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RESEARCH ARTICLE

Brainstem auditory evoked potentials in the older population

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ABSTRACT

Background: The central nervous system is no exception to the effects of aging. Physiologic changes due to aging have been suggested to impair the neurotransmission in the auditory pathways. Brainstem auditory evoked potential (BAEP) allows for the evaluation of such age-related transmission delays within the auditory system. **Aims and Objectives:** The present study, hence, intended to study healthy older subjects to attain a BAEP data normalized for age and gender for this less routinely studied age group. **Materials and Methods:** BAEP was recorded in 80 healthy normoacusic subjects (40 males and 40 females) in the age group of 41-80 years. BAEP latencies were compared in different age groups by one-way ANOVA. Correlations of latencies with age were performed using Pearson correlation coefficient. Gender differences in the older subjects were studied by unpaired *t*-test. $P < 0.05$ was considered as statistically significant. **Results:** Age-related increase with statistical significance was observed for the absolute latencies of Wave III and V and interpeak latencies (IPLs) I-III and I-V. Males exhibited increased absolute and interpeak BAEP latencies as compared to females, with statistical significance for Wave V and I-V IPL. **Conclusion:** The study supports the impairment of central conduction time in the healthy older subjects due to aging with the possibility of the involvement of both superior olivary complex and the inferior colliculus in the auditory pathways. Older subjects also demonstrate gender variations in BAEP latencies in the form of increased latencies in males. The available data can increase the accuracy of electrophysiological evaluation in the older subjects.

KEY WORDS: Aging; Brainstem Auditory Evoked Potentials; Older; Absolute Latency; Interpeak Latency

INTRODUCTION

Older people constitute a rapidly growing proportion of the world's population. India's population share of 60 years and older is suggested to climb from 8% in 2010 to 19% in 2050, according to the United Nations Population Division (UN, 2011).[1] This profound shift in the older population also brings with it, a variety of social and economic challenges. It is emphasized to understand the course and implications of aging and provide the data for this proportion of population. Newer and advanced recording techniques have increased our understanding of the detailed physiologic functions and might serve to provide insight into the aging physiology. Aging involves many physical, biological, chemical, and psychological changes, and the brain is no exception to this phenomenon. Slower or compromised neurotransmission in the neural auditory pathways based on the physiologic changes due to aging has been suggested by several studies.[2,3] A significant loss of spiral ganglion cells is one of the most definitive consequence of human aging.[4] Otte et al. (1978) showed that audiograms and basic speech reception thresholds are often fairly normal despite substantial loss of spiral ganglion cells in elderly people. A loss of ganglion cells would be expected to reduce

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the number of information channels from cochlea to central auditory system.[5]

Brainstem auditory evoked potentials (BAEPs) allow for the evaluation of central neural conduction and age-related transmission delays within the auditory pathways can be measured. Birren and Fisher, 1995, suggested that the measurement of evoked potentials provides a window into the temporal nature of neural processing.[6] More specifically, the latencies of BAEP can provide information regarding the time involved in processing the information as it travels through the various segments of the auditory pathway.

BAEP occurs as a series of seven waves generated in brainstem auditory areas within around 10 milliseconds of an auditory stimulus. The best waveforms are suggested to be produced using broadband click stimuli. Of the seven waveforms, termed as I-VII, the most clinically useful waves are Waves I, III, and V which are suggested to arise from auditory nerve, superior olivary nucleus, and inferior colliculus, respectively.[7] BAEP interpeak intervals are considered to represent true central conduction time within the auditory pathways and are used diagnostically in many focal brainstem pathologies, for example, acoustic neuromas, demyelination, and brainstem infarcts. It is essential, however, to have a control data of the same, excluding age-related hearing loss.

Studies in the past document aging changes affecting the BAEP latencies.[8-11] Such aging changes have been reported as increase in both absolute and interpeak latencies (IPLs) of auditory evoked potentials. However, the findings exhibit lack of uniformity in the different studies. Trune et al. (1988) have observed significant prolongation of Wave III only.[9] Costa et al. (1990) obtained an age-related prolongation of latency values which was marked for Wave I only, and the findings were not in agreement with the possibility of central conduction delays in the aging.[10] Hence, the evidence for age-related increase in IPLs has still been controversial.[10,12,13]

On the other hand, gender, which is another confounding variable, has also been suggested by majority of the studies to affect BAEP latencies. The effect is evident as increased BAEP latencies in males as compared to females. Although gender influence has been widely studied in the adults, yet studies providing data for older subjects are fewer in comparison.[14-16] Hence, the aim of the present study was to contribute to researches on aging and auditory system by recording BAEPs in the healthy older subjects. The study intended to provide a data comprising the effects of age and gender for this older age group, so that it could make the clinical assessment, in this group of subjects, valid and adequate.

