International Journal of Biomedical and Advance Research
ISSN: 2229-3809 (Online); 2455-0558 (Print)
Journal DOI: 10.7439/ijbar
CODEN: IJBABN

Original Research Article

Visual evoked potentials: Impact of age, gender, head size and BMI

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Abstract

Background and Objectives: Pattern-reversal visual evoked potential (PRVEP) is an objective, sensitive and non-invasive neurophysiological test that can prove to be a useful clinical tool in investigating the physiology and pathophysiology of human visual system. A successful clinical application of the test, however, is not possible without the acquisition of a normative data adjusted to known confounding physiological variables. Hence, this study attempted to obtain PRVEP values in different age-groups and gender in healthy adults and also to find out the influence of head size and body mass index on PRVEP parameters.
Methods: PRVEP was recorded in 52 healthy adults in the age-group of 18-70 years. PRVEP parameters were compared in different age-groups and gender using one way ANOVA. Head size and BMI were correlated with PRVEP parameters by Pearson correlation coefficient and the significance of difference analysed.
Results: The study demonstrated statistically significant differences in mean P100 latency among various age-groups. Gender difference revealed statistical significant differences in both the PREVP parameters (P100 latency and N75-P100 amplitude). The correlation of head size and BMI with PRVEP parameters could not be found to be statistically significant.
Conclusion: Clinical interpretation of PRVEP should be based on age and sex matched normal subjects besides standardizing the technical parameters of the laboratory. This study also suggests that endocrinal differences should be borne in mind besides the anatomical differences for gender variation in PRVEP-P100 latency.
Key message: For adequacy and accuracy of neurophysiological tests like visual evoked potentials, normal values have to be adjusted for physiological variables. Every neurophysiology laboratory should have its own normative data based on age and gender. A possibility of the role of endocrinal influences should be borne in mind for gender variation in P100 latency.
Keywords: Pattern reversal, Visual evoked potentials.

1. Introduction

Visual evoked potentials (VEPs) have emerged as an objective and non-invasive methods for investigating the visual pathways, providing important diagnostic information regarding the functional integrity of the visual system. VEPs record visually evoked electrophysiological signals extracted from the electroencephalographic activity in the visual cortex. Responses evoked by patterned stimuli constitute pattern visual evoked potentials and pattern reversal is the preferred stimulus for most clinical purposes because of its relative simplicity and reliability with less intra-individual and inter-individual variability. However, certain physiological and physical factors like age, gender, body mass index (BMI) and head size can influence the PRVEP (pattern reversal visual evoked potential) waveforms. Head size indirectly reflects the brain size and the length of the visual pathway and hence the conduction time. Hence, it is one of the variables hypothesised to influence VEPs. The construction of a normal sample for laboratory norms should include all these variables known to influence the VEPs. As the successful clinical application of evoked potentials depends, in large measure, on the availability of carefully collected and skilfully analysed normative data, hence, it is necessary to evaluate the role of these physiological factors on the visual evoked responses of normal subjects. Among these factors, the effects of age and gender have been studied more extensively in different parts of the world while those including data for effects of head size and BMI which depends on height and weight of the individuals, are sparse yet. Moreover, majority of the studies which have reported increased latencies in males as compared to females have explained the difference on the basis of anatomical differences (head size and body size).[1][2]

Hence, this study was planned to evaluate the influence of physiological variables like age and gender on the PRVEP records and also to assess the relationship of BMI and head size with the PRVEP parameters in the healthy individuals of Central India.

2. Materials and methods

It was a cross-sectional analytical study consisting of 52 healthy adults in the age-group of 18-70 years with normal visual acuity. Approval from the Institutional Ethical committee was taken to carry out the research work. A complete neuro-ophthalmologic examination of each subject was done after obtaining a written informed consent and a detailed clinical history. The height (cm) and weight (kg) of the subject were measured as a part of the general examination and body mass index calculated as weight (kg)/height (meters)^2. Head size was measured (from nasion to inion) by a measuring tape prior to VEP recording.

