International Journal of Biomedical Research
ISSN: 0976-9633 (Online); 2455-0566 (Print)
Journal DOI: 10.7439/ijbr
CODEN: IJBRFA

Original Research Article

Study of age-influences on brainstem auditory evoked potentials in healthy adults

Sangeeta Gupta[*1], Gaurav Gupta[2] and Surjit Singh[3]

[1]Associate Professor, Department of Physiology, M.M.I.M.S.R., Mullana-Ambala (Haryana) 133 207 India
[2]Professor, Department of Surgery, M.M.I.M.S.R., Mullana-Ambala (Haryana) 133 207 India.
[3]Professor, Department of Physiology, M.M.I.M.S.R., Mullana-Ambala (Haryana) 133 207 India

***Correspondence Info:**
Dr. Sangeeta Gupta,
F-23, M. M. University campus,
M.M.I.M.S.R., Mullana-Ambala (Haryana) 133 207 India.
E-mail: drsangeeta77.65@rediffmail.com

Abstract

Background and objectives: Brainstem auditory evoked potentials (BAEPs) have widespread clinical utility**.** BAEP responses exhibit a normal variability due to various non-pathologic factors and age is one of the variables suggested to have considerable influence on normal BAEP responses. Aging changes in the auditory system may significantly influence the interpretation of the auditory brainstem responses in comparison with younger adults. Hence, the study was planned to evaluate the influence of age on absolute and interpeak latencies in healthy subjects in the age-group of 18-70 years.
Methods: The test was conducted on 150 healthy adults in the age-group of 18-70 years (75 males and 75 females). BAEP latencies were compared in different age groups by one way ANOVA. Correlations of latencies with age were performed using Pearson correlation coefficient. P value<0.05 was considered as statistically significant.
Results: Absolute latencies of all BAEP waves (I, II, III, IV and V) increased with age. Interpeak latency I-III and I-V increased significantly with age but a decrease was found in subjects with 58-70 years of age. III-V interpeak latency variations were insignificant till the group with 48 years of subjects but exhibited a significant decrease in subjects with >48 years of age.
Conclusion: Age contributes to the normal variations in BAEP latencies. Acquisition of a normative data for different age-groups can improve the clinical utility of the test. The pattern of interpeak latency changes with age in the present study indicates a greater possibility of involvement of peripheral auditory functions in the elderly subjects.
Keywords: Brainstem auditory evoked potentials, Absolute latency, Interpeak latency.

1. Introduction

Brainstem auditory evoked potentials are electrophysiological investigations with well established clinical utility in neurology, audiology, neonatology and anaesthesiology. BAEPs represent the electrical activities generated in the auditory pathways between cochlea and the brainstem in response to the auditory stimuli. Activation of the eighth nerve, cochlear nucleus, tracts and nuclei of the lateral lemniscus and inferior colliculus result in the generation of BAEP waveform [1]. BAEP recorded from a normal human subject consists of a series of waves with different latencies and amplitudes appearing within 10 ms of the stimulus onset. The tests are potentially useful in objective assessment of hearing disorders, brainstem lesions, demyelinating diseases, intra-operative monitoring and in monitoring traumatic brain injury patients. BAEP responses exhibit a normal variability due to various non-pathologic factors including stimulus variable like stimulus intensity, stimulus rate, stimulus mode and phase, recoding parameters like electrodes and filter settings. Technical parameters can be standardized for each laboratory but subject's factor or inter-individual variability due to age, sex, temperature and anthropometric data can also vary BAEP latencies and amplitudes, thus limiting the clinical value of the test. Age is known to have considerable influence on BAEP responses and one of the important factors in the clinical interpretation of the test as progression in age has been found to affect BAEP absolute latencies and interpeak latencies [2-6**].**

The effect of age on BAEP responses is reflected as developmental or maturational changes in infants and children and also as aging changes thereafter in older subjects. However, developmental or maturational changes in BAEP latencies as demonstrated by various studies are evident till only upto 3-5 years of age, while aging changes that is, increases in latency attributable to increased conduction time have been demonstrated thereafter [7-10].

Aging changes in the auditory system may significantly influence the interpretation of the auditory brainstem responses in comparison with younger adults. Such aging changes have been reported by various authors as increase in the absolute and interpeak latencies (IPLs) of auditory evoked potentials. However, the findings are not uniform in the different studies. Trune *et al* (1988) have reported significant prolongation of wave III only [11]. Costa P *et al* (1990) obtained an age-related prolongation of latency values which was particularly marked for wave I, while other waves (particularly wave III) do not show a significant change [12]. Some studies stated no significant differences in BAEP latencies with age [13-15]. Also, evidence for age-related increase in interpeak latencies is still a matter of controversy [12, 16-18]. Hence, the present study was planned to evaluate the effect of age on the latencies of brain stem auditory evoked potentials in the healthy adults from North India.

