Age and Gender Effects on Auditory Brain Stem Response (ABR)

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Objectives: Auditory Brain Stem Response (ABR) is a result of eight nerve and brain stem nuclei stimulation. Several factors may affect the latencies, inter-peak latencies and amplitudes in ABR especially sex and age. In this study, the effects of age and sex on ABR were studied.

Method: This study was performed on 120 cases (60 males and 60 females) at a Rehabilitation Center in Tehran, Iran. Cases were divided into three age groups: 18-30, 31-50 and 51-70 years old. Each age group consists of 20 males and 20 females. Age and sex influences on absolute latency of wave I and V, and IPL of I-V were examined.

Results: Independent t test showed that females have significantly shorter latency of wave I, V, and IPL I-V latency (P-value <0.001) than males. Two way ANOVA showed that latency of wave I, V and IPL I-V in the 51-70 year old group was significantly higher than the 18-30 and 31-50 year old groups (P-value<0.001).

Conclusions: According to the results of the present study and similar studies, in clinical practice, different norms for older adults and both genders should be established.

Keywords: ABR, gender, presbycusis, central auditory pathway, brain stem time

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Introduction
Auditory Brain Stem Response (ABR) is an onset response (1, 2) and is a set of waves that occur in about 10 milliseconds (ms) after delivering a transient stimulus, mainly a click. This response is a result of eight nerve and brain stem nuclei (up to midbrain) stimulations (1, 3). This objective response is widely used for detecting auditory thresholds in infants and patients who have difficulty in behavioral auditory tasks like mentally retarded patients (4). In addition, ABR is one of the non-invasive and inexpensive diagnostic tests for eight nerve and brain stem pathologies, especially acoustic schwannoma (4, 5). In humans ABR generally has seven waves, I through VII. Each is originated from different parts of the auditory pathway (3). The most important components of ABR are waves I, III and V. Other components are highly variable and may not present even in normal cases (1, 3).

Generators of wave I to V are: distal part of the eighth nerve, proximal part of eighth nerve, cochlear nucleus, superior Olivary complex, and lateral leminiscus near the inferior colliculus (1, 5).

In humans, ABR can be recorded from about 26 weeks of gestational age (GA). After that, waves develop rapidly until term birth. From birth ABR continues development more slowly and in 18-24 month children, all the components are completely mature and adult-like (1, 5).

ABR is an early auditory evoked potential (AEP) and is not affected by sedatives (6, 7), and general anesthetics (8) so this test is a useful tool for assessing non-cooperative populations such as infants, young children and severe mentally retarded patients (1, 4, 5).

In general the ABR changes can be seen with neurological maturation and functional integrity of the brainstem (5). In particular, wave V is the most constant and most prominent of the ABR, and is widely used for objective audiometry. The analysis of this wave can identify pathological processes in the brainstem (1, 5). In diagnostic audiology, inter-peak latency interval (IPL) or inter-wave interval (IWI) of main ABR components especially I-V are very important because IPL I-V reflect the central conduction time (CCT) or brain stem conduction...
time (BCT). CCT reveals the functional state of brain stem and its deficit indicates neurological pathologies (5, 9, 10).

Several factors may affect the peak latencies, IPL and wave amplitudes in ABR. These factors are classified as recording variables (electrodes, reference, filters), stimulus variables (stimulus intensity, stimulus rate, stimulus mode and stimulus phase) and subject variables (age, sex, body temperature, and cochlear hearing loss). Subject variables especially ‘age’ and ‘gender’ have powerful influences on ABR (11). It has been shown that females may have shorter ABR latencies and IPL latencies than males. Also, in the elderly ABR waves have delayed latencies in comparison to young adults (12-15).

In interpretation of ABR in individual patients, it is important to consider subject variables affecting ABR waves, especially IPLs. Otherwise, our findings would be misleading. In this study, age and sex effects on ABR were studied. The Aim of this research was to determining age and sex influences on absolute latency of wave I and V, and IPL of I-V in four age groups from 18 to 70 years old. Most previous studies have not considered hearing loss in the elderly as a confounding variable so their findings are uncertain, but in this study only normal-hearing cases with hearing thresholds $\leq 30$ dBHL were used. This study was performed on 120 participants at the ‘University of Social Welfare & Rehabilitation Sciences’ Akhavan Rehabilitation Center in Tehran, Iran, SPSS software version 13 was used for statistic data analysis. Independent t test and two-way ANOVA were applied.

