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Detection of ophthalmic arterial doppler signals with Behcet disease using multilayer perceptron neural network

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Abstract

Doppler ultrasound is known as a reliable technique, which demonstrates the flow characteristics and resistance of ophthalmic arteries. In this study, ophthalmic arterial Doppler signals were obtained from 106 subjects, 54 of whom suffered from ocular Behcet disease while the rest were healthy subjects. Multilayer perceptron neural network (MLPNN) employing delta-bar-delta training algorithm was used to detect the presence of ocular Behcet disease. Spectral analysis of the ophthalmic arterial Doppler signals was performed by least squares (LS) autoregressive (AR) method for determining the MLPNN inputs. The MLPNN was trained with training set, cross validated with cross validation set and tested with testing set. All these data sets were obtained from ophthalmic arteries of healthy subjects and subjects suffering from ocular Behcet disease. Performance indicators and statistical measures were used for evaluating the MLPNN. The correct classification rate was 96.43% for healthy subjects and 93.75% for unhealthy subjects suffering from ocular Behcet disease. The classification results showed that the MLPNN employing delta-bar-delta training algorithm was effective to detect the ophthalmic arterial Doppler signals with Behcet disease.

Keywords: Doppler ultrasound; Spectral analysis; Multilayer perceptron neural network; Delta-bar-delta; Ocular Behcet disease; Ophthalmic artery

1. Introduction

Doppler ultrasound has been a widely used noninvasive technique in clinical applications for detecting and evaluating blood flow in vessels. Doppler systems are based on the principle that ultrasound, emitted by an ultrasonic transducer, is returned partially towards the transducer by the

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moving targets, thereby inducing a shift in frequency. When ultrasound is used to interrogate the flow within a blood vessel there are numerous targets in the ultrasound field with a range of velocities, and the Doppler shift signal therefore contains not just a single frequency but rather a spectrum of frequencies which varies in shape as the velocity distribution within the vessel changes with time [1–3]. Therefore, Doppler power spectrum has a shape similar to the histogram of the blood velocities within the sample volume and thus spectral analysis of the Doppler signal produces information concerning the velocity distribution in the artery. The estimation of the power spectral density (PSD) of the Doppler signal is performed by applying spectral analysis methods [1–3]. Doppler ultrasonography is a reliable technique, which demonstrates the flow characteristics and resistance of ophthalmic arteries in various ocular and orbital disorders such as Behcet disease [3–10]. Behcet disease is a chronic, recurrent and multisystem inflammatory disorder characterized by orogenital ulcers, ocular and skin lesions. Ocular involvement is the most frequent serious complication of Behcet disease and therefore, blood flow velocity changes of ophthalmic arteries are defined as the most evident symptoms of Behcet disease [5,6,9,10].

Artificial neural networks (ANNs) are computational tools for pattern classification that have been the subject of renewed research interest during the past 15 years [11,12]. They have been successfully used in a variety of medical applications [13–16]. Recent advances in the field of ANNs have made them attractive for analyzing signals. The application of ANNs has opened a new area for solving problems not resolvable by other signal processing techniques [11,12]. However, ANN analysis of Doppler shift signals is a relatively new approach [17–21]. These numerous applications exhibit the suitability of ANNs in pattern classification including detection of medical outcomes. Presently the most widely used ANN type is a MLPNN which has been playing a central role in applications of ANNs [12]. There are a number of training algorithms used to train the MLPNNs [11,22]. A frequently used one is called backpropagation training algorithm and reportedly has some problems [11,22]. Various related algorithms such as delta-bar-delta have been introduced to address the problems of backpropagation algorithm [23].

In the present study, the MLPNN employing delta-bar-delta training algorithm was used for the interpretation of ophthalmic artery Doppler waveforms. The ophthalmic arterial Doppler signals used in this study were obtained from Medical Faculty Hospital of Erciyes University and the usage of the data in our study was approved by the ethic board of the institution. The MLPNN was used to detect the presence of ocular Behcet disease. In order to determine the MLPNN inputs spectral analysis of the ophthalmic arterial Doppler signals was performed using the LS AR method. The performance of the MLPNN was evaluated by the classification results of the ophthalmic arterial Doppler signals.

