

A novel approach for analysis of altered gait variability in amyotrophic lateral sclerosis

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Abstract Gait variability reflects important information for the maintenance of human beings' health. For pathological populations, changes in gait variability signal the presence of abnormal motor control strategies. Quantitative analysis of the altered gait variability in patients with amyotrophic lateral sclerosis (ALS) will be helpful for either diagnosing or monitoring pathological progression of the disease. Thus, we applied Teager energy operator, an energy measure that can highlight the deviations from moment to moment of a time series, to produce an instantaneous energy time series. Then, two important features were extracted to assess the variability of the new time series. First, the standard deviation statistics were used to measure the magnitude of the variability. Second, to quantify the temporal structural characteristics of the variability, the permutation entropy was applied as a tool from the non-linear dynamics. In the classification experiments, the two proposed features were input to the support vector machine classifier, and the dataset consists of 12 ALS patients and 16 healthy control subjects. The experimental results showed that an area of 0.9643 under the receiver operating characteristic curve was achieved, and the classification accuracy evaluated by leave-one-out cross-validation method could reach 92.86 %.

Keywords Teager energy · Permutation entropy · Gait variability · Amyotrophic lateral sclerosis

1 Introduction

Ambulation, as a fundamental capability of human beings, is a complex process that requires sophisticated control of the neural systems and muscles. On the surface, both the kinetics and kinematics of gait in the normal condition show a considerable degree of stability under multichannel accurate controls. However, a closer examination of the gait reveals that gait dynamics, i.e., the stride-to-stride fluctuations of stride intervals, which are defined as the time between one heel strike of one foot and the next heel strike of the same foot [17], show a certain extent of variability when measured with millisecond precision.

Amyotrophic lateral sclerosis (ALS) disease is a type of neurodegenerative disorder that affects the motor neurons of the cerebral cortex, brain stem, and spinal cord [19]. Due to the interruption of the pathway from the cerebrum to the muscle, the lower limbs may not properly perform voluntary movements, which can result in gait patterns being altered for a patient with ALS [14]. Thus, clinically, gait evaluation is an important component in providing an accurate diagnosis and risk assessment. However, the available means of evaluation are often based on clinical observations and patients' self-reports, which are often qualitative and without much guarantee. As the measurement of gait dynamics becomes more and more precise and convenient [27, 40], a quantitative evaluation of gait variability based on signal processing and machine learning is possible. Hausdorff et al. [19] studied the altered gait rhythm of ALS patients with regard to the fluctuation magnitude and the fluctuation dynamics. By using the coefficient of variation

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and the SD of the first difference of the time series, they found that the magnitude of the stride-to-stride fluctuations was significantly increased in subjects with ALS compared to the control (CO). However, for the measures that evaluate the fluctuation dynamics, such as the fractal scaling index, the autocorrelation decay time and the nonstationarity index, they reported no significant difference between ALS patients and CO subjects. Wu and Krishnan [36] applied the signal turns count method to measure the fluctuations in the swing-interval time series, and they derived a parameter called the swing-interval turns count (SWITC). They found that the mean values of the SWITC for the ALS patients were significantly larger than those of the healthy CO subjects. In another work [37] by the same authors, they estimated the probability density functions (PDFs) of the stride-interval time series by using the nonparametric Parzen-window method, and they found that the spread of the PDFs of the ALS patients was much wider than that of the CO subjects. Aziz and Arif [4] introduced normalized corrected Shannon entropy (NCSE) of symbolic sequences to quantitatively characterize the variability of gait time series. The calculation of the NCSE feature depended on the distribution of different symbols that were generated by a threshold-based symbolization process. Their work revealed that the distribution of symbols in the CO subjects was more uniform than that of the ALS subjects with a short threshold. Recently, Zeng and Wang [42] proposed another method, which was based on the local approximation of gait dynamics via deterministic learning. A set of estimators, which were represented by the radial basis function (RBF) neural network, was trained beforehand. Then, the classification was realized by using the pretrained estimators to represent the test gait pattern, and the one with the minimum error had the same class as the testing pattern.

Although previous studies have observed an increase of gait variability in ALS patients, further quantitative studies should use more statistical models to better characterize the gait variability of ALS patients. The present study proposed a novel method, which is a hybrid of the Teager energy operator (TEO) [22] and permutation entropy (PE) [5], for the evaluation of gait variability. Due to its high time resolution and good adaptability to the instantaneous changes of signals, TEO has the capability of enhancing the transient features of a time series [29]. In the present study, TEO was applied firstly to the stride-interval time series to generate an instantaneous energy time series. We then extracted two parameters, the standard deviation (linear) and the PE (nonlinear), from this new time series to examine the gait variability. The former was calculated to quantify the magnitude of the variability, while the later was used to evaluate the temporal structure of the variability. Next, these two parameters were entered into the SVM

classifier to discriminate the gait of ALS patients from that of the healthy subjects. We expected that the proposed gait-variability-evaluation method could help to build up a noninvasive and highly accurate assessment tool to be used either in clinics or in everyday gait monitoring.