MATERIALS AND METHODS

The study was conducted on 80 healthy adults in the age group of 41-80 (40 males and 40 females). It was a cross-sectional analytical study. BAEP was recorded in electrophysiology laboratory in the Department of Physiology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala and the subjects were selected after having fulfilled the inclusion criteria of the study. Approval from the Institutional Ethical Committee was obtained to carry out the research work. The subjects underwent a complete neuro-otological examination. A written informed consent was taken for the test and a detailed clinical history obtained

Inclusion criteria for the study comprised adult healthy subjects in the age group of 41-80 years with normal neuro-otological examination. Exclusion criteria included otological disorders, systemic diseases such as diabetes-mellitus and hypertension, endocrine disorders, 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.

BAEP recording was done on Allengers Scorpio-EMG, EP, NCS in electrophysiology laboratory in a quiet environment. Subjects were informed about the test, 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 the American Clinical Neurophysiology Society.[17] Preparation of scalp skin was done before the electrode placements. 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.[17] Monaural auditory stimulus with rarefaction clicks (0.1 ms pulse) was provided. Click intensity of 80 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 Waves I, III, and V and IPLs I-III, III-V, and I-V. All the data were expressed as mean ± standard deviation.

The subjects were classified into four different age groups: Group I (41-50 years), Group II (51-60 years), Group III (61-70 years), and Group IV (71-80 years). The effect of age in different age groups was compared and analyzed using one-way ANOVA and *post hoc* test (Tukey multiple comparison test). Correlations of age with BAEP latencies were obtained using Pearson correlation coefficient. The effect of gender

was obtained by unpaired *t*-test. Statistical analysis was done using SPSS (Statistical package for social science) version 20.0 statistical software. The analysis was done at 5% level of significance.

RESULTS

Mean age of the study group (40 males and 40 females) was 60.2 ± 11.1 years demographic and anthropometric data for males and females revealed no statistically significant differences in mean ages for males (60.3 ± 11.3 years) and females (60.08 ± 11.2 years) while height, weight, and head sizes (measured from nasion to inion) were statistically significantly different (Figure 1).

Subjects were classified into 4 categories based on the age groups. Group 1: 41-50 years, Group 2: 51-60 years, Group 3: 61-70 years, and Group 4 comprised 71-80 years of subjects. BAEP absolute and IPLs were compared among the subjects in four different age groups (Figure 2). Absolute latencies of Wave III and V increased with age (one-way ANOVA). The statistical significance was found between Group 1 and Group 4 for Wave III and Group 1 and 3 as well as Group 1 and 4 for Wave V (*post-hoc* tests) (Table 1). IPL

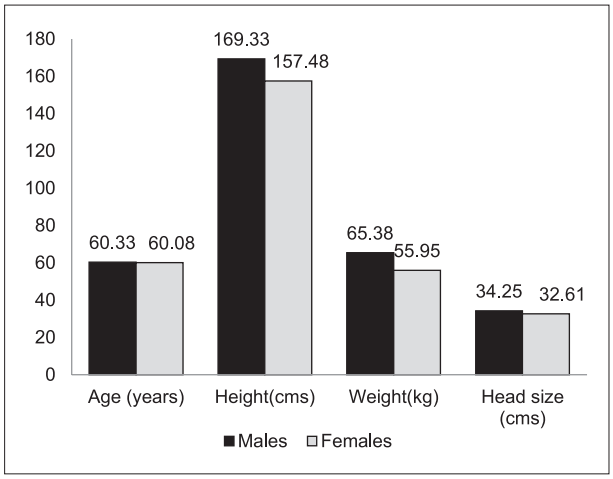

Figure 1: Demographic and anthropometric data compared in older males and females