2. Materials and methods

The study was conducted on 150 healthy adults in the age-group of 18-70 years (75 males and 75 females). It was a cross-sectional analytical study. BAEP was performed in Electrophysiology laboratory in the department of Physiology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala and the subjects selected were the students and staff of the institute and others belonging to the area of study after having fulfilled the inclusion criteria of the study**.** Approval from the Institutional Ethical committee was taken to carry out the research work. All the subjects underwent a complete neuro-otological examination. A written informed consent was obtained for the test and a detailed clinical history taken.

2.1 Inclusion criteria

Adult healthy subjects in the age group of 18-70 years with normal neuro-otological examination.

2.2 Exclusion criteria

Subjects with otological disorders, systemic diseases like Diabetes-mellitus and hypertension, HIV infection, hereditary and degenerative diseases, chronic use of ototoxic drugs, previous history of head trauma, tobacco-chewing, chronic alcoholism or cigarette smoking, ear surgery, radiotherapy or chemotherapy.

2.3 BAEP Recording

BAEP was performed on Allengers Scorpio-EMG, EP, NCS in Electrophysiology laboratory in a quiet environment. Subjects were informed about the procedure, reassured and made to relax before starting the procedure. Methodology for the test employed was standardized as recommended by guidelines on short latency auditory evoked potentials by American Clinical Neurophysiology society [19]. Preparation of scalp skin was done prior to the electrode application. Standard disc surface electrodes were placed according to the International 10/20 system of electrode placement, with active electrode at Mi, reference electrode at Cz and ground electrode at Fpz [19]. Monaural auditory stimulus with rarefaction clicks **(**0.1 ms pulse) and click intensity of 60 dB nHL was delivered through headphones at a rate of 11.1/s. The contralateral ear was masked with white noise 30 dB below the BAEP stimulus. The low filter setting was adjusted at 100 Hz and high filter setting at 3000 Hz. Responses to 2000 click presentations were averaged to obtain a single BAEP waveform pattern. To verify the reproducibility of the waveform, two responses were recorded and superimposed.

Parameters for the study were absolute latencies of wave I, II, III, IV and V and interpeak latencies I-III, III-V and I-V. All the data was expressed as mean ± S.D. The subjects were classified into five different age-groups: Group I (18-27 years), Group II (28-37 years), Group III (38-47 years) Group IV (48-57 years) and Group V (58-70 years). The effect of age in different age groups was compared and analysed using one way ANOVA and post hoc test (Fisher's least significant difference test). Correlations of age with BAEP latencies were obtained using Pearson correlation coefficient. Statistical analysis was done by using SPSS (Statistical package for social science) version 20.0 statistical software. The analysis was done at 5 % level of significance.

3. Results

The study comprised of 150 healthy subjects in the age-group of 18-70 years. BAEP absolute and interpeak latencies were compared among the subjects in five different age-groups with each group consisting of 30 subjects. Comparison of absolute latencies in different age groups revealed statistically significant difference ($P<0.0001$) by one way ANOVA (table 1)(Figure 1). Absolute latencies of all the waves I, II, III, IV and V increased with age. The statistical significance was found between the groups too, except between group 2 (28-37 years) and 3 (38-47 years) for wave I, III and V, group 2 and 3 and between 3 and 4 (48-57 years) for wave II and that between group 2 and 3 and between group 4 and 5 (58-70 years) for wave IV by post hoc tests. Correlation studies also revealed a significant positive correlation of absolute latencies with age ($p<0.0001$) (Pearson correlation coefficient) (Table 2).

The interpeak latencies I-III, III-V and I-V varied among the different age groups with $P<0.0001$ (one way ANOVA). I-III increased with age (except between the groups 2 and 3). Also, a decrease was noted in the last age-group (58-70 years of subjects) which was statistically significant when compared with the other groups (1, 2, 3 and 4) (post hoc tests). I-V interpeak latencies also increased with age (except between group 2 and 3). A decrease was noted in the last age group (group 5) which was statistically significant when compared with group 1 and 2. For III-V interpeak latency, one way ANOVA revealed significant variations ($p<0.0001$) but the increase with age observed till the age-group of 38-47 was statistically insignificant between the groups (post hoc tests) (Table 3). The statistical significance was obtained for the decrease in III-V interpeak latency in group 4 (48-57 years) and group 5(58-70 years) as compared with the other groups by post hoc tests (table 3)(Figure 2).