2. Materials and methods

The procedure used in the development of the classification system is shown in Fig. 1. It consists of four parts: (i) measurement of ophthalmic arterial Doppler signals, (ii) spectral analysis using the LS AR method (MLPNN inputs were selected), (iii) classification using MLPNN, (iv) classification results (healthy subjects and subjects suffering from ocular Behcet disease). These procedures are explained in the remainder of this study.

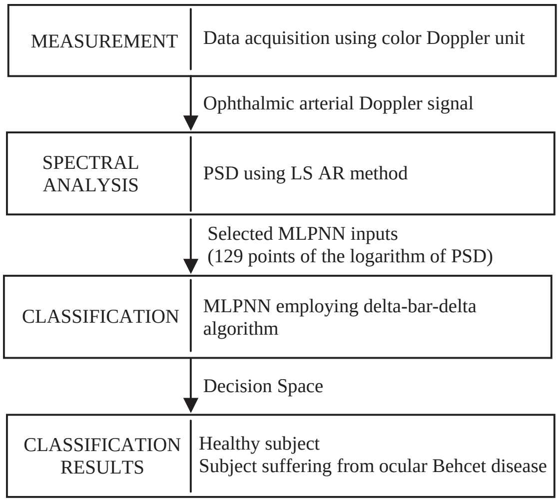

Fig. 1. The procedure used in the development of the classification system.

2.1. Subjects

In the present study, ophthalmic arterial Doppler signals were recorded from 106 subjects. The group consisted of 50 females and 56 males with ages ranging from 18 to 63 years and a mean age of 31.5 ± 0.5 years. Diasonics Synergy color Doppler ultrasonography was used during examinations and sonograms were taken into consideration. According to the examination results, 54 of 106 subjects suffered from ocular Behcet disease and the rest were healthy subjects (control group) who had no ocular or systemic pathology. The group suffering from ocular Behcet disease consisted of 25 females and 29 males with a mean age 35.5 ± 0.5 years (range 21–63) and the healthy subjects were 25 females and 27 males with a mean age 30.0 ± 0.5 (range 18–61).

The adequate functioning of ANN depends on the sizes of the training set and test set. In this study, 46 of 106 subjects were used for training and the rest of them were used for testing. A practical way to find a point of better generalization is to use a small percentage (around 20%) of the training set for cross validation. For obtaining a better network generalization 10 of training subjects, who were selected randomly, were used as cross validation set. The training set consisted of 22 subjects suffering from ocular Behcet disease and 24 healthy subjects. The testing set consisted of 32 subjects suffering from ocular Behcet disease and 28 healthy subjects. The cross validation set consisted of 5 subjects suffering from ocular Behcet disease and 5 healthy subjects.

2.2. Measurement of ophthalmic arterial Doppler signals

Doppler ultrasound system is used as a noninvasive method to observe the hemodynamics of the ophthalmic artery [3–10]. Ophthalmic artery examinations were performed with a color Doppler unit using a 10 MHz ultrasonic transducer. The measurement system consisted of 10 MHz ultrasonic transducer, analog Doppler unit (Diasonics Synergy color Doppler ultrasonography), recorder (Sony), analog/digital interface board (Sound Blaster Pro-16 bit), a personal computer with a printer

[2,3]. The ultrasonic transducer was applied to the closed eyelids using sterile methylcellulose as a coupling gel. The probe was most often placed at an angle of 60° from the midline pointing towards the orbital apex. Care was taken not to apply pressure to the eye in order to avoid artifacts.

