

Effect of Stimulus Rate and Gender on Auditory Brainstem Response in Korean Young Adults

Chul-Hee Choi, Ki-Hyeon Jang, and Seong Hee Choi

Department of Audiology and Speech-Language Pathology, Research Institute of Biomimetic Sensory Control, and Catholic Hearing Voice Speech Center, Catholic University of Daegu, Gyeongsan, Gyeongbuk, Korea

ABSTRACT

The main objective of this study was to determine the effect of stimulus rate and gender on auditory brainstem response (ABR) latency and amplitude in Korean young adults. A total of thirty young adults consisting of fifteen males and fifteen females participated in the study. We performed this study by analyzing the latencies and amplitudes of ABR wave I, III, and V as a function of low stimulus rate and gender. The stimulus repetition rate was changed in five steps: 8, 16, 21, 32, and 64/s. Experimental results showed that when stimulus rates increased, significant differences in the latency and amplitude of wave I, III, and V were observed while a gender effect was found on the latency of wave III and the amplitudes of wave I and III. As stimulus rates increased, the latencies of wave I, III, and V consistently and progressively increased, whereas the amplitudes of ABR waves inconsistently changed. The latency shift became longer in wave V than wave I and III. The amplitude of wave I, III, and V was greatest at a stimulus rate of 21/s and least at a stimulus rate of 32/s, compared to those of other stimulus rates. This study will provide beneficial information in developing proper strategies that optimize and enhance the ABR wave latencies and amplitudes in different gender groups, saving the ABR test time in clinical applications, and establishing a quantitatively normative database for clinical purposes.

Key words: Stimulus rate, Gender, Auditory Brainstem Response (ABR), Latency, Amplitude

INTRODUCTION

After the auditory brainstem response (ABR) had been reported as a transient electrical response resulting from synchronous neural activity of many neurons occurring within the first 10 ms after the introduction of a signal, ABR has been clinically used as an objective measure of auditory function. After

ABR had been introduced in Korea, its clinical efficacy has been widely investigated in a variety of topics such as non-automated (conventional) or automated ABR in screening premature and newborn infants (Choi, 2006; Choi et al., 2004; Jung, 2007; Kim, 2007; Kim et al., 1995), newborns with hyperbilirubinemia (Jo, 2013), normal adults (Cha, 2004; Lee, 2000; Lee & Baek, 1983; Kim & Kim, 2002; Kim et al., 1999; Kim & Lim, 1992; Woo et al., 1995), its usefulness as early predictor of kernicterus in early breast-feeding jaundice (Jang et al., 2007), its value in diagnosing acoustic neuroma (Park et al., 2010), its relationship with hearing thresholds of other hearing tests (Seo et

Submitted: Mar 3, 2015

Revised: Apr 9, 2015

Accepted: Apr 11, 2015

Corresponding Author: **Chul-Hee Choi**

Department of Audiology & Speech-Language Pathology, Research Institute of Biomimetic Sensory Control, and Catholic Hearing Voice Speech Center, Catholic University of Daegu, 13-13 Hayang-ro, Hayang-up, Gyeongsan-si, Gyeongsanbuk-do, 712-702, Korea

Tel +82 53 850 2541, Fax +82 53 850 2540, E-mail cchoi@cu.ac.kr

al., 2012), and the effects of ototoxicity (salicylate, gentamicin, furosemide, cisplatin, lidocaine, and so on), noise-induced hearing loss, and acute acoustic trauma in animal models (Choi, 2011; Lee et al., 2002; Rhee et al., 2012).