When interpeak latencies were correlated with age, significant positive correlations were obtained for interpeak latencies I-III and I-V but a statistically significant negative correlation was obtained for III-V interpeak latencies. Also, since I-III and I-V interpeak latencies showed a characteristic decrease in the last age-group studied, a separate correlation study was performed including only the subjects between 48 to 70 years. The results of the study revealed a negative correlation for both I-III and I-V interpeak latency with statistical significance (p<0.05) for I-V (Table 4).

Table 1: Mean BAEP absolute latencies in different age-groups

Age- group (years)	No. of subjects	Absolute latency Wave I **(ms ± SD)**		Absolute latency Wave II **(ms ± SD)**		Absolute latency Wave III **(ms ± SD)**		Absolute latency Wave IV **(ms ± SD)**		Absolute latency Wave V **(ms ± SD)**	
		R	**L**	**R**	**L**	**R**	**L**	**R**	**L**	**R**	**L**
18-27	**30** (M=15, F=15)	1.568 ±0.05	1.57 ±0.053	2.72 ±0.107	2.725 ±0.108	3.54 ±0.08	3.55 ±0.09	4.85 ±0.08	4.86 ±0.09	5.56 ±0.07	5.57 ±0.08
28-37	**30** (M=15, F=15)	1.627 ±0.03	1.626 ±0.029	2.82 ±0.05	2.81 ±0.07	3.66 ±0.04	3.658 ±0.03	4.95 ±0.05	4.95 ±0.06	5.675 ±0.025	5.68 ±0.03
38-47	**30** (M=15, F=15)	1.646 ±0.02	1.64 ±0.025	2.84 ±0.037	2.85 ±0.035	3.7 ±0.045	3.68 ±0.05	4.99 ±0.04	4.986 ±0.045	5.72 ±0.02	5.71 ±0.025
48-57	**30** (M=15, F=15)	1.68 ±0.06	1.683 ±0.066	2.88 ±0.03	2.86 ±0.05	3.839 ±0.059	3.833 ±0.065	5.05 ±0.05	5.065 ±0.048	5.77 ±0.03	5.765± 0.04
58-70	**30** (M=15, F=15)	1.799 ±0.07	1.81 ±0.09	2.92 ±0.076	2.93 ±0.078	3.926 ±0.049	3.93 ±0.06	5.08 ±0.07	5.097 ±0.19	5.87 ±0.09	5.88 ±0.094

M- Males, F- Females, R-Right, L-Left.

P<0.0001 for differences among the age-groups (one way ANOVA). The difference was significant between all the age groups except between group 2 and 3 for wave I, III and V, group 2 and 3 and between 3 and 4 (wave II) and group 2 and 3 and between group 4 and 5(wave IV)(post hoc test).

Table 2: Correlation coefficient (r) between age and absolute BAEP latencies

	Wave I		**Wave II**		**Wave III**		**Wave IV**		**Wave V**	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
	0.82	0.78	0.69	0.67	0.94	0.92	0.8	0.66	0.9	0.89
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Table 3: Mean BAEP interpeak latencies in different age-groups

Age group (years)	**No. of subjects**	**I-III (ms±SD)**		**III-V (ms±SD)**		**I-V (ms±SD)**	
		R	**L**	**R**	**L**	**R**	**L**
18-27	**30** (M=15, F=15)	1.967±0.056	1.97±0.06	2.02±0.05	2.01±0.058	4.013±0.07	4.017±0.06
28-37	**30** (M=15, F=15)	2.035±0.03	2.03±0.02	2.01±0.05	2.02±0.03	4.048±0.06	4.05±0.03
38-47	**30** (M=15, F=15)	2.05±0.05	2.04±0.056	2.02±0.03	2.026±0.06	4.06±0.05	4.07±0.03
48-57	**30** (M=15, F=15)	2.16±0.05	2.15±0.07	1.932±0.045	1.93±0.056	4.1±0.02	4.0947±0.04
58-70	**30** (M=15, F=15)	2.127±0.05	2.12±0.08	1.95±0.077	1.952±0.09	4.069±0.045	4.079±0.05

M- Males, F- Females, R-Right, L-Left

P<0.0001 for the differences in I-III, III-V and I-V interpeak latencies among the different age groups by one way ANOVA.

