Journal of Advanced Research in Computer Technology and Software Applications
Volume 7, Issue 1 - 2023, Pg. No. 15-20
Peer Reviewed Journal

Review Article

Advances in Diabetic Retinopathy: A review of Detection and Progression Assessment Techniques

Prarthana Sharma

DAV Institute of Engineering and technology, Jalandhar, Punjab, India.

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E-mail Id:

How to cite this article:
Sharma P. Advances in Diabetic Retinopathy: A review of Detection and Progression Assessment Techniques. *J Adv Res Comp Tech Soft Appl* 2023; 7(1): 15-20.

Date of Submission: 2023-05-01
Date of Acceptance: 2023-06-21

A B S T R A C T

One of the most prevalent consequences of diabetes is diabetic retinopathy. Unfortunately, many patients are unaware of their signs and symptoms until it is already too late for appropriate therapy. The investigation of induced potential responses of the retina, optical nerve, optical brain centre will clear the way for early diagnosis and prognosis throughout therapy. We present in this article an artificial-neural-network-based method for classifying diabetic retinopathy subjects based on changes in visual evoked potential spectral components, as well as an anatomically realistic computer systems model of the human eye in normal and retinopathy conditions in a virtual environment using 3D Max Studio and Windows Movie Maker.

Keywords: Diabetic Retinopathy, Retina, Virtual

Introduction

Diabetic retinopathy is a common cause of visual loss diagnosed globally and it is a potentially blinding complication of diabetes that affects the blood vessels of the retina and damages it.[1-13] Non-insulin-dependent diabetes mellitus (NIDDM) may be the most rapidly growing chronic disease in the world. Its long-term complications, including retinopathy, nephropathy, neuropathy, accelerated macro vascular diseases, which cause major morbidity and mortality.[14-17] At first, you may notice no changes in your vision. But do not let diabetic retinopathy fool you. It might worsen over the years and threaten your good vision.

Growth of new blood vessels, known as proliferative retinopathy, may lead to blindness through haemorrhage and scarring. A deterioration of retinal blood vessels, causing loss of blood vessels and leakage into the retina is known as maculopathy and leads to visual impairment and may progress to blindness.

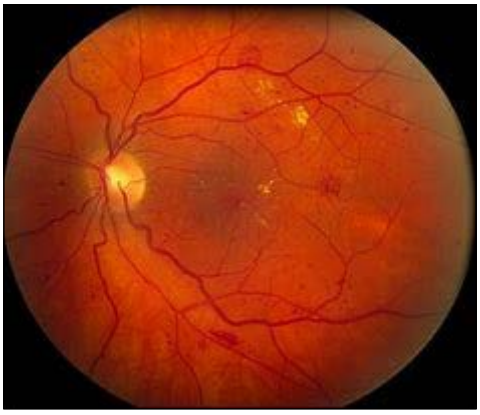

Figure 1.Diabetic-Retinopathy

Electrophysiological tests reveal an abnormal function of the visual system in patients with diabetic retinopathy.18,19 Visual Evoked Potential (VEP) has been used in the clinical environment as a diagnostic tool for long time.[20-22] VEP is one of the non-invasive tools in analysing diabetic retinopathy.[23-25] So far, not much of the work has been taken

up to identify the effect of retinopathy on optical response and variation in the functioning of the optic nerve.[26] Through analysis of evoked potential response of the optical nerve and optical brain centre, a way will be paved for early diagnosis of diabetic retinopathy and prognosis during the treatment process.[27-34]

In general, the clinical use of VEP is based on the peak amplitude and the latencies of the N75, P100, N145.[22, 35-37] The amplitude and the latencies of these peaks are measured directly from the signal.[38, 39] This requires precise definition of the starting and the end points. Latency measure depends on the point at which the latency is calculated, usually irregular peaks occur due to background EEG, so that averaging, interpolation are required. Therefore, the diagnosis based on amplitude and latency in time domain is not alone sufficient. Hence, other components should also be taken into consideration.

In recent years, many researchers have described a variety of approaches to extract the evoked potentials from the background ongoing EEG.[40-47] The investigation of the frequency domain characteristics of VEP is an attractive analytic approach because it allows detection of subtle waveform abnormalities that may escape detection with normal latency measurements.[48-50] The spectral analysis of VEP can yield useful information when it is performed carefully.[51-60]

Classification of the severity of diabetic retinopathy and quantification of diabetic changes are vital for assessing the therapies and risk factors for this frequent complication of diabetes. Current clinical studies use the standardized, validated Wisconsin grading system of retinopathy, which is performed by an experienced ophthalmologist or grader using standard photographs in this method. Diabetic Retinopathy Analysis 21 is a time-consuming process which requires significant training and exercise and is vulnerable to observer error.[61-63]

The Artificial Neural Network (ANN) has been used in a number of different ways in medicine and medically related fields. The principal advantages of ANNs are that, they are able to generalize, adapting to signal distortion and noise without loss of robustness, that they are trained by example and do not require precise description of patterns to be classified or criteria for classification.[62, 69, 70] Computer simulation is well established as a powerful and effective way of modelling health care systems.