Stimulus properties such as rate, duration, intensity, and polarity exert important and profound effects on ABR latencies and amplitudes (Hall, 2007; Parthasarathy et al., 1998). Among stimulus factors, stimulus rate refers to the number of stimuli presented per second to evoke electrical responses. This stimulus parameter must be selected and manipulated by an audiologist measuring ABRs because it reduces test time or allows administration of an accurate and reliable assessment in a given time if properly set up (Hall, 2007). Stimulus rate, an important factor affecting the diagnostic power of ABRs, differentiates neuropathological lesions in the nervous system (e.g. hypoxia and hypercapnia) and demyelinating diseases (e.g. multiple sclerosis) from normal or other lesions (Freeman et al., 1991; Hyde et al., 1976; Palludetti et al., 1983; Santos et al., 2004; Yagi & Kaga, 1979). In general, it has been known that when the stimulus rate increases, ABR latencies increase while ABR amplitudes decrease. However, there have been considerable disagreements between proper stimulus rate and latencies and amplitudes of ABR in normal adults and infants (Sininger & Hyde, 2009). Specifically, increasing stimulus rates (40 and 90.9/s) above 30/s at an intensity level of 55 dB nHL decreased the ABR peak amplitude (Hyde et al., 1976; Suzuki et al., 1986), while an increase in stimulus rate up to 80/s showed no significant differences (Picton et al., 1981). In infants, when the stimulus rate increased, ABR latencies showed larger increases while ABR amplitudes displayed greater reductions (Klein et al.,

1992; Sininger & Hyde, 2009). In cases of high stimulus rates (e.g. 90/s), infants were more vulnerable to the ABR amplitude reduction (Klein et al., 1992). With the stimulus rate up to 50/s, no elevated ABR thresholds were reported in infants (Lasky, 1997). In addition, it has been reported that high stimulus rates ranging from 88.8 to 1,000/s can be used to estimate hearing thresholds along with the maximum length sequence technique, a mathematical method allowing extraction of overlapping ABR stimuli and responses (Lasky, 1997; Leung et al., 1998). Recently, the effects of stimulus rate have been emphasized to reveal the relationship between stimulus timing and temporal processing of speech, because stimulus rate can affect the onset of speech-evoked responses to a greater extent than click-evoked responses by comparing a click and a consonant-vowel speech syllable presented at three low stimulus rates ranging from 6.9 to 15.4/s (Krizman et al., 2010). Although several studies regarding the effects of stimulus rate exist, considerable debate among investigators has occurred regarding the optimal stimulus rate which leads to the proper latency and maximal amplitude of click-evoked ABRs and establishes the criteria or boundary line between low and high stimulus rates. In neurodiagnostic testing, it has been reported that relatively slow stimulus rates less than 20/s are preferable due to its stability, while at high stimulus rates of 50/s, the amplitude of wave V is relatively stable compared to those of wave I and III (Schwartz & Morris, 1991). In contrast, with fast stimulus rates, the amplitudes of ABR wave I and V reduced progressively and consistently (Jiang et al., 1991). There is misunderstanding with regard to the relationship between stimulus rate and stimulus presentation levels in commercially available ABR

systems among audiologists, researchers, and equipment manufacturers (Lightfoot et al., 2007). In Korean literatures of ABR, it was often mentioned that stimulus rate is an important factor affecting ABR results (Kim & Lim, 1992; Lee & Baek, 1983; Woo et al., 1995) but there were no direct research that investigated the systematic effects of changing stimulus rates on ABR amplitude and latency except one study simply compared the stimulus rate of 9/s from that of 20/s (Cha, 2004).

Moreover, subject factors such as gender, age, hearing loss, body temperature, state of arousal, and drugs significantly impact ABR latencies and amplitudes (Hall, 2007). Gender is one of the most influential subject factors affecting the latencies and amplitudes of ABR wave components. Many previous studies regarding gender effects have reported that the ABR latencies of females are shorter than that of males, while the amplitudes of females are significantly larger than males (Hall, 1992). The effect of gender on ABR latency and amplitude may result from physical differences (e.g. smaller head size and less brain volume in females) which result in shorter latencies due to a shorter distance between the neurogenerators and a larger amplitude due to relatively closer recording electrodes (Chambers et al., 1989). In addition, physiological and biochemical differences between females and males can affect the neurotransmitter (Hall, 1992). Thus, gender is also an important factor that must be considered in order to understand how important variables relating to subjects can affect the ABR responses and to establish normative database for clinical purposes. In Korean literature of ABR, significant gender effects were found on the absolute latency of wave V and on the latencies of wave I-III and wave III-V in 90 dB nHL

and 70 dB nHL (Woo et al., 1995) and on the latencies of the 500 Hz tone burst evoked ABR (Cha, 2004). These studies did not also show the systematic effects of changing stimulus rate and gender on ABR amplitude and latencies.

