Analysis of Gait Rhythm Variability in Patients with Amyotrophic Lateral Sclerosis

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Abstract—**Gait rhythm patterns in neurodegenerative diseases could become abnormal due to deterioration of motor neurons. In the present study, we used the turns count (TC) method to measure the variability of gait rhythm (swing interval) in amyotrophic lateral sclerosis (ALS). The number of turns detected with the threshold of 0.06 s in the swing-interval time series exhibits a significant difference (p < 0.001) between 16 healthy control subjects and 13 patients with ALS. The pattern classification experiments were implemented using the linear discriminant analysis (LDA) and the least-squares support vector machine (LS-SVM), with the input features of TC and averaged stride interval (ASI, p < 0.0001). The results showed that the TC and ASI features may serve as excellent indicators to characterize the gait variability in ALS. The LS-SVM with sigmoid kernels was able to provide 89.7% classification accuracy and an area of 0.9568 under the receiver operating characteristic curve, which were superior to the diagnostic performance of the LDA.**

Keywords— **Amyotrophic lateral sclerosis, gait dynamics, linear discriminant analysis, support vector machine.**

I. INTRODUCTION

Motor neurons in the brain stem and spinal cord control voluntary muscle movement. Degeneration of motor neurons will result in neurological pathologies and lead to motor skill dysfunction. Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder caused by the degeneration of motor neurons or their myelin sheath [1]. With the ALS disorder, muscles cannot receive the sensory information in the central nervous system. Early clinical symptoms of ALS include twitching and cramping of the arms or legs, muscle fatigue, difficulty speaking, and swallowing or breathing [2]. The patient may gradually lose the ability to initiate and control voluntary movement [3, 4].

Analysis of gait dynamics in neurodegenerative diseases can assist the neurologist to develop computer-aided tools in order to monitor the progression of a specific neurological pathology. Sekine *et al.* [5] used a maximum likelihood estimation method to compute the fractal parameters in the acceleration signals recorded during climbing stairs and walking along a corridor. The results of their study showed that the fractal dimensions of the gait rhythm present in the acceleration signals recorded from patients with Parkinson's disease tend to be higher than those of healthy elderly subjects [6]. Hausdorff *et al.* [7] estimated the variation of gait cycle duration, also referred to as stride interval, in healthy elderly subjects and patients with Huntington's disease. Their study suggested that the coefficient of variation is associated with the degree of severity of Huntington's disease. Hausdorff *et al.* [8] studied the gait fluctuation in patients with ALS, by using the detrended fluctuation analysis method. Their results showed that the temporal gait-rhythm variability parameters (stride-to-stride fluctuation magnitude and fractal dimensions) of patients with ALS are significantly different from those of healthy subjects. In addition to stride interval, it is hypothesized that the gait patterns extracted from swing-interval time series of ALS patients might become abnormal as well. In the present study, we applied the turns count method to study the swing-interval variability in ALS patients, and also carried out the linear and nonlinear classification experiments to analyze the ALS gait patterns.

II. METHODS

A. Data Description

The gait database used in the present study was the same as used in the previous study of Hausdorff *et al.* [8], and can be downloaded via PhysioNet (http://www.physionet.org) [9]. The database consists of the time series of stride interval (along with its two subphases: swing and stance intervals) recorded from 16 healthy control (CO) subjects, including 2 men and 14 women aged 20-74 years (39.3 ± 18.5 years, mean ± standard deviation, thereafter), and 13 patients with ALS, including 10 men and 3 women aged 36-70 years (55.6 ± 12.8 years). The duration of the neurological pathology since diagnosis of ALS ranges from 1 to 54 months (18.3 ± 17.8 months). These ALS patients were free from other pathologies that might affect the gait. Height and weight of the CO subjects was not significantly different from those of the ALS patients.