2.3. MLPNN employing delta-bar-delta training algorithm

In the present study, the MLPNN consisted of one input layer, one hidden layer, and one output layer and the decision about the number of hidden layer in use was determined empirically. In the hidden layer and the output layer, sigmoidal function was used. The MLPNN was implemented by using MATLAB software package (MATLAB version 6.0 with neural networks toolbox). The advantage of using the MLPNN is the rapid execution of the trained network, which is particularly advantageous in signal processing applications [11,12,22,23]. The applications in the literature demonstrate the suitability of ANNs in detecting medical outcomes of Doppler signals when ANNs have trained satisfactorily [17–21]. The process of adapting the weights to an optimum set of values is called training ANN [11,12,22,23]. There are a number of training algorithms used to train a MLPNN and a frequently used one is called the backpropagation training algorithm. However, backpropagation has some problems for many applications [11,22]. One of the main problems of MLPNN employing backpropagation is that long training sessions are often required in order to find an acceptable weight solution because of the well known difficulties inherent in gradient descent optimization [11,22]. There exist a number of modifications to this algorithm which are designed to overcome this problem. The delta-bar-delta training algorithm is a modified backpropagation algorithm developed to speed up the training of the MLPNN [23]. The delta-bar-delta training algorithm is based on the hypothesis that a learning coefficient suitable for one weight may not be appropriate for all weights. Since the delta-bar-delta training algorithm has rapid execution and has widely used in pattern classification problems, MLPNN employing delta-bar-delta training algorithm was used to detect the presence of ocular Behcet disease.

The delta-bar-delta training algorithm [23] is invoked to adjust all the weights in the MLPNN and gives the change $\Delta w_{ji}(k)$ in the weight of the connection between neurons i and j at iteration k ($w_{ji}(k)$) as

$$\Delta w_{ji}(k) = -\alpha_{ji}(k)\,\frac{\partial E}{\partial w_{ji}(k)}, \tag{1}$$

where $\alpha_{ji}(k)$ is the learning coefficient assigned to the connection from neuron i to j, E is the sum of squared differences between the desired and actual values of the output neurons.

The learning coefficient change is given as

$$\Delta\alpha_{ji}(k) = \begin{cases} A, & D_{ji}(k-1)\,\dfrac{\partial E}{\partial w_{ji}(k)} > 0, \\ -\varphi\alpha_{ji}(k), & D_{ji}(k-1)\,\dfrac{\partial E}{\partial w_{ji}(k)} < 0, \\ 0, & \text{otherwise}, \end{cases} \tag{2}$$

where $D_{ji}(k-1)$ represents a weighted average of $\partial E/(\partial w_{ji}(k-1))$ and $\partial E/(\partial w_{ji}(k-2))$ given by

$$D_{ji}(k-1) = (1-\theta)\,\frac{\partial E}{\partial w_{ji}(k-1)} + \theta\,\frac{\partial E}{\partial w_{ji}(k-2)}, \tag{3}$$

and φ, θ and A are positive constants.

From Eq. (2), it can be noted that the algorithm increments the learning coefficients linearly but decrements them geometrically. By assigning a learning coefficient to each weight and permitting it to change over time, more freedom is introduced to facilitate convergence towards a minimum value of $E(w_{ji})$ [23]. In this study, the values of the training parameters adopted for the algorithm were determined empirically and they were as follows:

$$A = 0.01, \quad \varphi = 0.5, \quad \text{and} \quad \theta = 0.6.$$

3. Results

The collection of well-distributed, sufficient, and accurately measured-simulated input data is the basic requirement to obtain an accurate model. In the following sections, determination of the MLPNN input parameters are explained and performance analysis of the MLPNN is presented for determining whether the MLPNN is effective to detect the ophthalmic arterial Doppler signals with Behcet disease.

3.1. Determination of MLPNN input parameters

Feature selection is the key to pattern classification so that it is the most important component of designing ANN based on pattern classification since even the best classifier will perform poorly if the features are not selected well. Feature selection has two meanings: (1) which components of a pattern, or (2) which set of features best represent a given pattern [1]. The MLPNN input parameters were determined by taking into consideration of feature selection.

