Original Article

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Visual Evoked Potentials: Normative Values and Gender Differences

Physiology Section

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ABSTRACT

Introduction: Visual evoked potentials (VEP) are used to assess the visual pathways through the optic nerves and brain. A normal VEP response to a pattern-reversal stimulus is a positive mid occipital peak that occurs at a mean latency of 100 ms. VEP may be affected by variety of physiological factors including age, sex, visual acuity and pupillary size.

Aims and Objectives: The present study was performed on healthy medical students to determine the normative values and to investigate the effect of sex and anthropometric parameters on visual evoked potentials.

Materials and Methods: The study was conducted on 100 healthy medical students of Government Medical College, Patiala in the age group of 17-20 years, in which there were 50 males and 50 females. The anthropometric parameters including age, height, weight, BMI, BSA and Head circumference were recorded in all the subjects. VEP was recorded with a PC based, 2 channel, RMS EMG EP mark II machine and standard silver-silver chloride disc electrodes. A VEP monitor displaying checker board was used to give the pattern reversal stimulus. The VEP parameters recorded were latencies to N70, P100 and N155 waves, and peak to peak amplitude of P100 wave.

Results: Our results showed that the latencies of N70, P100 and N155 waves were significantly longer in males as compared to females. The amplitude of P100 wave was higher in females in both left and right eye as compared to males. No significant correlation was found between VEP parameters and head circumference in both male and female subjects in our study.

Conclusion: Gender is an important variable affecting the VEP. The exact reason of gender difference is not clear, but it may be related to anatomical or endocrinal differences in the two sexes.

Keywords: Amplitude, P100 Latency, Pattern Reversal, Visual Pathway

INTRODUCTION

Evoked potentials are noninvasive studies that measure the electrophysiological response of the nervous system to different sensory stimuli including brainstem auditory evoked potentials (BAEP), visual evoked potentials (VEP), short-latency somatosensory evoked potentials (SSEP) [1]. Visual evoked potentials (VEP) are used to assess the visual conduction pathways through the optic nerves and brain. To measure VEP, visual fields are stimulated, usually with a checkerboard visual stimulus, and the evoked response is recorded using surface recording electrodes over the occipital lobe. A unilateral defect in the visual pathway may be missed if both eyes are stimulated simultaneously; therefore, monocular stimulation is usually recommended except for special circumstances like in infants [2]. Three standard stimulus protocols are defined for recording VEP [3]: (a) Pattern-reversal VEP, (b) Pattern onset/offset VEP and (c) Flash VEP. The pattern reversal VEP is the preferred stimulus for most purposes because it has relatively low variability of waveform and peak latency both within a subject and over the normal population [4]. A normal VEP response to a pattern-reversal stimulus is a positive peak that occurs at a mean latency of 100 ms. There are three separate phases in the VEP waveform: an initial negative deflection (N70), a prominent positive deflection (P100), and a later negative deflection (N155). The peak latency and peak to peak amplitudes of these waves are measured [5].

VEP may be affected by variety of physiological factors including age, sex, visual acuity and pupillary size. It may also be affected by measures related to technique including check size, luminance, field size, etc [6]. Gender has been recognized as an important physiological factor which can affect both the amplitude and latency of pattern reversal VEP parameters. Many previous studies throughout the age span have found both larger P100 amplitudes and shorter P100 latencies in females [7].

To determine whether results of P100 latency in a given subject are normal or not, the results of VEP studies in normal subjects should be available in the laboratory. It is therefore recommended that each evoked potential laboratory preferably should have its own normative data [2]. Studies on normal subjects are required at the regional level to determine the standards for VEP parameters and the factors affecting it. Therefore, the present study was performed on healthy medical students to determine the normative values and to investigate the effect of sex and anthropometric parameters (Ht, Wt, BMI, BSA and Head size) on VEP.

