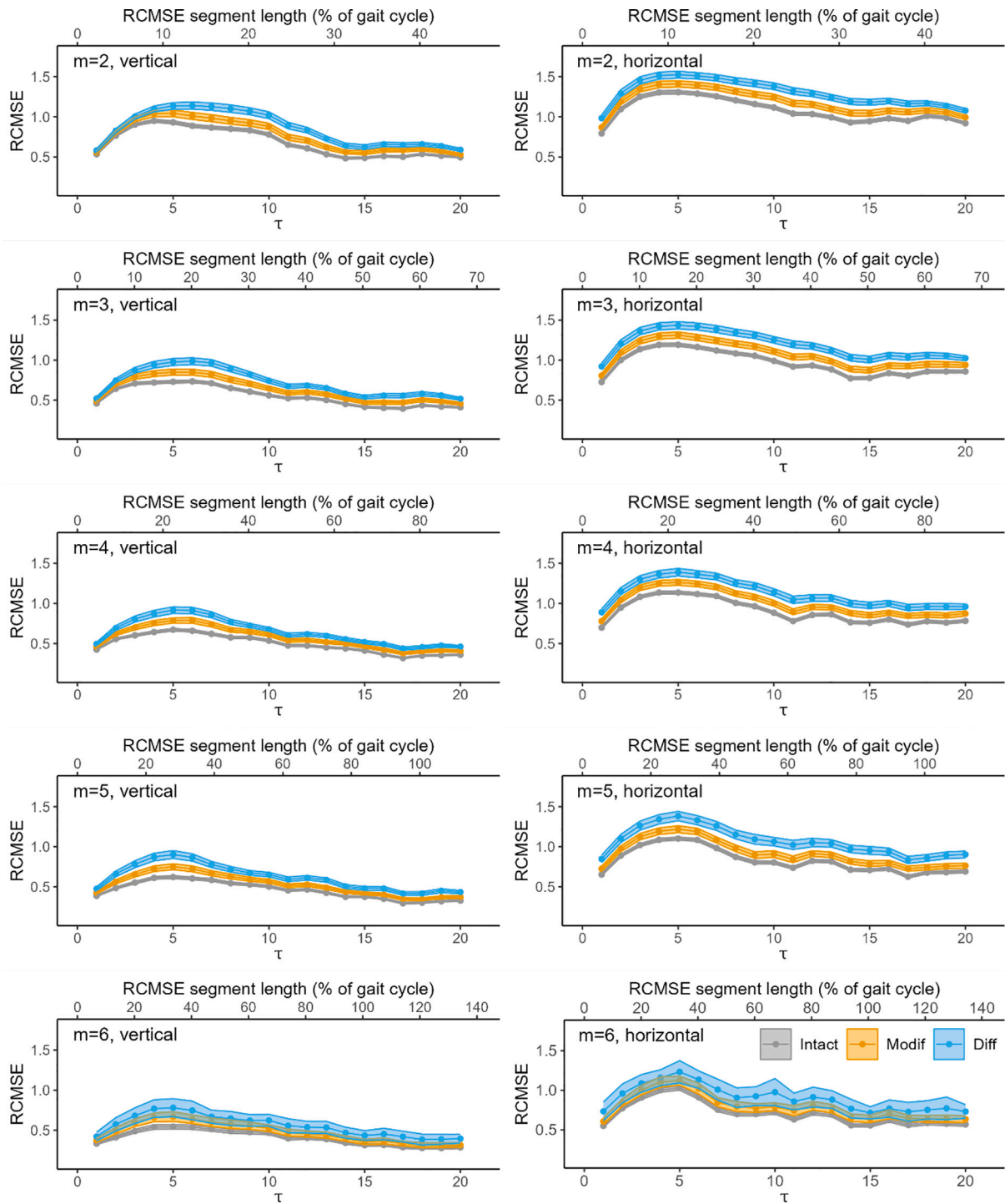


Fig. A.1. RCMSE calculated for vertical and resultant horizontal trunk acceleration during walking, with $r = 0.20 \cdot SD_{[v, h]}$. With $m = 8$, RCMSE did not produce enough matches for analysis.