In the first experiment, resistivity index (RI) and pulsatility index (PI) values, which are reflections of the resistance to flow, were taken as the MLPNN input parameters. RI and PI values are influenced by many factors including proximal stenosis, distal stenosis and peripheral resistance. RI and PI are defined as

$$\mathrm{RI} = (S-D)/S, \tag{4}$$

$$\mathrm{PI} = (S-D)/M, \tag{5}$$

where S is maximum systolic height, D is end diastolic height and M is mean height of the Doppler waveform as shown in Fig. 2 [1]. RI values of ophthalmic arteries of healthy subjects and subjects suffering from ocular Behcet disease were equal to 0.75 ± 0.05 and 0.76 ± 0.04, respectively. PI values of ophthalmic arteries of healthy subjects and subjects suffering from ocular Behcet disease were equal to 1.65 ± 0.25 and 1.66 ± 0.27, respectively. Independent-samples t-tests were used to compare RI and PI values of healthy subjects and subjects suffering from ocular Behcet disease. Independent-samples t-tests were performed with a statistical package (SPSS version 8.0). The level of statistical significance was taken as $p = 0.05$. The results of independent-samples t-tests showed

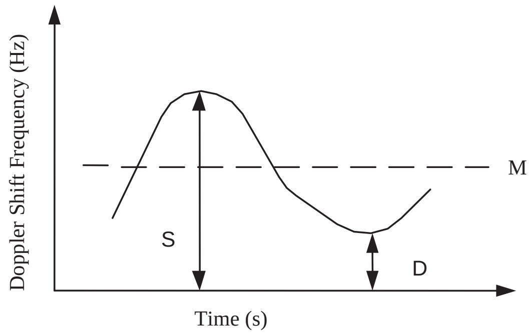

Fig. 2. Diagram illustrating the variables involved in the definitions of RI and PI. S is maximum systolic height, D is end diastolic height and M is mean height of the waveform.

that there was no statistically significant difference between RI and PI values of healthy subjects and subjects suffering from ocular Behcet disease ($p > 0.05$). Thus, it was concluded that RI and PI values were not appropriate features for predictions of ophthalmic arterial Doppler waveforms.

Doppler signal is conventionally interpreted by analyzing its spectral content. Diagnosis and disease monitoring are assessed by analysis of spectral shape and parameters. In order to obtain clinically useful information Doppler shift signal can be processed to achieve a Doppler PSD [1,17,18,20,21]. Therefore, in the second experiment ophthalmic arterial Doppler PSD values were taken as network input parameters. The PSD estimates of the ophthalmic arterial Doppler signals were calculated using the LS AR method for each subject. The LS AR PSD estimate is given by

$$\widehat{\mathrm{PSD}}_{\mathrm{LS}}(f) = \frac{\hat{\rho}_{\min}}{|1 + \sum_{k=1}^{p} \hat{a}_p(k) \mathrm{e}^{-\mathrm{j}2\pi f k}|^2}, \tag{6}$$

where $\hat{\rho}_{\min}$ is the estimate of minimum prediction error power, $\hat{a}_p(k)$ are the estimates of AR coefficients and p is the model order [3]. MATLAB software package (MATLAB version 6.0 with signal toolbox) was used for spectral analysis of the ophthalmic arterial Doppler signals. Mean of the PSD estimates of the ophthalmic arterial Doppler signals belonging to healthy subjects and subjects suffering from ocular Behcet disease are shown in Fig. 3. As it is seen from Fig. 3, ophthalmic artery Doppler PSD values of healthy subjects and subjects suffering from ocular Behcet disease are different. Doppler PSD values are related with the velocity distribution in the ophthalmic arteries and contain a significant amount of information about the Doppler signal. Therefore, in this study 129 points of the logarithm of the PSD values were used as the MLPNN inputs.

The outputs of the network were represented by unit basis vectors

[0 1] = healthy

[1 0] = ocular Behcet disease.

3.2. Performance analysis of MLPNN

The MLPNN employing delta-bar-delta was trained with the training set, cross validated with the cross validation set and checked with the test set. In this study, performance analysis of the MLPNN is examined in two parts as training performance and testing performance.

