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Gait pattern discrimination of ALS patients using classification methods

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Abstract: Amyotrophic lateral sclerosis (ALS) is a mortal and idiopathic neurodegenerative disturbance of the human motor system. The disturbances of locomotion due to neurodegenerative diseases (NDDs) consisting of ALS, Parkinson disease (PD), and Huntington disease (HD) cause some abnormal fluctuations in gait signals. The investigation into gait patterns of NDDs provides significant information in order to develop new biomedical diagnosis devices. The main objective of this study is to evaluate the best discrimination method of ALS among control subjects (Co.), PD patients, and HD patients. The D2, D4, D5, and D6 detailed components, which were determined as critical features extracted from gait signals using discrete wavelet transform analysis in our previous study, are used as the inputs of all classification methods of the present study. Multilayer perceptron neural networks (MLPNNs), radial basis function neural networks, generalized regression neural networks, support vector machines, and decision tree classifiers are evaluated in this study. The MLPNN classifier, for which the average accuracy percentage is calculated as 92.09%, is evaluated as the most accomplished method. The best leave-one-out cross-validation (LOOCV) score as testing% (all-training-all-testing%) in MLPNN is calculated as 96.55% (99.76%) for ALS vs. Co. discrimination. Other LOOCV scores with MLPNNs are calculated as 82.14% (99.36%) for ALS vs. PD, 78.79% (99.17%) for ALS vs. HD, 83.33% (98.87%) for ALS vs. HD+PD, and 82.81% (99.00%) for ALS vs. HD+PD+Co., respectively. Consequently, this study proposes a new classification method based on MLPNNs to discriminate ALS among other NDDs and Co. after comparing the results.

Key words: Amyotrophic lateral sclerosis, multilayer perceptron neural networks, radial basis functions neural networks, generalized regression neural networks, support vector machines, decision tree

1. Introduction

Amyotrophic lateral sclerosis (ALS) is a fatal and idiopathic neurodegenerative disease (NDD) that affects the human motor system [1]. Parkinson disease (PD), which is characterized by symptoms such as a tremor, muscle stiffness, and a reduction in voluntary locomotion, and Huntington disease (HD), which causes some movement abnormalities and mental retardation, are other NDDs examined in this study. There are some clinical analyses including blood tests, electrophysiological analysis, spinal tap, and genetic tests in order to diagnose these types of NDDs in the medical literature. However, these analyses may be time-consuming and misunderstood at first. Accordingly, before other analyses, the ability to make fast measurements and decisions is significant for early diagnosis. This study focuses on the development of an optimum classification algorithm that will be used with a new fast decision device to discriminate ALS among other NDDs and Control subjects (Co.).

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Many studies in the literature established that some neurological disorders may change the gait dynamics [2–6]. Hausdorff et al. observed that stride interval time series derived from gait dynamics show some fluctuations in PD, HD, and especially ALS in their study based upon detrended fluctuation analysis [4,5]. There are various methods to analyze gait dynamic signals in the literature [7,8]. Some studies based on multiscale entropy, wavelet analysis [9–11], and nonstationary analysis using statistical and time-frequency methods have been published in recent years [12,13]. Zheng et al. achieved 84.17% nonlinear accuracy in classification between Co. and HD and 86.4% nonlinear accuracy in classification between Co. and PD using statistical methods [12]. Sugavaneswaran et al. achieved 89.2% linear and 100% nonlinear accuracy in classification between Co. and ALS using a time frequency-based algorithm [13]. Liao et al. proposed a method based on multiresolution entropy analysis of stance time fluctuations in an investigation of gait asymmetry. They claimed that gait symmetry changed depending on the presence of PD, HD, and especially ALS [14]. Lee and Lim studied PD classification using gait signal analysis based on discrete wavelet transforms (DWTs) and achieved 81.10% accuracy [15]. Wu et al. obtained 82.8% linear and 89.7% nonlinear accuracy in classification between Co. and ALS using a method based on signal turn count [16–18] and they obtained 67.7% linear and 90.3% nonlinear accuracy in a classification between Co. and PD using the probability density function classification method [19]. Baratin et al. used a computer-aided automatic characterization method for certain neurological disorders. They achieved an average accuracy of 85% for all classifications using an unbiased cross-validation method. They also achieved 86.2% linear accuracy in the classification between Co. and ALS groups [20]. Sarbaz et al. obtained 96.6% nonlinear accuracy between Co. and HD using spectral analysis [21]. Kamath et al. achieved 96.1% nonlinear accuracy between ALS and other NDDs using entropy analysis [22]. Xia et al. achieved 92.86% accuracy between ALS and Co. using entropy-based analysis [23]. The studies in the literature thus clearly show that the dynamics of gait signals show differences among Co. and subjects having neurological disorders [12,13,16–28]. These types of studies have generally focused on stride interval time series analyses. Unlike such studies, for the classification of gait dynamics, the usage of the compound force signal (CFS) is the fundamental innovation of this study.

