Original article

Correlation between age and gender, and parameters of auditory brainstem evoked response

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Objective To analyze the correlation between age and gender, and the auditory brainstem response (ABR).

Materials and methods Adult volunteers with no history of ear disease were tested. ABR parameters; stimulated by click stimuli at 90 and 80 dBnHL, were analyzed. They included 1) absolute latencies of waves I, III and V, 2) interpeak latency of I-III, III-V and I-V, and 3) interaural latency difference of waves V between the ears.

Results Sixteen males and 34 females, aged 25-66 years (mean 42.3±10.4 years) were include in the analysis. ILD-V at 80 dBnHL clicks showed significant correlation with increased age, and the equation predicted its value at 0.012 + [0.003 * age (years)]. The absolute latency of waves III and V at 90 dBnHL clicks (*p*-value = 0.010, 0.024) in the males was significantly higher than the 80 dBnHL clicks (*p*-value = 0.014, 0.017) in the females. There was no significant correlation between 1) age and absolute latency at 80 or 90 dBnHL clicks; 2) age and interwave latency at 80 or 90 dBnHL clicks; and 3) age and ILD-V at 90 dBnHL clicks.

Conclusion ILD-V at 80 dBnHL clicks correlated with increased age. The absolute latency of waves III and V in the males was significantly higher than in the females at both 80 and 90 dBnHL clicks. Clinicians need to be cautious when interpreting ABR results in the elderly with increased ILD-V value at 80 dBnHL clicks, or in males with delayed absolute latency of waves III and V at 80 and 90 dBnHL clicks. **Chiang Mai Medical Journal 2015;54(4):163-9.**

Keywords: auditory brainstem response, absolute latency, interpeak latency, interaural latency difference

Introduction

An auditory evoked response is activity within the auditory system produced or stimulated (evoked) by sound (auditory or acoustic stimuli) via electrodes. In the simplest of terms, auditory evoked responses are brain waves (electrical potentials) generated and picked up by electrodes when a person is stimulated by sound. Their three major categories are classified by latency and an analysis period (epoch). Latency is the time interval (in milli-

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Received: July 1, 2015, **Accepted:** November 10, 2015.

seconds; msec) between stimulus presentation and the appearance of waveforms. The three categories are: 1) early response, e.g., electrocochleography (ECochG), which occurs at the first 1.5-2.0 msec, and auditory brainstem response (ABR) that occurs within 5-6 msec; 2) middle response, e.g., auditory middle-latency response (AMR), which occurs within 15-50 msec; and 3) late response, e.g., auditory latency response (ALR), which occurs within 75-200 msec, auditory P300 response that occurs at approximately 300 msec, and mismatch negativity (MMN) response occurring within 100-300 msec after specific stimuli. The two most common alternate terms for ABR are brainstem auditory evoked responses (BAER) and brainstem auditory evoked potential (BAEP)[1].

ABR is an objective response that assesses auditory function from the peripheral auditory system to the lower brainstem level[2]. Most ABR waveforms are plotted in the time domain, which is a sequence of peaks (amplitude of greater voltage) and valleys (amplitude of lower voltage) (in microvolts) occurring within a specific time period (in msec). ABR wave components are labeled with Roman numerals as wave I to wave VII[3]. Generators of ABR waves are based on many sources: e.g., recording in experimental animals with surgically induced central nervous system (CNS) lesions, or in humans during neurosurgical procedures. The presumed generators are in the medulla, pons, midbrain and thalamus, which include the ipsilateral distal auditory nerve (wave I), ipsilateral proximal auditory nerve (wave II), ipsilateral cochlear nucleus and superior olivary complex (wave III), bilateral multiple brain origins (wave IV), contralateral lateral lemniscus termination at the inferior colliculus (wave V), and medial geniculate body (wave VI and VII) [4]. These generators are in the retrocochlear pathway. Peaks often missing in normal ABR waveforms include wave IV, wave II, and wave VI[3]. Wave I, wave III, and wave V are usually well formed, repeatable, and commonly used for analysis.

The main parameters of the ABR waveform are latency and amplitude, and latency is used predominately as a neurodiagnostic test. When compared to wave latency, wave amplitude is more variable[5]. Latency is an absolute measurement calculated from the onset of stimulus to some point on or near the peak of an ABR waveform. Latency interval is calcu lated commonly between waves, including latency of wave I to wave III, wave III to wave V, and wave I to wave V[3]. The interaural latency difference (ILD) for wave V is the absolute latency difference of waveform V between the ipsilateral recordings of each ear. The ILD for wave V was used most often by early investigators of ABR[6].