2.1 Inclusion criteria

Adult subjects with normal visual acuity, normal fundus and visual field examinations.

2.2 Exclusion criteria

Subjects with metabolic, endocrine or demyelinating pathologies; glaucoma, strabismus, amblyopia, optic neuropathies, inherited or acquired neurological disorders, compressive lesions of anterior visual pathways, HIV infections, history of drug-abuse and history of cerebro-vascular accidents.

2.3 Pre-test evaluation

For the best results of VEP testing, subjects were advised to come without applying oil or any hair chemical to the scalp, asked to put on their usual glasses. Subjects were instructed to have an adequate sleep the previous night to prevent the effect of drowsiness on the responses. Subjects were explained about the test to ensure full cooperation. Subjects were also instructed to avoid any mydriatic or miotic drug 12 hours before the test. Preparation of scalp skin was done before electrode application.

2.4 VEP recording

VEP was performed on RMS Polyrite-Ad in a specially equipped electro-diagnostic procedure room, made dark and sound attenuated for the test. Subjects were seated comfortably about 95 cm away from a video-monitor with a 30 cm screen. The video- monitor presented a black and white checker-board pattern with a fixation spot in the centre of the screen (mean luminance 50candela/m^2 and contrast 70%). The checks/pattern elements reversed alternately at the rate of 1.71 Hz. The visual angle subtended by the checks was 54.6 min and the screen subtended a visual angle of 19 degrees. The signals were amplified (gain 20,000), filtered with a system band pass filter of 2-200 Hz and 100 responses were averaged. Standard disc surface electrodes were placed according to the International 10/20 system of electrode placement, with active electrode at Oz, reference electrode at Fz and ground electrode at Fpz.[3] Head size measurements were taken from nasion to inion prior to the electrode placements by a measuring-tape. Volunteers were instructed to fix the gaze on a small red square at the centre of the screen of video-monitor. Monocular stimulation was done with an eye-patch covering the other eye. With the preset stimulus and recording conditions as mentioned above and keeping the electrode impedance <5 kΩ, the recording procedure was started. To verify the reproducibility of the waveform, two responses were recorded and superimposed. The replicated response measurements with P100 latency within 2.5 ms difference and N75-P100 (peak-peak) amplitude within a 15% difference was accepted.[3]

Parameters for the study were P100 latency, N75-P100 amplitude, Interocular latency-difference, N75 latency and N145 latency. All the data was expressed as mean ± S.D. The significance of difference between groups was calculated by using unpaired t-test, one way ANOVA and Tukey multiple comparison tests. Pearson's correlation coefficient was applied for obtaining relationship between influencing variables and PRVEP parameters. Statistical analysis was done by using SPSS version 14.0 (Statistical package for social science) and Grafpad (Prism 4) statistical softwares. The analysis was done at 5 % level of significance.

3. Results

This study comprised of 52 healthy adults in the age-group of 18-70 years. The subjects were distributed into four groups according to their age: <20 years, 21-40 years 41-60 years and >60 years. Mean P100 latency varied in the age groups with a statistically significant difference (one way ANOVA). The difference was significant between group 2 with 21-40 years and group 4 with > 60 years of subjects and also between group 3 (41- 60 years) and group 4 (> 60years) but the variations in mean N75-P100 amplitudes and mean inter-ocular latency differences were not found to be statistically significant (Table 1).

In a gender comparison, mean PRVEP parameters revealed a greater mean P100 latency in males and greater mean N75-P100 amplitude in females with statistically significant difference (unpaired t test). Other PRVEP parameters like N75 latency and N145 latency varied in males and females without statistically significant difference (Table 2).

The correlation of head size of the subjects with their PRVEP parameters (mean P100 latency, mean N75-P100 amplitude, mean N75 latency and mean N145 latency) was not found to be statistically significant (Pearson's correlation coefficient) (Table 3). A similar finding was obtained when BMI was correlated with the PRVEP parameters with p=0.066 (for P100 latency). Correlation with other VEP parameters revealed statistical insignificance too (Table 3). For gender variations, when mean P100 latencies were compared in males and females with comparable age and head sizes, the difference still revealed a statistical significance (Table 4).