2 Materials and methods

2.1 Gait data

The gait dataset in this study was given by Hausdorff et al. [19], and it is available at www.physionet.org. By placing the ultrathin force-sensitive switches inside the left and right shoes of the subjects, the gait signals were recorded when subjects walked at their normal pace along a straight hallway of 77 m in length in 300 s. The digitized force data were analyzed with the stride detection algorithm proposed by Hausdorff et al. [16]. As a result of such analysis, a stride interval (time from initial contact of one foot to the immediate subsequent contact of the same foot) was generated for each gait cycle of the walk from the original force signals. To eliminate the start-up effects, the first 20 s of each record was removed. Then, a preprocessing step, which will be presented in the next section, was applied to remove outlier data points that may have been caused by the turnaround at the end of the hallway. The original dataset consists of 13 ALS subjects (10 men and 3 women, age mean \pm SD: 55.6 ± 12.8 years) and 16 healthy CO subjects (14 women and 2 men, age mean \pm SD: 39.3 ± 18.5 years). However, one male ALS patient, who was 36 years old, was not included in this study because the stride intervals for his right foot were recorded erroneously with a constant value for the last 150 s or so. No significant difference existed between the heights and weights of the ALS subjects and those of the healthy CO subjects. Some stride-to-stride plots of the gait interval time series for a healthy and an ALS-affected subject are shown in Fig. 1.

2.2 Preprocessing method

As mentioned before, because of the limited length of the pressure-sensitive hallway, some singular stride-interval points were generated when the subjects had to turn back at the end of the hallway. In previous studies [19, 37] on the same dataset, a median filter was applied to remove data points that were 3 SD greater than or less than the overall median value (i.e., the so-called 3-sigma-rules). However, such a median filter relies heavily on the global median of the stride-interval series. If the median of one sequence is a data point with a relatively large value, then some local outliers will fail to be detected with the 3-sigma-rule-based filter [37]. To overcome this problem, we adopted

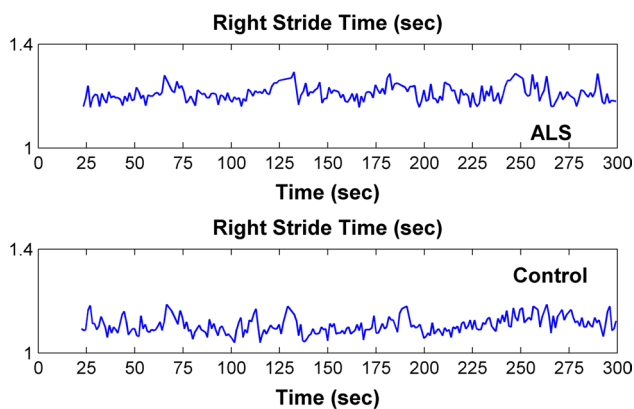


Fig. 1 Right stride-interval series of a 39-year-old ALS patient (disease duration 7 months) and a 61-year-old CO subject. The vertical axes of the plots represent the length of the stride interval during each gait cycle, and its labels are shown on top of each time series. The horizontal axes of the plots indicate when the stride interval begins

a distance-based algorithm [33] to detect the outliers that emerged in this dataset. The choice of this algorithm was based on the following observations: A turn-back outlier was a data point that had a value either very large or very small compared to its local neighbors, and it happened only several times for a finite sequence; therefore, its local density should be lower compared to that of most other data points. The key steps of the adopted outlier-detection algorithm are given as follows:

- Step 1: Sort the data points either in ascending or in descending order
- Step 2: Sweep the sorted data point series sequentially, and for each data point p , find its k nearest neighbors. Then, the distance denoted as k -distance, which is the maximum distance of p to its k nearest neighbors, is used to measure the local density of the data points around p . Thus, with a threshold η , a data point is deemed to be an outlier when its k -distance is greater than η

A general flowchart of the proposed preprocessing method is shown in Fig. 2, and the results are presented in Sect. 3.