Normative values of ABR parameters have a critical effect on determining abnormal results. The site of a lesion can be determined by other audiologic tests such as speech discrimination, the tone decay test and acoustic reflex test, and ABR is the most sensitive in detecting retrocochlear pathology[2]. Vestibular schwannoma is the pathology of most concern in the retrocochlear pathway by causing asymmetrical hearing loss. While magnetic resonance imaging (MRI) of the internal acoustic canal (IAC) with gadolinium is the most sensitive test for diagnosing retrocochlear pathology, it has some limitations. The high cost of MRI as a screening test is a major limiting factor. ABR at Chiang Mai University (CMU) hospital costs 15.8 times less (700 Baht) than for MRI of the IAC with gadolinium (11,100 Baht), which is similar to costs at the Christian Medical College and Hospital, Vellore, India (15 times greater)[2]. Other limiting factors of MRI include patients with claustrophobia, obesity, and noise intolerance[2]. Effective utilization of scarce funding and medical resources, as well as precise diagnosis in each disease should be balanced wisely, especially in developing countries. The higher the accuracy rate in ABR evaluation, the lower the MRI budget (fewer MRIs required).

The aim of this study was to analyze the correlation between age and gender, and the ABR response.

Materials and methods

Subjects without a history of ear disease, and aged 25-66 years were recruited into this study at CMU Hospital. Ear examination, tympanometry, and acoustic reflex of all volunteers showed normal findings. The pure tone audiometry test showed a normal air-bone gap of less than 10 dB in all tested frequencies, and the pure tone average (PTA) hearing threshold at 0.5, 1, and 2 kHz, as well as hearing threshold, was less than 50 dB at 4 kHz. Subjects with presbycusis could be enrolled into the study, but any with skin lesions on the areas of electrode application, high skin impedance after electrode placement, or absence of ABR in either ear were excluded. The study was approved by the CMU Ethics Committee. The subjects of this study gave their informed consent.

The skin was cleansed with alcohol and scrubbed with an abrasive skin preparation. Gold cup electrodes filled with conductive paste were placed on the right and the left mastoid tips (active or inverting electrode), high on the forehead (inactive or non-inverting electrode), and on the lower forehead (ground electrode). The subjects were allowed to lay down in supine position with their eyes closed. The testing room was quiet and air-conditioned, with the temperature set at a comfortable level. Rare fraction, with click stimuli at 90 and 80 dBnHL was presented ipsilaterally via an ER3A inserted earphone (Etymotic Research, Elk Grove Village, IL, USA) at a rate of 19.3 clicks/second. The signal was amplified and filtered (bandpass 100-3,000 Hz). The responses at the first 10 msec, total of 1,024 sweeps, were acquired for each recording by using the Intelligent Hearing System, Miami, Florida, USA. The waveforms were labeled by one technician and reviewed by the authors. Demographic data, and the following ABR parameters: 1) absolute latencies of waves I, III and V; 2) interpeak latency of I-III, III-V and I-V; and 3) interaural latency difference of wave V between the ears, were collected. Pearson's correlation was used to analyze the correlation between age and each parameter. If the value showed significant correlation, simple linear regression was used to analyze the equation predicting the value of each parameter. The difference between the parameters and gender was analyzed using the t-test. A *p*-value <0.05 was considered statistically significant. The SPSS 17.0 program (SPSS Inc, Chicago, IL, USA) was used for analysis.

Results

ABR was obtained from 51 volunteers (16 males and 35 females). One female subject was excluded for showing no ABR from her right ear. One hundred ears were analyzed. Ages of the subjects ranged from 25-66 years (mean 42.3±10.4 years± standard deviation; SD).

The *p*-value of Pearson's correlation between ABR and age is shown in Table 1. Only ILD-V at 80 dBnHL clicks showed significant correlation with age. Scatter plots of the ILD-V at 80 dBnHL clicks and slope estimates of response change by age (Figure 1). The equation predicting the ILD-V value at 80 dBnHL clicks was 0.012 + [0.003 * age (years)] (msec) (simple linear regression).