MATERIALS AND METHODS

The study was conducted on 100 healthy medical students of Government Medical College, Patiala in the age group of 17-20 years, in which there were 50 males and 50 females. The study was done in 2011 after approval from the ethical committee of the institute. Total duration of study was three months (Oct to Dec 2011). Correct procedure of the test was explained to all subjects and informed written consent was taken. Subjects having a history of any disorder which could influence the interpretation of the results, like CNS disease (Multiple Sclerosis, Stroke, Meningitis, Parkinsonism, etc), Ophthalmological conditions (cataract, glaucoma, retinopathy, optic atrophy, visual acuity <6/18 even with corrective glasses) and subjects taking drugs which may affect normal functioning of central nervous system (Antidepressants, antipsychotics, sedatives, opiods etc), were excluded from the study. The anthropometric parameters including age, height, weight, BMI, BSA and Head circumference were recorded in all the subjects. Head Circumference was measured by a measuring tape over the most prominent part on the back of the head (occiput) and just above the eyebrows (supraorbital ridges). Ophthalmological examination including visual acuity with Snellen's charts and fundus examination was done to rule out any visual disorder. The subject was instructed to take a sound sleep

in the previous night and to avoid using mydriatric/meiotic drops, atleast 12 hours before the test.

VEP was recorded with a PC based, 2 channel, RMS EMG EP mark II machine and standard silver-silver chloride disc electrodes. A one channel montage was used for recording the VEP. The scalp electrodes were placed relative to bony landmarks, in proportion to the size of the head, according to the International 10/20 system [8]. The active electrode was placed at Oz which is the highest point of the occiput, lies over the visual cortex. The reference and ground electrodes were put at Fz and Cz (vertex), respectively. The recording was done in a dark room with quiet surroundings. Visual stimulation was done with a checkerboard pattern generated on the monitor using the software installed, which consisted of black and white checks whose phase was reversed (black to white and white to black) at a fixed rate of two reversals per second. The subject was seated at a fixed distance of 100 cm from the screen and was asked to fixate at the center of the screen. Monocular stimulation was given to both the eyes separately. A sweep length of 250 ms was done, and more than 100 responses were averaged. An amplification range of 20,000 to 1,00,000 was used. To ensure reproducibility, the waveform was recorded twice. The electrode impedance was kept less than 5 KΩ. The VEP parameters recorded were latencies to N70, P100 and N155 waves, and peak to peak amplitude of P100 wave.

STATISTICAL ANALYSIS

The mean and standard deviation for latencies and amplitude of VEP waves was calculated. The data was analyzed statistically by using Student's unpaired t-test to compare the results in both groups and p-values were obtained. Correlation analysis of VEP and anthropometric parameters was done by using Pearson's coefficient 'r'. The statistical analysis was carried out with SPSS PC software version 13.0.

OBSERVATIONS AND RESULTS

[Table/Fig-1] shows the comparison of anthropometric parameters between male and female subjects. There was statistically significant difference in the height, weight, Body Surface Area (BSA) and Head circumference in the two groups, with males having higher mean values than the females. The difference in Body Mass Index (BMI) between the two groups was found to be statistically non significant.

The mean latencies (in milliseconds) of waves N70, P100 and N155 and peak amplitude of P100 (in microvolts) were noted and compared in both the eyes in the two groups [Table/Fig-2,3]. In this study, the latencies of N70, P100 and N155 waves were higher in males as compared to females, and the difference between the two groups was found to be statistically significant. Also the peak amplitude of P100 wave was higher in females in both eyes as compared to males. The difference in amplitude in the two groups was found to be statistically highly significant in both left and right eye.

Correlation analysis between anthropometric parameters (Ht, Wt, BMI, BSA and Head Circumference) and VEP latencies was done using Pearson coefficient 'r' [Table/Fig-4,5]. There was significant positive correlation of N70, P100 and N155 latencies with weight, BMI and BSA in female subjects. But in male subjects, significant correlation was found only between N155 latency and height.

