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VISUAL EVOKED POTENTIALS IN MALE PATIENTS OF PRIMARY OPEN ANGLE GLAUCOMA AND AGE MATCHED CONTROL MALES

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ABSTRACT

The aim of the study was to compare the latency and amplitude of P100 component of pattern reversal visual evoked potential (PRVEP) in a cohort of male patients having primary open angle glaucoma with those of age matched controls. This comparative case- control study was conducted in the Neurophysiology unit of the Department of Physiology of a rural Medical college of Central India. The study comprised of PRVEP recordings from 356 eyes (108 POAG eyes and 248 control eyes) which were performed with the stimulus configuration consisting of the transient pattern reversal method using an Evoked Potential Recorder (RMS EMG EP MARK II). Agewise comparison of VEP component in our study subjects revealed that the mean P100 latency of POAG patients was significantly ($p<0.05$) longer than the mean P100 latency of the controls in all the age groups (from 40-79 years). The mean amplitude of P100 in POAG patients was significantly ($p<0.05$) diminished compared to that of controls.

INTRODUCTION

Pattern reversal visual evoked potential (PRVEP) is an objective method known to be sensitive to glaucomatous neuropathy. It is a rapid and non invasive technique, avoiding the unknown risks of pressure elevation inherent in a provocative technique. The procedure requires no subjective responses from the subject, which can be a problem with some older or debilitated patients. P100, a major positive wave, the hallmark of full field VEPs, is the most consistent and least variable peak and maximal at mid-occipital electrode [1].

Numerous factors affecting the VEP waveform include the age, gender, height and head circumference of the subject. Shorter latency and larger amplitude of VEPs have been described in females as compared to males in some previous studies [2,3,4,5,6]. Longer P100 latency in adult males has been attributed to larger head size and lower core body temperature in males [7]. It has also been indicated that brain volume may be the relevant variable underlying the sex differences as brain volume of males is on an average 10% greater than in females [8]. Whether these changes are related to the smaller anatomic size of head of females or to hormonal factors were not clear. Also the differences observed between the two sexes were not significant in many of the earlier studies [2].

Further it is observed that there is not much data available in literature regarding changes in the visual evoked responses with all these parameters especially in visual disorders like glaucoma. Therefore a preliminary attempt was made by us to study the alterations of VEP components in a cohort of male glaucoma patients and to compare them with age matched controls.

EXPERIMENT WORK

The study was conducted in the Neurophysiology unit of the Department of Physiology of MGIMS, Sevagram. The study population consisted of 54 male patients diagnosed as having primary open angle glaucoma by the ophthalmologist at the Glaucoma Clinic of Department of Ophthalmology in Kasturba hospital, Sevagram and 124 healthy male volunteers comprised the age matched controls after proper screening as per inclusion and exclusion criteria. Both the eyes of two groups of the subjects each were included in the study. Thus, Pattern Reversal VEP recordings from 356 eyes (108 POAG eyes and 248 control eyes) in total were obtained for the present study.

Settings & Design: Tertiary care rural hospital based case control study

Sample characteristics

POAG patient group and the control group were recruited in the age range of 40-79 years. The mean age for POAG males was 60.44 ± 11.15 years and the mean age of control males was 57.17 ± 10.92 years. Statistical analysis of the mean age showed the paired difference between the glaucoma and control groups to be insignificant for all age groups. The p value was found not to be significant

statistically (p=0.63, p>0.05). Hence the normal population and the glaucoma subjects were statistically age matched.

The glaucoma group and control population was divided into 4 categories as-

Group I consisting of subjects in the age range of 40-49 years
Group II including subjects in the age range of 50-59 years
Group III comprising of subjects in the age range of 60-69 years
Group IV consisting of subjects in the age range of 70-79 years
Each subject gave informed consent to participate in this study.

Prior **Ethics approval** from the Institutional Ethics committee was obtained for the study.