2.3 Teager energy operator

The TEO is a nonlinear, high-pass filter that suppresses the low-frequency background signal while enhancing the high-frequency transient signal [34]. It was often used for the detection of a transient event [34], the modeling of nonlinear dynamics, [24] and the estimation of instantaneous frequency [43]. Its application to the measurement of gait variability in ALS patients was motivated by the

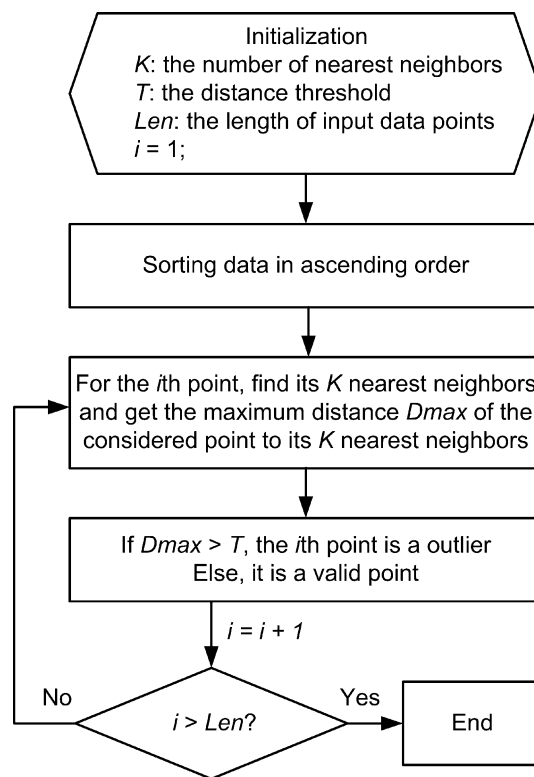


Fig. 2 Flowchart for the k -distance-based preprocessing method

observation that the gait of patients with ALS is less steady and more temporally disorganized than that of healthy controls [19]. Much of the earlier work on TEO was given by Maragos et al. [30, 31]. For a continuous signal $x(t)$, TEO is defined as:

$$\psi[x(t)] = \dot{x}^2(t) - x(t)\ddot{x}(t) \tag{1}$$

where $\dot{x}(t)$ and $\ddot{x}(t)$ are the first and second derivatives of $x(t)$, respectively. If a signal is represented as $x(t) = A \cos(\Omega t + \Phi)$, where A is the amplitude, Ω is the angular frequency, and Φ is the initial phase shift, then $\psi[x(t)] = A^2\Omega^2$. This expression tells us that the specialty of the TEO is that it measures the energy of the system that generates the signal based on mechanical and physical considerations rather than the energy of the signal itself [23]. Hence, any small deviations in the regular rhythmic activity of the gait are reflected in the Teager energy function. The discrete-time counterpart is given by the following [24]:

$$TE[x(n)] = x^2[n] - x[n-1]x[n+1] \tag{2}$$

From the above equation, one can find that at any instant the computation of energy, $TE[x(n)]$, only requires three samples; therefore, it is nearly instantaneous. Such excellent time resolution provides us with the ability to capture the energy fluctuations of gait stride-interval time series, and thus, it gives us another way to assess the gait variability.

2.4 Permutation entropy

The PE, first presented by Bandt and Pompe [5], is a complexity measure for time series based on comparing neighboring values, and it has been successfully applied to a number of applications. For instance, PE has been shown to be effective in disclosing abnormalities of cerebral activity in patients with typical absences from their scalp EEG [13]. It has also been used as a viable tool for detecting dynamic changes of the machine's working status [39]. Because the PE only makes use of the order of the values, it is robust to noise sources and artifacts, and it is particularly well equipped to capture the complex dynamics of the biological systems that are characteristic of rich temporal structures even at rest [41]. Several studies [10, 18] have indicated that the fluctuations of gait from one stride to the next display a subtle, "hidden" temporal structure in a healthy adult locomotor system. We hypothesize that the loss of motoneurons and potential degeneration of fine motor control in ALS [19] should alter the temporal structure, and therefore, the PE parameter should have significant differences between ALS patients and healthy subjects.