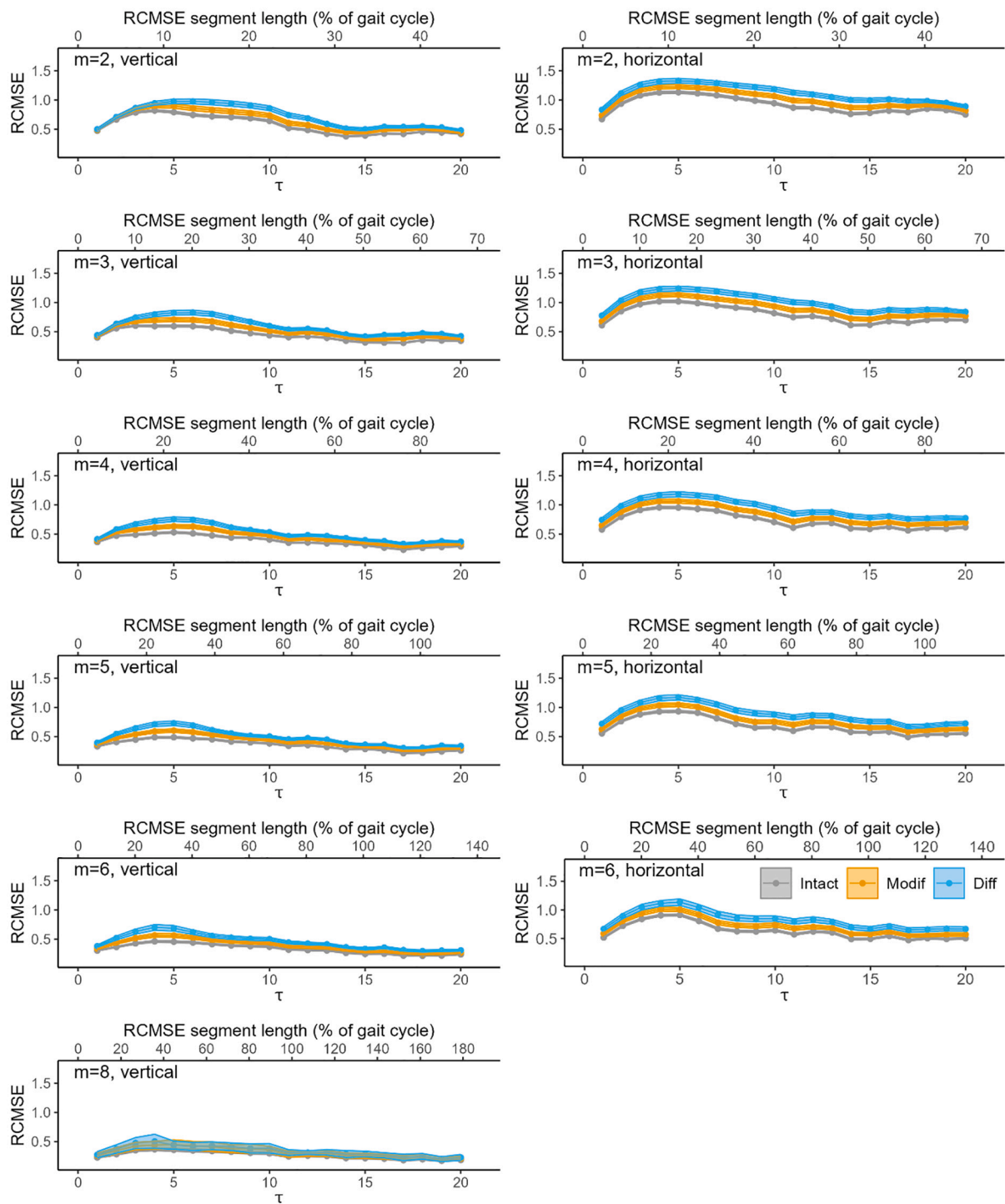


Fig. A.2. RCMSE calculated for vertical and resultant horizontal trunk acceleration during walking, with $r = 0.25 \cdot SD_{[v, h]}$. With $m = 8$, RCMSE did not produce enough matches for analysis for horizontal acceleration.

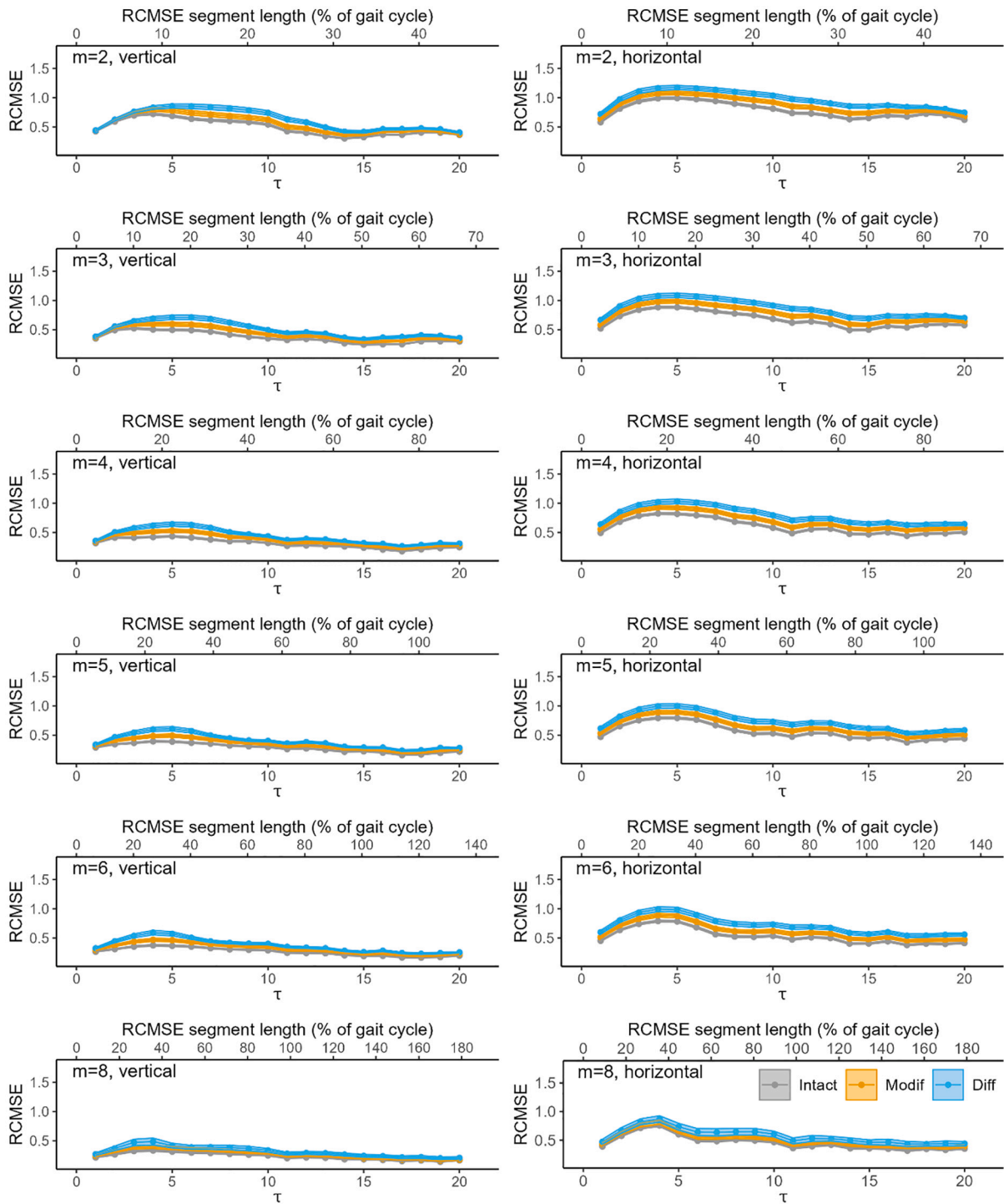