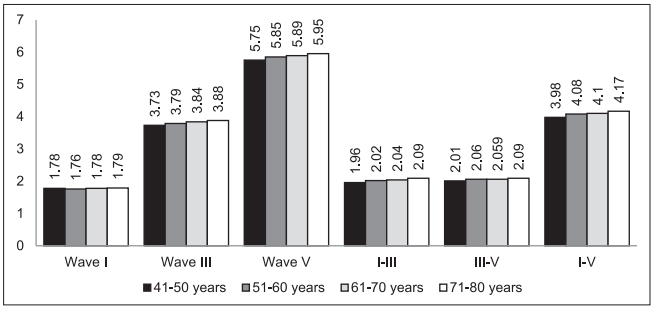

Figure 2: Mean brainstem auditory evoked potential absolute and interpeak latencies (mean ± standard deviation) in different older age groups

comparisons exhibited significant variations too with I-III and I-V showing statistically significant increase in Group 4 as compared to Group 1 (*post-hoc* test) (Table 2). Correlation studies for age and BAEP latencies revealed a statistically significant positive correlation ($P < 0.01$) for absolute latency of Wave III and V and IPL I-III and I-V with age (Table 3). The influence of gender was assessed by comparing the latencies in males and females by unpaired *t*-test. Absolute latency of Wave V and IPL I-V was found to be greater in males as compared to females with statistically significant difference $P < 0.01$ and $P < 0.05$, respectively (Table 4).

DISCUSSION

Recent trends in increase in the older population necessitate the importance of understanding the course and implications of aging. Acquisition of the data for this proportion of population can contribute to better clinical evaluations of this group of subjects. BAEP can prove to be a useful tool to document age-related signal transmission delays within the auditory brain stem. Aging, in the absence of age-related hearing loss (presbycusis) has been found to affect BAEP latencies.[10,13,18] There is some variability in this effect such that not all older systems demonstrate slowing.[19] Furthermore, age-related increase in IPLs has been inconsistent in previous studies.

The present study has included 80 normoacusic older subjects to obtain BAEP records to assess the influence of age and gender in the study group. The study demonstrates statistically significant increase ($P < 0.05$) in the absolute latency of Wave V and Wave III with nonsignificant variations in Wave I absolute latency (Table 1). IPLs I-III and I-V also exhibited increase with age ($P < 0.05$) (Table 2). Correlation studies revealed the similar results with statistically significant positive correlation of absolute latency of Wave III and Wave V and IPL I-III and I-V with age (Table 3). The results of the present study comply with previous similar study by Harinder et al. (2010) who studied 150 healthy adults in the age group of 15-29 years, 30-45 years and 46 years onwards.[20] Furthermore, Rowe (1978) reported prolongation of wave peak latencies and I-III IPL with age with no significant change in III-V IPL with age as found in our study.[8] In a similar previous study by Khatoon et al. (2012), older subjects with >50 years of age were compared with young adults and a similar prolongation of Wave III and V and IPLs I-III and I-V was reported.[15] Among other studies which report absolute as well as IPL prolongation, Allison et al. **(**1983) reported an increase in the peak as well as IPLs of BAEP in the normal subjects in the age group of 4-95 years.[21] Oku et al. (1997) demonstrated progressive delay of Wave I, Wave III, and Wave V and lengthening of the interpeak intervals of Waves III-V and I-V in the subjects aged 50-79 years.[22] The results from a study by Chu (1985**)** stated small prolongation in peak latency V and small increase in III-V and I-V in the subjects with 18-76 years of age group.[18]

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

Age group (years)	Number of subjects	(Mean±SD)					
		Absolute latency Wave I		Absolute latency Wave III		Absolute latency Wave V	
		R	L	R	L	R	L
41-50	20 (M=10, F=10)	1.78±0.086	1.77±0.088	3.75±0.1	3.71±0.14	5.77±0.095	5.71±0.088
51-60	20 (M=10, F=10)	1.77±0.08	1.74±0.095	3.79±0.12	3.788±0.12	5.85±0.11	5.84±0.11
61-70	20 (M=10, F=10)	1.766±0.14	1.799±0.11	3.84±0.16	3.84±0.14	5.89±0.17	5.889±0.13
71-80	20 (M=10, F=10)	1.78±0.07	1.79±0.066	3.86±0.07	3.9±0.06	5.94±0.07	5.96±0.06
Total	80 (M=40, F=40)	1.773±0.1	1.77±0.09	3.8±0.13	3.81±0.14	5.86±0.13	5.85±0.14

