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A PDF-Based Classification of Gait Cadence Patterns in Patients with Amyotrophic Lateral Sclerosis

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***Abstract*— Amyotrophic lateral sclerosis (ALS) is a type of neurological disease due to the degeneration of motor neurons. During the course of such a progressive disease, it would be difficult for ALS patients to regulate normal locomotion, so that the gait stability becomes perturbed. This paper presents a pilot statistical study on the gait cadence (or stride interval) in ALS, based on the statistical analysis method. The probability density functions (PDFs) of stride interval were first estimated with the nonparametric Parzen-window method. We computed the mean of the left-foot stride interval and the modified Kullback-Leibler divergence (MKLD) from the PDFs estimated. The analysis results suggested that both of these two statistical parameters were significantly altered in ALS, and the least-squares support vector machine (LS-SVM) may effectively distinguish the stride patterns between the ALS patients and healthy controls, with an accurate rate of 82.8% and an area of 0.87 under the receiver operating characteristic curve.**

I. Introduction

Caused by the deterioration of motor neurons in the central nervous system, amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, affects the muscular contractions during normal locomotor function [1, 2]. Due to the interruption of the pathway from the brain to the muscle, the lower limbs could not properly perform voluntary movements, which leads to a few altered gait patterns in patients with ALS [3,4]. The analysis of gait cadence in ALS patients may help study the movement disorders caused by the degeneration of motor neurons [5].

In recent studies [5–9], computer-aided methods have been utilized to assess the gait dynamics, and also to describe the distinct patterns of the gait in ALS. Hausdorff *et al.* [5] used the coefficient of variation (CV) to measure the instability of the gait in ALS. Their results suggested that the gait speed is apparently slower in ALS, and the CV value of the strides in ALS patients is much larger than that in healthy adults. They also observed that the stride-to-stride fluctuation dynamics are perturbed in ALS, but the changes of the gait variability (in terms of the fractal scaling index and nonstationary index) in ALS do not reach the significance level. The altered gait patterns in ALS could also be measured with other effective methods. Scafetta *et al.* [8] developed a supercentral pattern generator model to simulate human gait dynamics, and then discussed the stochastic and fractal properties of the gait in ALS, compared with those in Parkinson's disease and Huntington's disease. Wu *et al.* [7] applied the signal turns count method [10] to study the swing-interval fluctuations in ALS. Although some nonlinear methods have been used to investigate the complexity of human locomotion process, further quantitative studies still call for more computational tools that are suited for analysis of the gait in ALS [7].

The present study applied a statistical technique and a nonlinear classifier to study the changes of gait cadence (in terms of stride interval) in ALS. We first used the Parzen-window method to estimate the stride-interval probability density functions (PDFs) for healthy controls and ALS patients, respectively. Then we computed two statistical parameters (the mean of the left-foot stride interval and the modified Kullback-Leibler divergence), from the PDFs of stride interval. We also employed the kernel-based support vector machine as a nonlinear classifier to distinguish the stride patterns between the groups of healthy controls and ALS patients.

II. Methods

A. Gait data

The gait data we used were the same as used in the previous related studies [5, 7, 8], and can be accessed via the PhysioNet website [11]. A total of thirteen ALS patients (age: 55.6 ± 12.8 years, mean $\pm$ standard deviation, SD) were recruited from the Neurology Outpatient Clinic at Massachusetts General Hospital, Boston, MA, USA. The ALS patients were without visual, respiratory, cardiovascular, or other neurological diseases, which might lead to lower extremity weakness. The control (CO) group contained sixteen healthy subjects (age: 39.3 ± 18.5 years). The healthy CO subject group was established by physical examination and medical history. All the CO and ALS subjects provided informed consent as approved by the Institutional Review Board of the Massachusetts General Hospital.

According to the protocol [5], the subjects walk at their normal pace along a straight hallway of 77 m for 5 min, without stopping on level ground. The force underneath each subject's feet was recorded using a group of ultrathin pressure sensors sampled at 300 Hz, and the stride interval was obtained with the stride detection algorithm proposed by Hausdorff *et al.* [12].