Method
This study was performed on 120 cases (60 males and 60 females) at the ‘University of Social Welfare & Rehabilitation Sciences’ Akhavan Rehabilitation Center in Tehran (Iran) between 2010 and 2012. Participants were selected from patients with tinnitus, dizziness, or vertigo symptoms, and the Akhavan Rehabilitation Center (ARC) staff. All the participants signed a written consent and were volunteers. Cases were divided into three equal age groups: 18-30 years old, 31-50 years old and 51-70 years old. Each age group consisted of 20 males and 20 females.

Inclusion criteria were as follows: Normal otoscopy (Riesterotoscope), tympanogram $A_{a}$ (Zodiac 901 of Madsen), acoustic reflex being present (Zodiac 901 of Madsen), hearing threshold $\leq 30$ dBHL (Clinical Audiometer AC 33 and headphone TDH-39p of Telephonics) and good ABR morphology at 80 dBnHL (ICS Charter EP 2000, Madsen-Aurical and Insert phone ER-3A). Cases did not have any significant neurologic and audiologic problems.

For recording ABR, click stimulus at 80 dBnHL, with rarefaction polarity, the presentation rate of 11.1/s, 100-3000 HZ filtration was used. Response was average of 1024 accepted sweep and time window of recording was 15 msec. Stimuli were presented through Insert phone ER-3A. Disc gold electrodes with conductive gel were applied on the forehead (ground electrode), ipsi-lateral mastoid (active electrode) and contra-lateral mastoid (reference electrode). Before applying electrodes, mastoids and forehead were cleaned by using abrasive material. Impedance of electrodes was below 5 KOhms and inter-electrodes impedance was below 2 KOhms.

Results
The SPSS version 13 was used for statistic analysis. There were 60 males and 60 females aged 18 to 70 years old. Each gender group had three age groups: 18-30 years old (20 males and 20 females), 31-50 years old (20 males and 20 females), and 51-70 years old (20 males and 20 females). The right ears of all cases were selected to neutralize ear effect. Descriptive information about latencies in sex and in three age groups is summarized in table (1) and (2) respectively.

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<th>Table 2: Descriptive analysis of ABR latencies in three age groups</th>
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Charts (1), (2) and (3) show mean latency of wave I, V and I-V IPL for different gender and age groups.

**Chart 1. Mean latency of wave I**

**Chart 2. Mean latency of wave V**
Independent t test was done to compare ABR latencies between the two sexes. This analysis showed that females have significantly shorter wave I latency (male mean value=1.51, female mean value=1.40, with P-value<0.001), shorter wave V latency (male mean value=5.90, female mean value=5.60, with P-value<0.001), and shorter IPL I-V latency (male mean value=4.39, female mean value=4.19, with P-value<0.001) than males. Then two-way ANOVA was done to compare ABR latencies between three age groups in both sexes. Homogeneity of variances showed variances were equal for latency of wave I (P-value=0.08), wave V (P-value=0.10) and IPL I-V (P-value=0.14) in all age groups. There was an interaction between sex and age groups (P-value=0.003). Two-way ANOVA showed that latency of wave I in the 51-70 years old age group (mean=1.52 ms) was significantly higher than 18-30 (mean=1.41 ms) and 31-50 years old (mean=1.44 ms) age groups (P-value<0.001); latency of wave V in 51-70 age group (mean=5.88 ms) was significantly higher than 18-30 (mean=5.65 ms) and 31-50 years old (mean=5.73 ms) age groups (P-value<0.001), and latency of wave V in 31-50 years old age group was significantly higher than 18-30 years old age group (P-value<0.001). Moreover, it was shown that IPL I-V in the 51-70 year-old age group (mean=4.35 ms) was significantly higher than 18-30 (mean=4.23 ms) and 31-50 years old (mean=4.29) age groups (P-value<0.001), and that IPL I-V in 31-50 year olds was significantly higher than the 18-30 year-old age group (P-value<0.001).

**Discussion**

The results indicate that there is a significant difference between males and females in absolute latencies and IPLs of ABR, irrespective of age. Females have shorter absolute latencies and IPLs in ABR. Furthermore, this study shows that absolute latencies and IPLs of ABR increase with aging especially in the 51-70 year-old interval. These findings are in agreement with other studies (e.g. 5, 12, 13, 28, 29, 39).

It has been reported that females have shorter conduction times and ABR latencies than age-matched males (5, 12, 13), and that gender has more powerful effects on ABR than aging (14-16). Allison et al. (1983) explained this result by difference of body size in males and females (5,17). Head size and consequently the length of the auditory neural pathway is different between the sexes and can lead to ABR waves latency and amplitude discrepancies. Stockard et al. (1978) suggested that the anatomical distance of auditory pathway in females (CCT) might be shorter than males (12) because generators
of ABR components are closer to each other and to the surface electrodes (1). On the other hand, some researchers insist that head size cannot be the only factor for gender difference in ABR latencies (12, 18, and 19).

