Identification of Transient Visual Evoked Potential Latency Using Spectral Components

R. Sivakumar and G. Ravindran

Abstract—Transient visual evoked potential (TVEP) has been used as one of the valuable diagnostic tool in clinical environment. Various types of analyze have been performed on TVEP recordings for identifying diagnostically significant information. Conventional methods of detection of visual anomalies, based on TVEP require long periods of testing and averaging. Hence the problem of patient fatigue affects the accuracy of the results. This paper presents an approach to analysis TVEP latency using spectral components. This new approach was successfully tested on 300 normal and 450 abnormal subjects with certain disorders to identify the change in latency.

Index Terms—Transient visual evoked potential, latency, spectral components.

I. INTRODUCTION

The use of sensory evoked brain potentials in the study of attention and cognitive processing has a long history [1]-[4]. Transient visual evoked potential (TVEP) is an important diagnostic test for specific ophthalmological and neurological disorders [5]-[11]. VEP recordings are obtained in a simple and non-invasive way. The precision of clinical interpretation depends on the amount of information available. This requires long periods of stimulation. TVEP investigation focuses on the dominant peaks N75, P100, N135, a negative deflection followed by a positive and then a negative deflection. The peak P100 occurs after about 100 ms following the stimulation in all normal patients. The amplitude and latencies of these peaks are measured directly from the TVEP signal. Quantification of these latency changes can contribute to the detection of possible abnormalities [12],[13]. This requires the precise definition of the starting and end points of TVEP peaks. Latency measure depends on the point at which the latency is calculated and usually the peak presents irregularities, so that interpolation is required. The EP signal is always accompanied by the ongoing EEG signal, which is considered as noise in EP analysis. The SNR may be as low as -10dB. Overcoming the effects of noise is a major issue in EP analysis.

Many researchers have described a variety of approaches to extract the evoked potential from the background EEG [14]-[17]. Traditionally, the clinical use of VEPs is based on visual reading. Given the fact that useful data are completely buried in the ongoing EEG, averaging techniques are usually applied to estimate the VEP. Conventional methods of detection of visual anomalies, based on TVEP require long periods of testing and averaging, which requires a large number of trials. Hence, the problem of patient fatigue affects the accuracy of the results. These factors imply that the analysis in the time domain, based on amplitude and latency, is not reliable.

The failure of time domain analysis has compelled researchers to investigate the frequency domain characteristics of the VEP response. According to a working hypothesis published earlier [18], EPs are considered as stimulus-induced EEG rhythmicities. Accordingly, it is advantageous to analyze EPs in the frequency domain. The development of the FFT algorithm has facilitated the estimation of spectral functions [19]. Investigation of the frequency domain characteristics of VEP’s is an attractive analytic approach because it allows detection of suitable waveform abnormalities that may otherwise escape detection with normal latency measurements [20]-[22].

Several researchers have proposed methods using both TVEP and steady state VEP (SSVEP). Most of these methods utilize the latency and amplitude of P100 values of TVEPs to identify the abnormality. SSVEPs were Fourier analyzed, and phase and amplitude of the second harmonic response were measured to identify the disease condition. In most of the methods Fourier analysis was applied to SSVEP only [23],[24].

Previous studies have made extensive use of “transient” evoked potentials, which are computed by averaging a large number of repetitive responses to separate the desired signal from concurrent "noise". Only few studies adopted the spectral analysis to TVEP. Apaydin et al. studied the effects of oxygenated free radicals on VEP spectral components in experimental diabetes using TVEP [21]. Kulkarni and Udipiak recorded thirty normal subjects at a flash rate of 1.8 Hz [25]. Their result showed that the dominant response frequencies lie in the range of 4 to 16 Hz. Finally they suggested that the power spectrum analysis of VEP could be used as a non-invasive, objective technique to assess the stage of in any ocular diseases.