In our analysis, we first present a method to classify diabetic retinopathy subjects according to changes in VEP spectral components using feedforward ANN. Second, we present an anatomically realistic computer model of the human eye under normal and retinopathy conditions in a virtual environment using 3D Max Studio and Windows Movie Maker.

Materials and Methods

Subjects

Experiments were carried out with 50 normal and 300 subjects with indication (135 females and 165 males in the age group of 39-65 years). The subjects were obtained from the diabetic department with duration of diabetes and type of diabetes, that is, insulin-dependent diabetes mellitus (IDDM) and NIDDM. Only NIDDM patients were enrolled for further analysis. After papillary dilation the subjects were screened in the ophthalmology department with both direct and indirect ophthalmoscopy. Further, vision test, refraction test and intraocular pressure was measured. High intraocular pressure subjects were eliminated from further analysis. The NIDDM subjects were divided based on ophthalmoscope results into 4 groups: first group: control (normal) and the other 3 groups had diabetic retinopathy second group: Background Diabetic Retinopathy (BDR), third group: Pre-Proliferative Diabetic Retinopathy (PDR) and fourth group: Proliferative Diabetic Retinopathy (PPDR).

VEP Recordings

All the VEP recordings were performed in a specially equipped electrodiagnostic procedure room in the neurology department (darkened, sound-attenuated room). At the beginning, the patient was seated comfortably approximately 1 meter away from the pattern-shift screen and the viewing distance was adjusted based on the subject's visual acuity. The visual stimuli were checkerboard patterns (contrast 70%, mean luminance 110 cd/m^2) generated on a TV monitor and reversed in contrast at the rate of two reversals per second. At the viewing distance of 114 cm, the check edges subtended 15 minutes of visual angle and the screen of the monitor subtended 12.5°. The refraction of all subjects was corrected for the viewing distance. The stimulation was monocular, with occlusion of the contralateral eye.

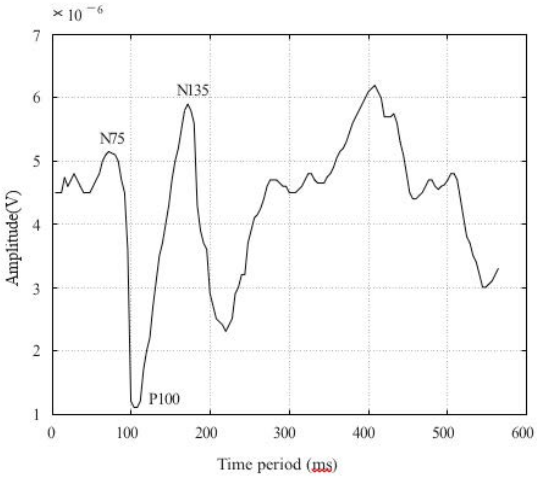

Figure 2.Normal Subject VEP Waveform

Standard silver-silver chloride disc surface electrodes were fixed in the following positions: active electrode at Oz, reference electrode at Fpz, ground on the left ear (according to the international 10/20 electrode system). The inter electrode resistance was kept below 3 kΩ. The bioelectric signal was amplified (gain 20000), filtered (bandpass, 1–100 Hz), averaged (200 events free from artefacts were averaged for every trial) with sweep speed 50 ms/div and sensitivity 2 µv/div using Nicolet Viking IV NT machine. The analysis time was 500-millisecond intervals following a stimulus.

VEP Data Analysis

The recorded averaged VEP data appears as a waveform with characteristics points N75, P100, N135 shown in Figure 1 with potential on the vertical axis (Y component) and time on the horizontal axis (X component).

The analogue signal was digitized at a sampling rate of 1024 samples/s. Using Welch's averaged periodogram method, the spectral components of the sampled data were identified using MATLAB signal processing toolbox functions with 95% confidence level.

Feature Extraction and Classification

First, two dominant peaks' amplitude and corresponding frequency values in the spectrum were extracted. Correlation between the spectral components and diabetic retinopathy stages were identified. These VEP features are classified by feedforward neural network into normal, BDR, PPDR, PDR categories.

Neural Network Configuration

We implemented the three-layer feedforward backpropagation neural networks, i.e., one input layer, one hidden layer, one output layer. The ANN had 6 input nodes, 4 hidden nodes, 4 output nodes.