A single expert ophthalmologist conducted a complete ophthalmic examination of each subject which included Visual acuity, Anterior Segment Examination, Posterior segment examination (Fundoscopy), Intra-ocular Pressure by Non-contact tonometry and Automated Perimetry.

VEP recordings were done in accordance to the standardized methodology of International Federation of Clinical Neurophysiology (IFCN) Committee Recommendations [9] and International Society for Clinical Electrophysiology of Vision (ISCEV) Guidelines [10] and montages were kept as per 10-20 International System of EEG Electrode placements [11].

The stimulus configuration was transient pattern reversal method in which a black and white checker board was generated (full field) on a VEP Monitor by an Evoked Potential Recorder (RMS EMG EP MARK II). Each subject was seated comfortably at a distance of 1 meter away from the screen of the VEP monitor. A fixation point (red square) was positioned at a corner of four checks which were located at the center of the field. The rate of pattern reversal was 1 Hz. The recording sensitivity was kept at 2μV. The electrode impedance was kept below 5KΩ. The 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 was 80%. The signals recorded were filtered by low cut and high cut frequency filter through a band spread of 2-100 Hz.

RESULTS

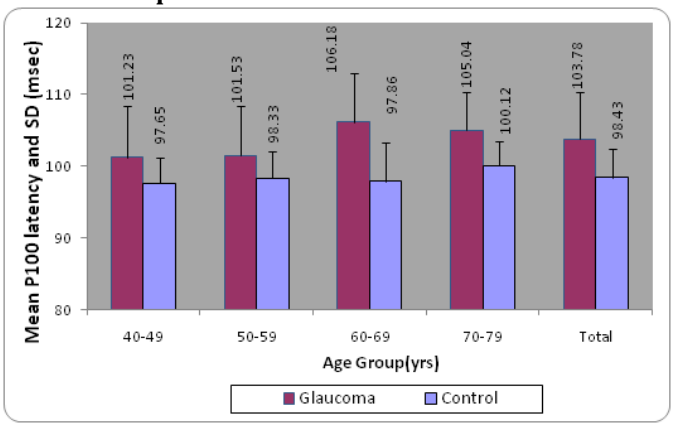
Table 1 compares the mean ± SD of P100 latency in males of glaucoma group with that of males in control group. The data elucidates that the P100 latency for males of age from 40 to 49 and 50 to 59 years in glaucoma group is significantly delayed as compared to males of same ages of control group. For the age groups 60-69 and 70-79 years, the males show prolonged latencies in comparison with the control group. The difference is statistically significant (p<0.05) in all the age groups.

Table 1. Age wise & Gender wise Comparison of P100 latency between Males of Glaucoma & Control Groups

Age Groups (years)	Mean ± SD of P100 Latency (msec)		
	Glaucoma	Control	p value
40-49	101.23±7.18 (n = 12)	97.65±3.51 (n = 35)	<0.05
50-59	101.53±6.86 (n= 14)	98.33±3.82 (n = 42)	<0.05
60-69	106.18±6.82 (n=11)	97.86±5.45 (n = 22)	<0.05
70-79	105.04±5.23 (n=17)	100.12±3.43 (n = 25)	<0.05
Total	103.78±6.54 (n=54)	98.43±4.04 (n = 124)	<0.001

Overall gender wise comparison in all the age groups as illustrated in Figure 1 shows that P100 latency of males in glaucoma group is highly significantly (p<0.001) prolonged than the control group.

Figure 1. Age wise comparison of P100 latency in males of both the Groups



The mean ± SD of the absolute latencies of the peak of positive wave P100 in each of the monocular recordings along with their inter-ocular differences that were recorded in males of the POAG patients in each group are shown in Table 2. The largest inter-ocular difference in males was found in group I.