Fig. A.3. RCMSE calculated for vertical and resultant horizontal trunk acceleration during walking, with $r = 0.30 \cdot SD_{[v, h]}$.

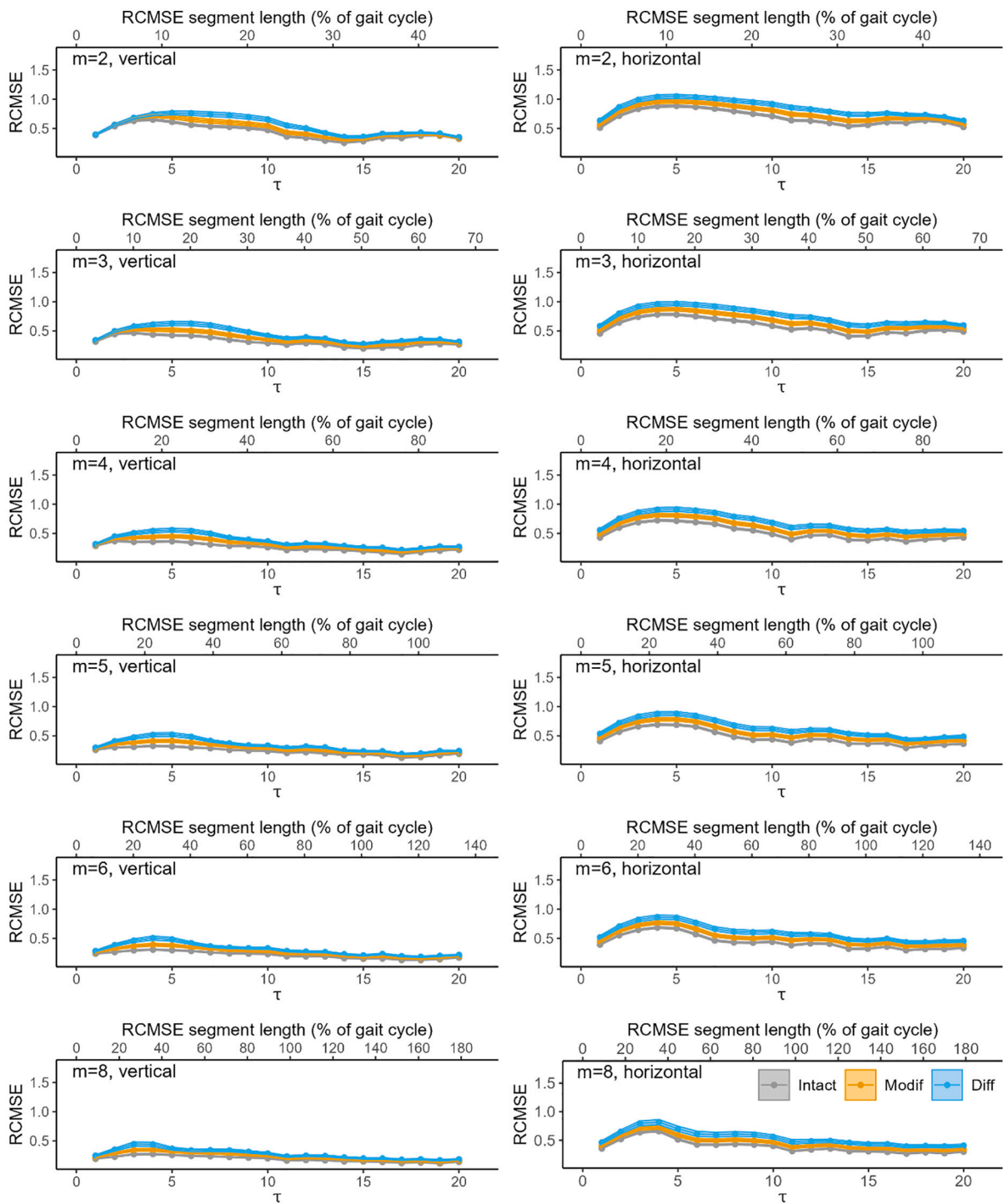


Fig. A.4. RCMSE calculated for vertical and resultant horizontal trunk acceleration during walking, with $r = 0.35 \cdot SD_{[v, h]}$.