According to the experimental protocol [8], each subject was instructed to walk at his or her normal pace along a 77-

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m-long straight hallway for 5 min. The force applied to the ground for each stride was recorded using ultrathin force-sensitive switches placed inside each subject's shoes and a small and lightweight recorder worn with a wallet on the ankle. The signal from the foot switches was digitized by an on-board analog-to-digital converter at the sampling rate of 300 Hz with 12-bit resolution per sample. Each subject provided informed consent as approved by the Institutional Review Board of the Massachusetts General Hospital.

B. Median Filtering

In order to minimize start-up effects, the stride-interval and swing-interval samples recorded in the first 20 s were excluded. We applied a median filter to remove the stride-interval samples that were 3 standard deviations (SDs) greater or less than the median value over the entire time series. These stride-interval outliers had very large values because the subject had to turn around at the end of the hallway during the 5-min walking. In addition, the corresponding swing-interval samples in the time series associated with the hallway turns were also removed for the variability analysis and the further pattern classification experiments. Fig. 1 shows the stride-interval time series of a 50-year-old ALS patient. Two stride-interval outliers detected by the median filter are marked with diamonds in Fig. 1.

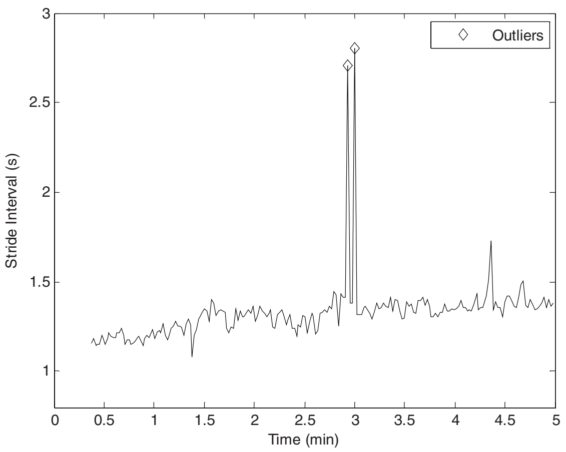

Fig. 1 An example of the raw stride-interval time series of a 50-year-old male subject with amyotrophic lateral sclerosis (ALS). Outliers were 3 SDs greater than the median stride interval over the entire time series.

C. Turns Count

The turns count (TC) can be used to characterize the degree of signal variability in a time series [10]. According to Rangayyan and Wu [11], the TC feature extracted from the knee-joint vibroarthrographic (VAG) signal analysis may serve as one of the useful indicators for the screening of articular cartilage disorders.

A signal sample in the time series can be identified as a "turn" if it satisfies the following two conditions: 1) it represents a change in direction in the signal; 2) the difference between its amplitude and that of the preceding sample should be over a certain threshold.

In the present work, the threshold used to detect the number of the signal turns in the swing-interval time series was varied from 0.05 to 0.1 s, increased by a step of 0.01 s. The Student's *t*-test was used to check whether or not the TC numbers of the ALS patients were different from those of the healthy CO subjects. Fig. 2 plots the p values of the Student's *t*-test on the TC numbers determined by different thresholds. It can be observed that the TC numbers present a significant difference ($p < 0.01$) between the ALS patients and the healthy CO subjects. With the threshold of 0.06 s, the lowest p value (0.0002) of the Student's *t*-test was obtained, which indicated that the TC numbers determined with such a threshold was the best choice in the detection procedure. The mean and SD values of the TC numbers for the healthy CO subjects and the ALS patients were 4.69 ± 4.59 and 28.77 ± 22.18, respectively.

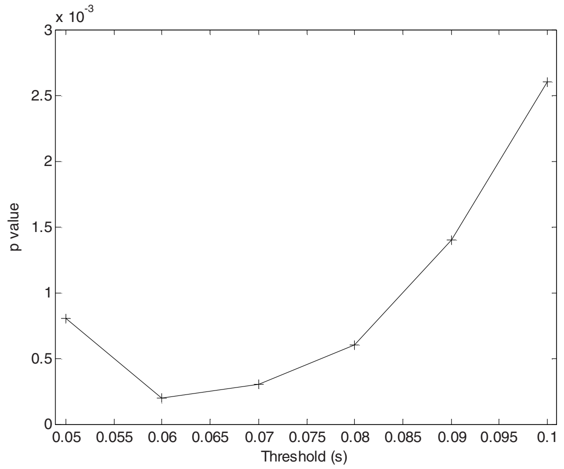

Fig. 2 The p values with regard to different thresholds that were used to determine signal turns in the swing-interval time series recorded from the healthy control and amyotrophic lateral sclerosis (ALS) subjects.