In order to eliminate the start-up effects, the stride-interval samples recorded in the first 20 s was removed, which was the same as implemented in the previous studies [5, 7]. The stride outliers associated with the turning events at the end

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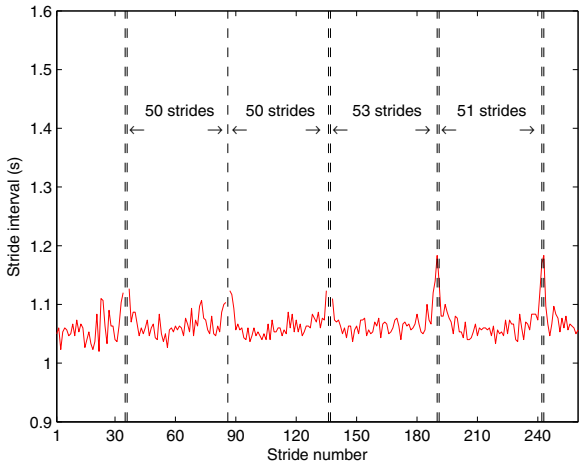
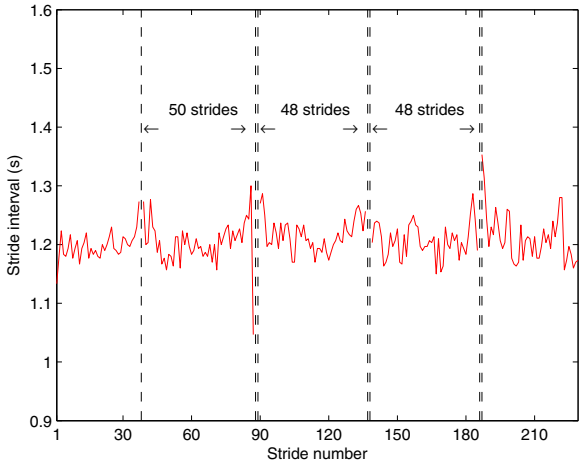
of the hallway were also removed, using the 3-SD median filter presented in study of Wu *et al.* [7]. For the purpose of probability-density-function-based comparative study, the right-foot time series of stride interval were calibrated with the left-foot time series. Figure 1 illustrates the detections of stride outliers present in the left-foot time series of a healthy CO subject (female, age: 22 years) and of an ALS patient (male, age: 40 years), respectively. According to the outlier annotations, three unabridged 77-m walking distances can be segmented (see the *dashed lines* in Fig. 1).



(a)



(b)

Fig. 1. Illustrations of the time series of left-foot stride interval recorded from (a) a healthy control subject, and (b) an ALS patient. *Dashed lines* locate the outlier strides which were 3 standard deviations greater or less than the median value of stride interval over the entire time series.

B. Probability density function (PDF) estimation

Before estimating the PDF of stride interval, we first computed the histogram as a reference for the PDF models. For each subject, the histogram of stride interval was established with B bins, which helped calculate the probability of occurrence with B containers of equal length in the amplitude range of stride interval [13]. The optimal number of bins were obtained in accordance with Scott's choice [14], the minimization criterion of the mean-squared error between the estimated histogram and the Gaussian density function.

For each subject, the nonparametric estimate of the stride-interval PDF was obtained with the Parzen-window method [15]. Supposing the situation where a time series of stride interval contains a collection of M samples, sorted in amplitude as $\{x_1, x_2, \cdots, x_M\}$, the estimated PDF $\hat{p}(x)$ can be provided by the function [9, 16]:

$$\hat{p}(x) = \frac{1}{M}\sum_{m=1}^{M} w(x - x_m), \tag{1}$$

where $w(\cdot)$ represents the Gaussian window function as

$$w(x - x_m) = \frac{1}{\sigma_{\mathrm{P}}\sqrt{2\pi}} \exp\left[-\frac{(x - x_m)^2}{2\sigma_{\mathrm{P}}^2}\right], \tag{2}$$

where σ_{P} denotes the spread parameter. In the present study, the estimated PDF was allocated into the same B containers as computed for the histogram, so that the Parzen-window PDF can be presented as $\hat{p}(g_b)$, in which g_b, $b = 1, 2, \cdots, B$, indicating the range of stride interval g. The optimal spread parameters that minimize the mean-squared error between the Parzen-window PDF and the histogram were 0.02 and 0.03 for the groups of healthy controls and ALS patients, respectively.