BAEP: Brainstem auditory evoked potential, SD: Standard deviation, M: Males, F: Females, R: Right, L: Left. $P<0.05$ for the increase in Wave III and Wave V absolute latencies (one-way ANOVA). The difference was statistically significant between Group 1 (41-50 years) and Group 4 (71-80 years) for Wave III ($P<0.05$) and Group 1 and Group 3 (61-70 years) and Group 1 and Group 4 ($P<0.01$) for Wave V (both the ears) by *post-hoc* test

Table 2: Mean BAEP IPL in different older age groups

Age group (years)	Number of subjects	(Mean±SD)					
		IPL I-III		IPL III-V		IPL I-V	
		R	L	R	L	R	L
41-50	20 (M=10, F=10)	1.966±0.118	1.96±0.12	2.03±0.09	2.0±0.13	4.0±0.15	3.95±0.11
51-60	20 (M=10, F=10)	2.03±0.17	2.01±0.12	2.05±0.17	2.07±0.19	4.076±0.15	4.087±0.16
61-70	20 (M=10, F=10)	2.058±0.12	2.023±0.07	2.065±0.15	2.053±0.15	4.12±0.145	4.09±0.14
71-80	20 (M=10, F=10)	2.077±0.06	2.11±0.04	2.095±0.09	2.077±0.097	4.16±0.086	4.17±0.087
Total	80 (M=40, F=40)	2.03±0.13	2.027±0.11	2.06±0.13	2.05±0.15	4.09±0.15	4.075±0.15

M: Males, F: Females, R: Right, L: Left, SD: Standard deviation, BAEP: Brainstem auditory evoked potential, IPL: Interpeak latency. $P<0.05$ for the increase in I-III and I-V IPL (one-way ANOVA). The difference was statistically significant between Group 1 (41-50 years) and Group 4 (71-80 years) for I-III ($p<0.05$) and I-V IPL ($P<0.01$) for both the ears by *post-hoc* test. III-V IPL variations were nonsignificant ($P>0.05$)

Table 3: Correlation coefficient (r) for age and mean BAEP absolute and interpeak latencies (mean±SD)

Correlation coefficient (r) and P value	Absolute latency Wave I		Absolute latency Wave III		Absolute latency Wave V		I-III interpeak latency		III-V interpeak latency		I-V interpeak latency	
	R	L	R	L	R	L	R	L	R	L	R	L
r	0.031	0.18	0.34	0.49	0.41	0.62	0.3	0.35	0.094	0.13	0.3	0.44
P	0.78^{NS}	0.12^{NS}	<0.01	<0.0001	<0.001	<0.0001	<0.01	<0.01	0.4^{NS}	0.25^{NS}	<0.01	<0.0001

R: Right, L: Left, NS: Not significant, SD: Standard deviation, BAEP: Brainstem auditory evoked potential

Similarly, Otto et al. (1982), who studied 86 male subjects in the age group of 60-86 years, reported statistically significant correlation ($P \leq 0.001$) between Wave V and I-V with age.[23]

The age-related significant prolongation of IPLs in the present study along with the many previous studies supports the fact that central conduction time delays in the elderly. However, there are also some studies which only report the prolongation of absolute latencies with no significant variations in IPLs and are not in agreement with the affection of central conduction time in the older subjects. Among such studies, Martini et al. (1990) studied 36 healthy subjects with mean age of 67.2 ±5.8 years and reported latency shift of all wave but did not support central conduction time impairment in the elderly.[12] Harkins (1981) has stated that the elderly group had delayed peak latencies for all BAEP components, but ILs did not reveal variations in the elderly subjects (71.2 years).[13] Similarly, Costa et al. (1990) found age-related prolongation of latency values of only Wave I and the involvement of central acoustic pathways were suggested to be doubtful.[10] Furthermore, Trune et al. (1988) could only found correlation of age with the latency of Wave III.[9]

Our results support the possibility of the fact that age affects neural propagation both at the level of olivary complex (Wave III and I-III) and inferior colliculus (Wave V and I-V). Regarding the studies investigating the physiological changes within the aging auditory system, some investigators have reported primary degeneration of the spiral ganglion cells or loss of fibers that can occur even in the absence of loss sensory

