ASSOCIATION OF PATTERN REVERSAL VEP PARAMETERS WITH THE MEAN DEFECT OF HUMPHREY VISUAL FIELD IN PATIENTS OF PRIMARY OPEN ANGLEGLAUCOMA

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Abstract: Glaucoma is a chronic, progressive bilateral optic neuropathy which disturbs the structural or functional integrity of the optic nerve that causes characteristic atrophic changes in it, which leads to specific visual field defects over time with loss of visual function. Primary open angle glaucoma (POAG) is the most common form of glaucoma in India and is fast emerging as a major cause of bilateral blindness. This rural hospital based study was conducted to evaluate whether glaucomatous visual field defects particularly the mean defect of Humphrey visual field could be related to VEP parameters of patients having POAG. Visual field by Humphrey perimeter and simultaneous recordings of pattern reversal visual evoked potential (PRVEP) were assessed in 100 patients with POAG. There was a significant (P<0.05) negative correlation of P100 latency, N155 latency and P100 duration and a highly significant (P<0.001) positive correlation of P100 amplitude with mean deviation (index of global visual field damage, MD) of Humphrey visual field in the subjects of POAG in various age groups. N70 latency showed a non-significant positive correlation with MD. The VEP changes observed by us in POAG patients were consistent with the progressing mean defect quantitatively. Therefore, it can be concluded that the VEP parameters can be useful quantitative indices in the evaluation of glaucomatous visual function damage.

Key words: pattern reversal mean defect visual field
P100 latency P100 amplitude

INTRODUCTION

Glaucoma is a progressive irreversible optic neuropathy characterized by a specific pattern of optic nerve head and visual field damage due to the death of retinal ganglion...
cells. Primary open angle glaucoma (POAG), one of the most prevalent type of glaucoma in India, is a disorder characterised by open iridocorneal angles and progressive optic disk cupping with resultant irreversible loss of vision. The past few years have seen an increasing interest in electrophysiological testing in glaucoma because it is well accepted that significant ganglion cell damage can occur before functional deficits are detected with static automated achromatic perimetry, the “gold standard” for detecting and monitoring glaucomatous damage.

The recording of visual evoked potentials (VEPs) has been an important means of obtaining reproducible, quantitative data on the function of the anterior visual pathways (1). VEPs are visually evoked electrophysiological signals extracted from the electro-encephalographic activity in the visual cortex recorded from the overlying scalp (2).

Pattern reversal visual evoked potential (PRVEP) is known to be an objective method for checking the visual function and has been shown to be sensitive to glaucomatous neuropathy. PRVEP is generated in the cortical and sub-cortical visual areas when the retina is stimulated with patterned light.

When assessing a patient with glaucoma, it is essential to estimate the amount of glaucomatous damage to set appropriate treatment targets. The relationship between functional and anatomical measurements in POAG is of fundamental importance to our ability to infer the extent of glaucomatous damage and to estimate rates of disease progression from such measurements. It is important to understand how field loss and ganglion cell loss are related to each other to identify correctly the stage of disease. Similarly, when assessing the rate of glaucomatous progression, it is important to know whether the relationship between the amount of ganglion cell loss and the measurement of visual function is linear. Thus the present study was conducted to study the association of changes in VEP parameters in patients of primary open angle glaucoma with the mean defect of their Humphrey visual field.

METHODS

This study was conducted in the Neurophysiology unit of the Department of Physiology, Mahatma Gandhi Institute of Medical Sciences, Sevagram. The study population consisted of 100 patients diagnosed as having primary open angle glaucoma by the ophthalmologist at the Glaucoma Clinic of Department of Ophthalmology in a tertiary care rural hospital after proper screening as per inclusion and exclusion criteria. Both the eyes of the subjects were included in the study. Thus, Pattern Reversal VEP recordings from 200 eyes in total were obtained for the present study. POAG patient group included 54 males and 46 females in the age range of 40-79 years. The mean age of POAG patients was 57.94±11.14 years. Each subject gave informed consent to participate in this study.

Detailed systemic and thorough ophthalmological examination was carried out for all the subjects. All the subjects' visual fields were assessed by the static perimeter Humphrey visual field analyzer II; using SITA Standard protocol with stimulus
size III, white object, (30-2 central WITH Fovea-ON). The main index of the Humphrey perimetry is the Mean deviation (MD). MD represents an index of severity of global damage. It is a measure of overall field loss (2).