C. Statistical parameters

The mean value of stride interval can be computed from the estimated PDF, $\hat{p}(g_b)$, as

$$\mu = \sum_{b=1}^{B} g_b \hat{p}(g_b). \tag{3}$$

For each subject, the mean values of stride interval for the left foot and right foot are presented as μ_{L} and μ_{R}, respectively. Either the variance of stride interval or the coefficient of variation was not considered in this paper, because these two statistical parameters have been discussed in the study of Hausdorff *et al.* [5].

In probability theory, the Kullback-Leibler divergence is commonly used to measure the difference between two PDFs [17]. However, such a relative-entropy-based parameter does not fit the metric criterion, due to its asymmetry. In order to measure the difference between the stride-interval PDFs estimated from the left foot and right foot, we used the modified Kullback-Leibler divergence (MKLD), defined as

$$\begin{aligned}\mathrm{MKLD} &= D[\hat{p}_{\mathrm{L}}(g_b)\,|\,\hat{p}_{\mathrm{R}}(g_b)] + D[\hat{p}_{\mathrm{R}}(g_b)\,|\,\hat{p}_{\mathrm{L}}(g_b)] \\ &= \sum_{b=1}^{B} \hat{p}_{\mathrm{L}}(g_b) \ln\left[\frac{\hat{p}_{\mathrm{L}}(g_b)}{\hat{p}_{\mathrm{R}}(g_b)}\right] + \sum_{b=1}^{B} \hat{p}_{\mathrm{R}}(g_b) \ln\left[\frac{\hat{p}_{\mathrm{R}}(g_b)}{\hat{p}_{\mathrm{L}}(g_b)}\right],\end{aligned} \tag{4}$$

where $D[\hat{p}_{\mathrm{L}}(g_b)\,|\,\hat{p}_{\mathrm{R}}(g_b)]$ denotes the Kullback-Leibler divergence of the Parzen-window PDF of right-foot stride interval, $\hat{p}_{\mathrm{R}}(g_b)$, from the PDF of stride interval estimated for the left foot, $\hat{p}_{\mathrm{L}}(g_b)$. The logarithms in the definition of the MKLD are taken to base e (i.e., natural logarithms) so that the information is presented in nats (about 1.44 bits). The MKLD is nonnegative, i.e., $\mathrm{MKLD} \geq 0$. The minimum $\mathrm{MKLD} = 0$ occurs if and only if $\hat{p}_{\mathrm{L}}(g_b) = \hat{p}_{\mathrm{R}}(g_b)$, for all $b = 1, 2, \cdots, B$.

D. Pattern classification

In the present study, the least-squares support vector machine (LS-SVM) was employed to distinguish the stride patterns between the groups of healthy controls and ALS patients. The LS-SVM has some modifications to the Vapnik SVM formulation [18]. Similar to the Vapnik SVM, the LS-SVM is also a type of kernel-based artificial neural network, the learning of which follows the structural risk minimization rule [18]. With different inner-product kernels, the LS-SVM is able to perform the same function as the polynomial learning machine (with polynomial kernels), the radial basis function network (with Gaussian kernels), or the multilayer perceptron with a single hidden layer (with sigmoid kernels) [18]. Compared with the Vapnik SVM, the LS-SVM can be regarded as a regularization network that solves linear Karush-Kuhn-Tucker equations, so that the LS-SVM has an improvement of moderate complexity.

