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Original Research Article

Normative values of pattern reversal visual evoked potentials in adult population of Mewat region, North India

Navneet K. Kaushik*, Abhishek K. Jaiswal, Anil Kumar

Department of Physiology, Shaheed Hasan Khan Mewati Government Medical College, Nuh, Haryana, India

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***Correspondence:**
Dr. Navneet K. Kaushik,
E-mail: navneetkk24@gmail.com

ABSTRACT

Background: Visual evoked potentials (VEPs) are a sensitive neurodiagnostic tool used to evaluate the functional integrity of visual pathways non-invasively. The present research was aimed at establishing the normative values of the VEP parameters among healthy adults in Mewat region, North India.
Methods: This cross-sectional study was conducted on 130 healthy adults, 91(70%) males and 39 (30%) females, in the age group of 18 to 60 years. Single channel recording was done using transient pattern (checkerboard) reversal stimuli (check size 13") presented at a reversal rate of 1 Hz. A total of 100 responses were recorded twice monocularly in each subject.
Results: We observed P100 latency of 103.77±5.74 msec (right eye), 102.88±5.14 msec (left eye) for males and 98.80±6.59 msec (right eye), 98.09±5.54 msec (left eye) for females. P100 latency was significantly longer in males than females ($p<0.001$). N75-P100 amplitude was 5.61±2.74 µV (right eye), 5.73±3.06 µV (left eye) in males and 5.53±2.86 µV (right eye), 5.50±3.24 µV (left eye) in females. P100 amplitude was comparable between the two sexes.
Conclusions: Gender based reference values of P100 latency and N75-P100 amplitude for the regional population were established. P100 latency was comparable to the values reported in most of the previous studies; however, reported N75-P100 amplitude was significantly lower which might be due to variation in technical factors.

Keywords: Amplitude, Latency, P100, Pattern reversal, Visual evoked potentials

INTRODUCTION

Evoked potentials (EPs) refer to electrical activity elicited in brain by sensory stimuli such as visual, auditory or tactile, measured using neurophysiological techniques such as electroencephalography. These are non-invasive neurodiagnostic tools used to assess the integrity of neural pathways.[1] EPs can provide valuable insights into the functioning of the central nervous system and help diagnose conditions like multiple sclerosis, traumatic brain injury, and other neurological disorders. These have the advantages of being objective and often more sensitive than detailed neurological examination allowing for detection of subclinical derangement of functional integrity of neural pathways.[2]

Visual evoked potentials (VEPs) represent electroencephalographic activity generated in the visual cortex in response to visual stimuli. VEP is primarily a reflection of central 3° to 6° of the visual field and depends upon functional integrity of central vision at all level of the visual pathway from eye, retina, optic nerve, optic radiations right up to the occipital cortex.[3] VEPs are a valuable non-invasive tool that can help diagnose a range of neurological and ocular conditions, monitor the progression of diseases, and guide clinical treatment decisions.[2]

VEPs have been shown to be influenced by various technical (type of stimulus, size of stimulus, contrast, luminance) and subjective factors (age, sex, size of pupil,

state of refraction, subject's attention).[4-6] Therefore, it is essential for any clinical neurophysiology lab to strictly control these parameters in order to obtain accurate, reproducible, and reliable data for VEPs in a normative study. Lack of normative data which can be used as a reference for our regional population prompted us to undertake this research to gather information regarding the normal values of latency and amplitude of VEPs in healthy adults in Mewat region, North India. Impact of gender and anthropometric measures (height, weight and body mass index) on VEP parameters was also explored and normative values were presented accordingly.

METHODS

Study design and settings

This institution-based descriptive, cross-sectional study was conducted in the Electrophysiology laboratory at a tertiary-care center (Shaheed Hasan Khan Mewati Government Medical College, Nuh) in Southern Haryana, North India over a period of one year from June 2023 to May 2024.

Inclusion and exclusion criteria

Healthy subjects of either sex within the age group of 18 to 60 years were considered for inclusion in the study. Exclusion criteria included the following: Presence of ophthalmological conditions such as cataract, glaucoma, retinopathy, any other ocular or systemic disease (such as multiple sclerosis) known to affect visual pathways, visual acuity (with or without corrective lenses) worse than 6/60, history of major illnesses like diabetes, hypertension, chronic kidney disease etc., history of routine alcohol consumption, chronic smokers.