Hausdorff *et al.* [8] reported that the gait cycle duration, also referred to as the stride interval, is usually longer for patients with ALS, compared with that of healthy subjects. Thus we considered the averaged stride interval (ASI) as the other dominate feature for classification of the ALS gait patterns. In the feature extraction procedure, the ASI value was averaged over the entire stride-interval time series. The mean and SD values of the ASI feature for the healthy CO subjects and the ALS patients were 1.09 ± 0.09 s and 1.36 ± 0.21 s, respectively. And the p value of the ASI evaluated with the Student's t-test was lower than 0.0001, which indicated high statistical significance of separability between the healthy CO subjects and the ALS patients.

In the ASI-TC feature space, depicted in Fig. 3, the gait patterns of the healthy CO subjects and the ALS patients are marked with circles and crosses, respectively. It is clear that the TC numbers of the healthy CO subjects congregate in the range from 0 to 20, and the ASI values concentrate in the range from 0.9 to 1.2 s, except for a 74-year-old healthy CO subject who possesses an ASI of 1.14 s. And the gait patterns associated with the ALS patients are dispersive in the feature space. In addition, we may also observe that the gait patterns of the healthy CO subjects exhibit distinct characteristics compared with those of the ALS patients.

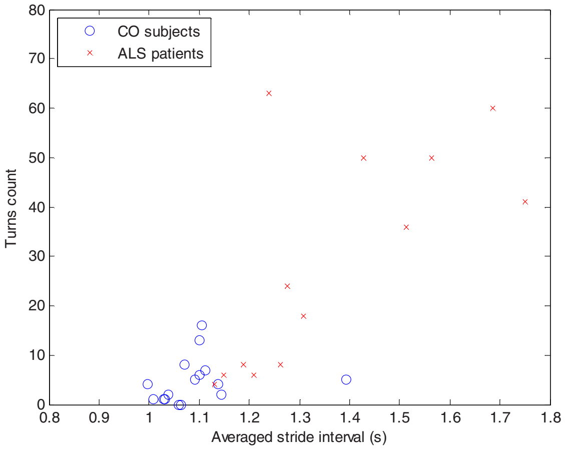

Fig. 3 Scatter plot of the averaged stride interval (ASI) and turns count (TC) features of the healthy control (CO) subjects, marked as circles, and of the patients with amyotrophic lateral sclerosis (ALS), marked as crosses.

D. *Classifiers*

The computer-aided analysis of the ALS gait patterns was implemented using the linear and nonlinear classifiers with the ASI and TC features. The linear classification was performed with the linear discriminant analysis (LDA), a commonly used statistical technique to find the linear combination of features which best separate two or more classes [12]. The nonlinear classifier used in the gait pattern analysis was the least-squares support vector machine (LS-SVM) proposed by Suykens *et al.* [13].

The LS-SVM is a reformulation to the standard support vector machine (SVM). The learning is implemented by minimizing a regularized least-squares cost function with equality constraints, and a subset of training data is selected as the support vectors. By choosing a specific type of nonlinear inner-product kernels in the hidden layer, the LS-SVM is able to perform the same function as the polynomial learning machine, radial-basis function network, or multilayer perceptron [14]. The major advantage of the LS-SVM is that the network has moderate complexity, which makes the training process become more efficient than the standard SVM. The detailed theoretical framework of the LS-SVM is described in the work of Suykens *et al.* [13]. In the experiments, we compared the performance of the LS-SVM with the polynomial, sigmoid, and Gaussian kernels, which were assigned with different model parameters. The classification performance was evaluated with the leave-one-out (LOO) cross validation method [15]. By checking the accuracy results of the LS-SVM with different kernels, we chose the sigmoid kernel function with the zero bias, unity scale parameter, and the regularization parameter equal to 5, which were well suited for the gait classification task.