Parameter	Females (Mean ± SD)	Males (Mean ± SD)	p-value
Age(yrs)	18.44 ± 0.704	18.62 ± 0.753	>0.05
Height (cm)	158.68 ± 6.116	166.36 ± 6.635	<0.01
Weight(kg)	56.64 ± 8.439	65.9 ± 10.075	<0.01
BMI(kg/m^2)	22.596 ± 3.849	23.824 ± 3.499	>0.05
BSA (m^2)	1.569 ± 0.104	1.733 ± 0.135	<0.01
Head Circumference(cm)	54.6 ± 2.483	56.27 ± 2.112	<0.01

[Table/Fig-1]: Comparison of anthropometric parameters between female and male subjects

Parameter	Females (Mean ± SD)	Males (Mean ± SD)	p-value
N70 latency	62.84 ± 6.386	66.97 ± 7.622	<0.01
P100 latency	88.31 ± 8.799	93.214 ± 10.656	<0.05
N155 latency	144.864 ± 9.521	149.012 ± 10.499	<0.05
Amplitude P100	6.393 ± 0.667	5.688 ± 0.499	<0.01

[Table/Fig-2]: Comparison of VEP parameters between female and male subjects in left eye

Parameter	Females (Mean ± SD)	Males (Mean ± SD)	p-value
N70 latency	63.058 ± 6.502	66.348 ± 7.954	<0.05
P100 latency	88.788 ± 8.984	93.41 ± 10.628	<0.05
N155 latency	145.358 ± 9.677	150.478 ± 9.295	<0.01
Amplitude P100	6.373 ± 0.665	5.708 ± 0.485	<0.01

[Table/Fig-3]: Comparison of VEP parameters between female and male subjects in right eye

DISCUSSION

VEP is an important procedure for evaluating visual function and is highly sensitive to lesions of the optic nerve and anterior chiasm [2]. The activation of visual cortex primarily occurs by the central visual field. VEP may be affected if there is abnormality anywhere along the visual pathway including the eye, retina, the optic nerve, optic radiations, and occipital cortex [3].

In our study, the mean latency (in milliseconds) of P100 wave in normal female subjects was 88.31 ± 8.799 and 88.788 ± 8.984 in the left and right eye respectively. The mean latency (in milliseconds) of P100 wave in normal male subjects was 93.214 ± 10.656 and 93.41 ± 10.628 in the left and right eye respectively. In a study done by Shibasaki H and Kuroiwa Y [9], the mean peak latency of N70, P100 and N145 waves in normal subjects were 67.8 ± 4.04, 92.5 ± 4.44 and 136.0 ± 12.11 respectively. In a previous Indian study of Visual Evoked Potentials in young adults, Tandon OP and Sharma KN [10] reported P100 latency of 95.37 ± 6.85 msec for males and 91.07 ± 49 msec for females. The difference in the values in this study and in past literature may be due to the difference in the recording instruments, which differs from institute to institute, therefore there is need for each institute to have its own parameters according to the device.

Our results showed that the latencies of N70, P100 and N155 waves were significantly longer in males as compared to females. The amplitude of P100 wave was higher in females in both left and right eye as compared to males. Our results were in agreement with the results of previous studies [11-16] which showed shorter latencies and higher amplitude in females. On the contrary, some studies showed no significant gender difference in VEP latencies [17,18].

In our study, there was significant positive correlation of N70, P100 and N155 latencies with weight, BMI and BSA in female subjects. But in male subjects, significant correlation was found only between N155 latency and height. This difference in correlation in our data may be due to small sample size. Further studies with larger number of subjects are required to establish any correlation with these parameters. Importantly, no significant correlation was found between VEP parameters and head circumference in both male and female subjects.