The main objective of this research is to obtain the best results for the classification of ALS among other neurological disorders and Co. We propose an efficient method based on DWT and artificial neural networks (ANNs) for the discrimination of ALS in this study. Five different binary classifications (BCs) are created for the discrimination of ALS. These are ALS vs. Co. (BC1), ALS vs. PD (BC2), ALS vs. HD (BC3), ALS vs. PD+HD (BC4), and ALS vs. PD+HD+Co. (BC5). Wavelet analysis is a time frequency-based signal processing method commonly used in engineering and biomedicine. It is an efficient tool especially for low-frequency biomedical signals like gait signals. ANNs are also among the most common methods for the classification of gait signals [8,29,30].

During the study, first, each digital raw gait signal obtained from the left and right feet of subjects is compounded separately to compose the CFS. Afterwards, these signals are decomposed into subfrequency bands by means of DWTs for feature extraction using linear discriminant analysis (LDA) and the naïve Bayesian (NB) algorithm [31]. These analyses were realized in a previous study [31]. In this study, these features are applied to the inputs of multilayer perceptron neural networks (MLPNNs), radial basis function neural networks (RBFNNs), generalized regression neural networks (GRNNs), support vector machines (SVMs), and decision tree (DT) classifiers and the accuracy scores of these methods are evaluated. The optimum classification method is thus determined.

2. Materials and methods

2.1. Database

A database downloaded for gait dynamics in the NDD database at www.physionet.org is used in the study [32]. This database consists of 64 left and right gait dynamic signals recorded from 13 subjects with ALS, 15 subjects with PD, 20 subjects with HD, and 16 Co. [4,33]. All subjects, including 28 males and 36 females, are aged between 20 and 79 years. The website's database was created using force-sensitive resistors that refer to the force under the right foot and left foot. These raw data, downloaded from the database, are denoted as left and right foot force signals in the study [33,34]. Some limitations exist in the database [5] and some solutions to such limitations are presented within the scope of the study. In the study, it is noticed that a CFS sampled at 300 Hz brings some advantages compared to other gait dynamics. First, a suitable match is not available among the classification groups with respect to sex and age. Although it is found that NDDs generally do not show any variation depending on sex and age groups of the scope in some studies about gait dynamics [4–6,34], further studies are needed to demonstrate the effects of age and sex in them. Second, the small number of subjects in each group may cause a bad match between the clusters used during the classification. Cross-validation processing is applied to classification models to overcome this limitation. In this study, three-fold cross-validation (TFCV) and leave-one-out cross-validation (LOOCV) methods are used for the validation of the classification algorithms. Third, the heights of subjects were not matched in a balanced way. This limitation can affect the increase of stride time fluctuation, but it does not affect the CFS patterns and analysis. Fourth, the database in the literature contains 5-min walking records. While the 5-min gait could be simple for some subjects, it might be challenging for others. For this reason, a loss of effort may occur in challenged subjects. Some bad signals may also occur in the 5-min recordings due to discontinuities and difficulties in walking. Therefore, the usage of 1-min records makes gait signal analyses relatively faster, and it will reduce the distortions in them.

2.2. Overview of the study

An overview of the study is shown in Figure 1. In a previous study, each CFS was decomposed using a DWT. These analyses were also evaluated and feature extraction was performed [31]. In this study, these features were applied to the inputs of MLPNN, RBFNN, GRNN, SVM, and DT structures, respectively, and their accuracy scores were compared to perform the ALS classification.

Figure 1. Overview of the study.

2.3. Feature extraction

The DWT, which can investigate signals in the time and frequency domains, was used for feature extraction in the previous study. Each CFS was decomposed into an approximation and detailed coefficients and reconstructed during 6 levels of DWT analyses [31,35]. Then the energy ratio values (E_{Per}) of each detailed component were calculated as follows:

$$E_{Per} = \frac{E_{Det}}{E_{Total}} \times 100, \tag{1}$$

where E_{Det} denotes each reconstructed detailed component energy value and E_{Total} is the total energy of the CFS. The classification performances of features were determined using LDA and the NB algorithm considering E_{Per} values. The best results obtained in the previous study are listed in Table 1.