The mathematical foundation of the PE can be found in Ref. [5]. According to the Takens–Maine theorem, the phase space of a scalar time series $\{x_t, t = 1, 2, \dots, T\}$ can be reconstructed as

$$\begin{cases} X(1) = \{x(1), x(1 + \tau), \dots, x(1 + (m - 1)\tau)\} \\ \vdots \\ X(i) = \{x(i), x(i + \tau), \dots, x(i + (m - 1)\tau)\} \\ \vdots \\ X(T - (m - 1)\tau) = \{x(T - (m - 1)\tau), x(T - (m - 2)\tau), \dots, x(T)\} \end{cases} \quad (3)$$

where τ is the time delay and m is called the embedding dimension that determines the length of each vector. To calculate the PE, the values contained in each vector $X(i)$ are sorted in an ascending order as follows:

$$x_{i+r_0 \times \tau} \leq x_{i+r_1 \times \tau} \leq \dots \leq x_{i+r_{m-2} \times \tau} \leq x_{i+r_{m-1} \times \tau} \quad (4)$$

where r_i is the offset of the sorted value to the start position and r_i takes its value from $\{0, 1, \dots, m - 1\}$. Thus, a permutation pattern $\pi = (r_0, r_1, \dots, r_{m-1})$ is created for each vector. An example is given for better clarification. With the vector $\{6, 1, 5\}$ in the phase space, it is sorted in ascending order, which gives $\{1, 5, 6\}$, and the corresponding permutation pattern is then $\pi = (120)$ because $x_{t+1} < x_{t+2} < x_{t+0}$. For a dimension of m , there will be $m!$ possible different permutation patterns. Supposing there are k different patterns $\pi_1, \pi_2, \dots, \pi_k$ in the reconstructed phase space of the given time series, if their corresponding probability frequency is denoted as $p(\pi_j), j = 1, \dots, k$, and

$\sum_{j=1}^k p(\pi_j) = 1$, then the PE of order m for the time series $\{x_t, t = 1, 2, \dots, T\}$ can be defined as follows:

$$H_p(m) = - \sum_{j=1}^k p(\pi_j) \ln p(\pi_j) \quad (5)$$

When all the permutation patterns have the same probability frequency as $p(\pi_j) = 1/m!$, then $H_p(m)$ takes the maximum value as $\ln(m!)$. Therefore, the corresponding normalized PE of order m can be defined as follows [39]:

$$0 \leq H_p(m) = \frac{H_p(m)}{\ln(m!)} \leq 1 \quad (6)$$

The largest value of $H_p(m)$ is one, which implies the time series is completely random, and the smallest value is zero, which denotes that the time series is extremely regular. In the process of calculating PE, the dimension m and the delay τ are two parameters that need to be set properly. The former decides the number of possible states, which is given by $m!$. A too small m means that there are only very few distinct states, and thus, the scheme will not work. A too large m will bring out the homogenized vectors in the reconstructed phase space, and it will become difficult to detect small changes in the time series. As suggested in Ref. [39], the value of m is often recommended to be in the range of 3–7. As for the time delay τ , it is related to the intrinsic timescales of the studied system. Following the findings presented in Ref. [8], which performed the multiscale entropy analysis of gait dynamics, we take the scale parameter τ to be from 2 to 5. The parameter-choice procedure and the PE feature calculated from the gait instantaneous energy time series are presented in Sect. 3.

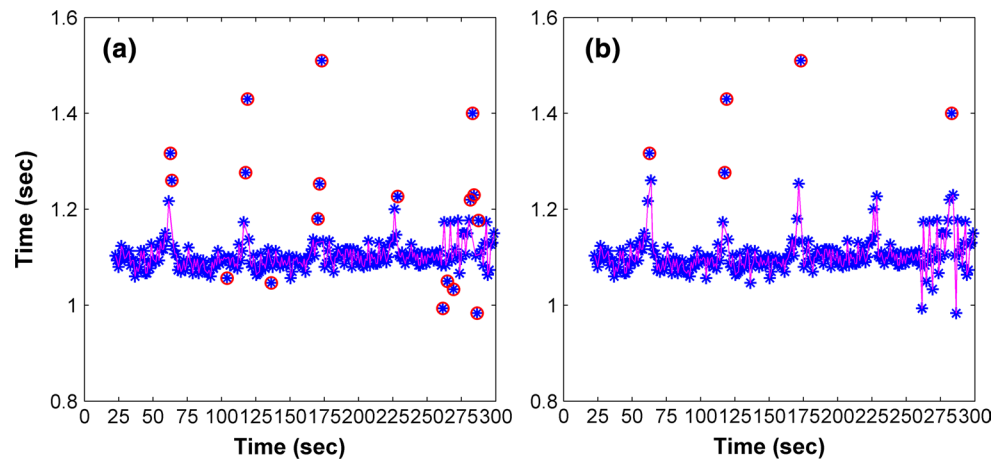
2.5 Statistical Analysis

The SPSS software (version 17.0, SPSS Inc, Chicago, IL, USA) was adopted for all statistical analyses. The continuous and categorical variables between the groups were compared using a Mann–Whitney U test. The differences between the two groups were considered statistically significant if the p values were < 0.05 .