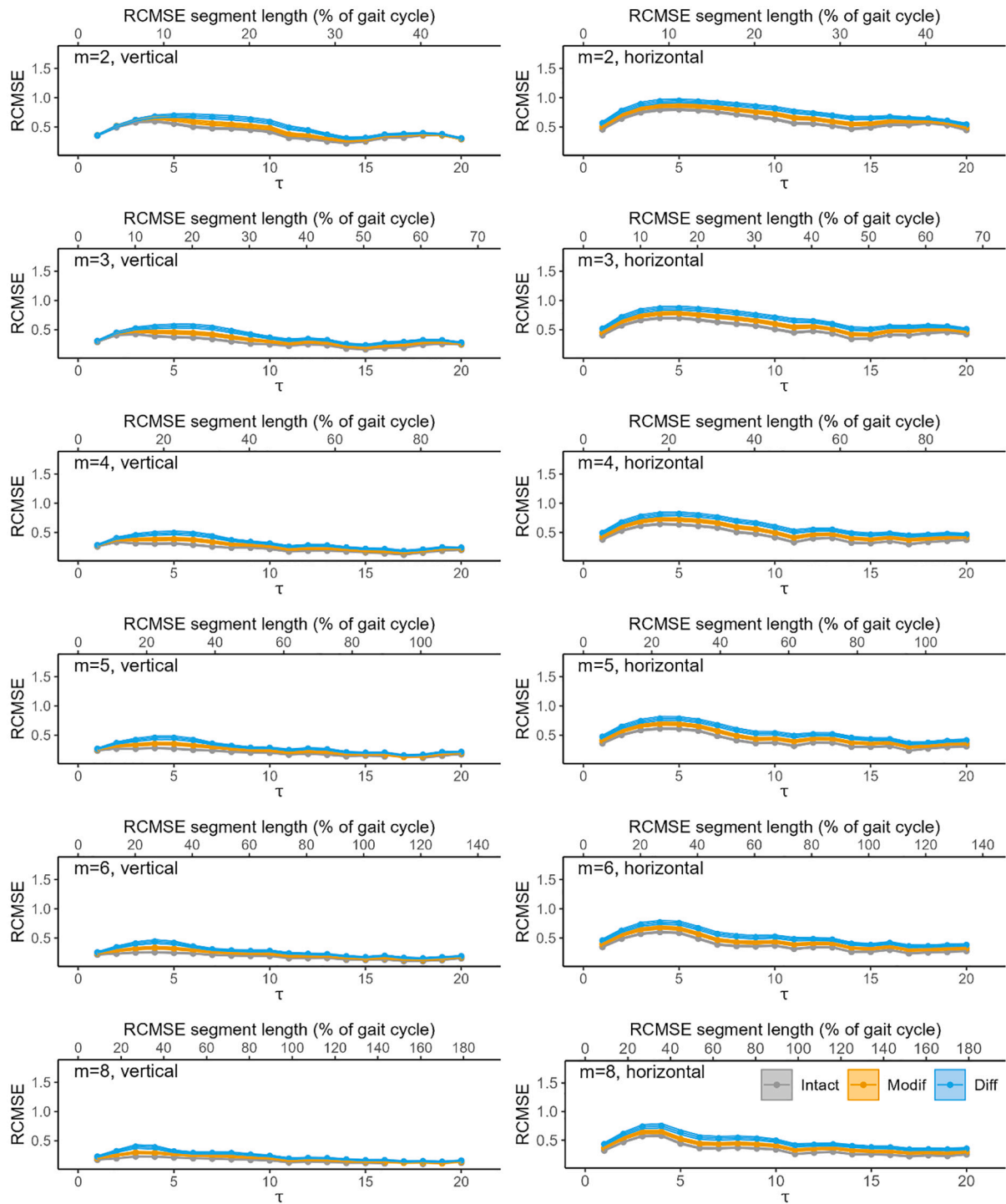


Fig. A.5. RCMSE calculated for vertical and resultant horizontal trunk acceleration during walking, with $r = 0.40 \cdot SD_{[v, h]}$.