Table 2. Age wise & Gender wise comparison of P100 latency in Both eyes of Glaucoma Group

Age Groups (Years)	Mean ± SD of P100 latency (msec)		
	RE	LE	IOD
40-49	99.60±3.22	102.86±13.90	7.71±12.13
50-59	103.48±7.80	101.58±7.19	3.98±4.98
60-69	105.98±7.67	106.38±7.02	4.13±3.40
70-79	105.50±7.16	104.59±5.64	4.84±5.72
Total	103.76±7.04	103.79±8.65	5.11±7.13

The mean ± SD of the absolute latencies of the peak of positive wave P100 in each of the monocular recordings along with their inter-ocular differences that were recorded in males among the controls in each group are shown in Table 3.

It is clear from the above table that there is negligible inter-ocular difference between the two eyes. However, the inter-eye difference of the VEP parameters in the POAG group was significantly greater than controls. The reason for this difference could be the severe glaucomatous damage in the one of the eyes having producing greater abnormality of VEP response as compared to the other which possessed mild to moderate glaucomatous changes.

In RE of control males, the maximum P100 latency was obtained was 106.90 msec. In LE, the maximum P100 latency recorded was 105.90 msec in the older ages of 70-79 years.

Table 3. Age wise & Gender wise comparison of P100 latency in Both eyes of Males of Control Group

Age Group (Years)	Mean ± SD of P100 latency (msec)		
	RE	LE	IOD
40-49	97.80±3.65	97.49±3.71	1.58±1.52
50-59	98.61±4.10	98.06±4.03	1.87±2.08
60-69	98.36±5.31	97.36±5.67	1.27±1.19
70-79	100.58±3.08	100.36±3.37	1.61±1.93
Total	98.73±4.10	98.25±4.25	1.63±1.76

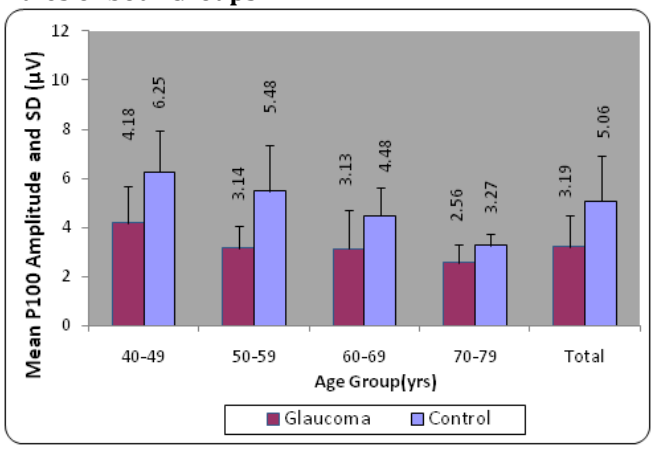
Table 4 compares the mean ± SD of P100 amplitude in males of glaucoma group with that of males in control group. The data enumerated in the above table shows that the P100 amplitude in males of ages from 40 upto 79 years in glaucoma group is significantly reduced (p<0.05) as compared to that in males of same ages of control group.

Table 4. Age wise & Gender wise Comparison of P100 amplitude between Males of Glaucoma & Control Groups

Age Groups (Years)	Mean ± SD of P100 amplitude (µ volts)		
	Glaucoma	Control	p value
40-49	4.18±1.48	6.25±1.70	<0.05
50-59	3.14±0.91	5.48±1.85	<0.001
60-69	3.13±1.59	4.48±1.12	<0.05
70-79	2.56±0.76	3.27±0.47	<0.05
Total	3.19±1.28	5.06±1.84	<0.001

Overall gender wise comparison in all the age groups as depicted in Figure 2 shows that P100 amplitude of males in glaucoma group is highly significantly (p<0.001) diminished than the control group.

Figure 2. Age wise comparison of P100 Amplitude in males of both Groups



The mean ± SD of P100 amplitude in each of the monocular recordings along with their inter-ocular differences that were recorded in males among the POAG patients in each age group are shown in Table 5. The data implies that smallest amplitude and largest inter-eye difference was found in the eldest age group i.e. in 70-79 years. The maximum value of P100 amplitude recorded for males was 6.69 µv in RE of a patient in group I.