2.6 Gait classification

To implement an automatic detection of abnormal gait with the proposed gait-variability features, the classical SVM classifier, which is a powerful statistical learning tool developed by Vapnik [35], was utilized. The goal of SVM is to find the hyper-plane with the maximal margin to separate the training samples in the feature space. To set up a linear separating hyper-plane for nonlinear problems, SVM employed kernel methods to map data to a

Fig. 3 Comparison of two different outlier elimination methods: **a** the distance-based method and **b** the 3-sigma method. The original time series marked with *stars* is the right-foot stride-interval sequence recorded from a 47-year-old CO subject. The detected outliers are marked with *circles* in the graph



higher-dimensional feature space. Several types of kernels, such as sigmoid, polynomial, and RBF, can be used for the mapping. Generally, no analytical or empirical study has conclusively established the superiority of one kernel over another, so the performance of SVMs in a particular task may vary with this choice [6]. We have tested the aforementioned three nonlinear kernels together with the linear kernel, and we found that the best classification performance was achieved with the Euclidean-distance-based RBF kernel by checking the classification accuracy with the corresponding optimal classifier parameters. As for the implementation of the SVM classifier, in this study, we utilized the OSU-SVM, which is a SVM toolbox developed in the Department of Electrical and Computer Engineering, Ohio State University, USA.

2.7 Performance evaluation

The leave-one-out cross-validation (LOOCV) procedure was applied to validate the classification performance of the proposed gait-variability measure. The test performance of the proposed feature was evaluated by the following statistical measures: specificity (S_p), sensitivity (S_n), classification accuracy (C_a), and the receiver operating characteristic curve (ROC) area (A_c), which was calculated by using the ROCKIT software provided by the University of Chicago, Chicago, IL, USA [32].

3 Results

3.1 Preprocessing results

Figure 3 illustrates the effectiveness of the distance-based method compared to the previous “3-sigma-rules” method. From the annotations in the figure, one can find that some apparent outliers failed to be detected when using the

“3-sigma-rules,” while they were captured by the distance-based method. The parameters used in this filtering process were tuned manually in the same way as practiced in other density-based or distance-based algorithms [26, 33]. It was found that the disturbed gait strides around the turning-back often have a number below 10. Therefore, we chose the nearest neighbor number k as 9, and then, after several adjustments according to the outlier-detection results, the distance threshold was set to 40 ms.

3.2 Results for gait-variability representation

3.2.1 Results of the Teager energy operator

As demonstrated by Wu and Shi [37], the stride time series for the left and right foot is highly correlated. Therefore, only the right-foot stride time series was analyzed in this study. Figure 4a, c shows representative Poincaré plots of Teager energy time series for two subjects, one healthy CO subject, and one ALS patient with a pathological duration of 17 months, respectively. Figure 4b, d shows Poincaré plots of the stride-interval time series for the same two subjects, respectively. Comparing the plots in Fig. 4, one can find that the dispersion of points for the ALS patient exhibits a greater tendency than that for the normal control in the Teager energy Poincaré plots and in the stride-interval Poincaré plots. Greater dispersion tendency indicates a higher variability, and therefore, gait variability in ALS patients is higher than that in healthy adults. These results are consistent with previous studies [19, 37]. In addition, it is also observed that the Teager energy Poincaré plots tend to have a wider dispersion compared with the stride-interval Poincaré plots for the same subject. This observation is more apparent in the case of the ALS patients. We further calculated the standard deviation of each Teager energy time series and used statistical analysis to compare the SD values between the ALS group and the normal group. As a

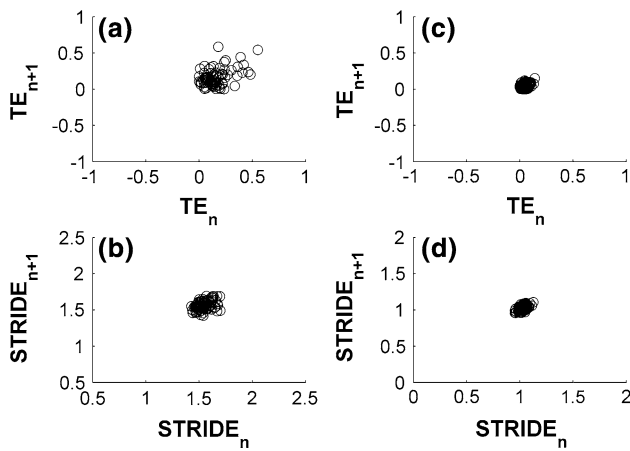


Fig. 4 Poincaré plots of the right-foot gait stride-interval time series (b, d) and their corresponding instantaneous Teager energy sequences (a, c). Plots of a, b are for a 30-year-old female healthy CO subject, while c, d are for a 43-year-old male ALS patient

comparison, the same calculation was also performed for the corresponding stride-interval time series. The results are shown in Table 1. According to the *p* values listed in Table 1, one can find that the difference in SD features between the two subject groups is more significant for the Teager energy time series than for the stride-interval time series.