Therefore, finding the optimal stimulus rate leading to the proper latency and maximal amplitude of click-evoked ABRs is still meaningful for both research and clinical application because this could suggest procedural strategies that may result in the enhancement of ABR recordings (Jang, 2014). Therefore, This study investigated whether the latency and amplitude of ABR responses produced by the different stimulus rates and genders will affect the amplitudes and latencies of ABR in Korean young adults. We attempted to seek the most optimal and stable stimulus rates maximizing the amplitudes and latencies of ABR. In addition, because there is no systematic comparison of different stimulus rates in ABR responses in Korea, we investigated the changes of the amplitudes and latencies of ABR according to different stimulus rates and genders in Korean young adults with normal hearing. For this goal, we measured the latencies and amplitudes of ABR wave I, III, and V with stimulus rates ranging from low (8/s) to high rates (64/s) in five different levels in different gender groups. This will be helpful in developing proper strategies that optimize and enhance the latencies and amplitudes of ABR waves in different gender groups and establish a normative database for clinical purposes.

MATERIALS AND METHODS

1. Subjects

Thirty young adults consisting of fifteen males (mean = 25, SD = 3.7) and fifteen females (mean = 21, SD = 1.4) participated in the study. The right ears of the participants were tested. All subjects received an otoscopic examination (Vision-System INV-150, INNOTECH, Korea), tympanometry (Impedance Audiometer AT235, Interacoustics, Denmark), and reported no positive history of head injury, ear surgery, audiological and neurological disorders. Measuring with a two-channel diagnostic audiometer (Acoustic Analyzer 1200, Starkey, Eden Prairie, MN, USA), none of the subjects had a hearing threshold greater than 20 dB Hearing Level (HL) at octave intervals between 250 to 8,000 Hz.

2. Stimuli and ABR Recording

Auditory brainstem responses (ABRs) were recorded using a GSI Audera system (2012, Grason-Stadler, Eden Prairie, MN, USA). Before recording, the subjects were comfortably seated and relaxed in an armchair located in a sound booth. The skin for electrode placement was cleaned with a generic alcohol prep pad and a gel (NuPrep) with fine pumice granules to help gently exfoliate the skin. Also, a conductive electrode cream was applied to the spot. In the ABR recording, electrical responses were obtained via an active electrode (+) indicating the non-inverting electrode placed on the middle of the forehead, the reference electrode (-) meaning the inverting electrode placed on the ipsilateral earlobe, and the ground electrode placed on the contralateral earlobe, which were connected to the amplifier and filter by shielded wires. Impedances among three electrodes were within

5 k Ω . Electrical responses were elicited by rarefaction clicks generated by rectangular electrical pulses of 100 μ s durations. The stimuli were presented at 75 dB normal Hearing Level (nHL) with a masking level of 35 dB nHL through an electromagnetically-shielded insert earphone (ER-3A, Etymotic Research Inc., Elk Grove Village, IL, USA). The stimulus repetition rate was changed in five steps: 8, 16, 21, 32, and 64/s. The electrical responses were amplified (100,000 times), band-pass filtered from 30 to 3,000 Hz, digitalized through an A/D converter, and averaged at a sample rate of 2,000 sweeps for each test condition. Analysis time was 15 ms, and the test time to complete each test condition was 200s.

3. Data Analysis

For click-evoked ABRs, peak latency and peak amplitude for waves I, III, and V were visually identified and obtained from each subject at 5 different stimulus rate conditions (8, 16, 21, 32, and 64/s). The latency and amplitude data were compared and analyzed between gender groups and within five different stimulus rate conditions. To make sure whether the ABR latencies and amplitudes were present for each experimental condition, three independent observers thoroughly examined the ABR data. All data in the study was reported as a mean \pm S.E.M. All graphic presentations were made by SigmaPlot (version 9, Systat Software, San Jose, CA, USA).