The differences in ABR included absolute latencies of waves I, III and V, interpeak latency of I-III, III-V and I-V of 100 ears, and interaural latency differences of wave V and *p*-value between males and females. These results are shown in Table 2. The absolute latency

Table 1. The r and *p*-value of correlation between ABR and age at 90 and 80 dBnHL clicks

Correlation between		r (*p*-value#)	
		80 dBnHL clicks	90 dBnHL clicks
Age and absolute latency of	I	-0.022 (0.83)	0.024 (0.81)
	III	0.044 (0.67)	0.084 (0.41)
	V	0.051 (0.61)	0.037 (0.72)
Age and interwave latency of	I-III	0.059 (0.56)	0.064 (0.53)
	III-V	0.029 (0.77)	-0.19 (0.85)
	I-V	0.064 (0.53)	0.022 (0.83)
Age and ILD-V		0.305 (0.03*)	0.208 (0.15)

Note: #Pearson's correlation, *statistically significant

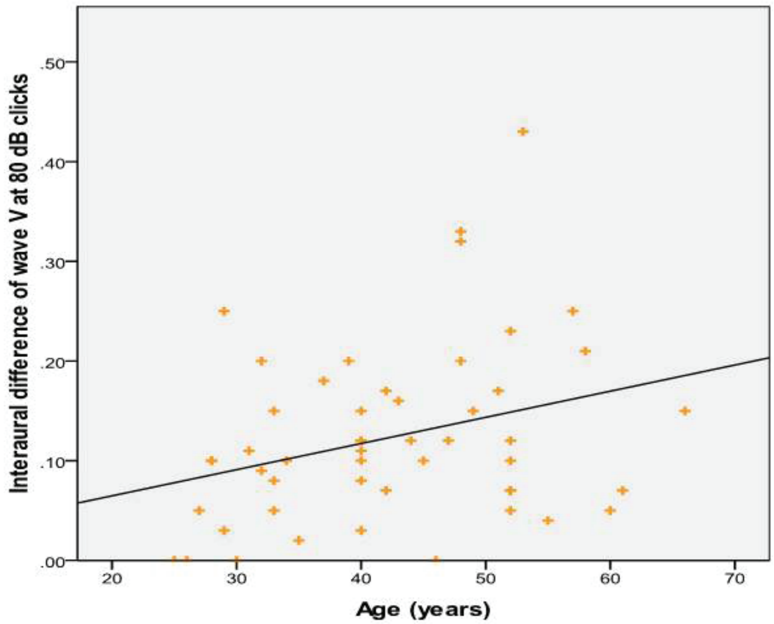

Figure 1. Scatter plots showing ILD-V at 80 dBnHL clicks and slope estimates of response changes by age.

of waves III and V at 90 and 80 dBnHL clicks in males was significantly higher than that in females. No other parameters displayed any gender differences.

Discussion

To develop normative ABR values, a variety of factors that affect ABR waveforms must be controlled. These factors include: 1) non-pathological subject factors: e.g., age, gender, body temperature, muscular artifact, medication, and hearing level; 2) stimulus factors: e.g., stimulus type (click, tone burst), rate, and intensity; and 3) acquisition factors: e.g., electrodes, amplification, filtering, and analysis time[3]. In this study, all subjects were examined by the authors, with no abnormal clinical symptoms detected. Before their enrollment, the hearing level of the subjects was evaluated by pure tone audiometry. Only subjects with acceptable audiogram results were recruited. During the test, the subjects were asked to relax, and the muscular artifact was then recorded and controlled. Recording of the ABR was performed in the same room with identical environment, and the stimulus was set up in the same setting. The ABR was acquired, amplified, and filtered using a single machine. Norms of ABR to click stimulus in this study were comparable to those of other studies, as shown in Table 3. Delayed ABR norms in this study certainly conformed to the pathology of the subject.

In this study, ABR parameters: 1) an ILD-V value at 80 dBnHL clicks stimulation (difference by age); and 2) absolute latency of waves III and V at 90 and 80 dBnHL clicks stimulation (difference by gender), may need to be considered when using age and gender. Adult females showed shorter latency values and larger amplitudes than males for wave III and V. The explanation offered for gender effect is smaller head size and brain dimensions, better hearing sensitivity, and higher average body temperature in females[3,14]. Watson DR (1996) reported earlier wave V latencies and shorter I-V intervals in females than in males[6]. Solanski JD (2010) also reported shorter I-III and III-V interwave latencies in teenage females than in teenage males[14]. Therefore, clinicians should consider the clinical significance of the parameters that show statistically significant differences between males and females.