Table 1. Extracted features.

Class	Wavelet function	Features (frequency ranges (Hz))
BC1	bior2.6	D5 (4.6875–9.375) – D6 (2.3438–4.6875)
BC2	sym4	D4 (9.375–18.75) – D5 (4.6875–9.375)
BC3	bior2.6	D2 (37.5–75) – D5 (4.6875–9.375)
BC4	sym4	D4 (9.375–18.75) – D5 (4.6875–9.375)
BC5	sym4	D4 (9.375–18.75) – D5 (4.6875–9.375)

From the table, it is seen that bior2.6 is the best distinctive wavelet function of the BC1 and BC3 classifications while sym4 is the best for the others. Each feature obtained from DWT decomposition was evaluated as dyadic during LDA and NB feature extraction processing because the classification accuracy was observed to decrease when trying triple and higher combinations. Considering the results, it is observed that the D5 and D6 detailed components for BC1, the D2 and D5 detailed components for BC3, and the D4 and D5 detailed components for the others are the best distinctive features [31].

2.4. Classification methods

During the previous study, the LDA and NB structures were used in order to measure the classification performances and extract the features. Although these methods are useful and practical for feature extraction, they are insufficient for more comprehensive classification operations. Therefore, more comprehensive classification methods are needed to distinguish ALS using gait analysis features. Although there are many classification methods in the literature, one of the most used methods is the ANN for gait data analysis [8]. Therefore, three types of ANN models, consisting of the MLPNN, RBFNN, and GRNN, are used for the classification. SVM and DT structures, which are new approaches for the classification, are also evaluated during the study.

2.4.1. Multilayer perceptron neural network (MLPNN)

The MLPNN is a type of ANN algorithm that consists of two or more layers having neurons within each layer [30]. The MLPNN structure is based on a perceptron model fundamentally [36]. A perceptron model in the jth layer is calculated mathematically as:

$$y = f(\sum_{i=1}^{N} x_i.w_{ij} + \theta_j)\,, \quad (j = 1, 2, \ldots, M), \tag{2}$$

where N refers to the number of neurons in the input layer, M is the number of layers, x_i is the ith neuron in a hidden layer, w_i is weights for each input, θ_j is the bias of the perceptron, $f(.)$ is the activation function, and y refers to the output of the perceptron in the jth layer.

In the study, the features obtained in the previous study are applied to MLPNN inputs respectively. In the first part of the study, BC1 is classified in the MLPNN structure, which includes one input layer with 2 neurons, 2 hidden layers with 10 neurons, and one output layer with one neuron. The numbers of layers and neurons are determined depending on their classification achievement. The activation function is selected as tangent sigmoid within each neuron in all structures experimentally with respect to performance. All of the models are trained using the Levenberg–Marquardt method owing to the fact that it has the best performance in the MLPNN. The percentage energy values of D5 and D6 detailed components having the best distinctive specifications are applied to the MLPNN in BC1. BC2 is investigated in the next step. The MLPNN is composed of one input layer with 2 neurons, 2 hidden layers with 20 neurons, and one output layer with one neuron. The classification accuracy scores are diminished when the number of neurons and layers is decreased or increased. Also, when more neurons and layers are selected, the duration of the classification processing gets longer. For BC3 classification, the percentage energy values of D2 and D5 detailed components are applied to the inputs of the network. An MLPNN that is the same as the model used for BC3 is applied for BC2, BC4, and BC5. The inputs of the MLPNN are selected as the percentage energy values of D4 and D5 detailed components for these classifications.

2.5. Radial basis function neural network (RBFNN)

The RBFNN is another type of ANN model that is comprised of one input layer, one kernel layer, and one output layer [36]. The input variables are passed directly through the nodes in the input layer and connected to the kernel layer without weights. The transfer function of the kernels is the radial basis function (RBF) that is defined as a symmetrical function centered on a given mean value of a space. The RBFNN is optimized by means of parameter optimization using distance weighted regression in training.