4. Statistical Analysis

A one-way repeated measure ANOVA was performed for the significant differences of five different levels of stimulus rates (8, 16, 21, 32, and

64/s). If Mauchly’s sphericity was assumed for the repeated measures, the sphericity value was used to determine statistical significance. If the sphericity was not assumed for the repeated measures, the Greenhouse-Geisser correction was applied to determine the *p* values. Additionally, within-subjects contrasts were performed for multiple comparisons following the one-way repeated measure ANOVA. Significant differences in gender groups for each ABR wave (I, II, V) were statistically analyzed with independent t-test (IBM SPSS 19.0, IBM corp., Armonk, NY, USA). A

statistical significance was determined by *p* < .05.

RESULTS

We evaluated statistical differences in the latencies and amplitudes of ABR waves I, III, and V according to stimulus rate and gender. Table 1 shows the descriptive statistics of latencies and amplitudes of ABR wave I, III, and V as a function of stimulus rate (8, 16, 21, 32, and 64/s).

Table 1. Means and standard deviations for latencies and amplitudes of ABR waves in five different stimulus rate levels

Type	Rate	8	16	21	32	64	<i>p</i> -value
Wave I	latency	1.60±.20	1.67±.19	1.73±.19	1.73±.24	1.79±.18	.000 †
	amplitude	.23±.18	.19±.24	.28±.17	.09±.19	.19±.15	.000 †
Wave III	latency	3.56±.32	3.62±.34	3.66±.36	3.73±.43	3.78±.71	.072
	amplitude	.22±.18	.16±.16	.28±.15	.02±.20	.14±.18	.000 †
Wave V	latency	5.43±.33	5.58±.24	5.63±.25	5.75±.26	5.89±.50	.000 †
	amplitude	.37±.13	.27±.15	.41±.19	.14±.18	.20±.12	.000 †

* *p* < .5 , † *p* < .1, and ‡ *p* < .001

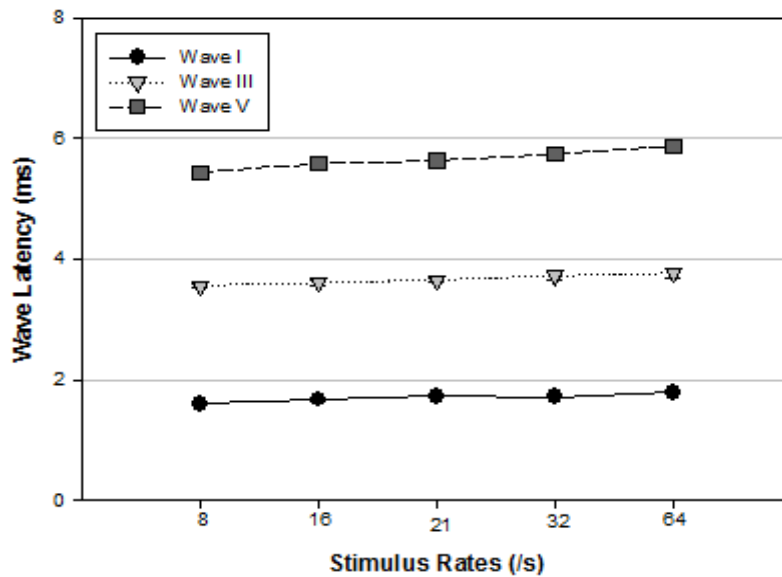


Figure 1. The latencies of ABR wave I, III, and V as a function of five different stimulus rate conditions

Figure 1 displays the latencies of ABR wave I, III, and V as a function of five different stimulus rate conditions. When the stimulus rate increased from 8 to 64/s, the latencies of wave I, III, and V increased from 1.60 to 1.79, 3.56 to 3.77, and 5.44 to 5.88 ms, respectively. The one-way repeated measure ANOVA yielded that there were significant differences among the five different

stimulus rates for the latencies of ABR wave I, III, and V ($F(4, 232) = 10.382, p < .001$; $F(4, 232) = 4.649, p < .01$; $F(4, 232) = 29.006, p < .001$, respectively).