A total of 130 subjects were enrolled following consecutive (convenient) sampling approach. They were explained the purpose of the study and nature of assessment following which informed written consent was obtained. Study protocol was ratified by the institutional ethics committee.

VEP examination

VEP examination was conducted using SCORPIO® 4.0 NCS EMG EP system (Allengers Global Healthcare private limited, Punjab, India) with checkerboard stimulus displayed on 19-inch Lenova® LED monitor. Subjects were instructed to have a sound sleep in the previous night and to avoid any mydriatic/miotic eye drops, atleast 12 hours before the test. VEP examination was conducted monocularly with the occlusion of non-tested eye using an opaque eye patch. Pattern stimulus (checkerboard), with a red colored rectangle at the center acting as fixation point, was displayed on the monitor. Distance between subject and monitor was 1 meter (full field size ~ 13°). Following settings were used: band pass 1-100 Hz, Check size-13", reversal rate-2/s (1Hz), analysis time-300 milliseconds, sensitivity -2 µV/division. Luminance and contrast levels were customized by the manufacturer. A total of 100 responses were recorded twice to ensure reproducibility. Disc type silver-silver chloride electrodes placed as per the 10-20 international system were used to pick up the evoked activity from the scalp. Single channel recording was done with active electrode on the occiput in the midline few centimeters above inion (Oz), reference electrode at Fz (30% of nasion-inion distance) and ground electrode on vertex (Cz). Skin to electrode impedance was kept below 5 KOhms. Pattern reversal visual evoked potential (PRVEP) response comprises of three deflections designated as N75, P100 and N145. Peak latencies and peak-to-peak amplitude were measured. Only the most reliable parameters indicative of clinically significant alterations in visual pathways i.e. P100 latency and N75-P100 amplitude were included in the analysis.

Statistical analysis

Data were compiled and analyzed using Statistical Package for Social Sciences (SPSS) version 20.0 (SPSS Inc., Chicago, IL, USA). Datasets were assessed for normality distribution using Shapiro-Wilk test. Since most of the study variables exhibited non-Gaussian distribution, therefore descriptive statistics for them were presented using median and interquartile range. Interocular comparisons of the primary outcome variables (P100 latency and amplitude) were done using Wilcoxon signed rank test. Gender differences in mean P100 latency and amplitude were explored through independent t-test. Potential confounding effect on observed gender relationship with P100 latency was examined using multiple regression. Linear relationship between age and anthropometric parameters with P100 latency and amplitude was determined using Spearman's rank correlation analysis. Two-tailed p value <0.05 was considered for statistical significance.

RESULTS

Study sample comprising of 130 apparently healthy adults had median age of 25.50 years. Males were more than twice the female participants, 91 versus 39 respectively. Other demographic and anthropometric characteristics of the subjects are summarized in Table 1. Majority (79.2%) of the participants were within the normal weight BMI category.

Table 2 presents the descriptive statistics of the peak latency and peak-to-peak amplitude (N75-P100) of the P100 component of PRVEP waveform for each eye separately. Median P100 latency of the averaged values of both eyes was 102.20 milliseconds (IQR=6.3) and averaged N75-P100 amplitude of the two eyes had a median of 5.17 microvolts (IQR=4.2).

Table 1: General characteristics of the study participants (n=130).

Attribute		Median (IQR[a])	Min, Max
Age (years)		25.50 (13)	18, 60
Height (cm)		166.50 (15)	150, 184
Weight (Kg)		62.50 (13)	42, 90
BMI (Kg/m^2)		22.49 (4.07)	17.63, 29.41
Sex (%)	Male	91 (70)	
	Female	39 (30)	
BMI categories (%)	Underweight	5 (3.8)	
	Normal weight	103 (79.2)	
	Overweight	22 (16.9)	

[a]IQR-Interquartile range, Min-minimum, Max – maximum

Table 2: Descriptive statistics of P100 latency and N75-P100 amplitude (n =130).

PRVEP parameter		Percentiles			Min, Max
		25th (Q1)	50th (Median)	75th (Q3)	
P100 latency (ms)	Right eye	98.63	102.50	105.78	87.50, 124.10
	Left eye	97.35	102.50	105.0	89.40, 119.80
N75-P100 amplitude (µv)	Right eye	3.29	5.41	7.32	0.61, 13.20
	Left eye	3.31	5.25	8.15	0.46, 14.50

Ms-milliseconds, µv-microvolts

P100 latency exhibited significant interocular asymmetry, W=49, p=0.023. Average P100 latency was longer in right eye than left eye, median difference =0.60, IQR=3.98. However, the observed interocular P100 latency difference could reach statistical significance only in males, W=32, p=0.037. Mean N75-P100 amplitude was comparable between the two eyes. Interocular amplitude ratio differed significantly from 1, t (129) =12.39, p<0.001 (Table 3). No significant linear relationship was observed between P100 latency and N75-P100 amplitude in either eye.