The RBFNN is expressed theoretically as:

$$y = \omega_0 + \sum_{i=1}^{n_h} \omega_i f(\|\mathbf{X} - \mathbf{c_i}\|), \tag{3}$$

where the f function refers to the RBF, $\mathbf{c_i}$ represents the centers related to the basis functions, n_h is the number of basis functions in the network, ω_i is weights in the output layer, ω_0 presents the output offset value, vector $\mathbf{X}$ that has n elements expresses the inputs of the network as $\mathbf{X} = [x_1\ , \ldots, \ \ x_n]$', and the $\|\cdot\|$ mathematical term defines the Euclidean norm. It is denoted as:

$$\|\mathbf{X}\| = \left(\sum_{i=1}^{n} x_i^2 \right)^{\frac{1}{2}}. \tag{4}$$

The nonlinear basis function is expressed mathematically by a Gaussian function:

$$f(x) = e^{-\frac{(x-c)^2}{\sigma^2}}, \tag{5}$$

where σ is the radius of the basis function while c is the center of the same function.

In this paper, RBFNN inputs are the same as the inputs in the MLPNN. Spread parameter σ, which is a variable parameter in the RBF, is selected experimentally as 1.9 for BC1, 1.4 for BC2, 1.7 for BC3, and 0.9 for BC4 and BC5 depending on the classification achievement. If σ is selected as larger, there will be a smoother function approximation. However, it can also cause numerical problems when selected as too large. The goal parameter that is a squared error goal of the network during training is selected as 10^{-3} for all RBFNNs.

2.5.1. General regression neural network (GRNN)

The GRNN is a type of ANN structure consisting of an input layer, a pattern layer, an addition layer, and an output layer. It has a dynamic network structure that uses regression analysis [37]. In this model, p and q are measured values for input and output of the GRNN, respectively. The joint probability density function $\hat{f}(pq)$ is expressed by:

$$\hat{f}(pq) = \frac{1}{(2\pi)^{(d+1)/2}} \times \frac{1}{k} \sum \left[e^{\left(\frac{(p-p_i)^T (p-p_i)}{2\sigma^2} \right)} \times e^{\left(\frac{(q-q_i)^2}{2\sigma^2} \right)} \right], \tag{6}$$

where σ is the spread parameter, k is the sample observations, and p_i is the ith training vector related to output q_i.

The GRNN allows the changing of the only σ, like in the RBFNN. The σ is altered in each classification during analysis. The σ is selected as 2 experimentally for the all of the classifications. The inputs of the network are applied the same as in the RBFNN.

2.5.2. Support vector machine (SVM)

The SVM method is a supervised learning algorithm proposed by Vapnik in 1992 for solving classification and regression problems [38]. It solves any classification or regression problem, without interfering with local solutions, by transforming it into a quadratic programming problem, which is one of its advantages. In addition, it has the ability to make high generalizations.

The output signal y of a SVM network is determined as the function of variable x:

$$y = \sum_i w_i k\left(s_i, x\right) + b, \tag{7}$$

where s_i parameters are the support vectors, w_i parameters are the weights, b is the bias, and k is a kernel function. In the case of a linear kernel, k is the dot product. If $y \geq 0$, then variable x is classified as a member of the first group; otherwise, it is classified as a member of the second group.

The results are observed using four kernel functions including the RBF, linear function, Gaussian function, and 2nd degree polynomial function. The best results are obtained with the Gaussian function. The soft-margin constant (SMC) that controls the maximum penalty imposed on margin-violating observations is adjusted to 12 values, from 10^{-5} to 10^6, by a factor of 10 to take into account unbalanced groups to prevent overfitting. The increasing of the SMC decreases the number of support vectors. The kernel scale (KS) is calculated between 0.24 and 3.76 using a heuristic procedure based on subsampling. For small values of KS, the decision boundary is nearly linear. Large values of KS lead to over?tting.

2.5.3. Decision tree (DT)

The DT, a simple and understandable classification algorithm, is widely used in the literature [39]. It uses a multistage or sequential approach to the realization of the classification process. The basic structure of the DT consists of three basic parts called nodes, branches, and leaves. In this tree structure, each feature is represented by a node. The branches and leaves are the other components of the tree structure. The basic principle of the DT structure is to achieve results in the shortest time by dividing the data into small parts.

In this study, DT inputs were implemented as they were in all other methods in the study.