Further analysis for within-subjects contrasts was performed to identify significant differences among five different stimulus rates in latencies of each ABR wave.

Table 2. Multiple comparisons of the latencies of ABR wave I, III, and V among five different levels of stimulus rate (8, 16, 21, 32, and 64/s)

Type	Rate	p-value	Rate	p-value
Wave I	8 ~ 16	.366	16 ~ 32	1.000
	8 ~ 21	.000 †	16 ~ 64	.004 †
	8 ~ 32	.013*	21 ~ 32	1.000
	8 ~ 64	.000 †	21 ~ 64	.047*
	16 ~ 21	.840	32 ~ 64	.349
Wave III	8 ~ 16	.573	16 ~ 32	.008 †
	8 ~ 21	.016*	16 ~ 64	.609
	8 ~ 32	.000 †	21 ~ 32	.132
	8 ~ 64	.128	21 ~ 64	1.000
	16 ~ 21	1.000	32 ~ 64	1.000
Wave V	8 ~ 16	.019*	16 ~ 32	.000 †
	8 ~ 21	.001 †	16 ~ 64	.000 †
	8 ~ 32	.000 †	21 ~ 32	.000 †
	8 ~ 64	.000 †	21 ~ 64	.000 †
	16 ~ 21	1.000	32 ~ 64	.032*

* $p < .5$, † $p < .1$, and ‡ $p < .001$

As shown in Table 2, the ABR latency for wave I showed significant differences at stimulus rates of 21, 32, and 64/s, respectively, compared with a stimulus rate of 8/s. Compared with a stimulus rate of 64/s, significant differences were displayed in the stimulus rates of 16 and 21/s, respectively. In the latency of ABR wave III, compared with a stimulus rate of 8, significant differences were shown in the stimulus rates

of 21 and 32/s, respectively. Significant differences were also found between the stimulus rates of 16 and 32/s. The latencies of ABR wave V were significantly different between a stimulus rate of 8/s and each different level of stimulus rate (16, 21, 32, and 64/s), respectively. Compared with a stimulus rate of 16/s, significant differences were observed in three other stimulus rates of 8, 32, and 64/s, respectively. Compared

with a stimulus rate of 21/s, significant differences were also shown in three other stimulus rates of 8, 32, and 64/s, respectively. Significant differences were found between the stimulus rates of 32 and 64/s.

Additionally, one-way repeated measures showed that there were significant differences among five different stimulus rates for the amplitudes of ABR wave I, III, and V ($F(4, 232) = 12.176, p < .001$; $F(4, 232) = 41.260, p < .001$; $F(4, 232) = 45.178, p < .001$, respectively). Table 1 and Figure 2 present the amplitudes of ABR wave I, III, and V according to five different stimulus rate conditions. When the stimulus rate increased from 8 to 64/s, the amplitude of wave I, III, and V for the stimulus rate of 21/s was the largest but the amplitude for stimulus rate of 32/s was the smallest.

Furthermore, multiple comparisons were performed

to investigate the significant differences among five different stimulus rates in the amplitudes of ABR wave I, III, and V as shown in Table 3.

For the amplitude of ABR wave I, significant differences were observed between a stimulus rate of 32/s and all other stimulus rates of 8, 21, and 64/s, respectively. There were also significant differences between the stimulus rates of 21 and 64/s. In the amplitude of ABR wave III, significant differences were shown in the stimulus rates of 8, 21, and 32/s and all other stimulus rates. Other significant differences were found between a stimulus rate of 16/s and all other stimulus rates except a stimulus rate of 64/s. In the amplitude of ABR wave V, significant differences were observed in all other stimulus rates except between the stimulus rates of 8 and 21/s and between the stimulus rates of 32 and 64/s.