References

Adamowicz, L., Christakis, Y., Czech, M.D., Adamusiak, T., 2022. SciKit digital health: Python package for streamlined wearable inertial sensor data processing. *JMIR Mhealth Uhealth* 10, e36762. <https://doi.org/10.2196/36762>.
 Ahmadi, S., Sepehri, N., Wu, C., Szturm, T., 2018. Sample entropy of human gait center of pressure displacement: a systematic methodological analysis. *Entropy* 20, 579. <https://doi.org/10.3390/e20080579>.
 Alexander, N.B., 1996. Gait disorders in older adults. *J. Am. Geriatr. Soc.* 44, 434–451. <https://doi.org/10.1111/j.1532-5415.1996.tb06417.x>.

Bisi, M.C., Stagni, R., 2016. Complexity of human gait pattern at different ages assessed using multiscale entropy: from development to decline. *Gait Posture* 47, 37–42. <https://doi.org/10.1016/j.gaitpost.2016.04.001>.
 Bizovska, L., Svoboda, Z., Vuillerme, N., Janura, M., 2017. Multiscale and Shannon entropies during gait as fall risk predictors—a prospective study. *Gait Posture* 52, 5–10. <https://doi.org/10.1016/j.gaitpost.2016.11.009>.
 Bizovska, L., Svoboda, Z., Kubonova, E., Vuillerme, N., Hirjakova, Z., Janura, M., 2018. The differences between overground and treadmill walking in nonlinear, entropy-based and frequency variables derived from accelerometers in young and older women: preliminary report. *Acta Bioeng. Biomech.* 20, 93–100.

- Castiglia, S.F., Trabassi, D., Conte, C., Ranavolo, A., Coppola, G., Sebastianelli, G., Abagnale, C., Barone, F., Bighiani, F., De Icco, R., Tassorelli, C., Serrao, M., 2023. Multiscale entropy algorithms to analyze complexity and variability of trunk accelerations time series in subjects with Parkinson's disease. *Sensors* 23, 4983. <https://doi.org/10.3390/s23104983>.
- Challis, J.H., 2006. Aging, regularity and variability in maximum isometric moments. *J. Biomech.* 39, 1543–1546. <https://doi.org/10.1016/j.jbiomech.2005.04.008>.
- Costa, M., Goldberger, A.L., Peng, C.-K., 2002. Multiscale entropy analysis of complex physiologic time series. *Phys. Rev. Lett.* 89, 068102 <https://doi.org/10.1103/PhysRevLett.89.068102>.
- Costa, M., Peng, C.-K., L. Goldberger, A., Hausdorff, J.M., 2003. Multiscale entropy analysis of human gait dynamics. *Phys. Stat. Mech. Its Appl., RANDOMNESS AND COMPLEXITY: Proceedings of the International Workshop in honor of Shlomo Havlin's 60th birthday* 330, 53–60. <https://doi.org/10.1016/j.physa.2003.08.022>.
- Delgado-Bonal, A., Marshak, A., 2019. Approximate entropy and sample entropy: a comprehensive tutorial. *Entropy* 21, 541. <https://doi.org/10.3390/e21060541>.
- Fiogbé, E., Vassimon-Barroso, V., Catai, A.M., de Melo, R.C., Quitério, R.J., Porta, A., Takahashi, A.C. de M., 2021. Complexity of knee extensor torque: effect of aging and contraction intensity. *J. Strength Cond. Res.* 35, 1050. <https://doi.org/10.1519/JSC.0000000000002888>.
- Flood, M.W., Jensen, B.R., Malling, A.-S., Lowery, M.M., 2019. Increased EMG intermuscular coherence and reduced signal complexity in Parkinson's disease. *Clin. Neurophysiol.* 130, 259–269. <https://doi.org/10.1016/j.clinph.2018.10.023>.
- Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. Mini-mental state. *J. Psychiatr. Res.* 12, 189–198. [https://doi.org/10.1016/0022-3956\(75\)90026-6](https://doi.org/10.1016/0022-3956(75)90026-6).
- Fried, L.P., Bandeen-Roche, K., Williamson, J.D., Prasada-Rao, P., Chee, E., Tepper, S., Rubin, G.S., 1996. Functional decline in older adults: expanding methods of ascertainment. *J. Gerontol. A Biol. Sci. Med. Sci.* 51, M206–M214. <https://doi.org/10.1093/gerona/51A.5.M206>.
- Fried, L.P., Bandeen-Roche, K., Chaves, P., Johnson, B.A., others, 2000. Preclinical mobility disability predicts incident mobility disability in older women. *J. Gerontol.-Biol. Sci. Med. Sci.* 55, M43.
- Godfrey, A., Del Din, S., Barry, G., Mathers, J.C., Rochester, L., 2015. Instrumenting gait with an accelerometer: a system and algorithm examination. *Med. Eng. Phys.* 37, 400–407. <https://doi.org/10.1016/j.medengphy.2015.02.003>.