3.2.2 Results of the calculation of the PE feature

To determine the proper values for the parameter values of dimension *m* and delay τ , the significant difference of the PE values between the ALS patient group and the healthy subject group was investigated by using different combinations of the parameter values ($m = 3-7$ and $\tau = 2-5$) recommended in previous studies. We found that, in most cases, the calculated PE values in the CO subjects were significantly higher than those in the ALS patients with a *p* value <0.05 . Figure 5 illustrates the PE values for both ALS patients and CO subjects when calculated with *m* from 3 to 7 and $\tau = 2$. It was observed that a difference in the PE values between the two subject groups existed in all the cases. In fact, when $\tau = 2$ and *m* took a value from 3 to 7, the corresponding *p* value was 4.3×10^{-3} , 3.5×10^{-3} , 4.2×10^{-5} , 6.5×10^{-5} , and 1.5×10^{-4} , respectively. We then set $m = 5$ and $\tau = 2$ because they provided the PE

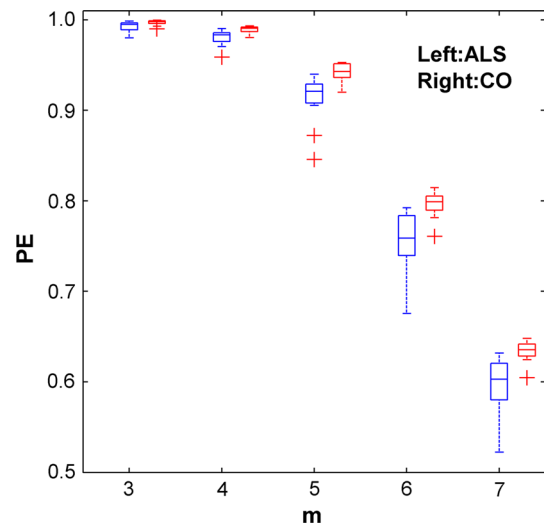


Fig. 5 Permutation entropy (PE) values of the instantaneous gait energy time series for the subjects in the ALS and CO groups, where scale $\tau = 2$ and dimension *m* takes a value from 3 to 7

feature with the lowest *p* value (i.e., the highest extent of separability), following the same parameter-setup method that was also utilized in Ref. [36].

Thus, two features were extracted and used in the classification experiments. One was the SD value of the Teager energy time series (SDTE), and the other one was the PE value of the same Teager energy time series (PETE). They formed a feature space that is shown in Fig. 6. The gait patterns associated with the ALS subjects and the healthy CO subjects were represented by using scatter markers of squares and stars, respectively. Note that most of the CO patterns congregated in a small region where $SDTE < 0.04 \text{ s}^2$ and $PETE > 0.93$. On the other hand, the ALS patterns were dispersed in a larger area of the SDTE–PETE feature plane.

3.2.3 Classification results

The classification results are shown in Table 2. It can be observed that, in general, the classification results evaluated with the features (i.e., the SD value, the PE value of the time series, and the combination of them) extracted from the Teager energy time series were more accurate than those from the original stride-interval time series. These results indicated again that the preprocessing by

Table 1 Comparison of the SD feature between the stride-interval time series and the Teager energy time series

Statistics name	Mean \pm SD		<i>p</i> values
	ALS	CO	CO versus ALS
Stride-interval SD (s)	0.059 \pm 0.026	0.026 \pm 0.006	1.23×10^{-03}
Teager energy SD (s ²)	0.088 \pm 0.050	0.030 \pm 0.008	1.79×10^{-05}