Table 4: Mean BAEP absolute and interpeak latencies in older males and females

Sex	(Mean±SD)									
	Absolute latency Wave I		Absolute latency Wave III		Absolute latency Wave V		I-III interpeak latency		III-V interpeak latency		I-V interpeak latency	
	R	L	R	L	R*	L*	R	L	R	L	R*	L*
Males (*n*=40)	1.78±0.09	1.79±0.1	3.82±0.13	3.84±0.13	5.9±0.12	5.9±0.13	2.05±0.12	2.04±0.11	2.08±0.13	2.07±0.15	4.13±0.14	4.11±0.15
Females (*n*=40)	1.77±0.12	1.76±0.08	3.79±0.12	3.78±0.14	5.82±0.13	5.798±0.12	2.02±0.14	2.058±0.18	2.04±0.14	2.02±0.14	4.06±0.15	4.04±0.15

n=number of subjects, **P*<0.01 for the decrease in the absolute latency of Wave V and *P*<0.05 for interpeak latency I-V in females as compared to males (both the ears) (unpaired *t*-test).
BAEP: Brainstem auditory evoked potential, SD: Standard deviation, M: Males, F: Females, R: Right, L: Left

hair cells.[24,25] Neuronal loss has also been reported in the cochlear nucleus, inferior colliculus, medial geniculate body, and the temporal lobe.[3,26,27] Konigsmark and Murphy found a relation between age and a decrease in the volume of the cochlear nucleus that appeared to be associated with changes in axon size and degree of myelination.[28] Degenerative changes in the myelin sheaths and axis cylinders have also been reported.[27] Other degenerative changes, such as cell size and cell shape irregularities and the possible accumulation of lipofuscin pigments, have been observed in the cochlear nucleus, superior olivary nucleus, inferior colliculus, medial geniculate body, and inferior olive.[3,26]

Gender comparison performed in the older subjects in our study revealed slight prolongation of all the absolute latencies studied (I, III and V) in males as compared to females with statistical significance for Wave V latency (Table 4) ($P < 0.05$) (unpaired *t*-test). IPL variations revealed statistical significance among the gender for I-V IPL (Table 4). The findings comply with the previous similar study by Patterson et al. (1981), who studied the subjects in the age group of 20-79 years and demonstrated Wave V latency prolongation in males.[14] Furthermore, in a study by Michalewski et al., (1980) males exhibited statistically significant Wave V latency prolongation as compared to females as found in our study.[29] Furthermore, Costa Neto et al. (1991) emphasized that significant difference between the gender was evident in Wave V latency.[30] The findings supported that the latency measures (especially Wave V) and interpeak intervals (especially in the I-V interval) are higher in male subjects compared with female subjects. However, Rosenhall et al. (1985) also reported prolongation of Wave III along with that for V and I-V IPLs in males.[31] Among some recent studies which included the older age groups, Yones Lotfi et al. (2012) found significant latency prolongation for Wave I, V, and I-V.[32] Khatoon et al. (2012) reported prolongation in Wave III, V, I-III, III-V, and I-V IPL.[15] Harinder et al. (2010) in their study demonstrated prolonged absolute latency of Wave III and V as well as prolongation of all IPLs in males.[20]

Head size has been speculated by many authors as a factor accounting for gender difference in BAEP latencies.[33-35] Furthermore, some have suggested the role of hormonal influences for gender difference in BAEP latency as the source of the gender variability.[36,37] In the present study, hormonal influences have little role to play as the study group comprised older subjects. Furthermore, evidence regarding hormonal influences causing gender differences in BAEP latencies is scarcer. In our study, head sizes varied significantly in males and females which can be attributed to the increased latencies in males.

CONCLUSION

BAEP can be used to document age-related signal transmission delays within the auditory pathways of normoacusic older

subjects. Prolongation of IPLs (I-III and I-V) in the present study, in addition to absolute latency prolongation, supports the affection of central conduction time in the older age group. The results indicate the possibility of the involvement of superior olivary complex and inferior colliculus in the auditory pathways as the levels of affection. Older subjects also demonstrate gender variations in BAEP latencies, revealing increased latencies in males. Older population should be clinically assessed based on the data normalized for age as well as gender to increase the accuracy of the electrophysiological evaluation of the auditory pathways.

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