- Govindan, R.B., Wilson, J.D., Eswaran, H., Lowery, C.L., Preißl, H., 2007. Revisiting sample entropy analysis. *Phys. Stat. Mech. Its Appl.* 376, 158–164. <https://doi.org/10.1016/j.physa.2006.10.077>.
- Guralnik, J.M., Simonsick, E.M., Ferrucci, L., Glynn, R.J., Berkman, L.F., Blazer, D.G., Scherr, P.A., Wallace, R.B., 1994. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J. Gerontol.* 49, M85–M94. <https://doi.org/10.1093/geronj/49.2.M85>.
- Harris, C.R., Millman, K.J., van der Walt, S.J., Gommers, R., Virtanen, P., Cournapeau, D., Wieser, E., Taylor, J., Berg, S., Smith, N.J., Kern, R., Picus, M., Hoyer, S., van Kerkwijk, M.H., Brett, M., Haldane, A., del Río, J.F., Wiebe, M., Peterson, P., Gérard-Marchant, P., Sheppard, K., Reddy, T., Weckesser, W., Abbasi, H., Gohlke, C., Oliphant, T.E., 2020. Array programming with NumPy. *Nature* 585, 357–362. <https://doi.org/10.1038/s41586-020-2649-2>.
- Hausdorff, J.M., 2005. Gait variability: methods, modeling and meaning. *J. NeuroEngineering Rehabil.* 2, 19. <https://doi.org/10.1186/1743-0003-2-19>.
- Hodt-Billington, C., Helbostad, J.L., Moe-Nilssen, R., 2008. Should trunk movement or footfall parameters quantify gait asymmetry in chronic stroke patients? *Gait Posture* 27, 552–558. <https://doi.org/10.1016/j.gaitpost.2007.07.015>.
- Huijben, B., van Schooten, K.S., van Dieën, J.H., Pijnappels, M., 2018. The effect of walking speed on quality of gait in older adults. *Gait Posture* 65, 112–116. <https://doi.org/10.1016/j.gaitpost.2018.07.004>.
- Ihlen, E.A.F., Weiss, A., Bourke, A., Helbostad, J.L., Hausdorff, J.M., 2016. The complexity of daily life walking in older adult community-dwelling fallers and non-fallers. *J. Biomech.* 49, 1420–1428. <https://doi.org/10.1016/j.jbiomech.2016.02.055>.
- Ihlen, E.A.F., van Schooten, K.S., Bruijn, S.M., van Dieën, J.H., Vereijken, B., Helbostad, J.L., Pijnappels, M., 2018. Improved prediction of falls in community-dwelling older adults through phase-dependent entropy of daily-life walking. *Front. Aging Neurosci.* 10.
- Kang, H.G., Dingwell, J.B., 2016. Differential changes with age in multiscale entropy of electromyography signals from leg muscles during treadmill walking. *PLoS One* 11, e0162034. <https://doi.org/10.1371/journal.pone.0162034>.
- Kassambara, A., 2023. rstatix: Pipe-friendly Framework for Basic Statistical Tests (Manual).
- Lipkin, D.P., Scriven, A.J., Crake, T., Poole-Wilson, P.A., 1986. Six minute walking test for assessing exercise capacity in chronic heart failure. *Br. Med. J. (Clin. Res. Ed.)* 292, 653–655.
- Lipsitz, L., Goldberger, A., 1992. Loss of “complexity” and aging potential applications of fractals and chaos theory to senescence. *JAMA* 267, 1806–1809. <https://doi.org/10.1001/jama.1992.03480130122036>.
- Mänty, M., Heinonen, A., Leinonen, R., Törmäkangas, T., Sakari-Rantala, R., Hirvensalo, M., von Bonsdorff, M.B., Rantanen, T., 2007. Construct and predictive validity of a self-reported measure of preclinical mobility limitation. *Arch. Phys. Med. Rehabil.* 88, 1108–1113. <https://doi.org/10.1016/j.apmr.2007.06.016>.
- Mänty, M., Heinonen, A., Viljanen, A., Pajala, S., Koskenvuo, M., Kaprio, J., Rantanen, T., 2010. Self-reported preclinical mobility limitation and fall history as predictors of future falls in older women: prospective cohort study. *Osteoporos. Int.* 21, 689–693. <https://doi.org/10.1007/s00198-009-0950-x>.
- McCarmley, J., Donati, M., Grimpampi, E., Mazzà, C., 2012. An enhanced estimate of initial contact and final contact instants of time using lower trunk inertial sensor data. *Gait Posture* 36, 316–318. <https://doi.org/10.1016/j.gaitpost.2012.02.019>.
- McCarmley, J.D., Denton, W., Arnold, A., Raffalt, P.C., Yentes, J.M., 2018. On the calculation of sample entropy using continuous and discrete human gait data. *Entropy* 20, 764. <https://doi.org/10.3390/e20100764>.
- Moe-Nilssen, R., Helbostad, J.L., 2004. Estimation of gait cycle characteristics by trunk accelerometry. *J. Biomech.* 37, 121–126. [https://doi.org/10.1016/S0021-9290\(03\)00233-1](https://doi.org/10.1016/S0021-9290(03)00233-1).