Different researchers studied the effect of chronic cadmium exposure on VEP and EEG spectral components on Swiss albino rats [26]-[28]. Amplitude maximal were obtained in the 2-4, 4-7, 8-13, 14-20, 20.5-36 Hz frequency bands. None of the above methods correlated the latency with spectral components.
This paper describes a method of classification of normal and abnormal TVEP’s based on the spectral components using Welch’s averaged periodogram method. In the first stage of this paper, the spectral components of normal and abnormal subjects have been identified using Welch’s averaged periodogram method. The Spectral components of each subject have been compared with the corresponding latency values measured by the averaging method and results have been presented in the second stage of this paper. This procedure has been repeated for all the subjects with fewer numbers of ensembles and the latency has been computed directly from the spectral components and the results has been statistically analyzed and presented.

II. MATERIAL AND METHOD

A. Subjects
Experiments were carried out with subjects in the Neurology Department of Sri Ramachandra Medical College and Research Institute, Chennai, India from 2000 to 2001. 250 cases data were analyzed. Of these patients, 50 normal and 100 abnormal subjects (35 females and 65 males in the age group of 39 – 52 years mean age 48) were chosen for further analysis. In 100 abnormal subjects, 35 subjects had multiple sclerosis (MS), 25 subjects had diminished vision, 15 subjects had Motor neural disorder, and 25 subjects had diabetic retinopathy.

B. Patient Preparation
The local institutional human experimentation committee approval was obtained before the procedure. The written consent was also obtained from each subject after complete explanation of the nature of study and possible consequence of the study. Subjects were requested to take routine medications in the morning of the procedure, including prescription ophthalmics, washing the hair the previous night (to facilitate electrode placement). They were requested to eat shortly before the investigation (to avoid relative hypoglycemia) and corrective lenses have also been brought to the testing room.

C. Equipment
Nicolet Viking IV-pattern-shift stimulator television screen, signal amplifier with filters, computer system for averaging were used for the analysis.

D. TVEP Recording
TVEP was performed in a specially equipped electro diagnostic procedure room (darkened, sound attenuated room). Initially, the patient was made to sit comfortably approximately 1 meter away from the pattern-shift screen. Subjects were placed in front of a black and white checkerboard pattern displayed on a video monitor. The checks alternate black/white to white/black at a rate of approximately twice per second. Every time the pattern alternates, the patient's visual system generates an electrical response that was detected and was recorded by surface electrodes, which were placed on the scalp overlaying the occipital and parietal regions with reference electrodes in the ear. The patient was asked to focus his gaze onto the center of the screen. Each eye was tested separately (monocular testing).

E. Stimulation Pattern
The visual stimuli were checkerboard patterns (contrast 70%, mean luminance 110 cd/m²) generated on a TV monitor and reversed in contrast at the rate of two reversals per second (Fig. 1). 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.

F. Electrodes and Electrode Placement
Cup-shaped Ag/AgCl electrodes were fixed with collodion in the following positions: active electrode at Oz, reference electrode at Fpz, ground on the left ear (Figure 2). The interelectrode resistance was kept below 3 kΩ. The bioelectric signal was amplified (gain 20,000), filtered (band-pass, 1-100 Hz), and 75 events free from artifacts were averaged for every trial [29]. The analysis time for each trial was 250 ms.
Fig. 3. Pre-stimulus TVEP waveform.

Fig. 4. Averaged TVEP waveform.

Fig. 5. Single trial TVEP waveform.

G. Eye Blink Removal

A common artifact that corrupts the TVEP data is eye blinks. This problem has been solved by an amplitude threshold method. The TVEP signals with magnitude above 50 microvolts are assumed to be contaminated with eye blinks and are discarded from the experimental study and additional trials were conducted as replacements.

H. Data Set Description

The experimental data was collected in terms of blocks of trials. First trial was the time period of 250 ms before the onset of stimulation. Remaining trials are 250 ms each after the onset of stimulation. One block of trial was the continuous collection of 20 trials displayed one after other. In a typical experiment, 3-4 blocks of trials were recorded. In the block of trials, the eye blink trials were eliminated. Entire trials were divided into three groups:
1. Pre-stimulus trials
2. Post-stimulus trials
3. Single trials

Fig. 3 shows the sample time scale data recorded before the stimulus and Fig. 4 shows the sample time scale data recorded after the stimulus, averaged over 75 trials. Fig. 5 shows the sample single trial data.