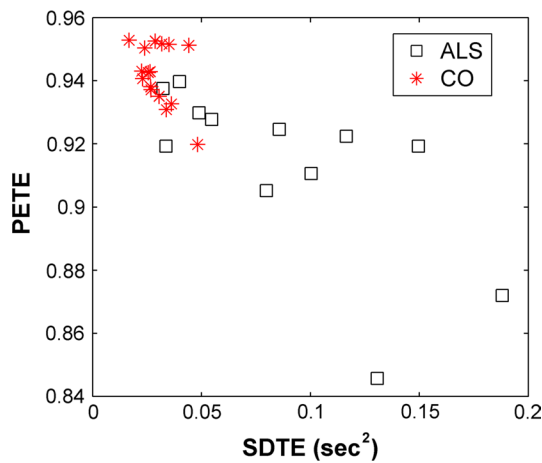


Fig. 6 Scattergram of the gait patterns of the subjects with amyotrophic lateral sclerosis (ALS), marked as *squares*, and of the healthy control (CO) subjects, marked as *stars*, in the two-dimensional feature space. The two features were the SD value of the Teager energy time series (SDTE) and the PE value of the same Teager energy time series (PETE)

TEO could help to improve the classification capability for the same features. Results with more accuracy were obtained with a combination of the two features. The best

classification result was obtained with the combination of the SDTE and PETE features. That included a specificity of 93.8 %, a sensitivity of 91.7 %, an accuracy of 92.86 %, and a ROC area A_z of 0.9643 [standard error (SE) 0.04].

The comparison of the classification performances of the proposed variability measures with other variability measures on the same dataset is tabulated in Table 3. We note that, for two gait-variability measures, the coefficient of variation and the nonstationarity index [19], the results were generated by our own realization of classification because only statistical p values were reported in the original paper. From the results, it can be observed that the proposed features achieved the best classification results. We also noticed that the accuracy evaluated by an all-training–all-testing (ATAT) scheme in Duta’s study [12] was 91.7 %, which is close to the 92.86 % in our study. However, the classification accuracy provided by our proposed features was 96.43 % when evaluated with the ATAT scheme, which is higher than that obtained in the LOOCV scheme. The classification performance with the proposed gait-variability features implies that they are characteristic of the stride-interval signals, and they can facilitate a more accurate separation of the normal and abnormal gaits when

Table 2 Confusion matrix for the classification performance of different combinations of features extracted from the original stride-interval time series and their corresponding Teager energy time series

Time series name	Feature	Positive class (ALS)		Negative class (CO)		Specificity (S_p)	Sensitivity (S_n)	Accuracy (C_a) (%)
		TP	FN	TN	FP			
		Teager energy	SD	10	2			
	PE	10	2	15	1	0.938	0.833	89.29
	SD, PE	11	1	15	1	0.938	0.917	92.86
Original stride interval	SD	9	3	14	2	0.875	0.75	82.14
	PE	9	3	15	1	0.938	0.75	85.71
	SD, PE	10	2	15	1	0.938	0.833	89.29

TP, TN, FP, FN true positives, true negatives, false positives, and false negatives, respectively

Table 3 A comparison of the classification capability of the proposed variability features with other variability measures on the same gait dataset for discriminating abnormal (ALS) gait and normal (control) gait

Extracted features	Classifier	Evaluation method	ROC area	Accuracy in %
Signal turns count [36]	LS-SVM	LOOCV	0.9629	89.66
Kullback–Leibler divergence [37]	LS-SVM	LOOCV	0.869	82.8
Symbolic entropy [4]	NA	NA	0.85	NA
Model of gait dynamics [42]	RBFNN	LOOCV	NA	89.66
Cross-correlation [12]	ERNN	ATAT	NA	91.7
Coefficient of variation* [19]	SVM	LOOCV	0.9244	85.71
Nonstationarity index* [19]	SVM	LOOCV	0.7669	78.57
Proposed features	SVM	LOOCV	0.9643	92.86

LS-SVM least squares support vector machine, ERNN Elman’s recurrent neural network, RBFNN radial basis function neural networks, ATAT all-training–all-testing, NA information not available in the literature

* The results were generated by our own realization of classification

Table 4 Confusion matrix for the classification performance of the two proposed gait-variability features for discriminating ALS patients with a mild degree from those with an advanced degree

Features	Positive class (mild)		Negative class (advanced)		Specificity (S_p)	Sensitivity (S_n)	Accuracy (C_a)
	TP	FN	TN	FP			
SDTE, PETE	2	1	8	1	$8/9 = 0.889$	$2/3 = 0.667$	83.33 %

combined with other features such as the average, maximum, and minimum stride interval [9, 38].

We have also investigated the degree of functional impairment of ALS patients using the proposed gait-variability features. Following a method used in two previous studies [4, 19], diseased ALS subjects were divided into two subgroups: advanced functional impairment (stride time above 1.2 s, which corresponds to the upper quartile among all subjects) and mild functional impairment (stride time less than or equal to 1.2 s). Based on this criterion, three of the ALS patients (no. 2, 8, and 10) had mild functional impairment, and the other nine patients (nos. 1, 3, 4, 6, 7, 9, 11, 12, and 13) had severe functional impairment. The classification results between these two subgroups are shown in Table 4. As one can see, a classification accuracy of 83.3 % was obtained, which indicates the potential use of the proposed features for tracking the progress of the ALS disease or other similar diseases that cause abnormal gaits.

