International Journal of Basic and Applied Medical Sciences ISSN: 2277-2103 (Online)
An Online International Journal Available at http://www.cibtech.org/jms.htm
2013 Vol. 3 (3) September-December, pp.180-185/Kothari et al.
Research Article

NORMATIVE DATA OF PEAK LATENCIES OF N70, N155 WAVES AND INTER-PEAK LATENCY OF PATTERN REVERSAL VISUAL EVOKED POTENTIALS IN CENTRAL INDIAN POPULATION

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ABSTRACT
The aim was to report the normal values of the N70 latency, N155 latency and interpeak latency of Visual evoked potential [VEP] of central Indian population. This study was conducted in the Neurophysiology unit of the Department of Physiology of our institute. The study comprised of pattern reversal visual evoked potential (PRVEP) recordings by an electronic pattern regenerator inbuilt in an Evoked Potential Recorder (RMS EMG EP MARK II) from 200 eyes of 100 carefully screened visually normal, healthy middle aged and elderly individuals having age in the range of 40 to 79 years.This was an observational cross-sectional study. The mean age of the subjects was 56.08 ± 10.87 years (minimum age of 40 years and maximum of 79 years). 57.17 ± 10.92 years was the mean age for males and for females it was 54.30 ± 10.62 years. The overall mean interpeak latency in all the 200 subjects was 68.79±9.49 msec, N70 latency was 66.64±5.59 msec and N155 latency was 135.44±8.31 msec. The normative values of N70 latency, N155 latency & interpeak latency of PRVEPs in the normal adults of central India have been reported in the present study. These can be used for evaluation and interpretation of various VEP abnormalities especially the ones encountering extended temporal dispersion.

Key Words: *Pattern Reversal, N70 Latency, N155 Latency, Interpeak Latency, Normative Data*

INTRODUCTION

Visual evoked potentials provide a sensitive indication of abnormal conduction in the visual pathway. VEP is a useful clinical tool in the diagnosis and documentation of visual impairment in many neurological and ophthalmological disorders. Like any other neurophysiological test, exquisite attention to the technical details, acquisition of reproducible and reliable waveforms, proper interpretation based on laboratory control values and correlation with the clinical picture are essential for optimal utilization of this technique.

Every clinical neurophysiology lab need to set up its own normative data for its population required in clinical practice to identify the abnormal subjects.

The preferred stimulus for clinical investigation of the visual pathways is a reversal of a high contrast black and white checkerboard pattern, as it tends to evoke larger and clearer responses than other patterns. The standard clinical test involves the recording of the pattern reversal VEPs (PRVEPs). Pattern-reversal VEPs are less variable in waveform and timing than the VEPs elicited by other stimuli (Odom *et al*., 2010).

Normal VEP Waveform

The starting point of VEP waveform is stimulus onset. The waveform of a VEP depends upon the temporal frequency of the stimulus. At low temporal frequencies, the waveform consists of a number of discrete deflections and is termed a transient VEP. The transient responses have the advantage of component analysis (Birch and Subramanian, 2012). The usual PRVEP waveform is the initial negative peak (N1 or N70), followed by a large positive peak (P1 or P100) and followed by another negative peak (N2 or N155). Positive wave P100 is shown with downward polarity and the negative waves are shown with upward polarity in the recording.

Interpeak Latency is one VEP parameter that is measured between the peaks of N70 and N155 (N70-N155) and so its quantum depends upon the onset latencies of the two negative peaks.
The attributes of PRVEP are affected by a number of factors including the brightness and contrast of the stimulus and the angle subtended by the squares in the checkerboard. It is therefore customary and pertinent to base the values used to define the range of normal variation on data obtained from normal subjects using the local equipment. Although P100 is the most consistent and least variable peak as compared with N70 and N155 waves yet the inter-peak latency of PRVEP has to be given special weightage in assessing the normality of a recording as this has been found to produce increased "temporal dispersion" (term for prolonged P100 duration) as a unique characteristic of optic nerve compression (Livingstone *et al.*, 1981; Onofrj and Bodis-Wollner, 1982) as well as demyelination (Holder, 1985) of the optic nerve. Not many studies have been published in literature regarding reference values for N70 latency, N155 latency and interpeak latency of PRVEPs. The key purpose of this study was to provide normative visual electrophysiological data for these parameters of commonly used PRVEPs in visually normal central Indian population using standard distance and temperature control.