I. P100 Latency Measurements

For each subject 75 trials were carried and corresponding waveforms were stored in the system hardware. From the 75 trials, 70 artifact free trials waveforms were selected and using the averaging method all 70 trials were averaged to get the TVEP waveform. By manually moving the cursor over the averaged waveform the characteristic points such as N75, P100, and N145 were identified and corresponding latency values identified. Only P100 values were taken for further analysis.
TABLE I
NORMAL SUBJECTS SPECTRAL COMPONENTS

<table>
<thead>
<tr>
<th>S. No</th>
<th>Subjects</th>
<th>Eye</th>
<th>Sex</th>
<th>Age</th>
<th>Freq. (Hz)</th>
<th>Magnitude</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>F1</td>
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</tr>
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<td>M</td>
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<td>2</td>
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<td>R</td>
<td>M</td>
<td>47</td>
<td>2</td>
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</tr>
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</table>

J. Spectral Components Identification

The TVEP waveform was sampled at 1024 Hz (as per IFCN Guidelines issued by Nuwer [30]). The spectral components of the each pre-stimulus waveform and post-stimulus averaged waveform were identified by Welch’s averaged periodogram method with a frequency resolution of 1 Hz. Beyond 10 Hz no major spectral components were obtained for all subjects (Figs. 6 and 7), so the values on the frequency band 1-10 Hz were normalized according to the maximum value in that band. Specifically, the first two dominant peaks were extracted from the spectral plot along with the corresponding magnitudes (A1, A2) and frequency values (F1, F2). A program to extract the magnitude and frequency of the first two dominant spectral component values has been developed. In the second stage the spectral components of single trial waveforms were identified and the results were compared with the averaged waveform spectral components.

K. P100 Calculation Using Spectral Components

In the subjects with different P100 latency value, there were different spectral peaks in the periodogram. Correlation between the spectral components and P100 value has been obtained. The latency values obtained by the averaging method and the spectral components obtained by the periodogram method have been compared. Correlation between the spectral components and latency values were identified using Pearson’s correlation coefficient. For single trial waveform the latency were calculated using the spectral components values.

L. Classification

After identifying the correlation between spectral components with patient abnormality, the patients were classified based on the spectral components. Patient classifications based on spectral components were compared with clinician classification.
The dominant spectral components for all the 50 normal subjects TVEP averaged waveform have been identified and the sample results are presented in Table I. Figs. 8 and 9 show TVEP waveform of two normal subjects and corresponding periodograms. The statistical results are shown in Table II. It has been found that all normal subjects had a dominant peak at 2 Hz, with a secondary peak occurring in the range 6-12 Hz.

The dominant spectral components for all the 100 abnormal subjects have been identified and the sample results are presented in Table III. Figs. 10 and 11 show the TVEP waveform of two abnormal subjects and corresponding periodograms. The statistical results are presented in Table IV. It has been found that the abnormal subjects had a dominant peak around 3-5 Hz and secondary peak in the range 6-12 Hz.

The spectral components of the pre-stimulus TVEP waveform for both normal and abnormal subjects had a single dominant peak in 6-12Hz ranges. The representative results are shown in the Figure 12. For both the prestimulus and post stimulus TVEP, it has been found that the peak occurred in the range 6-12 Hz. It was found that the second peak corresponds to the background EEG. The dominant peak value in the 2-5 Hz range was significantly different for normal and abnormal subjects (p<0.001). The results indicate that the subject could be classified based on dominant spectral component. The results also indicate that the best classification of subjects could be obtained without removing the background of the signal.

