Analysis of Transient Visual Evoked Potential (TVEP) Using Phase Spectral Periodicity Components

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Abstract: Transient Visual Evoked Potential (TVEP) is an important diagnostic test for specific ophthalmological and neurological disorders. The precision of clinical interpretation depends on the amount of information available. This paper describes the method of classification of normal and abnormal TVEP's based on the phase spectral periodicity using Welch's averaged periodogram method. The phase spectral components of normal and abnormal subjects have been identified using Welch's averaged periodogram method. The phase Spectral periodicity of each subject have been compared with the corresponding latency values measured by the averaging method and results have been presented. The advantage of this method is that one can directly identify the latency more precisely than the magnitude domain method.

Key words: Transient Visual Evoked Potential (TVEP), spectral components, phase spectral periodicity, welch averaged periodogram

INTRODUCTION

The use of sensory evoked brain potentials in the study of attention and cognitive processing has a long history[1-4]. The 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 focused on the dominant peaks N75 P100 N135, a negative deflection followed by a positive and then a negative deflection. The peak P100 occurring about 100 msec following the stimulation in all the normal patients. The amplitude and latencies of these peaks are measured directly from the 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 the end points. Latency measure depends on the point at which the latency is calculated and usually the peak presents irregularities, so that interpolation is then 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 becomes 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 based on visual reading. Given the fact that the 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 TVEPs require long periods of testing and averaging. 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 escape detection with normal latency measurements[20-22].

Several researchers have proposed methods using both the TVEP and SSVEP. Most of these methods utilize the latency and amplitude of P100 values of TVEPs to identify the abnormality and SSVEPs were Fourier analyzed and phase and amplitude of the second harmonic response were measured. In most of the methods Fourier analysis was applied to only SSVEP[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 adapted the spectral analysis to (TVEP).

Apaydin *et al.*[21] studied the effects of oxygenated free radicals on VEP spectral components in experimental diabetes using TVEP. Kulkarni and Udpikar[25] recorded the thirty normal subjects at a flash rate of 1.8 Hz. Their result showed that the dominant frequencies 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.

Agar *et al.*[26], Yargicoglu *et al* .[27] and Yargicoglu *et al.*[28] studied the effect of Chronic Cadmium exposure on VEP and EEG spectral components on Swiss albino rats. Amplitude maximal were obtained in the 2-4, 4-7, 8-13, 14-20, 20.5-36Hz frequency bands. Many research works have been carried out in the magnitude spectra and few studies only concentrated on the phase spectra[29,30]. None of the above methods correlated the latency with spectral components.

Our previous results show that the 100, 120, 140 and 160 msec latency values can be identified precisely using the magnitude spectral components[31,32].

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 msec, 140,160 etc.

This paper describes the method of classification of normal and abnormal TVEP's based on the phase spectral periodicity using Welch's averaged periodogram method. In the First stage of this paper, the phase spectral components of normal and abnormal subjects have been identified using Welch's averaged periodogram method. The phase Spectral periodicity of each subject have been compared with the corresponding latency values measured by the averaging method and results have been presented. The same 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.

MATERIALS AND METHODS

Subjects: Experiments were carried with subjects in the Neurology Department of the leading Medical Institute from 2000 to 2001. 250 cases with complete 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 taken for further analysis.

Fig. 1: Nicolet viking IV machine

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.

Patient preparation: The local institutional human experimentation committee approval has been obtained before the procedure. The written consent has also been 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) and they were requested to eat shortly before the exam (to avoid relative hypoglycemia) and corrective lenses have also been brought to the testing room.

Equipment: Nicolet Viking IV-Pattern-shift stimulator television screen, signal amplifier with filters, computer system for averaging were used for the analysis (Fig. 1).