We tested the classification performance of the LS-SVM based upon three types of nonlinear kernels (i.e., the polynomial, sigmoid, and Gaussian kernels). The highest classification accuracy was provided by the Gaussian-kernel LS-SVM with variance parameter $\sigma_\kappa^2 = 0.25$. The Gaussian kernel function $\kappa(\cdot)$ used in the experiment can be written as

$$\kappa(\mathbf{f}_i, \mathbf{f}_j) = \exp\left[\frac{-\left\|\mathbf{f}_i - \mathbf{f}_j\right\|^2}{\sigma_\kappa^2}\right], \qquad (5)$$

where $\mathbf{f}_i$ denotes the input feature vector associated with the ith subject, and σ_κ^2 represents the variance parameter of the Gaussian kernel. The performance of the LS-SVM was evaluated with the leave-one-out (LOO) cross-validation method, and the classification results were also characterized the receiver operating characteristic (ROC) curve.

III. Results

Figure 2 illustrates the histogram graphics and the Parzen-window PDFs of stride interval shown in Fig. 1. It can be observed that the mean of stride interval in the ALS patient was significantly increased, and the spread of the stride interval PDF of the ALS patient was much wider than that of the CO subject. We computed the mean values of the left-foot and right-foot time series for each subject, and observed that μ_L and μ_R were highly correlated (over 0.99 in terms of Pearson's correlation coefficient). The statistics of the mean of left-foot stride interval for the CO and ALS subject groups were 1.093 (SD: 0.091) and 1.354 (SD: 0.196), respectively. Compared with the control group, the value of μ_L in the ALS group was increased by 23.9% (an increment of 0.261 s). The p-value obtained with the Student's t-test was lower than 0.001, which indicated that the mean of the left-foot stride interval was significantly different in ALS patients.

The MKLD value of the ALS subject group (0.445 ± 0.499 nat) was much higher than that of the CO subject group (0.106 ± 0.160 nat). Such results indicated that the symmetry of stride interval has been disturbed in the ALS patients. The p-value of the MKLD ($p < 0.02$) also reached the level of significant difference. In the present study, we used the the mean of the left-foot stride interval and the MKLD values as the distinct features for the classification The stride patterns of the groups of the CO and ALS subjects were shown in Fig. 3 (the support vectors marked as solid data points). It is worth noting that most of the CO patterns congregated in a restricted region where $\mu_L < 1.2$ s and MKLD < 0.6 nat, whereas the ALS patterns were widely dispersed in the upper district where $\mu_L > 1.1$ s.

The classification accuracy of the LS-SVM, evaluated by the LOO cross-validation method, was 82.8% (sensitivity: 0.769; specificity: 0.875). For the purpose of comparison, we also implemented the linear discriminant analysis (LDA) method to perform a linear classification. In the classification experiment, the LS-SVM can provide a higher accurate rate than the LDA (accuracy: 65.5%; sensitivity: 0.462;