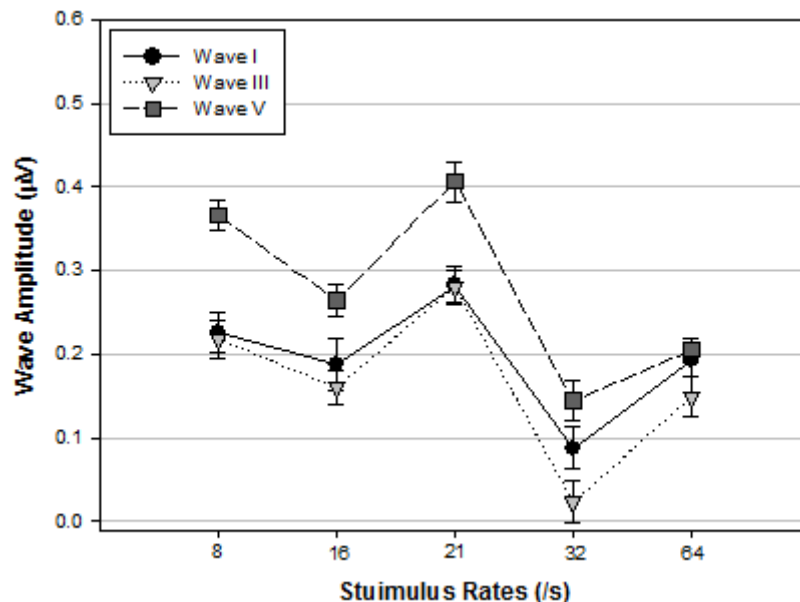


Figure 2. The amplitudes of ABR wave I, III, and V as a function of five different stimulus rate conditions

Table 3. Multiple comparisons of the amplitudes of ABR wave I, III, and V among five different levels of stimulus rates (8, 16, 21, 32, and 64/s)

Type	Rate	<i>p</i> -value	Rate	<i>p</i> -value
Wave I	8 ~ 16	1,000	16 ~ 32	.026*
	8 ~ 21	.589	16 ~ 64	1,000
	8 ~ 32	.000 ‡	21 ~ 32	.000 ‡
	8 ~ 64	1,000	21 ~ 64	.001 †
	16 ~ 21	.057	32 ~ 64	.000 ‡
Wave III	8 ~ 16	.010*	16 ~ 32	.000 ‡
	8 ~ 21	.030*	16 ~ 64	1,000
	8 ~ 32	.000 ‡	21 ~ 32	.000 ‡
Wave III	8 ~ 64	.015*	21 ~ 64	.000 ‡
	16 ~ 21	.000 ‡	32 ~ 64	.000 ‡
Wave V	8 ~ 16	.000 ‡	16 ~ 32	.000 ‡
	8 ~ 21	.830	16 ~ 64	.028*
	8 ~ 32	.000 ‡	21 ~ 32	.000 ‡
	8 ~ 64	.000 ‡	21 ~ 64	.000 ‡
	16 ~ 21	.000 ‡	32 ~ 64	.058

* $p < .5$, † $p < .1$, and ‡ $p < .001$

We also investigated the gender effect on the latencies and amplitudes of each ABR wave. Table 4 shows the descriptive statistics of latencies and amplitudes of ABR wave I, III, and V according to gender (female and male). Figure 3 and 4 present the latencies and amplitudes of ABR wave I, III, and V in different gender groups. However, for latency, the female group was higher than the male group.

Independent t-test showed that the latency of ABR wave III was significantly higher in the female group than the male group ($t(298) = 3.185$, $p < .1$) but not significantly different between female and male groups in both ABR wave I and V. Meanwhile, the amplitudes of ABR wave I and III were significantly higher in the male group than the female group ($t(298) = -2.362$, $p < .5$, $t(298) = -5.099$, $p < .001$, respectively).