4 Discussion

By using three consecutive samples, the calculation of the Teager energy for discrete time series can capture an energy variation with excellent time resolution. Therefore, it is often used to detect transient events that happen in a regular rhythmic activity, such as heart rate signals [24] or machine vibration signals [3]. Though the stride-interval time series for healthy controls also varies in a complex and nonlinear fashion [18], the fluctuation amplitude is still more “regular” than that of the ALS patients, which was verified in many previous studies [4, 19]. Thus, the enhancement of variation provided by TEO is still noticeable when it is applied to gait stride-interval time series. Such enhancement can be observed either from the Poincaré plots in Fig. 4 or from the corresponding calculation results shown in Table 1.

Because a special characteristic of TEO is the consideration of the instantaneous frequency during the calculation of Teager energy, the benefits brought by TEO in this work indicate that it should be very helpful in representing the time-varying gait signal in a joint time–frequency space. For this purpose, the quadratic time–frequency distribution (QTFD) is a popular choice, as it can provide good

time and frequency resolution and has been successfully applied to many other signals for similar purposes, such as electrocardiogram (ECG) signals [11], machine vibration signals [20], and power quality signals [1]. When applying the QTFD to gait signals, a critical task is choosing a suitable kernel function that can effectively reduce the cross-terms caused by the quadratic nature of the QTFD. Many solutions were available, such as the smooth-windowed Wigner–Ville distribution (SWWVD), the compact-support kernel TFDs [2], and the modified B-distribution (MBD) [21]. For gait signals, the MBD with a gamma function as its kernel is perhaps a good choice because it is very suitable for signals with slowly varying FM components [11].

Permutation entropy is associated with the order structure of events in a phase space. Therefore, it is very suitable for revealing the temporal structure of a time series. We calculated the PE value of the time series generated by the TEO. The results indicate that the temporal structures of gait variability for healthy adults are more varied than those of the ALS patients in a reconstructed phase space with certain dimensions and certain scales. As we know, physiological complexity is associated with the ability of living systems to adjust to an ever-changing environment [4]. However, under pathological conditions, this adaptability could be weakened and lead to rigid, periodic, and regular behavior [15]. Thus, the loss of variability of a temporal structure may be a generic feature of pathological dynamics, and similar results have also been reported in previous studies on gait variability [4, 28].

We have noted that, during the classification experiments, the results of the specificity are often higher than those of the sensitivity. This phenomenon may be explained by the wide spread of ALS samples compared with the small distribution range of CO samples as shown in Fig. 6. As for the wide spread of gait variability for the ALS group, it could be attributed to the wide spread of the subjects’ disease duration from onset, which is in a range from 1 to 54 months with a mean \pm SD of 18.3 ± 17.8 months.

Indeed, this study has certain limitations. First, in the current dataset, the age and gender distributions are not well matched between the different gait groups. The exact mechanism of how these two factors act on gait variability is still not clear. For age, slower walking leads to greater variability in young adults, but slow speeds are also typical in older adults [25]; for gender, the study presented by

Cho et al. [7] showed that the female walking speed was significantly slower than the male's, but the duration of the stance phase and the double support period expressed as a percentage of the gait cycle were not different between the genders. Therefore, for the purpose of underlining the ALS disease's role in altering gait variability, it is better to design a more reasonable protocol to balance the age and gender distribution in the different gait groups. Second, in the current experiments, turning back happens at the end of the testing hallway because it has a limited length. During this process, the walking rhythm can be disturbed. Therefore, the method for producing gait stride-interval time series should be modified to allow for continuous and barrier-free walking. For this purpose, perhaps the wearable inertial-sensor-based system [40] could be a good option due to its convenience and easy operation for use outside of the laboratory.

5 Conclusion

The aim of the present study was to assess the altered gait variability in ALS patients. As a new attempt, we evaluated the gait variability on the instantaneous energy time series that was generated by applying the TEO to the gait stride-interval time series. Two features were extracted to quantify the variability of the gait energy time series. The standard deviation value was used to capture the fluctuation magnitude from one stride to the other stride, while the PE was applied to represent the temporal structure of such variability. The results of the statistical analysis and classification experiments indicated that the two features, along with the SVM classifier, constituted a promising tool that could be used in rehabilitation-related applications such as gait monitoring for ALS patients.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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