MATERIAL AND METHODS

A total of 200 carefully screened visually normal, healthy middle aged and elderly individuals were included in this study. Inclusion criteria were normal eyes without systemic or ocular diseases that would affect the values of VEP. Exclusion criteria were the persons who were not co-operative and who had systemic or ocular diseases that would affect the normal values. These subjects were further stratified into 4 age groups (Table 1) comprising of 64 (32%) subjects in **Group I** with age range of **40-49** years, 62 (31%) in **Group II of 50-59** years, 42 (21%) in **Group III** of **60-69** years and 32 (16%) subjects in the **Group IV** of **70-79** years (Table 1 , Figure 1).

Study Design

This was an observational cross-sectional study.
Out of 200 subjects, 124 (62%) were males and 76 (38%) were females (Figure 1).

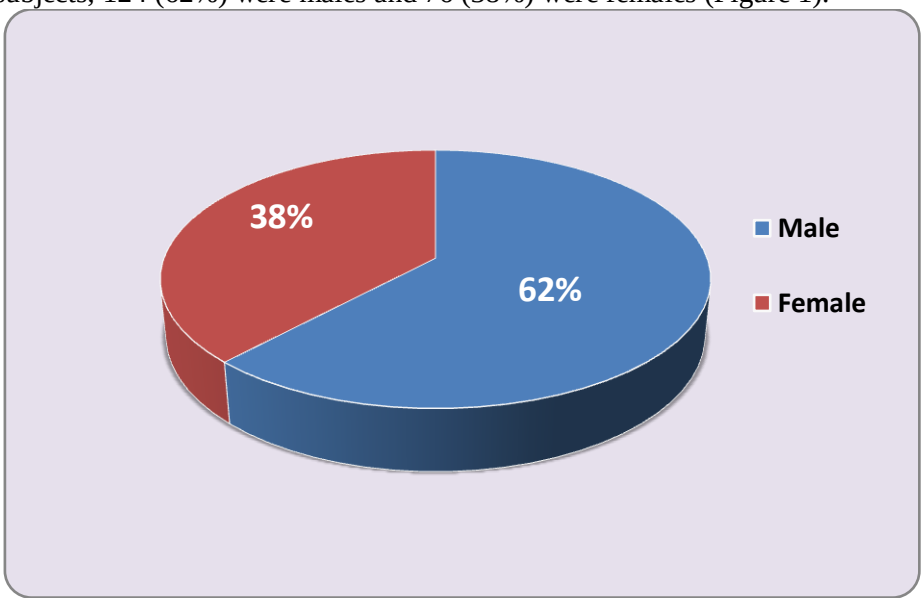

Figure 1: Sex distribution of subjects

Methodology for VEP

VEP recordings were done in accordance to the standardized methodology of International Federation of Clinical Neurophysiology (IFCN) Committee Recommendations (Celesia *et al.*, 1993) and International Society for Clinical Electrophysiology of Vision (ISCEV) Guidelines (Odom *et al.*, 2010) and montages were kept as per 10-20 International System of EEG Electrode placements (American Clinical Neurophysiology Society, 2006).

PRVEP recordings were performed in the Neurophysiology unit of the Department of Physiology of our institute with the stimulus configuration consisting of the transient pattern reversal method in which a black and white checker board was generated (full field) and displayed on VEP Monitor by an electronic pattern regenerator inbuilt in 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.

Ethics Consideration

Each subject gave informed consent to participate in this study. Ethics approval from the Institutional Ethics committee was obtained prior to the study.

Statistical Method

Analysis was done using statistical package for social sciences (SPSS) 13.0 version. Values obtained were expressed in the form of mean and standard deviation (SD).

RESULTS AND DISCUSSION

Results

The mean age of the subjects was 56.08 ± 10.87 years (minimum age of 40 years and maximum of 79 years). 57.17 ± 10.92 years was the mean age for males. Similarly, for females the mean age was 54.30 ± 10.62 years (Table 1). The overall mean ± SD of interpeak latency in all the 200 subjects was 68.79±9.49 msec. The mean ± SD of interpeak latency in males was 68.51±8.59 while that in females was 69.25±10.85 msec.