Table 4. Means and standard deviations for the latencies and amplitudes of ABR waves in two gender groups

Type	Gender	Male	Female	<i>p</i> -value
Wave I	latency	1,69±.24	1,72±.17	.140
	amplitude	.22±.22	.17±.17	.019*
Wave III	latency	3,59±.48	3,75±.42	.002 †
	amplitude	.22±.18	.11±.19	.000 ‡
Wave V	latency	5,62±.40	5,69±.32	.104
	amplitude	.28±.17	.27±.19	.680

* $p < .5$, † $p < .1$, and ‡ $p < .001$

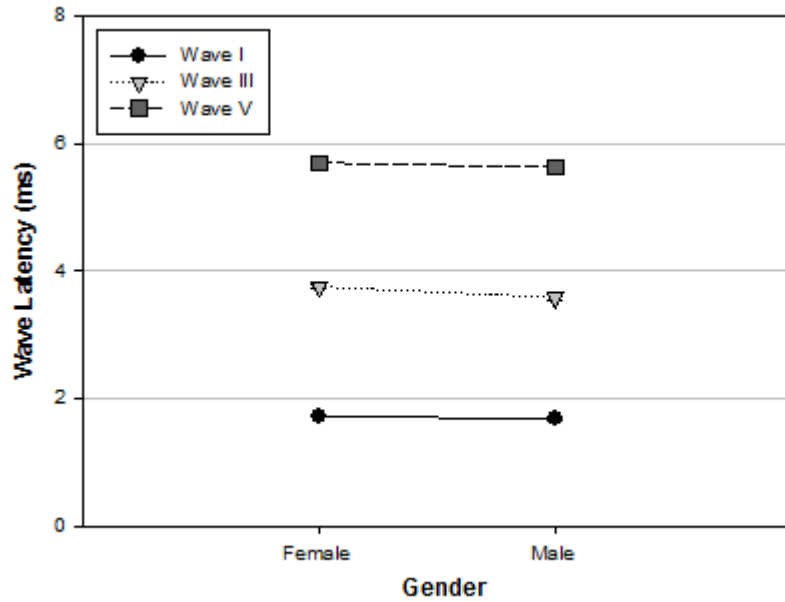


Figure 3. The latencies of ABR wave I, III, and V according to different gender groups

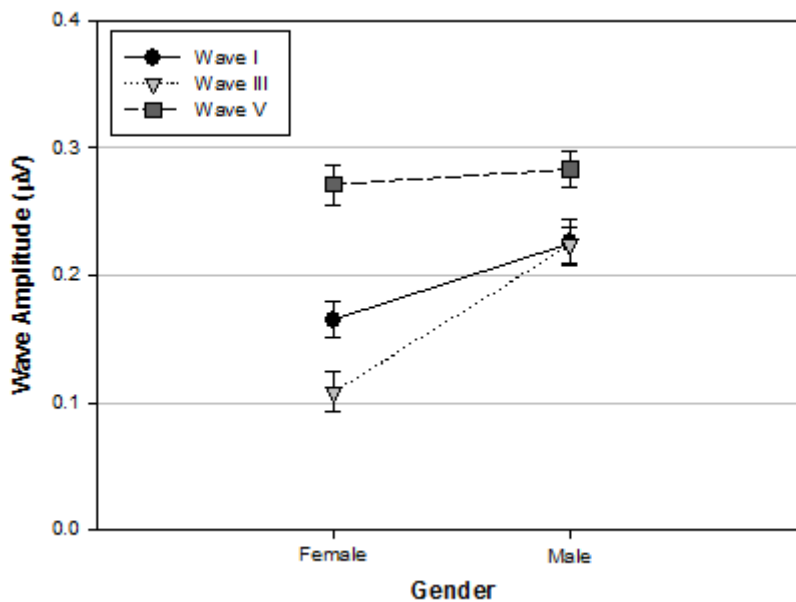


Figure 4. The amplitudes of ABR wave I, III, and V according to different gender groups