Relationship between P100 latency and N75-P100 amplitude with gender and age

Our study revealed a significant impact of gender on P100 latency, t (128) =4.84, p<0.001, effect size (Cohen's d) =0.93. Average P100 latency was longer in males as compared to their female counterparts, mean difference =4.88, 95% confidence interval =2.89, 6.88. Gender-wise normative values of P100 latency and amplitude for each eye are summarized in Table 4. A part of observed gender effect was due to differing average height of male and female subjects, β (unadjusted) =0.39, β (adjusted for height) =0.32. With regards to age, no significant linear relationship was observed between age and P100 latency; however, P100 latency differed significantly between 18-40 years age group as compared to 41-60 years group, U=418.50, p=0.048. Average P100 latency was longer in the latter age group i.e. 41-60 years, mean difference =3.92, 95% confidence interval =0.41, 7.43. However, it seems that the observed difference was due to the confounding effect of height variable. N75-P100 amplitude did not demonstrate any significant relationship with either gender or age.

Table 3: Interocular comparisons of P100 latency and N75-P100 amplitude (n=130).

Parameter	Percentiles			Min, Max
	25th (Q1)	50th (Median)	75th (Q3)	
Interocular P100 latency difference (R-L[a]) (ms)	-1.20	.60	2.78	-14.60, 19.80
Interocular N75-P100 amplitude ratio (L/S[b])	1.07	1.18	1.33	1.00, 2.11

[a]R-L: Rt eye minus Lt eye, [b]L/S-Larger value/Smaller value

Association of P100 latency and N75-P100 amplitude with anthropometric parameters

Among the anthropometric parameters, height was found to have significant positive relationship with P100 latency, r_s=0.27, p=0.002. However, when controlled for gender effect, the aforesaid association was no longer significant. Pearson's correlation analysis demonstrated a negative relationship between normally transformed BMI and P100 latency variables, r=-0.22, p=0.011 (Figure 1). Likewise, BMI based categories variable was also found to be negatively associated with P100 latency, r_s=-0.22, p=0.011. Overweight participants were found to have lower average P100 latency in comparison to underweight and normal weight subjects, F(2,129) =5.42, p=0.006. However, the aforementioned relationships were no longer

apparent when adjusted for the confounding effect of BMI and BMI category variable on each other. None of the anthropometric variables seem to have any significant effect on N75-P100 amplitude.

Table 4: Gender-based normative values of P100 latency and N75-P100 amplitude for each eye.

	PRVEP parameters					
	P100 Latency (ms)		N75-P100 Amplitude (µV)		Gender difference [Mean Difference (95% Confidence Interval)]	
	Males (n=91)	Females (n=39)	Males (n=91)	Females (n=39)	P100 Latency	N75-P100 Amplitude
Right eye	103.77 (5.74)	98.80 (6.59)	5.61 (2.74)	5.53 (2.86)	4.97*** (2.70 , 7.25)	0.08 (-0.97, 1.13)
Left eye	102.88 (5.14)	98.09 (5.54)	5.73 (3.06)	5.50 (3.24)	4.79*** (2.80, 6.78)	0.23 (-0.95, 1.40)

***p<0.001 (statistical significance determined using Independent t-test), †Data are presented as mean (standard deviation)

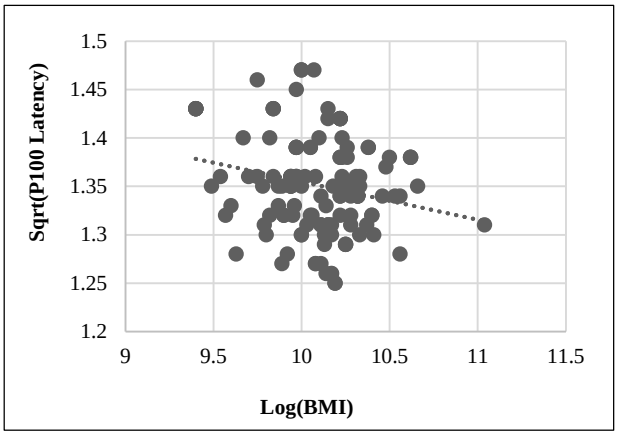

Figure 1: Relationship between P100 latency and body mass index (BMI).