Table 4: Correlation coefficient (r) between age and interpeak BAEP latencies

No. of subjects		**I -III**		**III-V**		**I-V**	
		Right	**Left**	**Right**	**Left**	**Right**	**Left**
150 (18-70 years)	**r**	0.76	0.67	-0.49	-0.44	0.6	0.46
	P	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
60 (48-70 years)	r	-0.24	-0.20	0.136	0.0896	-0.31	-0.32
	P	0.06[NS]	0.125[NS]	0.3[NS]	0.496[NS]	0.016	0.013

[NS]- Not significant

Figure 1: Mean Absolute latencies in different age-groups

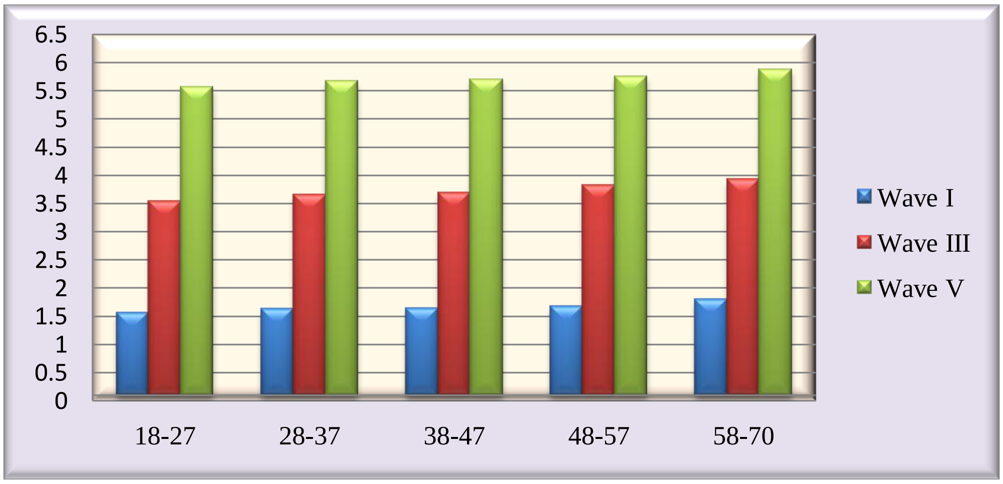
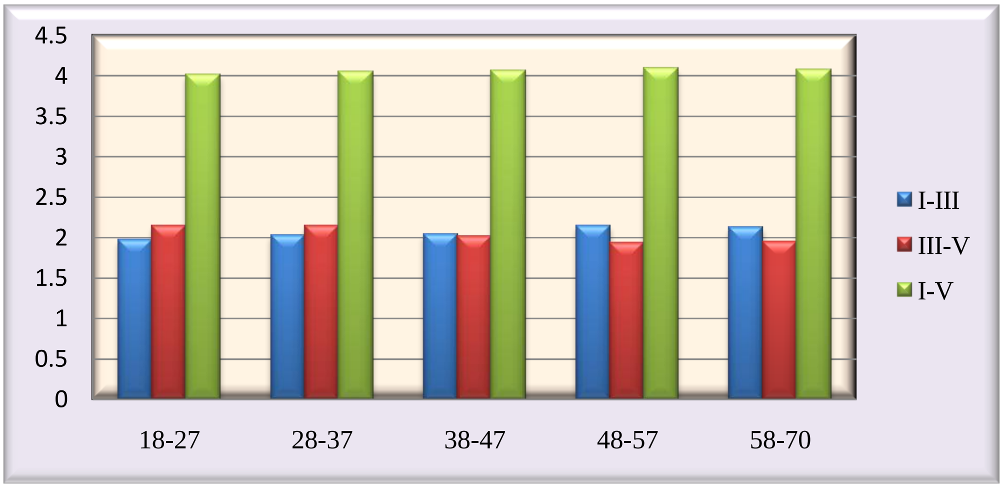


Figure 2: Mean Interpeak latencies in different age-groups



4. Discussion

BAEPs possess widespread clinical utility owing to their relative stability and reproducibility. The test can assess both peripheral and central components of the auditory functions. The clinical application of the test largely depends on the normal values adjusted for the various confounding variables. As a confounding variable, age appears to play an important role in the variability of the BAEP parameters in normal healthy subjects. Regarding age-influences on BAEP responses, many previous studies argue that aging process is essentially a peripheral phenomenon and it does not involve the central part of the acoustic pathway [12]. A prolonged wave I latency and poor evidences for interpeak latency differences (considered as the changes in the true central conduction time through the acoustic pathways) demonstrated in previous studies in elderly subjects have been largely attributed to the changes in peripheral auditory structures [4,17,20]. The contribution of intrinsic brainstem dysfunction to age-related differences in the BAEP is still controversial. The present study attempted to determine the age-related differences in healthy adults in the age-group of 18-70 years in absolute and interpeak latencies of BAEP and to compare the data with the previous similar studies.