Table 2. Differences of mean (SD) and *p*-value of the ABR parameter at 90 and 80 dBnHL clicks in males and females

parameter	I	III	V	I-III	III-V	I-V	IAD-V	I	III	V	I-III	III-V	I-V	IAD-V
Males	1.63 (0.18)	3.83 (0.14)	5.76 (0.23)	2.20 (0.14)	1.95 (0.14)	4.13 (0.25)	0.11 (0.10)	1.71 (0.13)	3.88 (0.13)	5.83 (0.21)	2.17 (0.12)	1.95 (0.14)	4.12 (0.21)	0.11 (0.07)
Females	1.56 (0.09)	3.70 (0.16)	5.60 (0.22)	2.14 (0.16)	1.89 (0.17)	4.03 (0.22)	0.13 (0.09)	1.65 (0.10)	3.76 (0.18)	5.66 (0.24)	2.10 (0.18)	1.89 (0.17)	4.00 (0.22)	0.10 (0.07)
p-value#	0.195	0.010*	0.024*	0.201	0.270	0.156	0.437	0.076	0.014*	0.017*	0.171	0.270	0.073	0.437

#t-test, *statistically significant

Table 3. Mean and standard deviation of ABR in adults with normal hearing

Author	Subject	Click intensity	I	III	V	I-III	III-V	I-V	IAD-V
Kaewsiri 2015	50 adults	80 dBnHL	1.67 (0.12)	3.81 (0.17)	5.72 (0.24)	2.14 (2.14)	1.91 (0.17)	4.05 (0.23)	0.13 (0.09)
		90 dBnHL	1.58 (0.13)	3.75 (0.16)	5.65 (0.22)	2.17 (0.16)	1.9 (0.15)	4.07 (0.23)	0.10 (0.07)
Konrad-Martin 2012[7]	81-95 adults (40-79 years)	75 dBnHL	1.67 (0.2)	3.83 (0.2)	5.72 (0.3)	2.16 (0.2)	1.90 (0.3)	4.04 (0.3)	NA
Petrova 2009[8]	NA	60-70 dB above nHL or SL	1.59 (0.12)	3.76 (0.12)	5.69 (0.20)	2.17 (0.15)	1.93 (0.12)	4.10 (0.21)	0.09 (0.08)
Musiek 1986[9]	46 ears	80 dB nHL	NA	NA	NA	2.05 (0.25)	1.85 (0.45)	3.88 (0.5)	NA
Schwartz 1989[10]	20 ears	80 dB nHL	2.44 (0.098)	4.60 (0.15)	6.50 (0.19)	2.20 (0.16)	1.84 (0.17)	4.04 (0.18)	NA
Antonelli 1987[11]	NA	100 dBpeSPL	1.54 (0.20)	3.73 (0.25)	5.52 (0.96)	2.19 (0.45)	1.79 (0.63)	3.98 (0.58)	NA
Ness DA 2009[5]	20 adults	80 dBnHL	1.59 (0.11)	3.77 (0.11)	5.46 (0.20)	2.18 (0.11)	1.70 (0.16)	3.87 (0.20)	NA
Joseph, West, Thorton, Herman 1987[12]	786 adults	NA	1.65 (0.14)	3.80 (0.18)	5.64 (0.23)	2.15 (0.14)	1.84 (0.14)	3.99 (0.20)	0.00 (0.11)
Mohammad FT 2007[13]	19 adult 40-50 years	90 dBHL	1.67 (0.015)	3.82 (0.122)	5.75 (0.032)	2.15 (0.003)	1.93 (0.090)	4.08 (0.017)	NA
Solanki JD (2010)[14]	23 teenage males	60 dB	1.76 (0.18)	3.73 (0.14)	5.75 (0.79)	2.29 (0.26)	1.77 (0.20)	4.03 (0.20)	NA
	23 teenage females		1.70 (0.19)	3.71 (0.17)	5.72 (0.08)	1.95 (0.22)	2.05 (0.18)	4.00 (0.18)	NA

Both ABR peaks and interpeak latencies became higher with advancing age[7,13,15]. All parameters, except for absolute latency of wave I and interwave III-V, showed a positive correlation in this study. No previous studies reported a negative correlation of ABR with age. Increased hearing loss, rise of age-related systemic disorders, delayed synaptic transmission associated with age-related loss of neurons, and changes in neuron membrane permeability, all contribute to delayed wave response[3]. Konrad-Martin (2012) reported increased latency of wave V at 0.214 msec over a span of 40 years[7]. Mohammad (2007) found increased I-III, III-V and I-V interpeak latencies with age[13], but the I-V interpeak latency reported by Burkard (2001) showed no difference with age[15]. Rupa and Dayal (1993) proposed a formula to predict wave V latency, i.e. (ms) = 4.911 + 0.007 x hearing loss + 0.004 x age + 0.081 x gender (where the chronological age is in years, and gender is expressed with a value of 1 for females and 2 for males)[16]. This study found a difference in only ILD-V at 80 dBnHL clicks, which showed significant correlation with age. The formula for predicting ABR was analyzed only for this parameter. Data analysis of ILD-V value changes with age from other studies was not available. The formula predicting ABR is helpful when considering ABR abnormalities in patients of advanced age.