Grading of glaucomatous damage (Anderson's Criteria)

The glaucomatous eyes were graded as below based on Humphrey perimetry visual field defects:

a) Early glaucoma group with mild glaucomatous damage (Grade 1): having MD < –6 dB

b) Moderate glaucoma group with moderate glaucomatous damage (Grade 2) : having MD from –6 dB to –12 dB

c) Late or Advanced glaucoma group with severe glaucomatous damage (Grade 3): having MD > –12 dB.

Methodology for VEP

VEP recordings were done in accordance to the standardized methodology of International Federation of Clinical Neurophysiology (IFCN) Committee Recommendations (3) and International Society for Clinical Electrophysiology of Vision (ISCEV) Guidelines (4) and montages were kept as per 10-20 International System of EEG Electrode placements. The stimulus configuration in the present study consisted of the transient pattern reversal method in which a black and white checker board (8x8 pattern) was generated (full field) and displayed on a VEP Monitor (colour 14") by an Evoked Potential Recorder (RMS EMG EP MARK II) (Fig. 1). A fixation point (red square) was positioned at the center of the field. The rate of pattern reversal was 1 Hz. The recording sensitivity was 2 µV and the electrode impedance was below 5 KΩ. The analysis time (sweep duration) was maintained at 300 ms. Responses to 200 stimuli were amplified and averaged for each eye and two trials for each eye were obtained. The pattern stimulus luminance was 59 cd/sqm and the contrast between black and white squares was kept as 80%. The signals recorded were filtered by low cut and high cut frequency filter through a band spread of 2-100 Hz. Each subject was seated comfortably at a distance of 1 meter away from the screen of the VEP monitor.

The PRVEP waveform consisted of the initial negative peak (N70) followed by a large positive peak (P100) and followed by another negative peak (N155) (Fig. 2).

Statistical analysis

The correlation of all electrophysiological parameters with mean deviation (MD) of Humphrey visual field was evaluated by Pearson’s correlation co-efficient (r).

RESULTS

The data in the Table I represents the agewise distribution of MD values of both the eyes of POAG patients. It clearly depicts that maximum proportion of the POAG population 118 (59%) out of 200 eyes had mild glaucomatous defect. Moderate glaucomatous defect was found in 47 (23.5%) eyes and severe glaucomatous defect was observed in 35 (17.5%) eyes.
moderate defects was seen in the eldest age group followed by 25% in 60-69 years and 20% in 50-59 years. Again the least number of eyes (16.67%) fell in the youngest age group. Regarding the mild glaucomatous defect, this category included maximum eyes (70.37%) from 40-49 years and 50-59 years (65%) followed by 60-69 years (50%) and 70-79 year groups (45.65%) respectively. To summarise, as the age increased from 40-79 years, there is a decrease in proportion of eyes having mild glaucomatous defects whereas an increase in proportion of eyes having moderate and severe glaucomatous defects is observed. Figure 1 illustrates the total proportion (sum of right and left eyes) showing abnormally prolonged P100 latency.

The table also indicates that majority (25%) of the severe defects were in ages 60-69 years followed by 19.56% in 70-79 years and 15% in 50-59 years. The least number of eyes (12.96%) with severe defects fell in the youngest age group i.e. 40-49 years. Likewise, major proportion (34.78%) of moderate defects was seen in the eldest age group followed by 25% in 60-69 years and 20% in 50-59 years. Again the least number of eyes (16.67%) fell in the youngest age group. Regarding the mild glaucomatous defect, this category included maximum eyes (70.37%) from 40-49 years and 50-59 years (65%) followed by 60-69 years (50%) and 70-79 year groups (45.65%) respectively. To summarise, as the age increased from 40-79 years, there is a decrease in proportion of eyes having mild glaucomatous defects whereas an increase in proportion of eyes having moderate and severe glaucomatous defects is observed. Figure 1 illustrates the total proportion (sum of right and left eyes) showing abnormally prolonged P100 latency.
(using the 95\textsuperscript{th} percentile of the normative data as a definition of abnormal) in each of the age groups with respect to the three grades of glaucomatous visual field defects as per the Anderson’s criteria. It can be deduced from the Figure 1 that maximum number of eyes in each age group had mild defects. Further as we proceed from younger to older age groups there is progressive increase in proportion of abnormality in P100 latency (from 2 in 40-49 years it rises to 16 in 70-79 years). With the exception of 50-59 years, highest proportions of eyes with abnormal latency are observed under severe (grade 3 of) glaucomatous defect. In 50-59 year group, highest proportion of eyes with abnormal latency is observed under grade 2 of glaucomatous defect [4 out of 7 (57.14\%)]).

Table II depicts the correlation of mean of MD of the 200 eyes with their mean VEP parameters in the glaucoma group. The
Fig. 3: PRVEP Waveform of a 69 Years Male POAG patient showing.
- Prolonged P100 latency, markedly prolonged N70 latency and
- markedly reduced P100 amplitude in both eyes.