3. Results

The accuracy values are evaluated for five different classifications at the end of the study. Here, Sp denotes specificity, Se sensitivity, and Acc accuracy values. These parameters are calculated as follows:

$$Sp = \frac{TN}{TN + FP} \times 100, \tag{8}$$

$$Se = \frac{TP}{TP + FN} \times 100, \tag{9}$$

$$Acc = \frac{TP + TN}{TP + FN + TN + FP} \times 100, \tag{10}$$

where TP is true positive, TN is true negative, FP is false positive, and FN is false negative. These parameters are used for the measurement of classification performance.

Also, TFCV and LOOCV are used for evaluation and validation of the classifications. TFCV is a cross-validation method taking into account the database partitioning rules in ANN methods. LOOCV in this study offers the opportunity to compare results with other methods. Mean values of accuracy percentages are determined by simulations. In this study, the classification accuracies were evaluated for validation using TFCV and LOOCV methods based on all-training-all-testing (ATAT) and testing data. In order to determine the most successful classification method, the calculated TFCV and LOOCV values of all classifications are shown in Figure 2. The average classification performances, which are the average values of BC1, BC2, BC3, BC4, and BC5 accuracy scores for each method, were calculated for both testing and ATAT values. Finally, the overall percentages, which are the average of all TFCV and LOOCV scores, were obtained. According to the figure, the overall accuracy percentages are calculated as 92.09% in MLPNN, 83.55% in RBFNN, 79.79% in GRNN, 86.32% in SVM, and 81.50% in DT for the mean of all validation results. Therefore, it is observed that MLPNN is strongest among the classification methods according to the comparison of the results. The TFCV and LOOCV results of MLPNN for the testing and ATAT data are shown in Table 2. These results are the best for all classifications. According to the table, the maximum accuracy values of MLPNN were acquired by LOOCV method based on ATAT. LOOCV accuracy scores of MLPNN for BC1 are obtained as 96.55% in testing and 99.76% in ATAT. Besides, it is shown that the LOOCV accuracy scores as testing% (ATAT%) are 82.14% (99.36%) for BC2, 78.79% (99.17%) for BC3, 83.33% (98.87%) for BC4, and 82.81% (99.00%) for BC5.

4. Discussion

The objective of our previous study, which used CFS for the first time in the literature, was a feature comparison and the researching of the impacts of frequency characteristics in gait signals. The LDA and NB methods used in the past study are basic methods that are used only for the evaluation of feature extraction. Therefore, the purpose of the study was not to make a classification. As a result, our previous study focused on the occurring of the CFS and the most effective time-frequency analysis method in the CFS was investigated [31]. On the other hand, the present study focused on the evaluation of the classification methods. The fundamental novelty of this study is applying the features of CFS to the classification methods to obtain the best classification algorithm for the discrimination of ALS. The data used in previous studies in the literature included 5-min recordings [13,16,19,20,23]. These types of recordings may cause difficulties and discontinuities during gait. A 1-min CFS recording, which has a sufficient sample for DWT analyses and is the most important novelty in this

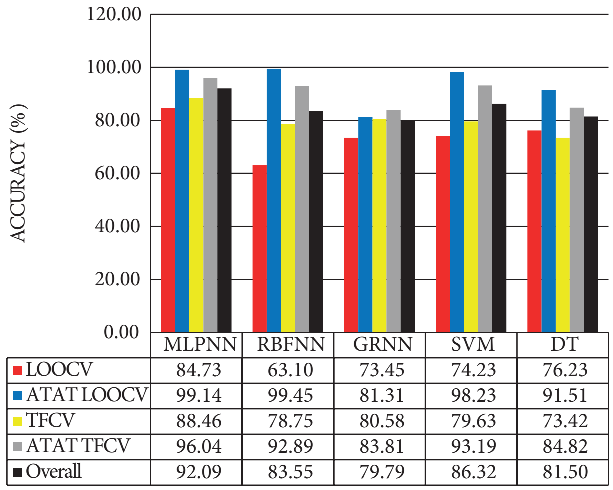

Figure 2. The accuracy comparison of ANN models.

Table 2. The comparison results of MLPNN.