Table 1: Mean P100 latencies, mean N75-P100 amplitude and mean inter-ocular latency difference in different age-groups of the subjects

Age-group	No. of subjects	Mean P100 latency (ms±SD)			Mean N75-P100 amplitude (µv±SD)			Mean interocular latency Difference (ms±SD)
		Right eye	Left eye	Mean of both the eyes	Right eye	Left eye	Mean of both the eyes	
<20 years	3	98.33±0.97	98.76±1.85	98.55±1.40	6.73±1.32	5.08±2.77	5.90 ± 2.02	0.83±0.32
21-40 years	17	97.88±1.09	97.73±1.12	97.81±0 .98	6.25±1.85	6.32±1.65	6.29± 1.69	0.67±0.79
41-60 years	27	98.24±0.74	98.15±0.92	98.19± 0.75	7.37±2.28	7.08±2.20	7.23± 2.16	0.55± 0.63
>60 years	5	99.28±0.26	99.64±1.44	99.46 ±0.77	6.07±2.13	6.74±1.70	6.40± 1.90	0.88±1.05
Total	52	98.23± 0.92	98.19±1.19	98.21± 0.96	6.84±2.11	6.69±2.03	6.77±1.99	0.64 ±0.71

Mean P100 latency in the controls varied in the age groups with a statistically significant difference with P=0.006 (p<0.05) (One way ANOVA). The difference was significant between the group 2 with 21-40 years and group 4 with >60 years of subjects (Tukey multiple comparison test) and also between group 3 (41-60 years) and group 4 (>60 years) (P<0.05). The variations in mean N75-P100 amplitudes and mean interocular latency differences among the different age-groups were not found to be significant statistically, P=0.378 (P> 0.05) (one way ANOVA).

Table 2: **PRVEP parameters compared in males and females**

Sex	No. of subjects	Mean P100 latency (ms±SD)	Mean N75-P100 amplitude (µv±SD)	Mean N75 latency (ms±SD)	Mean N145 latency (ms±SD)
Male	31	98.84± 0.86	6.64±1.68	65.04± 5.29	136.6± 6.3
Female	21	98.21± 1.38	7.9 ±1.54	63.54± 5.54	133.0± 5.8
Total	52	98.58± 1.13	7.27±1.6	64.29± 5.42	134.8± 6.03

Mean P100 latency was greater in the males and mean N75-P100 amplitude was found to be greater in the females with statistically significant difference (0.048, p<0.05 and 0.0074, p<0.05 respectively by (unpaired t-test). Mean N75 latency and mean N145 latency varied without statistical significance.

Table 3: Correlation of head size and BMI with PRVEP parameters

Mean Head size (cms± SD)	Parameters	r*	P value
	Mean P100 latency	0.1432	0.311
	Mean N75-P100 amplitude	-0.119	0.40
	Mean N75 latency	0.169	0.23
34.89±1.24	Mean N145 latency	0.073	0.6
Mean BMI (kg/meters^2 ± SD)	Mean P100 latency	0.257	0.066
22±2.45	Mean N75-P100 amplitude	-0.173	0.22
	Mean N75 latency	-0.122	0.39
	Mean N145 latency	-0.164	0.24

*Pearson's correlation coefficient

Correlation between head size and BMI with PRVEP parameters was not found to be statistically significant (at 0.05 level).

Table 4: Comparison of mean P100 latency in males and females with comparable age and head size

	Age (years)	Head size (cms)	Mean P100 latency
Males (n=20)	35.3±5.22	34.68±1.32	98.9± 0.8
Females (n=18)	35.1±5.45	34.68±1.32	98.2± 1.26

Mean P100 latency difference in males and females is statistically significant (p=0.046) by unpaired t test.