Table 5. Age wise & Gender wise comparison of P100 amplitude in Both eyes of Males of Glaucoma Group

Age Groups (Years)	Mean ± SD of P100 Amplitude (µ volts)		
	RE	LE	IOD
40-49	4.35±1.60	4±1.62	2±0
50-59	3.37±1.23	2.92±1.01	3±0
60-69	2.81±1.49	3.45±1.81	4±0
70-79	2.59±0.89	2.54±0.82	5±0
Total	3.23±1.42	3.15±1.39	3.61±1.15

The mean ± SD of P100 amplitude in each of the monocular recordings along with their inter-ocular differences that were recorded in males among the controls in each age group are shown in Table 6. The data in the above table indicates that smallest amplitude was found in the eldest age group i.e. in 70-79 years. The maximum value of P100 amplitude recorded for males was 13.89 µv in LE of a normal subject in group II.

Table 6. Age wise & Gender wise comparison of P100 amplitude in Both eyes of Males of Control Group

Age Groups (Years)	Mean ± SD of P100 Amplitude (µ volts)		
	RE	LE	IOD
40-49	6.22±1.66	6.27±1.87	0.76±0.50
50-59	5.37±1.96	5.59±1.84	0.61±0.60
60-69	4.31±0.84	4.64±1.55	0.72±0.88
70-79	3.29±0.46	3.25±0.62	0.36±0.40
Total	5±1.84	5.13±1.94	0.62±0.61

DISCUSSION

Gender has not been quoted as a strong risk factor in most studies of POAG according to Weih [12], although men have been found to have greater risk for presence of disease or progression than women. However, reports on sex predilection differ in their view. Although some age-controlled studies have reported significantly higher mean Intra-Ocular Pressure values in women than in men, others have failed to find such a difference and some others have even shown males to have a higher prevalence of glaucoma.

Due to the prominent gender based differences in VEP latencies and amplitude reported in the literature we analyzed the data of the present study in males throughout the age span of 40-79 years. Since glaucoma is found to be more prevalent in the aging population, such separate analyses appear to provide more useful descriptions of PRVEP latency and amplitude changes across this age range which is most susceptible to POAG.

In our study when control males were compared with glaucoma males, we found that P100 latency of males in glaucoma group was prolonged than the control group. The difference was statistically significant in males of all the age groups Overall gender wise comparison in all the age groups shows that P100 latency of males in glaucoma group is highly significantly (p<0.001) prolonged than that of controls.

POAG is one such optic neuropathy in which age related morphological changes in the optic nerve head like loss of neuroretinal rim and increase in optic cup size parallel the loss of optic nerve axons as is found by histologic studies. This loss of axons possibly is reflected by the increase in latency of VEP in our POAG patients. It has been well documented by Garway Heath et al [13] that ganglion cell axon number correlates with the neuroretinal rim area.

Significant loss of lateral geniculate nucleus relay neurons terminating in the primary visual cortex occurs in the magnocellular and parvocellular layers in an experimental monkey model of glaucoma as reported by Yucel et al [14]. This further adds substance to the notion that in glaucoma, degenerative changes are occurring in the striate cortex, which is the generator site of VEP.

Substantial evidence demonstrates that loss of optic nerve fibers precede the glaucomatous field loss. For example optic disc cup enlarges before detectable field loss. This cup enlargement can be best explained by loss of nerve fibers according to Quigley et al [15]. One of the possible manifestations of this nerve fiber damage in glaucoma could be the significant reduction (p<0.001) in P100 amplitude of POAG patients.

CONCLUSION

In a nutshell, on performing the age wise case control comparison of P100, the right and left eyes of males of POAG group have shown longer P100 latencies and produced diminished amplitude than the control eyes. Our findings of latency delays and amplitude reductions in glaucoma patients support the hypothesis that the dysfunction of retinal layers may be the root cause of histological and functional changes at the dorsal lateral geniculate nucleus and this involvement could induce an impaired (delayed and/or reduced) bioelectrical activity in those cells in which the visual cortical responses have their source.

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