Table 1: Age distribution of study subjects

Age Group (years)	MALES n (%) (%)	FEMALES n (%) (%)	TOTAL n (%) (%)
40-49	35(28.22%) (17.5%)	29 (38.16%) (14.5%)	64(32%) (32%)
50-59	42(33.87%) (21%)	20(26.31%) (10%)	62(31%) (31%)
60-69	22(17.74%) (11%)	20(26.31%) (10%)	42(21%) 21%)
70-79	25(20.16%) (12.5%)	7(9.21%) (3.5%)	32(16%) (16%)
Total	124(100%)	76(100%)	200(100%)
Mean Age ± SD	57.17 ± 10.92	54.30 ± 10.62	56.08 ± 10.87

The mean ± SD of interpeak latency in each of the monocular recordings along with their inter-ocular differences that were recorded in males and females among the subjects in each age group are shown in Table 2. It can be deduced from the table that the duration of P100 wave is almost similar in both the sexes and there is negligible inter-ocular difference between the two eyes of the same sex. The mean values tend to rise with the increasing age and the longest P100 duration was observed in subjects of group IV.

Table 2: Age wise & Gender wise values of P100 duration in Both eyes of Subjects

Age Groups (Years)	Mean ± SD of P100 duration (msec)					
	Males			Females		
	RE	LE	IOD	RE	LE	IOD
40-49	65.81±9.75	65.87±10.41	3.37±3.43	64.79±9.20	64.19±10.19	3.48±3.74
50-59	69.19±7.05	68.88±8.25	4.19±4.15	70.40±8.31	69.55±9.09	4.64±4.85
60-69	71.21±10.62	70.44±9.93	3.88±3.97	73.89±12.16	72.71±10.47	4.86±4.97
70-79	71.09±11.61	72.01±10.94	3.15±2.85	74.24±17.08	76.49±16.42	2.25±1.82
Total	68.83±9.73	68.75±9.96	3.69±3.69	69.53±11.22	68.97±11.27	4.04±4.29

The mean ± SD of the absolute latencies of the peak of negative wave N70 in each of the monocular recordings along with their inter-ocular differences that were recorded in males and females among the subjects in each age group are shown in Table 3. It can be concluded from the table that the latency of N70 wave is longer in males than in females and there is negligible inter-ocular difference between the two eyes of the same sex. The overall N70 latency in all the 200 subjects was 66.64±5.59 msec.

Table 3: Age wise & Gender wise values of N70 latency in both eyes of subjects

Age Groups (Years)	Mean ± SD of N70 latency (msec)					
	Males			Females		
	RE	LE	IOD	RE	LE	IOD
40-49	67.88±5.15	68.27±5.02	1.87±2.25	67.54±4.40	68.16±4.57	1.30±1.83
50-59	66.96±5.84	66.69±5.32	2.06±2.62	66.18±5	65.84±4.96	2.68±3.16
60-69	66.76±6.74	66.92±6.05	1.64±1.44	62.20±6.49	62.44±6.32	2.69±2.99
70-79	67.44±6.90	66.53±6.91	2.92±3.13	65.19±6.18	65.79±6.86	2.21±2.24
Total	67.29±6	67.14±5.71	2.12±2.49	65.56±5.65	65.83±5.75	2.11±2.62

The mean ± SD of the absolute latencies of the peak of negative wave N7155 in each of the monocular recordings along with their inter-ocular differences that were recorded in males and females among the subjects in each age group are shown in Table 4.