DISCUSSION

VEPs are a sensitive neurodiagnostic tool that can used to evaluate the functional integrity of visual pathways non-invasively. Since VEP parameters are affected by a host of technical and biologic factors and neurophysiology laboratories across the globe conducting VEP examination not following uniform methodology, thus it is advised that every laboratory performing VEP testing should establish normative database to be used as reference for their local population. Keeping this is mind, the present study was carried out to establish normative values for our regional population.

In our study, median latency (in milliseconds) of P100 wave was 102.50 (IQR=7.15) and 102.50 (IQR=7.65) for the right eye and left eye respectively. It was also observed that P100 latency exhibited interocular asymmetry in males, p=0.037. These values corroborate with many previous studies while some authors reported values for P100 latency substantially different than observed in present study. Gupta et al. in their study in North Indian adults (n = 120) reported mean value of 100.78±2.21 for P100 latency.[7] In a recent study among adults (n = 126) in Eastern India by Roy and Ghosh, they observed mean value of 99.76±6.29 for P100 latency.[8] Similar values were reported by Aggarwal et al and Tandon et al in their studies among Indian populations.[9,10] Mahjoob et al in a study among Iranian adults (n = 59) also observed a comparable value for mean P100 latency (101±7.54). Additionally, they also documented interocular difference in P100 latency.[11] Contrary to the aforementioned studies, Sharma et al obtained a significantly different value (86±3.32) for mean P100 latency than observed in our research.[12] Gregori et al observed a similar value (89.75±2.32) in their study among adults (n = 54) in England.[13]

With regard to peak-to-peak (N75-P100) amplitude of P100 wave, we observed median value (in microvolts) of 5.41 (IQR = 4.03) for the right eye and 5.25 (IQR = 4.84) for the left eye. P100 amplitude between the two eyes was comparable; however, interocular amplitude ratio differed significantly from 1, median = 1.18, p<0.001. Our observed value is significantly lower than those reported by most of the other researchers. Roy and Ghosh reported a mean P100 amplitude value of 11.93±4.57 [8]. Quite similar values were obtained by Gupta, et al. (11.34±3.37) and Tandon et al (11.32±2.21) in their research.[7,10] Sharma, et al. reported mean P100 amplitude values (males -5.71±0.48; females -6.37±0.66) that are closer to the findings in the present study.[12] This discrepancy in P100 amplitude values could be due to variation in stimulus (check size) or other technical/subjective factors in the studies by different researchers.

Present study revealed significant gender differences in P100 latency; however, P100 amplitude was comparable between male and female group. Males were reported to have longer mean P100 latency than females. Sex differences in P100 latency have also been reported by other researchers.[13-15] Shorter P100 latency in females might be due to shorter axial eye length in them as compared to females.[16] Some researchers postulated that the shorter latency and higher amplitude of the P100 wave in females may be due to their smaller brain size.[17,18] Kaneda et al. proposed that the sex differences in P100 latency and amplitude could be attributed to genetically determined differences in neuroendocrinological systems.[19] Guthkelch, et al suggested that gender differences in VEP parameters might be due to variations

in head geometry, rather than to more general biological distinctions between males and females.[20] On the contrary, some studies demonstrated no significant gender differences in VEPs.[21,22] None of the anthropometric variables were found to have any significant impact on either P100 latency or amplitude in our study.

This study has few limitations. Though the present study had the advantage of using a bigger sample size than previous studies, there are few limitations that should be duly acknowledged. Firstly, generalizability of observed findings to the adult population of North-India is limited as the study subjects were recruited from a single territory (Mewat region) in North India. In addition, potential confounding role of head circumference on the observed sex differences in VEP parameters, as has been reported in some previous studies, could not be investigated as this anthropometric variable was not measured in study participants.

CONCLUSION

The P100 latency observed in our study is similar to the values found in several previous studies conducted on Indian and Western populations. However, the amplitude of P100 was notably lower than the values typically reported in the majority of existing studies, which may be due to the smaller stimulus (check) size used or variation in other technical factors. The study revealed significant gender differences in P100 latency, but anthropometric variables such as height, weight and BMI had no impact on either P100 latency or amplitude.

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