For the single trial TVEP waveform, the spectral results show that the dominant peak value is constant for all the trials and only slight variation in the second dominant peak. Finally, spectral components of each subject have been compared with the corresponding latency values measured by the averaging method and the sample results have been presented in Tables V-VII. It has been found that the
latency for single trial could be identified using the spectral components, but P100 amplitude value could not be identified from the waveform directly.

The results show that the 100 ms, 120 ms, 140 ms, and 160 ms latency values can be identified precisely using the spectral components. The results have been compared with the data obtained from all the 150 patients with the averaging method and statistically analyzed (p<0.001). For the intermediate latencies (such as 112, 123, 145 etc values), the results obtained shows that the latency cannot be predicted precisely. The intermediate latencies have shown as nearest latencies such as 112 and 123 displayed as latencies nearer to 100, 120, 140, 160 ms, etc.

IV. DISCUSSION

Characteristically, TVEPs are of low amplitude and require considerable amplification. Computer signal averaging must be used to diminish background electrical signals (EEG), and isolate the TVEP. The results of numerous consecutive trials are computer averaged. The composite signal appears as a waveform, with potential on the vertical axis and time on the horizontal. Minimum of 50 trials are required to extract the TVEP from the background EEG.

Due to the background EEG identification of P100, extraction of the exact value in TVEP becomes very difficult, and therefore several trials are averaged in order to enhance the TVEP. Since TVEP is time locked to the stimulus, their contribution will add while the on going EEG effect will be canceled. However, when averaging, information related to variations between the single trials is lost [31], [32]. This information could be relevant in order to study the behavioral and functional processes. Moreover, in many cases, compromise must be made while deciding on the number of trials in an experiment. If the large numbers of trials are considered then the subject could deal with the effects such as tiredness, which eventually corrupts the average results. The same procedure has been repeated for all subjects with fewer numbers of trials and the latency has been computed directly from the spectral components. It has been found that the latency could be computed from the spectral components with fewer numbers of trials.

In the analysis presented in this paper it has been found that the pre-stimulus spectrum is in the range of 6-12 Hz. Also, for the post-stimulus data, it has shown that the secondary peak was obtained in the range of 6-12 Hz. It has been found that the peak at 6-12 Hz range corresponding to the background EEG and it agrees with the previous results because those studies shows that the EEG spectrum during the evoked potential analysis falls in the alpha range [33].

Most of the frequency domain methods have been applied to denoising the averaged TVEPs and then the decision was taken again from time domain P100 [33]. But in the present method, it has identified the P100 latency directly from the spectral components. The method proposed in this paper can be used for analyzing both averaged TVEP and single trial TVEP.

All the 4 disorders analysed in this study found to have the common phenomenon. The latency is elongated when compared to normal condition. In the case of MS patient, previous reports indicate that the latency have been prolonged by 10 to 30 ms [34], [35]. As the severity of the disease increases, the prolongation will also increase. In the present study subjects with MS found to have prolongation of latencies by 30 to 38 ms when compared to normal. Main disorder associated with MS is demyelination of the optic nerve. Demyelination produces decrease in velocity of conduction, which in turn increases the latency. As the latency increases, it has been found that the peak frequency shifts towards the higher side. In the present results it has been found that the peak frequency was at 4 Hz.

<table>
<thead>
<tr>
<th>S. No</th>
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<th>P100 (ms)</th>
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<tr>
<td>10.</td>
<td>N10</td>
<td>2</td>
<td>100</td>
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</table>
The next disorder namely diminished vision, which results either due to hereditary or degenerative condition like MND has been found to have small increase in latency. In the present work, latency has been found to increase by 18 to 22 ms (i.e. latency of 118 to 122 ms). For these waveforms, peak response has been found to occur at 3 Hz. In the clinical findings, all these four diseases that have been analysed will have increased latencies compared to normal VEPs [36]-[38]. Thus, this result proves that the waveform with increased latencies will have a shift in the peak frequency range. The results have been compared with practical cases and were found to be consistent with the clinical findings. Thus the spectral response technique agrees with the pathological conditions. Its implementation is quite simple.

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REFERENCES


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