An age-related increase in all the absolute latencies (I, II, III, IV and V) with statistical significance ($p<0.0001$) was obtained in the present study (Table 1). Correlation studies also revealed a significant positive correlation with age (Table 2). Absolute latencies prolongation has been stated by majority of authors in the past. Martini A *et al* (1991) reported a latency shift of all principal components of ABR [16]. Harkins SW (1981) reported that the elderly group (mean age: 71.2 years) had delayed peak latencies for all BAEP components as compared to the young adults [17]. In a study by Rosenhall U *et al* (1985), the latencies of waves I, III and V were found to be increased by 0.1-0.2 milliseconds with increasing age [18]. Rowe M J (1978) demonstrated increase in all peak latencies [4]. Chu NS (1985) noted a small progressive prolongation in the peak latency with increasing age, particularly peak V [21]. According to Costa P *et al* (1990) data obtained showed an age-related prolongation of latency values which was particularly marked for wave I, while other waves (particularly wave III) do not show a significant change [12]. Among the more recent studies, Tafti FM *et al* (2007) and Khatoon M *et al* (2012) found variations in I, III and V wave latencies, while the results from the study by Patel KC *et al* (2014) showed wave

I, II and III and that by Hairnder JS *et al* (2010) revealed wave III and V absolute latency prolongation [2,22-24].

Absolute latency prolongation, hence, has been observed in many studies in the past which conforms to the present study. Only few authors like Costa P *et al*, however, have reported only wave I latency prolongation and concluded that aging does not involve the central part of the acoustic pathway [12]. Other authors like Beagley HA *et al* (1978), Kjaer M (1979), Manjuran T J *et al* (1982) reported no significant variations in BAEP latencies [13-15].

On the other hand, the results for BAEP interpeak latency variations with age have largely provided conflicting data from the different studies in the past. The present study observed significant variations for the all three interpeak latencies with age. The variations were in the form of significant increase in the latencies with age for I-III and I-V and not for III-V. Also a significant decrease was noted in the older age-groups, group 4 (48-57 years) and group 5 (58-70 years) for III-V latencies and in group 5 for I-III and I-V interpeak latencies. The statistically significant increase which was observed for I-III and I-V in the present study comply with the study by Rowe MJ (1978) who described I-III prolongation with III-V unaffected with age [4]. Harinder JS *et al* (2010) reported a similar finding in older males with an insignificant increase in III-V IPL [24]. We obtained a significant decrease in all the three IPLs in older subjects (58-70 years) and the fact that some previous similar studies could not state a decrease in IPLs can be explained on the basis of the age-group of the subjects included, as subjects in those studies were <60 years of age while we have observed the decrease after 60 years of age (58-70 years) [2, 22]. Also, correlation studies revealed a negative correlation for I-III and I-V in the subjects with 48-70 years. This attenuates the possibility of the delay in the central auditory pathway, as interpeak latencies are considered to represent true central conduction time through the acoustic pathways. The decrease in IPLs in the elderlies (58-70 years) indeed, points towards a greater extent of involvement of the peripheral component of acoustic functions in the elderlies. These findings are supported by Costa P *et al* (1990) who found a negative 'r' value for I-III and I-V did not show a significant change [12]. In addition, Harkins SW, Rosenhall *et al* and Martini *et al* although stated a significant prolongation of all the peak latencies could not found interpeak latency differences, further supporting the fact that aging affects the peripheral components of auditory pathways [16-18].

The increased absolute latencies and the interpeak latency changes with age have been attributed to the several structural changes in the auditory nerve that occur along the auditory pathway and retrocochlear cell degeneration leading to loss of synchrony of the auditory pathways and also to the changes in the peripheral auditory structures leading to peripheral hearing loss with age [17, 20, 25]. Cognitive alterations due to aging caused by the deterioration of the dopaminergic and the cholinergic systems also have been suggested for the latency prolongation of BAEP components [26]. The findings of the present study do not provide evidence in the favour of age-related slowing of central transmission time in the afferent auditory system, rather it supports the fact that in elderlies peripheral auditory structures are affected to a greater extent which prolongs the absolute latencies but the interpeak latencies remain unaffected or shortened.

5. Conclusion

Age is an important variable that influences BAEP latencies and hence can affect the clinical interpretation of the test. The accuracy and adequacy of the clinical interpretation of the test can be optimized by taking these normal variations into consideration and acquiring a normative data for the test for different age groups. The study also suggests a greater possibility of the involvement of peripheral components of the auditory functions in the elderly subjects as compared to the central conduction delay in the auditory pathway due to aging.

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