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
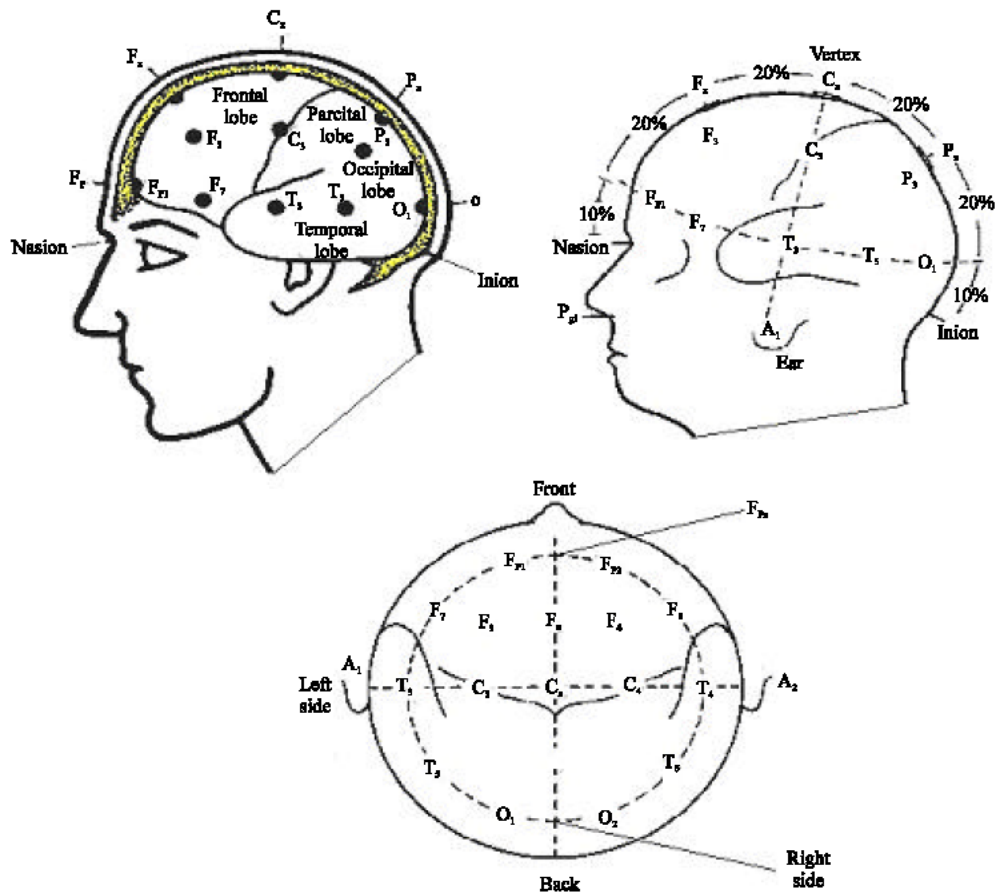
Fig. 2: 10-20 Electrode system with electrode position

Fig. 3: Pattern shift stimulation TV screen

Fig. 4: Electrode locations

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 (Fig. 2). The patient was asked to focus his gaze onto the center of the screen. Each eye was tested separately (monocular testing).

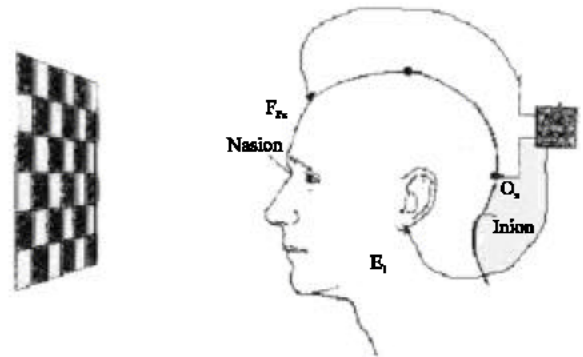**Stimulation pattern:** The visual stimuli were checkerboard patterns (contrast 70%, mean luminance 110 cd/m^2)

generated on a TV monitor and reversed in contrast at the rate of two reversals per second (Fig. 3). 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 contra lateral eye.

Electrodes and electrode placement: Cup-shaped Ag/AgCl electrodes were fixed with collodion in the

Table 1: Normal subjects periodicity values

S. No	Subjects	Eye	Sex	Age	Latency (msec)	Periodicity measure
1.	N1	R	M	39	100	0.6536
2.	N2	L	M	41	100	0.5145
3.	N3	R	F	50	100	0.5584
4.	N4	R	F	45	100	0.6495
5.	N5	L	M	52	100	0.6591
6.	N6	R	M	43	100	0.5586
7.	N7	R	F	48	100	0.5785
8.	N8	L	M	50	100	0.6007
9.	N9	L	M	40	100	0.6748
10.	N10	R	M	47	100	0.6321

following positions: active electrode at Oz, reference electrode at Fpz, ground on the left ear (Fig. 4). The interelectrode resistance was kept below 3 k. 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 (Odom et al 2004). The analysis time for each trial was 250 msec.