Humphrey Visual Field chart of Left Eye Showing severe field defect with Superior Arcuate Scotoma and Right Eye Visual Field Showing Moderate Glaucomatous Defect.
mean P100 latency, N155 latency and P100 duration have shown a significant negative correlation with mean MD and the mean P100 amplitude has depicted a highly significant positive correlation with mean MD of the POAG group.

Figure 2 illustrates the relationships between visual field loss as determined by the Mean Defect (MD) and the VEP parameters. The VEP parameters (on Y axis) are plotted as a function of MD (on X axis). The solid lines show the best linear correlation for the patients’ eyes. There was a rather trivial relationship between N70 Latency and MD, a good significant negative correlation of P100 latency and MD and a significant but not a very strong relationship of N155 latency and P100 duration. The most striking conclusion from the data in the above table and Figure 2 was a highly significant positive correlation of P100 amplitude with MD values.

**DISCUSSION**

The nature of the relationship between glaucomatous visual field loss and visual evoked responses in glaucoma is poorly understood. There have been various attempts in the past to obtain an electrophysiological measure of perimetric defects. Increased pattern VEP latency has been associated in previous studies with optic disc cupping (5) and the presence of visual field loss (6, 7, 8).

The visual field impairment in our POAG patients shown by reduced MD was significantly correlated with the abnormal cortical electrophysiological responses. This is in accordance with previous concept that a diminution of the sensitivity of the visual field caused by damage to nerve structures in the visual pathway as occurs in glaucoma may lead to changes in the visual evoked potentials such as a decrease in amplitude and/or increase in latency (9). Our finding of significant correlation between the values of MD and those of VEP parameters is consistent with the results reported in earlier studies in which abnormal VEP responses were related to visual field defects assessed by Goldmann perimetry (6, 10, 11, 12, 13) or by static perimetry (12, 13).

Our results are also in close agreement with Mokbel TH and Ghanem AA (14) who have reported that the MD values in their POAG patients were negatively correlated with the latency time of P100, which also corroborates the findings of Parisi V (15) and Parisi V et al (16). The mean MD value in our POAG group was −7.47±6.46 dB which closely resembles −7.41±5.35 dB that of Mokbel TH and Ghanem AA (14). However our results do not agree with those of Grippo TM et al (17) who observed that there was no clear relationship between the latency of the conventional VEP and the MD of the Humphrey Visual Field.

Because VEP latency and duration increases were associated with more severe
field defects, we construe that increased VEP delay as we have observed here is a manifestation of optic nerve damage. This observation is in accord with the significant retardation in blue on yellow VEP peak times with increase of glaucomatous defects showed by Horn FK et al (18).

On the other hand there was a corresponding drop in amplitude with the disease progression as indicated by a strong positive correlation between severe field defects and P100 amplitude in both the eyes of POAG patients. This decrement in mean P100 amplitude was observed when proceeding from mild to severe defects. In all when abnormally reduced P100 amplitude was correlated with field defects it was observed that maximum (60%) abnormalities were associated with severe field defects and 40% eyes with abnormally reduced had moderate field defects. This observation supports the contention that VEP is potentially helpful in monitoring the advancement of the disease. It is in accordance with reports of Galloway NR and Barber C (10) who indicated that the degree of visual field loss was related to the amplitude of VEP.

Our data analysis also illustrated that the mean P100 amplitude had a highly significant (P<0.001) positive correlation with mean MD of the POAG group. These results also correspond with Mokbel TH and Ghanem AA (14) who have reported that the MD values in their POAG patients were positively correlated with the amplitude of P100 (r=0.203). Our correlation co-efficient (r) between P100 amplitude and MD was 0.394. Our results also concur with the findings of Parisi V et al (16) who have shown highly significant positive correlation (P<0.001) between P100 amplitude and Humphrey Field Analyzer 24/2 MD.

Conclusion

The reduced MD observed in our POAG patients was significantly correlated with the abnormal cortical electrophysiological responses. This correlation between all the electrophysiological VEP parameters and MD of Humphrey static perimetry suggests that the impaired visual cortical responses observed in glaucoma patients can be revealed by both electrophysiological and psychophysical methods. In addition, the severity of global glaucomatous damage evidenced by reduction in MD could depend on the delay in neural conduction from retina to the visual cortex as revealed by the significant correlation between VEP latencies and MD. Further, in an attempt to procure an electrophysiological measure of perimetric defect, we found in the present study the incidence of VEP abnormality to be more in those POAG patients with “severe” and “moderate” field defects.

REFERENCES

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