Conclusions

ILD-V at 80 dBnHL clicks showed correlation with increasing age. The absolute latency of waves III and V at both 90 and 80 dBnHL clicks in males was higher than that in the females. Clinicians need to be cautious when interpreting ABR results from the increased ILD-V value at 80 dBnHL clicks in the elderly, or delayed absolute latency of waves III and V at 80 and 90 dBnHL clicks in males.

Acknowledgements

This work was supported by the Faculty of Medicine Research Fund, Chiang Mai University, Chiang Mai, Thailand

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ความสัมพันธ์ระหว่างผลการตรวจการได้ยินระดับก้านสมองกับอายุและเพศ

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วัตถุประสงค์ เพื่อวิเคราะห์หาความสัมพันธ์ระหว่างผลการตรวจการได้ยินระดับก้านสมองกับอายุและเพศ

วัสดุและวิธีการ อาสาสมัครผู้ใหญ่ 50 ราย ที่ไม่มีประวัติของโรคหูได้รับการตรวจการได้ยินระดับก้านสมอง โดยกระตุ้นด้วยเสียงคลิกที่ความดัง 90 และ 80 dBnHL วิเคราะห์ผลการตรวจ ได้แก่ 1) absolute latencies ของคลื่นที่ I, III, V, 2) interpeak latency ระหว่างคลื่น I-III, III-V, I-V, 3) ความต่างของ latency ของคลื่นที่ V (ILD-V) ระหว่างหูสองข้าง

ผลการศึกษา อาสาสมัครเป็นชาย 16 ราย หญิง 34 ราย มีช่วงอายุระหว่าง 25-66 ปี (เฉลี่ย 42.3±10.4 ปี) ค่า ILD-V เมื่อกระตุ้นด้วยเสียงคลิกที่ความดัง 80 dBnHL มีความสัมพันธ์กับอายุที่เพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ โดยสมการทำนายค่า ILD-V คือ 0.012 + (0.003 * อายุ (ปี)) absolute latency ของคลื่นที่ III, V ในอาสาสมัครชาย เมื่อกระตุ้นด้วยเสียงคลิกที่ความดัง 90 dBnHL (*p*-value = 0.010, 0.024) และที่ความดัง 80 dBnHL (*p*-value = 0.014, 0.017) มีค่ามากกว่าอาสาสมัครหญิงอย่างมีนัยสำคัญทางสถิติ ไม่พบว่ามีความสัมพันธ์ระหว่าง 1) อายุและ absolute latency เมื่อกระตุ้นด้วยเสียงคลิกที่ความดัง 80, 90 dBnHL; 2) อายุและ interwave latency เมื่อกระตุ้นด้วยเสียงคลิกที่ความดัง 80, 90 dBnHL; และ 3) อายุและ ILD-V เมื่อกระตุ้นด้วยเสียงคลิกที่ความดัง 90 dBnHL

สรุปผลการศึกษา ILD-V เมื่อกระตุ้นด้วยเสียงคลิกที่ความดัง 80 dBnHL มีค่ามากขึ้นเมื่ออายุเพิ่มขึ้น absolute latency ของคลื่นที่ III, V เมื่อกระตุ้นด้วยเสียงคลิกที่ความดัง 90 และ 80 dBnHL ในผู้ชายมีค่ามากกว่าผู้หญิง ดังนั้นหากผลการตรวจพบ ILD-V ที่มากขึ้น เมื่อกระตุ้นด้วยเสียงคลิกที่ความดัง 80 dBnHL ในผู้สูงอายุ หรือพบ absolute latency ของคลื่นที่ III, V ที่มากขึ้น เมื่อกระตุ้นด้วยเสียงคลิกที่ความดัง 90 และ 80 dBnHL ในผู้ชาย การแปลผลการตรวจ จึงควรนำข้อมูลดังกล่าวมาร่วมพิจารณาด้วย **เชียงใหม่เวชสาร 2558; 54(4):163-9.**

คำสำคัญ: การตรวจการได้ยินระดับก้านสมอง อายุ absolute latency, interpeak latency, interaural latency difference