III. Results

The classification performance was measured in terms of overall accuracy in percentage and the area (Az) under the receiver operating characteristic (ROC) curve. The ROC curve is commonly used in clinical applications to depict the patterns of sensitivities and specificities observed when the performance is evaluated at different diagnostic thresholds [16]. The ROC results were implemented using the ROCKIT software tool provided by Metz *et al.* (University of Chicago, Chicago, IL, USA) [17].

The LDA was able to provide 82.76% overall accuracy, and an Az of 0.9315 with the standard error (SE) of 0.0470. One healthy CO subject and four patients with ALS were misclassified, that is, the sensitivity and specificity were 0.6923 (11/13) and 0.9375 (15/16), respectively. On the other hand, the LS-SVM with the sigmoid kernels was able to provide higher percentage accuracy (89.66%) and a larger Az value (0.9568, SE: 0.0388), compared with the LDA. Although the LS-SVM cannot distinguish the same healthy CO subject as done by the LDA, only two ALS patients were misclassified by the LS-SVM. The sensitivity and specificity of the sigmoid-kernel-based LS-SVM evaluated with the LOO method were 0.8462 (11/13) and 0.9375 (15/16), respectively. Such results were superior to those obtained with the LS-SVM based on other kernels, such as the polynomial or Gaussian kernels.

Fig. 4 plots the ROC curves provided by the LDA and the LS-SVM, respectively. It can be observed that the LS-SVM improved the diagnostic performance, and its ROC curve was consistently over that provided by the LDA. Such results demonstrated that the nonlinear classifier performed better than the linear classifier for the analysis of ALS gait patterns based on the ASI and TC features.

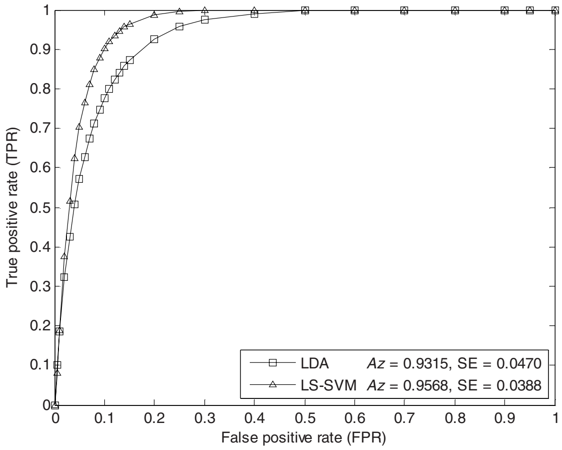

Fig. 4 ROC curves of the linear discriminant analysis (LDA) and the least-squares support vector machine (LS-SVM) evaluated with the leave-one-out (LOO) cross valuation method, respectively.

IV. Conclusion

ALS is a common neurodegenerative disorder in the central nervous system [18]. With the ALS, the gait rhythm from one gait cycle to the next would be affected due to deterioration of motor neurons in the central nervous system. Computer-assisted tools may help the neurologist better interpret and characterize a specific neurological degenerative pathology. Analysis of gait patterns based on signal processing and machine learning techniques is able to provide important diagnostic information that can be used to distinguish particular disorders of motor or sensory function, and to monitor the progression of a particular neurodegenerative disorder.

In the present work, we studied the variability of swing interval with the turns count (TC) method, and also measured the averaged stride interval (ASI). Two dominate statistical features, i.e., the TC numbers ($p < 0.001$) and the ASI ($p < 0.0001$), extracted from the swing- and stride-interval time series present significant differences between the healthy CO subjects and the patients with ALS. Both of the LDA and the LS-SVM were able to provide excellent diagnostic performance, in terms of the overall classification accuracy and the *Az* under the ROC curve. The pattern classification results obtained in our experiments showed the advantages of the TC and ASI features, as well as the nonlinear LS-SVM classifier, for the analysis of the ALS gait-rhythm patterns.

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