The exact cause of this gender difference in VEP parameters is not clear but it may be related to anatomical or endocrinal differences [19]. In a study conducted by Marsh MS et al., [20] to compare the differences in the pattern VEP between pregnant and non-

Parameter	Left Eye				Right Eye			
	N70	P100	N155	Amp	N70	P100	N155	Amp
Height	0.016	-0.060	-0.016	-0.367**	0.004	-0.085	-0.015	-0.383**
Weight	0.560**	0.521**	0.485**	0.004	0.565**	0.526**	0.473**	0.019
BMI	0.505**	0.502**	0.452**	0.168	0.517**	0.518**	0.426**	0.189
BSA	0.514**	0.442**	0.434**	-0.152	0.508**	0.438**	0.436**	-0.147
HC	-0.207	-0.064	-0.226	0.000	-0.220	-0.079	-0.209	0.003

[Table/Fig-4]: Correlation coefficient 'r' between anthropometric and VEP parameters in females
**Correlation is significant at the 0.05 level (2-tailed)

Parameter	Left Eye				Right Eye			
	N70	P100	N155	Amp	N70	P100	N155	Amp
Height	0.222	0.138	0.310*	-0.052	0.181	0.120	0.319*	-0.029
Weight	-0.001	-0.058	0.045	0.205	-0.022	-0.052	0.065	0.215
BMI	-0.131	-0.151	-0.152	0.257	-0.128	-0.134	-0.133	0.253
BSA	0.089	0.016	0.168	0.131	0.056	0.014	0.188	0.148
HC	-0.011	-0.176	0.089	0.069	-0.072	-0.208	0.038	0.070

[Table/Fig-5]: Correlation coefficient 'r' between anthropometric and VEP parameters in males
* Correlation is significant at the 0.05 level (2-tailed)

pregnant women, it was observed that the mean P100 latencies for all responses were shorter in the pregnant women. The difference in blood levels of sex steroids may be the likely cause of differences in P100 latencies between pregnant and non-pregnant women. They postulated that this endocrine difference may also account for the gender difference in VEP latency. Similarly, Kaneda Y et al., [21] postulated that the sex differences in VEP may be attributed to genetically determined sex differences in neuroendocrinological systems.

Our results showed no significant correlation between head circumference and VEP parameters in males and females. This is in contrast to earlier studies which identified Head size as an important variable responsible for gender difference. Guthkelch et al., [14] attributed these gender differences to differences in the geometry of the head rather than to more general biological differences between males and females. Gregori B et al., [15] observed that the slight sex difference in P100 latencies observed in a normal sample was mainly related to the slightly smaller average head size in females than in males. Recently, Dion et al., [16] analysed the sex differences in VEP in school-age children. They observed that shorter latencies in girls appeared mostly due to head size.

Clinical Application of VEP

VEP has been shown to be a very sensitive though non-specific diagnostic tool. When properly performed, VEP can contribute important information on the visual pathways in patients with diseases like optic neuritis, multiple sclerosis, compressive lesions of optic nerve and optic chiasm, and also in neurodegenerative diseases not primarily involving the visual pathways [22]. It is more sensitive in diagnosing abnormalities in anterior visual pathway, i.e. before the optic chiasm. Significant prolongation of P100 latency, with relative preservation of amplitude is seen in demyelinating diseases like Multiple sclerosis. On the contrary, compressive or ischemic lesions often show decrease in amplitude, with relative preservation of latency. Nonspecific VEP changes are seen in degenerative disease, with small changes seen in latency and amplitude [2].

LIMITATIONS

Our study had a limitation that we could not correlate this gender difference in VEP parameters with endocrine differences. Another limitation of our study might be the smaller sample size. Further studies are warranted to look for factors causing difference in VEP in males and females.

CONCLUSION

Every neurophysiological laboratory doing VEP studies should have its normative data for future reference. There is a definite gender difference in VEP parameters with females showing shorter P100 latencies and higher amplitudes. This gender difference may be due to anatomical or endocrinal differences in the two sexes.

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