4. Discussion

Visual evoked potentials can be a useful clinical tool in the diagnosis and documentation of visual impairment in various neurological disorders. But, like any other neurophysiological test, close attention to the technical details, acquisition of reproducible and reliable waveforms and proper interpretations based on availability of a carefully collected laboratory control values are essential for optimal utilization of this technique. Hence, apart from standardizing the technical parameters, normal values have to be adjusted for various confounding physiological factors.

In the present study, when mean P100 latencies were assessed among the various age groups, a statistically significant difference was found in the various age groups (p<0.05) (Table 1). Our findings comply with similar studies in the past.[2,4-6] Stockard et al, 1979, have reported in their study that age has been found to influence the latency of P100 at a rate of 2.5 ms per decade after fifth decade.[2] Mitchell et al, 1987 elicited VEP in 68 normal subjects (31 males, 37 females) in the age range 40-80 years. VEP latency showed a significant age effect, increasing values with age was demonstrated.[4] Age-related changes in P100 latencies can be attributed to the decline in the visual functions with aging.[1,6-8]

Mean N75-P100 amplitudes were not found to be statistically significant (p>0.05), when assessed in the different age groups (table 1). The mean amplitude for the right eye was 6.84µv±2.11 SD and for the left eye was 6.69 µv±2.03 SD, with the mean value of 6.77±1.99 S.D. The variation in the amplitudes with the age has been studied by many researchers in the past. But, the data for amplitude variation in different age-groups is conflicting, with some studies depicting a decrease in the amplitude with age while some suggested that in the adult life the amplitude remained reasonably stable while in the first decade of life the mean amplitude was almost double of the adult value.[6,9]

The present study could not find any significant variation in the amplitudes among the various age-groups. The mean interocular latency difference (0.64 ms±0.71) was another PRVEP parameter tested among the various age-groups but no statistically significant variation was found (Table 1).

Gender variation in PRVEP parameters was evident in all the parameters tested with statistically significant increase in mean P100 latency in males and statistically significant increase of mean N75-P100 amplitude in females. N75 latency and N145 latency varied, but without statistically significant difference. The studies in the past have reported that the Pl00 latency is longer in adult males as compared with the females.[8,10-12] The difference has been attributed to larger head size and lower core body temperature in males.[11-14] It was hypothesized that head size would indirectly reflect brain size and the length of the visual pathway and hence the conduction time. Hence, we measured the skull size (nasion to inion), correlated with PRVEP parameters to verify its impact on the differences in the results. But, head size was not found to be significantly correlated with P100 latency. Also, the gender difference in mean P100 latency was statistically significant in comparable age and head sizes too (Table 3 and 4). This can be explained by the fact that many neuro-endocrinological factors including gonadal steroids may also be relevant and fluctuation of the VEP latency in females could be related to the hormonal levels.[15,16] It has been suggested that estrogen facilitates synaptic conduction along the optic pathways.[16] Hence, the faster visual conduction time observed in females during the ovulatory and pre-ovulatory phase can be attributable to the high concentration of estrogen during that period.[15-17]

Another gender variation was exhibited by a statistically significantly greater mean N75-P100 amplitude in females as compared to males (table 2).[6,14] The amplitude increase in females as compared to males has been attributed to the hormonal differences.[18] No influence of anthropometric differences has been suggested to play role in the same.[19] Amplitude change has been found to persist even after head and body size adjustments.[20]

5. Conclusion

Age and gender constitute important physiological variables in establishing a laboratory's normative data for PRVEP and clinical interpretation of PRVEP should be based on age and sex matched normal subjects besides standardizing the technical parameters of the laboratory. The present study also suggests that for gender variation in PRVEP-P100 latency, endocrinal factors should be borne in mind besides the anatomical differences.

References

[1] Celesia GG, Kaufman D, Cone S. Effect of age and sex on pattern electroretinograms and visual evoked potentials. *Electroencephalography and Clinical Neurophysiology*, May1987; 68(3):161-171.