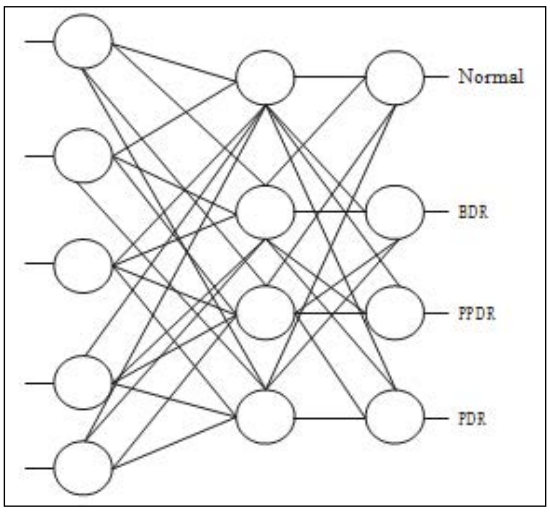

Figure 3.Feedforward Neural Network

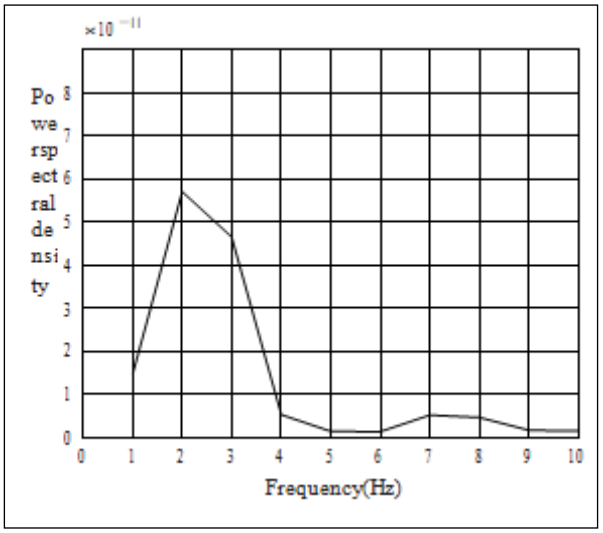

Figure 4.Normal Subject VEP Spectrum

The four output nodes corresponded to normal waveform, BDR waveform, PPDR waveform, PDR waveform. The neural network output vector is based on the VEP spectral components Figure 2.

Neural Network Training

The neural networks were trained by backpropagation algorithm. Gradient descent (GDM) was used to minimize the mean squared error between network output and the actual error rate. During the training period we utilized 6 input nodes, 6 hidden nodes, 4 output nodes, logs in transfer function, GDM training method, 6000 epochs, 0.9 learning rate, 0.0001 goal. The training error continues to decrease as the number of epoch's increases. Repeated experiments were performed to determine the size of the hidden layer and t.raining sample.

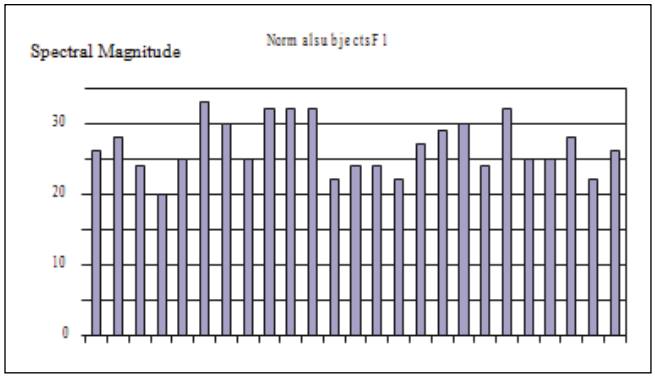

Figure 5(a).Normal patients' first spectral component 2D histogram

Our final ANN consists of 4 hidden units, which provide a compromise between the mapping error and the computational time. Weights were initialized to random values and networks were run until at least one of the following termination conditions was satisfied:

1. Maximum each,
2. Minimum gradient,
3. Performance goal.

Neural Network Testing

For testing, the input data was presented to the ANN without weight adjustment. The output of the ANN was compared with the clinician's classification based on the retinal blood vessel examination and VEP averaging latency methods. Results were compared, the percent of input patterns, which was correctly classified, was calculated.

Results

VEP Spectral Components Interpretation

The spectral response results show that the peak response occurs at specific frequencies like 2, 3, 4, 5, 6 Hz. The first two spectral components with considerable amplitude were extracted from the power spectrum plot. The important finding of this result showed that there are distinct differences at the peak frequencies for normal and diabetic retinopathy patients.

Positive correlation was obtained between the spectral components with the disease condition ($r = 0.987$). It was found that in all 50 normal subjects the dominant spectral component falls exactly at 2 Hz and the second dominant peak falls in the range of 4–7 Hz ($P < 0.0001$).

Figure 3 shows the spectral plot of normal subject. It is shown that the dominant spectral component falls at 2Hz and the secondary component at 7 Hz. 25 normal subjects' dominant spectral component magnitudes 2D histogram is presented in Figure 4 and the corresponding second dominant peak magnitude values are presented in Figure 5.

It is found that for all the BDR subjects the dominant spectral peak falls in the range of 2–3 Hz and the second dominant peak falls in the range of 5–9 Hz ($P < 0.0001$). Figure 6 shows the spectral plot of BDR subject.

Figure 5(b).Normal patients' second spectral component 2D histogram

Conclusion

After conducting a literature review, we learned about the various benefits and drawbacks of various research papers and proposed a system that predicts diabetes in an affordable and effective manner by requiring few inputs from the user and anticipating accurate results using trained Machine Learning algorithms. As a result, the diabetic retinopathy analysis system has been constructed utilizing the specified 5 Machine Learning algorithms, which have a maximum accuracy of 98.56%. As a result, the system is meant to provide a simple yet productive User Interface design with a compassionate approach to its users and patients. The system has potential for growth, which might lead to improved outcomes and greater satisfaction for users.

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