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 50microvolts are assumed to be contaminated with eye blinks and are discarded from the experimental study and additional trials were conducted as replacements.

Data set description: The experimental data was collected in terms of blocks of trials. First trial was the time period of 250msec before the onset of stimulation. Remaining trials are 250msec 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.

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 the 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 were identified. Only P100 values were taken for further analysis.

Phase Spectral periodicity identification: The TVEP waveform was sampled at 1024Hz (as per IFCN Guidelines issued by Nuwer *et al*.[33]. 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. The periodicity measure for each phase spectrum have been identified using the following formula

$$P_f = (\sum F_{iw} - \sum F_{(iw+w/2)})/(\sum F_{iw} + \sum F_{iw+w/2})$$

where F is the energy spectrum of the signal f and w is the frequency corresponding to the highest amplitude in the energy spectrum. The measure is normalized with respect to the total energy at the frequencies of interest so that it is one for a completely periodic signal and zero for a flat spectrum. In the second stage the spectral components of single trial waveforms were identified and the results were compared with the averaged waveform spectral components.

P100 calculation using spectral periodicity components: It was observed that the subjects with different P100 latency value, there was a different periodicity value in the periodogram. Correlation between the phase periodicity of spectral components and P100 value has been obtained. The latency values obtained by the averaging method and the phase periodicity obtained by the peridogram method have been compared. Correlation between the phase spectral periodicity and latency values were identified using Pearson's correlation coefficient.

Classification: After identifying the correlation between phase spectral periodicity with patient abnormality, the patients were classified based on the phase spectral periodicity. Patient classifications based on phase spectral periodicity were compared with clinician classification.

RESULTS

The periodicity measure of spectral components for all the 50 normal subjects TVEP averaged waveform have been identified and the sample results are presented in Table 1. Figs. 5 and 6 show the two normal subjects TVEP waveform and corresponding periodicity measure values.
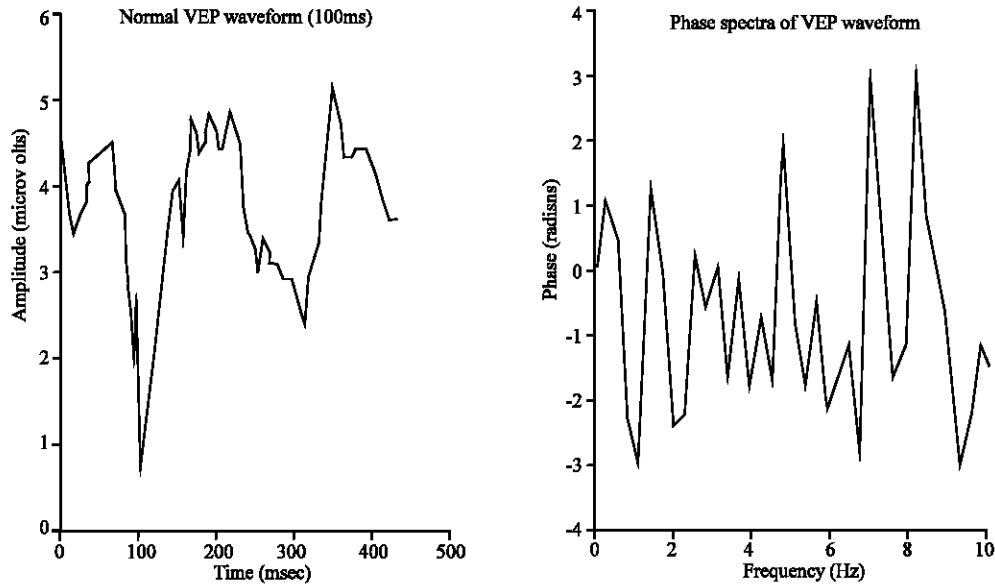
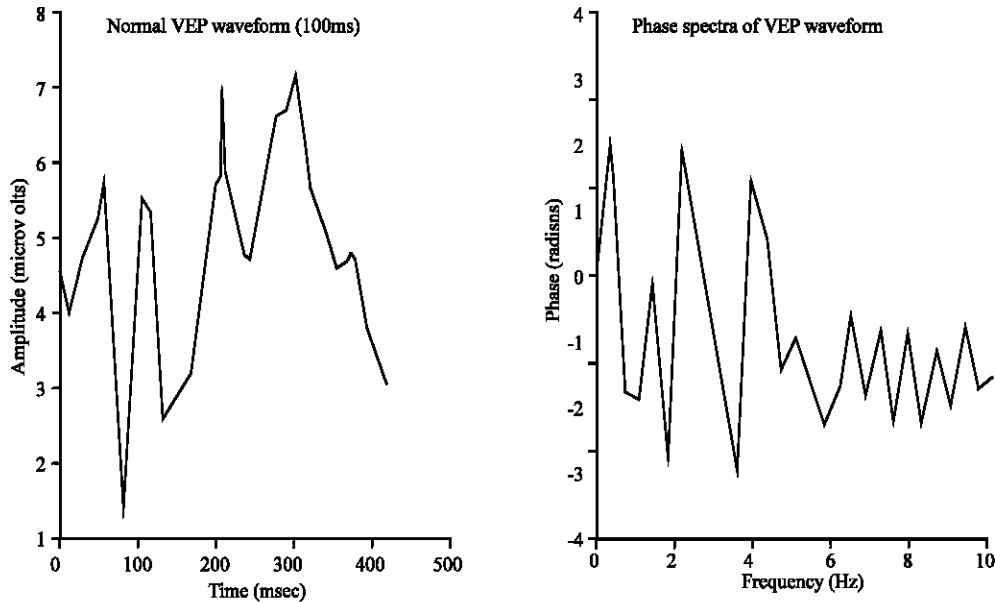Fig. 5: Normal TVEP waveform1 and its phase spectrum