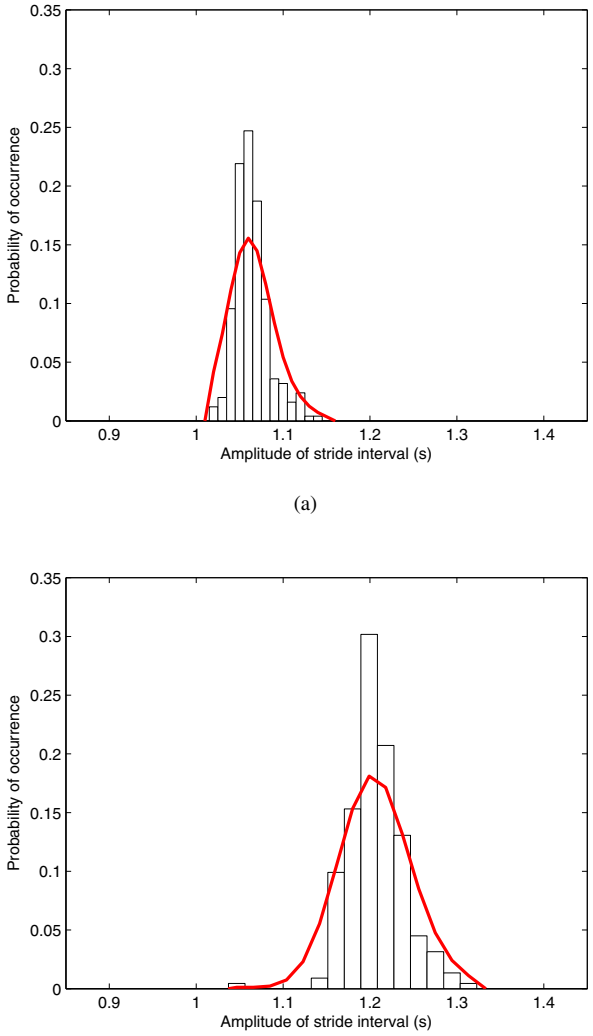


Fig. 2. Probability density functions (PDFs) of the left-foot stride interval estimated from (a) a healthy control subject, and (b) an ALS patient. The number of bins computed for the histograms of the healthy control and the patient with were 13 and 15, respectively. The spread parameters computed for the PDFs of the healthy control and the ALS patient were 0.02 and 0.03, respectively.

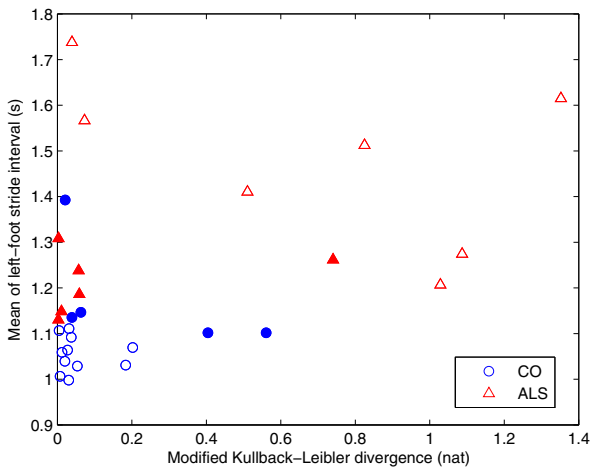


Fig. 3. Scatter plot of the stride patterns of the healthy CO subjects and of the patients with ALS. The stride patterns were displayed with the features of the MKLD and the mean of the left-foot stride interval (μ_L). The linear and nonlinear decision boundaries were provided by the linear discriminant analysis (LDA) and the LS-SVM with Gaussian kernels, respectively. Solid data points represent the support vectors.

specificity: 0.875). The LDA was not able to distinguish six ALS stride patterns from those of the CO group, which reflects a low sensitivity value (0.462). The area (A_z) under the ROC curve obtained by the LS-SVM was 0.87, much larger than that of the LDA (A_z: 0.52).

IV. Discussion and Conclusion

Both of the two statistical parameters presented in this paper could help the LS-SVM distinguish the ALS stride patterns with an excellent accurate rate. It is worth noting that either μ_L or μ_R can be used as an alternative feature for the pattern analysis, as they were highly correlated with each other. However, such a high correlation does not indicate the symmetry in the left-foot and right-foot gait rhythm time series of ALS patients, because the mean of stride interval computed based on the PDF does not contain any information about gait fluctuations. Although the MKLD parameter can be used to identify the stride patterns in ALS, it is worth noting that the MKLD is not suitable to serve as a measure of gait symmetry, as such a statistical parameter does not contain any temporal information. For example, two time series with completely different temporal structures could also cause a near-zero-value MKLD, as long as their samples produce similar probability distributions of amplitude, whereas the MKLD with a large value definitely indicates some degree of asymmetry in the gait. Therefore, the MKLD with a zero or near-zero value is a necessary but not sufficient condition for gait symmetry. In the present study, we only used the MKLD parameter as a discriminant feature, rather than a gait symmetry indicator, for the analysis of the stride patterns in two subject groups. The support vectors selected by the LS-SVM can highlight the boundary from the healthy subjects to the ALS patients, and may help study the pathological changes in the gait parameters. The methods presented in this paper also show high potential in monitoring of the gait during the progressive course of ALS. In addition to the conventional classification methods, the multiple classifier systems have recently been effectively used for medical diagnosis [19]. With the concept of "divide and conquer", a multiple classifier system combines a finite number of component classifiers with a certain fusion strategy to provide a consensus medical decision [19]. For the future work, we will consider the design of multiple classifier systems with a few fusion strategies, for a better and comprehensive analysis of the gait patterns of ALS patients.

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