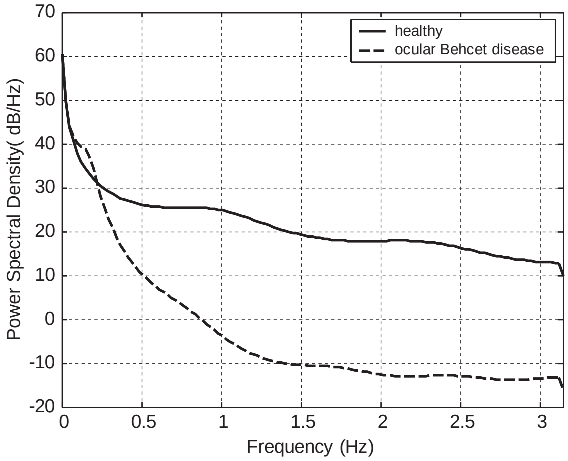

Fig. 3. Mean of the PSD estimates of the ophthalmic arterial Doppler signals: (—) healthy subjects, (- - -) subjects suffering from ocular Behcet disease.

3.2.1. Training performance of MLPNN

Training set provided to the MLPNN was representative of the whole state space of concern so that the trained MLPNN had the ability of generalization. In training, a representative training set with examples was presented iteratively to the MLPNN and the output activations were calculated using the MLPNN weights. An error term, based on the difference between the output of MLPNN and desired output, was then propagated back through the MLPNN to calculate changes of the interconnection weights. The square difference between the output of MLPNN and the desired output over training iterations was plotted for observing how well the MLPNN was trained. The curve of the mean square error (MSE) versus iteration is called as the training curve. In general, it is known that a network with enough weights will always learn the training set better as the number of iterations is increased. However, this decrease in the training set error is not always coupled to better performance in the test. When the network is trained too much, the network memorizes the training patterns and does not generalize well. The training holds the key to an accurate solution, so the criterion to stop training must be very well described. Cross validation is a highly recommended criterion for stopping the training of a network. When the error in the cross validation increases, the training should be stopped because the point of best generalization has been reached. In Fig. 4, the error in training set and the cross validation set is shown on the same graph. The values of minimum MSE and final MSE during training and cross validation are given in Table 1. In this study as it is seen from Table 1, training was done in 4200 epochs since the cross validation error began to rise at 4200 epochs. Since MSE (Fig. 4) converged to a small constant approximately zero in 4200 epochs, training of the MLPNN was determined as successful.

3.2.2. Testing performance of MLPNN

The trained MLPNN was tested using 60 test data which were composed of healthy subjects and unhealthy subjects suffering from ocular Behcet disease. This 60 test data, that the network had not seen before, was applied to the MLPNN for testing the MLPNN performance. The MLPNN applied

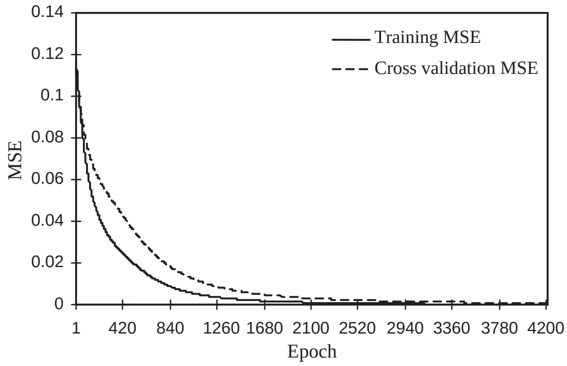

Fig. 4. Training and cross validation MSE curves of the MLPNN.

Table 1
The values of minimum and final MSE during training and cross validation

Best networks	Training	Cross validation
Epoch number	4200	4200
Minimum MSE	0.000256223	0.000360517
Final MSE	0.000256223	0.000360517

its past experience to test data and produced a good solution based on the successful training and the chosen topology of the MLPNN. The evaluation of testing performance of the MLPNN was performed by assessment of classification results and receiver operating characteristic (ROC) curve analysis.