Fig. 6: Normal TVEP waveform2 and its phase spectrum

It has been found that all normal subjects the spectral component periodicity falls in the range of 0.5-0.6 (p<0.01).

The periodicity measure of spectral components for all the 100 abnormal subjects have been identified and the sample results are presented in Table 2. Figs. 7 and 8 show the two abnormal subjects TVEP waveform and corresponding periodicity measure values. The statistical results are presented in Table 3. It has been found that all abnormal subjects the spectral component periodicity falls in the range of 0.2-0.4 (p<0.01).

Finally, phase spectral periodicity of each subject have been compared with the corresponding latency values measured by the averaging method . It has been found that the latency could be identified using the spectral components, but P100 value could not be identified from the waveform directly. The periodicity measure of spectral response has shown that the periodicity measure value occurs in the range between 0.1-0.6. The important finding of this result shown that there are distinct differences at the periodicity measure for normal and abnormal subjects. Negative correlation

Table 2: Abnormal subjects periodicity values

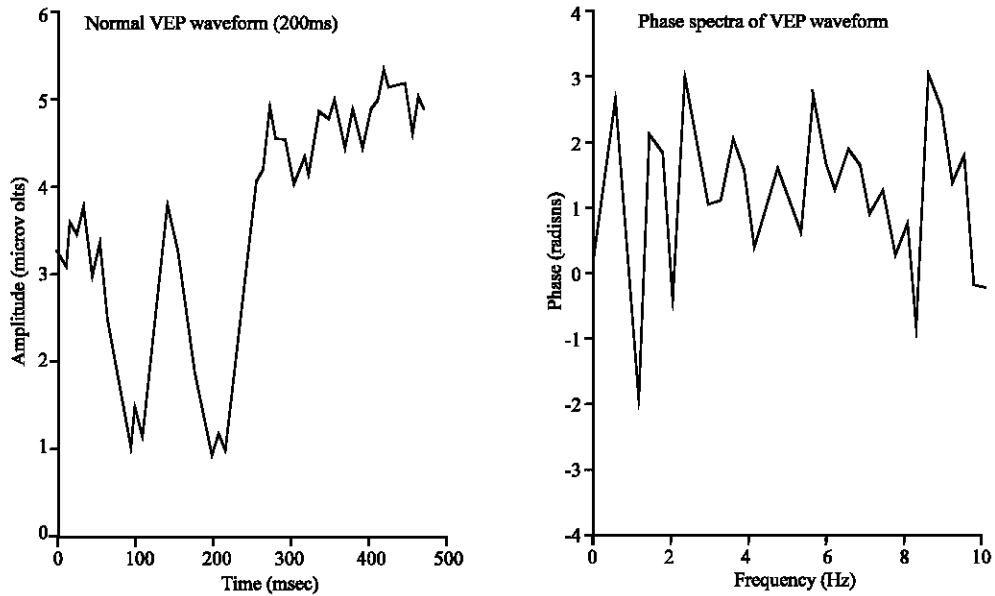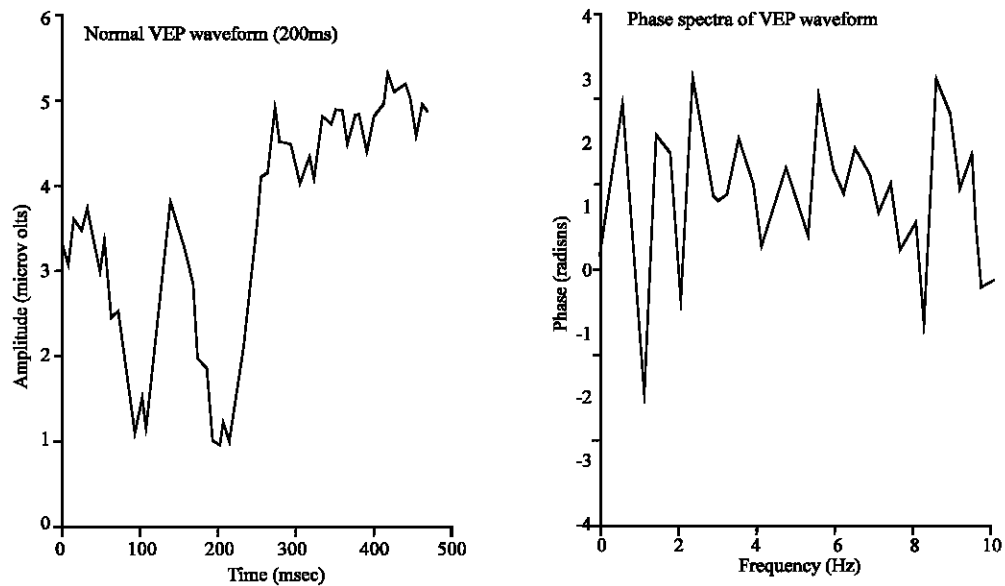| S. No	Subjects	Eye	Sex	Age	Latency (msec)	Periodicity measure
1.	MS1	L	F	45	118	0.3584
2.	MS2	R	F	52	118	0.4415
3.	MS3	R	M	43	138	0.3441
4.	MS4	L	M	48	140	0.3835
5.	MS5	R	F	50	146	0.3554
6.	MND1	R	M	40	180	0.2516
7.	MND2	L	M	47	192	0.3620
8.	MND3	L	M	51	207	0.2786
9.	MND4	R	M	52	208	0.2022
10.	DM1	R	M	52	210	0.1545
11.	DM2	R	F	40	210	0.2712
12.	DM3	L	F	45	223	0.2214

Fig. 7: Abnormal TVEP waveform1 and phase spectrum

Fig. 8: Abnormal TVEP waveform and phase spectrum

Table 3: Statistical analysis on periodicity values

S.No	Subject	Mean	Standard deviation
1	Abnormal	0.3020	0.0815
2	Normal	0.5830	0.0835

obtained between the spectral components periodicity measure with the disease condition (r = 0.987).

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, exact value in TVEP becomes very difficult and therefore several trials are averaged in order to enhance the TVEP. Since TVEP time locked to the stimulus, their contribution will add while the on going EEG will cancel. However, when averaging, information related to variations between the single trials is lost[34,35]. 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 the subjects with fewer numbers of trials and the latency has been computed directly from the spectral periodicity components. It has been found that the latency could be computed from the spectral periodicity components with fewer numbers of trials.

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[36]. But in the present method, it has been identified that the P100 latency directly from the phase spectral periodicity 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 30msec[37,38]. 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 38msec 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 phase periodicity shifts towards the lower side. In present result it has been shown that the periodicity measure was at .4.

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 22msec(i.e. latency of 118 to 122msec). For these waveforms, peak response has been found to occur at 3Hz. In the clinical findings, all these four diseases that have been analysed will have increased latencies compared to normal VEP's. Thus, this result proves that the waveform with increased latencies will have a shift in the periodocity.