Table 4: Age wise & Gender wise values of N155 latency in both eyes of subjects

Age Groups (Years)	Mean ± SD of N155 latency (msec)					
	Males			Females		
	RE	LE	IOD	RE	LE	IOD
40-49	134.54±9.97	135.54±9.82	2.68±3.17	132.33±8.35	132.36±9.08	2.66±3.12
50-59	135.58±7.86	135.26±8.13	2.90±2.90	136.59±6.57	135.40±7.03	3.11±3.05
60-69	135.42±6.76	135.21±7.67	2.45±1.94	136.09±8.34	135.15±7.15	2.56±2.90
70-79	137.69±8.60	137.34±9.11	1.67±1.79	139.43±11.20	142.28±10.51	3.52±3.67
Total	135.70±8.47	135.77±8.71	2.51±2.66	135.10±8.38	134.81±8.53	2.83±3.05

It can be inferred from the table that the N155 latency is almost similar in both the sexes and there is negligible inter-ocular difference between the two eyes of the same sex. The mean values depict a rising trend with the increasing age and the highest values of latency were obtained for group IV in both the sexes. The overall N155 latency in all the 200 subjects was 135.44±8.31 msec.

Discussion

Many clinical neurophysiology laboratories are rapidly emerging in our country and have added visual evoked potential study to their routine procedures as this method is non-invasive, low cost, real time, highly objective and informative about functional integrity of visual pathways. Since many stimulus parameters and physiological factors like age, sex, head circumference, body temperature affect VEP waveform so it becomes imperative on the part of any clinical neurophysiology laboratory to control these parameters rigidly in order to obtain reasonable, reproducible and reliable data of VEP in a normative study before using it as a diagnostic tool. This study estimates the peak latencies of N70, N155 waves and interpeak latency derived from the parameters of the pattern reversal VEPs of a visually healthy middle aged and elderly population of central India to provide the normative and reference values for our neurophysiology lab. These reference values differ from one population to another as the anthropometric parameters and the rate of aging also varies across the world. In the Indian scenario very few endeavours have been made to establish a normative data in this context. There are no detailed studies which have been reported till date with regard to peak latencies of negative waves and interpeak latency of PRVEPs which can be extrapolated and used in our fast developing clinical neurophysiology units. The time consuming nature of the study, the difficulties faced in singling out and selection of a "true" normal subject as well as the lack of practical experiences in the recording field are some of the obstacles in establishing such data. Moreover, most of the studies in the published literature have emphasized on the latency and amplitude of the major positive wave P100 which holds the ultimate clinical significance and very little clinical utility has been accredited to the two negative peaks of PRVEP. N70 is thought to reflect the initial activation of the visual cortex by a visual stimulus. Evidences indicate that N70 is generated in the striate cortex and it shows small and less significant aging changes (Allison *et al*., 1983; Allison *et al*., 1984) as was evident from the observations of the present study also. N155 is the second negative peak of the PRVEP waveform. N155 and similar later potentials are believed to be generated in extra striate cortex. There was an age related increase of N155 latency that was observed in the present study among both the sexes with the longest latencies found particularly in age group of 70-79 years (Refer Table 4). This finding is in consonance with earlier studies (Allison *et al*., 1983; Allison *et al*., 1984) where it was found that N145 have showed large changes after the age of 60. Furthermore, it has been postulated long back that vascular and biochemical changes occur in the elderly brain which may adversely affect various processing in the CNS including the visual process (Samuel *et al.,* 1983). This might also be the possible reason of the longer N155 latencies observed in elderly subjects. The overall mean value of interpeak latency in the subjects of the present study was 68.79±9.49 msec which is longer than the reported ones in literature. The value reported by Shahrokhi *et al.,* (1978) for interpeak latency was 63.0 ± 8.7 msec while Misra and Kalita (2011) who investigated 58 patients in the age range 15-58 years (mean age 34.6 years) msec have documented the mean interpeak latency as 55.9 ± 7.7 msec. The primary reason for this discrepancy could be the representative population which in our study comprised of middle aged and elderly subjects in whom the prolongation of peak latencies of negative waves and interpeak latency can be attributed to the age related changes in the striate and extra-striate part of the visual cortex.

Conclusion

Variability of VEP recording character depends on application of various stimulus parameters various methods of their presentations and many physiological factors. Consequently, every laboratory performing visual evoked potential examinations should establish age-related normative data of parameters of VEP with strictly defined standardized conditions of stimulation and recording to facilitate clinical interpretation. In conclusion, we have reported a normative data on peak latencies of negative waves and interpeak latency of PRVEP in central Indian population which will give working baseline criteria for interpreting various VEP abnormalities especially the ones encountering extended temporal dispersion.

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