[2] Stockard JJ, Hughes JR, SharVough FW. Visually evoked potentials to electronic pattern reversal: latency variations with gender, age and technical factors. *Am J EEG Technol*, 1979; 19(4):171-204.

[3] American Clinical Neurophysiology society Guideline 9 B: Guidelines on Visual evoked potentials. *J Clin Neurophysiol*. 2006; 23(2):138-56.

[4] Mitchell K W, Howe J W and Spencer S R. Visual evoked potentials in the older population: age and gender effects. *Clin. Phys. Physiol. Meas*., 1987; 8(4): 317.

[5] Tobimatsu S, Kurita-Tashima S, Nakayama-Hiromatsu M, Akazawa K, Kato M. Age- related changes in pattern visual evoked potentials: differential effects of luminance, contrast and check size. *Electroencephalogr Clin Neurophysiol.* 1993 Jan-Feb; 88(1):12-9.

[6] Allison T, Hume AL, Wood CC, Goff WR. Developmental and aging changes in somatosensory, auditory and visual evoked potentials. *Electroencephalogr Clin Neurophysiol*. 1984 Jul; 58(1):14-24.

[7] Onofrj M, Thomas A, Iacono D, D'Andreamatteo G, Paci C. Age-related changes of evoked potentials. *Clin Neurophysiol* 2001; 31:83-103.

[8] Emmerson-Hanover R, Shearer DE, Creel DJ, Dustman RE. Pattern reversal evoked potentials: Gender differences and age-related changes in amplitude and latency. *Electroencephalogr Clin Neurophysiol* 1994; 92:93-101.

[9] Shaw NA, Cant BR: Age dependent changes in the amplitude of pattern evoked visual potentials. *Electroencephatogr Clin Neurophysiol*. 1981; 51: 671.

[10] Fenwick PB, Brown D, Hennesey. The visual evoked response to pattern reversal in normal 6-11 year old children. *Electroencephalogr Ciin Neuro Physiol* 1981; 51:49 -6.

[11] Malcolm CA, MCCulloch DL, Shepherd AJ: Pattern-reversal visual evoked potentials in infants: gender differences during early visual maturation. *Dev Med Child Neurol* 2002; 44: 345-351.

[12] Gregori B, Pro S, Bombelli F, La Riccia M, Accornero N Vep latency: sex and head size. *Clin Neurophysiol* 2006; 117:1154-1157.

[13] Guthkelch AN, Bursick D, Sclabassi RJ: The relationship of the latency of the visual P100 wave to gender and

head size. *Electroencephalogr Clin Neurophysiol* 1987; 68: 219-222.

[14] Kaneda Y, Nakayama H, Kagawa K, Furuta N, Ikuta T: Sex differences in visual evoked potential and electroencephalogram of healthy adults. *Tokushima J Exp Med* 1996; 43:143-157.

[15] Shushtarian, S. M., & Yahyavi, S. H. Study of visual evoked potentials during normal monthly cycle in normal female subjects. *Biomedical Sciences Instrumentation* 1999; 35:165–167.

[16] Yilmaz, H., Erkin, E. F., Mavioglu, H., & Sungurtekin, U. Changes in pattern reversal evoked potentials during menstrual cycle. *International Ophthalmology* 1998; 22: 27–30.

[17] Gupta S, Singh S, Gupta G, Ovais. Variations in pattern reversal visual evoked potentials during menstrual cycle in healthy females. *Current Trends in Biotechnology and Chemical Research* 2013; 3(1):45-49.

[18] Celesia GG, Kauufman D, Cone S. Simultaneous recording of pattern electroretinography and visual evoked potentials. *Electroencephalogr Clin Neurophysiol*, 1987; 68:161.

[19] George Fein, Fiona F. Brown. Gender differences in pattern reversal evoked potentials in normal elderly *Psychophysiology*, 1987; 24(6): 683-690.

[20] Cynthia L. Darlington. Functional differences. In: The female brain, Dec 2010, 2nd edition (CRC press): 59-89.