In classification, the aim is to assign the input patterns to one of several classes, usually represented by outputs restricted to lie in the range from 0 to 1, so that they represent the probability of class membership. While the classification is carried out, a specific pattern is assigned to a specific class according to the characteristic features selected for it. In this study, there were two classes as healthy and ocular Behcet disease which were indicating situation of ophthalmic arteries of subjects. Classification results of the MLPNN were displayed by a confusion matrix. According to confusion matrix, 1 healthy subject was classified incorrectly by the MLPNN as a subject suffering from ocular Behcet disease and 2 subjects suffering from ocular Behcet disease were classified as healthy subjects. The other option in confusion matrix, is to display each cell as a percentage of the exemplars for the desired class. According to this confusion matrix, healthy subjects were classified correctly with 96.43% and incorrectly with 3.57%. Subjects suffering from ocular Behcet disease were classified correctly with 93.75% and incorrectly with 6.25%. In this case, the classifications of healthy subjects and subjects suffering from ocular Behcet disease were done with the accuracy of 96.43% and 93.75%, respectively.

Paired-samples t-tests were used to compare the detections of physician and the MLPNN for healthy subjects and subjects suffering from ocular Behcet disease. The results of the paired-samples

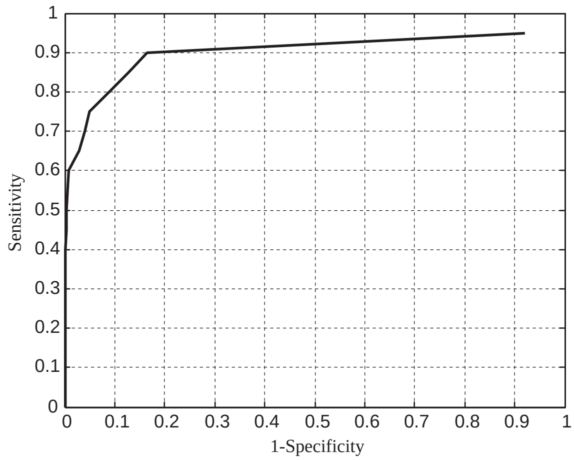

Fig. 5. ROC curve.

t-tests showed that there was no statistically significant difference between detections of physician and the MLPNN for healthy subjects and subjects suffering from ocular Behcet disease ($p > 0.05$).

The performance of a test can be evaluated by plotting a ROC curve for the test. For a given result obtained by a classifier system, four possible alternatives exist that describe the nature of the result: (i) true positive (TP), (ii) false positive (FP), (iii) true negative (TN), and (iv) false negative (FN) [24]. In this study, a TP decision occured when the positive detection of the MLPNN coincided with a positive detection of the physician. A FP decision occured when the MLPNN made a positive detection that did not agree with the physician. A TN decision occured when both the MLPNN and the physician suggested the absence of a positive detection. A FN decision occured when the MLPNN made a negative detection that did not agree with the physician. A good test (curve in Fig. 5) is one for which sensitivity rises rapidly and 1-specificity hardly increases at all until sensitivity becomes high. ROC curve which is shown in Fig. 5 represents the MLPNN performance on the test file.

The difference between the output of the network and the desired response is referred to as the error and can be measured in different ways. In this study, MSE, normalized mean squared error (NMSE), mean absolute error (MAE), minimum absolute error, maximum absolute error, percent correct, and correlation coefficient (r) were used for measuring error of the MLPNN. The correlation coefficient is limited with the range $[-1, 1]$. When $r = 1$ there is a perfect positive linear correlation between network output and desired output, which means that they vary by the same amount. When $r = -1$ there is a perfectly linear negative correlation between network output and desired output, that means they vary in opposite ways. When $r = 0$ there is no correlation between network output and desired output. Intermediate values describe partial correlations. The values of performance evaluation parameters of the presented MLPNN are given for healthy subjects and subjects suffering from ocular Behcet disease in Table 2. According to the results of performance evaluation and statistical measures, the MLPNN was found to be successful.