The results have been compared with practical cases and were found to be consistent with the clinical findings. Thus the phase spectral periodicity measure technique agrees with the pathological conditions. Its implementation is quite simple. The work presented in this chapter mainly concentrates with the different latencies corresponds to P100. Variations of latency with the severity of the diseases are not taken in to consideration.

REFERENCES

1. Spong, P., M. Haider and D.B. Lindsley, 1965. Selective attentiveness and cortical evoked responses to visual and auditory stimuli, Sci., pp: 395-397.
2. Naatanen, R., 1975. Selective attention and evoked potentials in humans-a critical review, Biological Psychology, pp: 237-307.
3. Regan, D., 1989. Human Brain Electro physiology: Evoked potentials and Evoked Magnetic Fields in Sci. and Med. Amsterdam, Elsevier, pp: 41-42.
4. Collura, T.A., 2001. Human steady state Visual Evoked potential and Auditory potential Components During a Selective Discrimination Task, J. of Neuropathy, pp: 1-13.
5. Plant, G.T., 1983. Transient visually evoked potentials to sinusoidal gratings in optic neuritis, J. Neurol Neurosurg Psychiatry., pp: 1125-1133.
6. Chiappa, K.H., 1990. Pattern shift visual evoked potential methodology, Evoked potentials in Clinical Medicine, K.H.Chiappa, Ed. Newyork: Raven Press, pp: 37-110.

7. Misra, J.K. and Kalith, 1999. Clinical Neurophysiology, I. Churchill Livingstone Pvt Ltd, New Delhi.

8. AbdelMageed, M.A.S. and H.M. Assem, 2002. Electroretinography and visual evoked potential in children with IDDM, Proceedings of ISLRR Vision 2002 Conference, pp: 150.

9. Lauritzen, L., M.H. Jorgensen and K.F. Michaelsen, 2004. Test-retest reliability of swept visual evoked potential measurements of infants visual acuity and contrast sensitivity, Pediatric Res., pp: 701-708.

10. Momose, K., M. Kiyosawa, N. Nemoto, M. Mochizuki and J.J. Yu, 2004. PRBS-determined temporal frequency characteristics of VEP in glaucoma, Documenta Ophthalmologica, pp: 41-46.

11. Suttle, C.M. and A.M. Turner, 2004. Transient pattern Visual Evoked Potentials in children with Downs syndrome, Ophthalmic and Physiological Optics, pp: 91.

12. Nogawa, T., K. Katayama, H. Okuda and M. Uchida, 1991. Changes in the latency of the maximum positive peak of visual evoked potential during anesthesia, Nippon Geka Hokan, pp: 143-153.

13. Xu, S., H. Wagner, F. Joo, R. Cohn and I. Klatzo, 1992. Reduced latency of the visual evoked potential cortical response following cryogenic injury to cerebral cortex – A neuroexcitatory phenomenon, Neurological Res., pp: 233-235.

14. Fotopoulos, S., A. Bezerianos and N. Laskaris, 1995. Latency measurement improvement of P100 complex in visual evoked potentials by FMH filters, IEEE Transactions on Biomedical Engineer., pp: 424-428.

15. Kong, X. and N.V. Thakor, 1996. Adaptive estimation of latency changes in evoked potentials, IEEE Transaction on Biomedical Engineer., pp: 189-197.

16. Gevins, A.S., N.H. Morgan, S.L. Bressler, J.C. Doyle and B.A. Cutillo, 1986. Improved event-related potential estimation using statistical pattern classification, Electroencencephalogr., Clin. Neurophysiol., pp: 177-186.

17. Davila, C.E., R. Srebro and I.A. Ghaleb, 1998. Optimal Detection of Visual Evoked Potentials, IEEE Transaction on Biomedical Engineer., pp: 800-803.

18. Basar, E., 1980. EEG-Brain Dynamics, Elsevier, Amsterdam.

19. Kelly, S., D. Burke, P.D. Chazal and R. Reilly, 2002. Parametric Models and Spectral analysis for Classification in Brain-Computer Interface, Proc. Of 14th Intl. Conference on DSP, pp: 1-4.