Class		TFCV			LOOCV		
		Sp mean	Se mean	Acc mean	Sp mean	Se mean	Acc mean
Testing	BC1	94.44	100.00	96.30	94.12	100.00	96.55
	BC2	87.78	86.11	85.56	81.25	83.33	82.14
	BC3	91.67	82.22	84.85	78.26	80.00	78.79
	BC4	91.54	88.89	89.58	84.62	77.78	83.33
	BC5	87.52	77.78	86.00	88.46	58.33	82.81
ATAT	BC1	98.04	100.00	98.85	99.59	100.00	99.76
	BC2	95.69	95.05	95.24	99.33	99.49	99.36
	BC3	96.97	93.17	94.95	99.00	99.57	99.17
	BC4	96.29	95.24	95.83	98.78	99.70	98.87
	BC5	95.57	94.19	95.31	99.00	97.87	99.00

study, provides the ability to eliminate such limitations. Thus, the analyses will be faster and signal distortions will be less. Moreover, this method is more successful in all classifications considering other studies in the literature. In order to realize the validation, while LOOCV using only testing data was applied in the study by Xia et al. [23], LOOCV ATAT was used in the other studies [13,16,19,20]. The performance comparison of the study among other past studies in the literature is shown in Table 3. According to the table, it is seen that the method having the best performance for BC1 is the time frequency-based study proposed by Sugavaneswaran et al. They obtained 100% accuracy for BC1. It is noticed that the accuracy evaluated using ATAT data in their study was 100% [13]. This is higher than 96.55% calculated using only testing data in our study. However, when our study is evaluated with ATAT, the accuracy value is 99.76%, which is higher than the value being obtained for LOOCV. Although the best performance is provided for BC1 in [13], their study was limited to the characterization of ALS and it requires more research. There are no comparisons with other NDDs (HD, PD) in their study. Wu et al. achieved 89.66% accuracy using a signal turn-count-based algorithm and 90.32% accuracy using statistical analysis and a least squares support vector machine (LS-SVM) [16,19]. Baratin et al.

proposed computer-aided automatic characterization for NDDs and reported 86.2% accuracy using an unbiased cross-validation strategy [20], and Xia et al. obtained 92.86% accuracy using the SVM for BC1 [23]. Therefore, the proposed algorithm can be used safely as a distinctive method for BC1 compared to other methods in the table. In addition, Baratin et al. also studied BC2 and obtained 80% accuracy [20]. However, the accuracy of this study is determined as 82.14% (99.36%) in the testing% (ATAT%) scheme for BC2. Liao et al. researched gait symmetry in BC2 and BC3 patterns using multiresolution entropy analysis and proposed parameters for the classifications, but they did not make any classifications [14]. Therefore, BC3, BC4, and BC5 were carried out in the study.

Table 3. Comparison of present and other methods (NA: Not available in the literature).

Class	Method	Classifier	Accuracy (%)
BC1	Signal turn-count-based [16]	LS-SVM	89.66
	Statistical analysis [19]	LS-SVM	90.32
	Time frequency-based [13]	NN-based	100
	Wavelet-based [20] Std statistics	LDA	86.2
	and temporal structural characteristics [23]	SVM	92.86
	Proposed	MLPNN	96.55
BC2	Wavelet-based [20]	LDA	80
	Proposed	MLPNN	82.14
BC3	Existing methods		NA
	Proposed	MLPNN	78.79
BC4	Existing methods		NA
	Proposed	MLPNN	83.33
BC5	Existing methods		NA
	Proposed	MLPNN	82.81

5. Conclusion

The main objective of this study is to achieve ALS discrimination among Co. and other NDDs. Most studies in the literature focused on the analysis of stride cycle time, stride length, and stride speed [2,7]. These types of signals obtained from the force signals must be at least 5 min long for DWT analysis. Signals recorded in less time may not be suitable for DWT analysis due to the small number of samples. However, 1 min of CFS recording at 300 Hz sampling frequency is sufficient for DWT analysis. The fundamental novelty of this study is the use of CFS for the first time for the classification, unlike other studies in the literature. The 1-min CFS provides an advantage of shortening the analysis time and reducing the distortions in the signal when compared to other analyses performed with 5-min records like stride cycle time, stride length, and speed of gait signals. In the study, five different classifications consisting of BC1, BC2, BC3, BC4, and BC5 are evaluated for ALS discrimination. The results of these classifications are higher when compared to other methods. The MLPNN is determined as the most accomplished classification method in the study according to analysis results. As a result, the best LOOCV accuracy scores as testing% (ATAT%) are obtained as 96.55% (99.76%) in BC1, 82.14% (99.36%) in BC2, 78.79% (99.17%) in BC3, 83.33% (98.87%) in BC4, and 82.81% (99.00%) in BC5 using MLPNN classification. The proposed algorithm, when used as a premonitoring tool, can facilitate early diagnosis of different NDDs and provide a better treatment process.

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