Table 2
The values of performance evaluation parameters

Performance	Result (healthy)	Result (ocular Behcet disease)
MSE	0.003565628	0.003710403
NMSE	0.315698741	0.372141745
MAE	0.095475511	0.099590421
Minimum absolute error	0.007361279	0.007595658
Maximum absolute error	0.918734692	0.921097517
r	0.946251742	0.924021453
Percent correct	96.42857361	93.75011523

4. Discussion

Color Doppler ultrasonography is a noninvasive method that is known to be useful in evaluating blood flow velocities in orbital and retinal vascular disorders. Owing to the sensitivity of Doppler analysis, the blood flow of very small vessels can be measured. Thus, color Doppler imaging is commonly performed in the evaluation of orbital vessels in various pathologic conditions. The results of the studies in the literature have shown that color Doppler imaging of orbital vasculature is valuable in subjects suffering from Behcet disease [3–10]. The studies in the literature have reported that ocular involvement is the most frequent serious complication of Behcet disease [5,6,9,10]. The rate of incidence of ocular involvement is reported to be 60–90% [5]. Color Doppler imaging studies on ocular Behcet disease are relatively new [3–10]. However, the studies have demonstrated that blood flow velocity changes of ophthalmic arteries enlighten clinical manifestations of Behcet disease.

In order to determine the MLPNN inputs in pattern classifying systems, the parameters which best represent the pattern should be selected. Toward achieving this purpose, Doppler PSD estimates of the ophthalmic arterial Doppler signals were obtained by using spectral analysis methods. The result of the previous study which applied various spectral analysis methods (fast Fourier transform, Burg AR, LS AR) to the ophthalmic arterial Doppler signals with Behcet disease showed that the LS AR method was the most appropriate one [3]. Therefore, PSD estimates of the ophthalmic arterial Doppler signals were calculated using the LS AR method for each subject. RI and PI values are two conventional parameters to demonstrate vascular resistance. However, the previous studies have shown that standard waveform indices such as RI and PI are inadequate to evaluate Doppler waveforms [17,21]. In the present study, no significant differences in the RI and PI of ophthalmic arteries were observed between the healthy subjects and subjects suffering from ocular Behcet disease. This result is in agreement with other published results [5,10]. Ophthalmic arterial Doppler PSD values were related with the velocity distribution in the ophthalmic arteries which is in agreement with other results in the literature [1,3]. Thus, ophthalmic arterial Doppler PSD values obtained by the LS AR method were used as the MLPNN inputs.

ANNs may offer a potentially superior method of Doppler signal analysis to the spectral analysis methods. In contrast to the conventional spectral analysis methods, ANNs not only model the signal, but also make a decision as to the class of signal. Another advantage of ANN analysis over existing methods of ophthalmic artery waveform analysis is that, after an ANN has trained satisfactorily and the values of the weights and biases have been stored, testing and subsequent implementation is rapid. When the ANN has demonstrated acceptable pattern recognition skills, its creation is complete and it is ready for use. The result of the previous study which applied various spectral analysis methods to the ophthalmic arterial Doppler signals with Behcet disease showed only the most appropriate spectral analysis method for modeling the ophthalmic arterial Doppler signals [3]. However, in the present study the MLPNN has made a decision as to the class of the ophthalmic arterial Doppler signals and can be used to detect the presence of ocular Behcet disease. In conclusion, the MLPNN presented in this study has become a potentially more powerful technique of ophthalmic arterial Doppler signal analysis than the described in the previous study [3], because the MLPNN has removed the decision making process from the operator and subsequent implementation is rapid.

5. Conclusion

Recent developments in the field of ANNs have made them very powerful tools for classification and analysis of Doppler signals. In this study, the MLPNN employing delta-bar-delta training algorithm was used to detect the presence of ocular Behcet disease. Performance indicators and statistical measures were used for evaluating the MLPNN. The classifications of healthy subjects and unhealthy subjects suffering from ocular Behcet disease were done with the accuracy of 96.43% and 93.75%, respectively. Based on the accuracy of the MLPNN detections, it can be mentioned that the classification of ophthalmic arterial Doppler signals with Behcet disease is feasible by the MLPNN employing delta-bar-delta training algorithm.

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