20. Skuse, N.F. and D. Burke, 1990. Power spectrum and optimal filtering for visual evoked potentials to pattern reversal, Electroencephalogr Clin Neurophysiol., pp: 199-204.

21. Apaydin, C., Y. Oguz, A. Agar, P. Yargicoglu, N. Demir and G. Aksu, 1993. Visual Evoked potential and optic nerve histopathology in normal and diabetic rates and effect of ginkgo biloba extract, Acta Ophthalmol., pp: 623-628.

22. Kramarenko, A.V. and U. Tan, 2002. Validity of Spectral analysis of evoked potentials in brain research, Intl. J. Neuroscience, pp: 489-499.

23. Tobimatsu, S. and M.M. Kato, 1996. The effect of binocular stimulation on each component of transient and steady-state VEPs, Electroencephalogr Clin Neurophysiol., pp: 177-83.

24. Nakayama, M., 1994. Transient and steady-state electroretinograms and visual evoked potentials to pattern and uniform-field stimulation in humans, Fukuoka Igaku Zasshi., pp: 225-234.

25. Kulkarni, G.R. and V. Udpikar, 1995. An integrated facility for data acquisition and analysis of biomedical signals. Case studies on VEP, IVS, Proc. 14th Conference of the Biomedical Engineer. Society of India, pp: 67-68.

26. Agar, A., P. Yargicoglu, B. Aktekin, M. Edremitlioglu and C. Kara, 2000. The effect of cadmium and experimental diabetes on EEG spectral data, J. Basic Clin. Physiol. Pharmacol., pp: 17-28.

27. Yargicoglu, P., A. Agar, V.N. Izgut-Uysal, U.K. Senturk and Y. Oguz, 1996. Effect of Chronic Cadmium exposure on VEP and EEG spectral components, Intl. J. Neuroscience, pp: 173-184.

28. Yargicoglu, P., A. Agar, Y. Oguz, V.N. Izgut-Uysal, U.K. Senturk and G. Oner, 1997. The effect of Development Exposure to Cadmium (cd) on Visual Evoked Potentials (VEPs) and Lipid Peroxidation, Neurotoxicology and Teratology, pp: 213-219.

29. Pecher, A. and P. Husar, 2003. Phase Estimation of Visual Evoked Responses, IEEE Transaction on biomedical engineering, 50, 3, pp: 324-353.

30. Micheli-Tzanakou, E. and S. Pavlopoulos, 1998. ANALYSIS OF VEP USING PHASE INFORMATION, Proc. Of IEEE EMBS 10th Annual Intl. Conference, pp: 1160-1161.

31. Sivakumar, R. and G. Ravindran, 2004. Automatic Discrimination of Abnormal Subjects Using the Visual Evoked Potential Spectral Components, Intl. J. Biomedicine and Biotechnology, pp: 5-9.

32. Sivakumar, R. and G. Ravindran, 2002. Visual evoked potential spectral component analysis, Proc. 2nd European Medical and Biological Engineering Conference-EMBEC02, Austria, pp: 18-20.

33. Nuwer, M.R., D. Lehmann, F.L. Silva, W. Sutherling and J.F. Vibert, 1994. IFCN guidelines for topographic and frequency analysis of EEGs and EPs. Report of an IFCN committee, Electroencephalography and clinical Neurophysiology, pp: 1-5.

34. Truccolo, W.A., M. Ding, K.H. Knuth, R. Nakamura and S.L. Bressler, 2002. Trial-to-trial variability of cortical evoked responses: implications for the analysis of functional connectivity, Clinical Neurophysiology, pp: 206-226.

35. Goodman, C., V. Rodionov, G.Z. Rosenstein and H. Sohmer, 2003. Analysis of visual evoked potentials and background electroencephalographic activity in young and elderly subjects, Journal of Basic Clinical Physiology Pharmacology, pp: 265-299.

36. Quiroga, R.Q., 2000. Obtaining single stimulus evoked potentials with wavelet denoising, Plysica D, pp: 278-292.

37. Alshuaib, W.B., 2000. Progression of visual evoked potential abnormalities in multiple sclerosis and optic neuritis, Electromyography Clinical Neurophysiology, pp: 243-252.

38. Gronseth, G.S. and E.J. Ashman, 2000. The usefulness of evoked potentials in identifying clinically silent lesions in patients with suspected multiple sclerosis, Neurology, pp: 1720-1725.