Indeed, cochlear duct is longer in males than in females, resulting in longer cochlear traveling times in males. In addition, shorter cochlear duct in females results in greater stiffness of the female basilar membrane and may cause earlier ABR latencies relative to males. When velocity of the traveling wave increases it leads to increments of neural synchrony (20). With frequency-specific ABR and high-pass masking, it has been revealed that cochlear response time in females is 13 percent shorter than males (21). Males and females are different in cochlear processes. It has been shown that SOAEs are more prevalent and stronger in females than males and TEOAEs have larger amplitude in females (22). Moreover, the activity of the olivo-cochlear bundle (OCB) which is a part of the efferent auditory system is different between males and females. Researches show that the auditory efferent system is more active in males and this could affect peripheral mechanisms (23). Additionally, behavioral and imaging studies have shown that in males and females the auditory cortex has different ways for processing acoustic stimuli. For example, fMRI studies have identified that in females, language areas of cortex show stronger activation (20). These differences are under the influence of hormones especially estrogen (19, 20, 24). Gender difference of hearing is reduced during menopause and in females who have a male twin. In support of this hormonal explanation, females with Turner syndrome, a chromosomal abnormality resulting in estrogen deficiency, demonstrate longer click-ABR latencies and earlier presbycusis, similar to males. Auditory thresholds show variations with the menstrual cycle in females (20). Electroencephalography (EEG) and ABR show fluctuations during menstrual cycle (25-27). In Menière's disease, auditory symptoms are exacerbated during the premenstrual phase because estrogen levels are in their lowest state during this phase (20).

Many authors have reported increments of ABR latencies with advancing age and decrement of neural conduction velocity (increment CCT) in older people. As mentioned in earlier studies, advancing age will directly affect the peak latencies and IPLs of ABR waveform components (28-31). Most studies have shown that in the age range of 25 to at least 55 years old, ABR latencies increase 0.2 ms (32). Between 60 and 86 years old, IPL I-V increases significantly (33-35). Allison et al. (1984) and Dorfman and Bosley (1979) explained this as an age-related decrease in the peripheral (cochlear) and central conduction velocity. Other explanations are axonal dystrophy especially in myelinated fibers, demyelination, neurotransmitter alterations, or vascular and biochemical changes (5). Moreover, central nervous system dysfunctions are common in patients with essential hypertension (36, 37). Dysfunction of brain in hypertension is a result of arterial and arteriolar spasm in cerebral blood vessels and micro-infarctions. A variety of clinical sensory and motor signs and symptoms along with dizziness, vertigo, tinnitus and occipital headache in patients of essential hypertension suggest the micro-vascular insufficiency of the brain. Such type of micro-vascular damage may alter ABRs. Essential hypertension may also be due to micro-vascular damage in the peripheral nervous system like peripheral neuropathy. Given the high prevalence of hypertension in older subjects, it could lead to reduction of neural conduction velocity and increase in ABR wave latencies and IPLs (37).

In many studies of presbycusis, the hearing thresholds of young and older participants are not matched and there is hearing loss in older people especially in high frequencies. This hearing loss is a confounding factor and makes it difficult to separate aging effects from threshold effects (1, 13, 38). Oku and Hasegawa (1997) compared the ABR and ECOG in young and older participants (50–89 years old). The old group had normal hearing thresholds at 0.5–2 kHz, but their thresholds were between 35 to 72 dB HL at 4–8 kHz. The latencies of Waves I, III, and V showed a progressive delay in the older group, but it was attributed to high frequency hearing loss and it was difficult to rule out hearing loss effects on the ABR latency (30, 39). Martini et al. (1991) reported that normal-hearing older adults in the frequency range of 0.25–2 kHz who had mild high frequency loss at 4 kHz and above, had delayed latencies for Waves I, III, and V compared to normal-hearing young adults. These differences were considered to be due to the mild hearing loss at 4 kHz and were not exclusively due to aging (39). But the present study showed that increase in ABR latencies is independent of hearing thresholds because all the participants had normal hearing thresholds.
Conclusion
The results of this study among others show that subject variables (age and sex) have statistically significant influence on ABR latencies. Therefore age and sex can affect ABR interpretation and clinicians should consider them in clinical settings. It is recommended that in clinical practice, different norms be established for different age groups and genders.
We conclude that if female norms be used for both sexes, then all males may fall into abnormal (late) ABR criteria and if male norms be applied to both sexes, neurological pathologies in females may not be detected. Furthermore, our study shows that irrespective of the hearing threshold, in the elderly, ABR latencies are longer than young adults and misinterpretations may take place if their norms are used interchangeably.

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