- Moon, Y., Sung, J., An, R., Hernandez, M.E., Sosnoff, J.J., 2016. Gait variability in people with neurological disorders: a systematic review and meta-analysis. *Hum. Mov. Sci.* 47, 197–208. <https://doi.org/10.1016/j.humov.2016.03.010>.
- Perera, S., Mody, S.H., Woodman, R.C., Studenski, S.A., 2006. Meaningful change and responsiveness in common physical performance measures in older adults. *J. Am. Geriatr. Soc.* 54, 743–749. <https://doi.org/10.1111/j.1532-5415.2006.00701.x>.
- Perkins, N.J., Schisterman, E.F., 2006. The inconsistency of “optimal” cut-points using two ROC based criteria. *Am. J. Epidemiol.* 163, 670–675. <https://doi.org/10.1093/aje/kwj063>.
- Pethick, J., Winter, S.L., Burnley, M., 2021. Physiological complexity: influence of ageing, disease and neuromuscular fatigue on muscle force and torque fluctuations. *Exp. Physiol.* 106, 2046–2059. <https://doi.org/10.1113/EP089711>.
- Piitulainen, H., Kulmala, J.-P., Mäenpää, H., Rantalainen, T., 2021. The gait is less stable in children with cerebral palsy in normal and dual-task gait compared to typically developed peers. *J. Biomech.* 117, 110244 <https://doi.org/10.1016/j.jbiomech.2021.110244>.
- Pincus, S.M., 1991. Approximate entropy as a measure of system complexity. *Proc. Natl. Acad. Sci.* 88, 2297–2301. <https://doi.org/10.1073/pnas.88.6.2297>.
- Portegijs, E., Karavirta, L., Saajanaho, M., Rantalainen, T., Rantanen, T., 2019. Assessing physical performance and physical activity in large population-based aging studies: home-based assessments or visits to the research center? *BMC Public Health* 19, 1570. <https://doi.org/10.1186/s12889-019-7869-8>.
- R Core Team, 2023. R: A Language and Environment for Statistical Computing (Manual). R Foundation for Statistical Computing, Vienna, Austria.
- Rantakokko, M., Mänty, M., Rantanen, T., 2013. Mobility decline in old age. *Exerc. Sport Sci. Rev.* 41, 19. <https://doi.org/10.1097/JES.0b013e3182556f1e>.
- Rantakokko, M., Portegijs, E., Viljanen, A., Iwarsson, S., Kauppinen, M., Rantanen, T., 2016a. Changes in life-space mobility and quality of life among community-dwelling older people: a 2-year follow-up study. *Qual. Life Res.* 25, 1189–1197. <https://doi.org/10.1007/s11136-015-1137-x>.
- Rantakokko, M., Portegijs, E., Viljanen, A., Iwarsson, S., Rantanen, T., 2016b. Mobility modification alleviates environmental influence on incident mobility difficulty among community-dwelling older people: a two-year follow-up study. *PLoS One* 11, e0154396. <https://doi.org/10.1371/journal.pone.0154396>.
- Rantakokko, M., Portegijs, E., Viljanen, A., Iwarsson, S., Rantanen, T., 2017. Task modifications in walking postpone decline in life-space mobility among community-dwelling older people: a 2-year follow-up study. *J. Gerontol. Ser. A* 72, 1252–1256. <https://doi.org/10.1093/gerona/glw348>.
- Rantalainen, T., Karavirta, L., Pirkola, H., Rantanen, T., Linnamo, V., 2020. Gait variability using waist- and ankle-worn inertial measurement units in healthy older adults. *Sensors* 20, 2858. <https://doi.org/10.3390/s20102858>.
- Rantanen, T., Era, P., Heikkinen, E., 1997. Physical activity and the changes in maximal isometric strength in men and women from the age of 75 to 80 years. *J. Am. Geriatr. Soc.* 45, 1439–1445. <https://doi.org/10.1111/j.1532-5415.1997.tb03193.x>.
- Rantanen, T., Saajanaho, M., Karavirta, L., Siltanen, S., Rantakokko, M., Viljanen, A., Rantalainen, T., Pynnönen, K., Karvonen, A., Lisko, I., Palmberg, L., Eronen, J., Palonen, E.-M., Hinrichs, T., Kauppinen, M., Kokko, K., Portegijs, E., 2018. Active aging – resilience and external support as modifiers of the disablement outcome: AGNES cohort study protocol. *BMC Public Health* 18, 565. <https://doi.org/10.1186/s12889-018-5487-5>.
- Richman, J.S., Moorman, J.R., 2000. Physiological time-series analysis using approximate entropy and sample entropy. *Am. J. Physiol.-Heart Circ. Physiol.* 278, H2039–H2049. <https://doi.org/10.1152/ajpheart.2000.278.6.H2039>.
- Riva, F., Toebes, M.J.P., Pijnappels, M., Stagni, R., van Dieën, J.H., 2013. Estimating fall risk with inertial sensors using gait stability measures that do not require step detection. *Gait Posture* 38, 170–174. <https://doi.org/10.1016/j.gaitpost.2013.05.002>.
- Row Lazzarini, B.S., Kataras, T.J., 2016. Treadmill walking is not equivalent to overground walking for the study of walking smoothness and rhythmicity in older adults. *Gait Posture* 46, 42–46. <https://doi.org/10.1016/j.gaitpost.2016.02.012>.
- Shema-Shiratzky, S., Gazit, E., Sun, R., Regev, K., Karni, A., Sosnoff, J.J., Herman, T., Mirelman, A., Hausdorff, J.M., 2019. Deterioration of specific aspects of gait during the instrumented 6-min walk test among people with multiple sclerosis. *J. Neurol.* 266, 3022–3030. <https://doi.org/10.1007/s00415-019-09500-z>.
- Simonsick, E.M., Guralnik, J.M., Fried, L.P., 1999. Who walks? Factors associated with walking behavior in disabled older women with and without self-reported walking difficulty. *J. Am. Geriatr. Soc.* 47, 672–680. <https://doi.org/10.1111/j.1532-5415.1999.tb01588.x>.
- Sing, T., Sander, O., Beerenwinkel, N., Lengauer, T., 2005. ROCr: visualizing classifier performance in R. *Bioinforma. Oxf. Engl.* 21, 7881. <https://doi.org/10.1093/bioinformatics/bti623>.
- Skantz, H., Rantanen, T., Palmberg, L., Rantalainen, T., Aartolahti, E., Portegijs, E., Viljanen, A., Eronen, J., Rantakokko, M., 2020. Outdoor mobility and use of adaptive or maladaptive walking modifications among older people. *J. Gerontol. A Biol. Sci. Med. Sci.* 75, 806–812. <https://doi.org/10.1093/gerona/glz172>.
- Skantz, H., Rantalainen, T., Karavirta, L., Rantakokko, M., Palmberg, L., Portegijs, E., Rantanen, T., 2021. Associations between accelerometer-based free-living walking

- and self-reported walking capability among community-dwelling older people. *J. Aging Phys. Act.* 29, 1018–1025. <https://doi.org/10.1123/japa.2020-0389>.
- Snijders, A.H., van de Warrenburg, B.P., Giladi, N., Bloem, B.R., 2007. Neurological gait disorders in elderly people: clinical approach and classification. *Lancet Neurol.* 6, 63–74. [https://doi.org/10.1016/S1474-4422\(06\)70678-0](https://doi.org/10.1016/S1474-4422(06)70678-0).
- Vähä-Yppä, H., Husu, P., Suni, J., Vasankari, T., Sievänen, H., 2018. Reliable recognition of lying, sitting, and standing with a hip-worn accelerometer. *Scand. J. Med. Sci. Sports* 28, 1092–1102. <https://doi.org/10.1111/sms.13017>.
- Vaillancourt, D.E., Newell, K.M., 2002. Changing complexity in human behavior and physiology through aging and disease. *Neurobiol. Aging* 23, 1–11. [https://doi.org/10.1016/S0197-4580\(01\)00247-0](https://doi.org/10.1016/S0197-4580(01)00247-0).
- Vaillancourt, D.E., Newell, K.M., 2003. Aging and the time and frequency structure of force output variability. *J. Appl. Physiol.* 94, 903–912. <https://doi.org/10.1152/japplphysiol.00166.2002>.
- Vaillancourt, D.E., Slifkin, A.B., Newell, K.M., 2001. Regularity of force tremor in Parkinson's disease. *Clin. Neurophysiol.* 112, 1594–1603. [https://doi.org/10.1016/S1388-2457\(01\)00593-4](https://doi.org/10.1016/S1388-2457(01)00593-4).
- Van Rossum, G., Drake, F.L., 2009. *Python 3 Reference Manual*. CreateSpace, Scotts Valley, CA.
- Wu, S.-D., Wu, C.-W., Lin, S.-G., Lee, K.-Y., Peng, C.-K., 2014. Analysis of complex time series using refined composite multiscale entropy. *Phys. Lett. A* 378, 1369–1374. <https://doi.org/10.1016/j.physleta.2014.03.034>.
- Yentes, J.M., Raffalt, P.C., 2021. Entropy analysis in gait research: methodological considerations and recommendations. *Ann. Biomed. Eng.* 49, 979–990. <https://doi.org/10.1007/s10439-020-02616-8>.
- Yentes, J.M., Hunt, N., Schmid, K.K., Kaipust, J.P., McGrath, D., Stergiou, N., 2013. The appropriate use of approximate entropy and sample entropy with short data sets. *Ann. Biomed. Eng.* 41, 349–365. <https://doi.org/10.1007/s10439-012-0668-3>.
- Zijlstra, W., Hof, A.L., 2003. Assessment of spatio-temporal gait parameters from trunk accelerations during human walking. *Gait Posture* 18, 1–10. [https://doi.org/10.1016/S0966-6362\(02\)00190-X](https://doi.org/10.1016/S0966-6362(02)00190-X).