DISCUSSIONS

The purpose of the current study was to investigate the amount of change in ABR latencies and amplitudes for wave I, III, and V with stimulus repetition rates increasing from 8 to 64/s in Korean young female and male adults with normal hearing. As stimulus rates increased, the latencies of each ABR wave were consistently longer. When the stimulus rates increased, the latencies of all ABR waves also gradually increased. The absolute latencies of wave I, III, and V in our study were 1.60 ~ 1.79, 3.56 ~ 3.77, and 5.44 ~ 5.88 ms, respectively. They were very comparable with the findings of previous studies which suggested the average normal wave I ($1.54 \pm .08$ ms), wave III ($3.73 \pm .10$ ms), and wave V ($5.52 \pm .15$ ms) for adults with normal hearing (Antonelli et al., 1987; ASHA, 1998). Furthermore, the amount of changes for wave I, III, and V latency with increasing rate in this study was .19, .21, and .44 ms, respectively. This indicates that the latency shifts with increasing rates are not the same for each wave component. These results were also consistent with the previous studies which reported that the latency shift was least for wave I and greatest for wave V (Hall, 2007; Schwartz et al., 1994).

As mentioned before, in previous studies, there were considerable disagreements as to the degree of each wave latency shift. For the wave I latency shift, some studies reported no stimulus rate effect (Hyde et al., 1976), while others showed the shift of .4 to .5 ms (Palludetti et al., 1983). The wave I latency shift was about .23 ms when the stimulus rate increased from 5 to 90/s (Yagi & Kaga, 1979). These latency shift amounts were higher than that of wave I in our study, but the mean latency shift of wave V was

approximately .5 ms when stimulus rate increased from 10 to 100/s indicating a 15 ~ 20 dB decrease in signal intensity at the stimulus rate of 10/s (Don et al., 1977). These previous results of latency shifts regarding wave V were very similar to our study. Based on cross-cultural results, our data were more stable in wave I than other countries. Another study reported that the latency shift of wave V increased from .4 to .6 ms with a stimulus rate increasing from 20 to 80/s (Gerling 1989). In addition, it has been reported that below the stimulus rate of 20/s, there was no main effect of stimulus rate on ABR but above the stimulus rate, ABR latency was longer when stimulus rate increased (Hall, 2007). However, the present study showed that as stimulus rate increased from 8 to 64/s, the absolute latency of ABR waves significantly increased without the boundary line of the stimulus rate of 21/s in all ABR waves. These discrepancies between our study and previous studies may result from a variety of factors such as difficulty identifying confident ABR waves and accurate determination of latency, greater contribution of synapses to later ABR waves, and different neural generators for each wave (Hall, 2007; Ponton et al., 1996).

In addition, the present study compared the amplitudes of ABR wave components as a function of stimulus rate. Results showed that the amplitude of wave V was greatest compared to those of other waves. This is consistent with the previous research showing that the amplitude of wave V is relatively stable and stronger compared to those of other early wave I and III (Schwartz & Morris, 1991; Schwartz et al., 1994). This study showed that the amplitude of wave III was less than that of wave I indicating the amplitude of wave III was most unstable and least. This was not consistent with other studies that

reported the amplitude was most reduced for wave I compared to those of other waves (Schwartz et al., 1994). In addition, in our study, the amplitudes of all ABR waves were largest for a stimulus rate of 21/s, least for a stimulus rate of 32/s and bounced back a little at a stimulus rate of 64/s. The amount of the decreased amplitude ranged from .09 to .28 for wave I, .02 to .28 for wave III, and .14 to .41 μV for wave V, respectively. The degree of amplitude shift for wave I, III, and V was .19, .19, and .27 μV , respectively, showing that wave V was largest in the degree of amplitude shift in our study. These results were not consistent with previous research reporting that the amplitude decreased consistently and progressively when the stimulus rate increased and the decreased amplitude may result from metabolic changes at the receptor level or changes in neural activity within the brainstem (Jiang et al., 1991). These discrepancies between our study and other investigations may result from different stimulus rates used in each research.

Generally, although the criteria for determining the amount of latency and amplitude as a function of stimulus rate have not been clearly mentioned, the clinical utility of stimulus rates in terms of ABR wave latency and amplitude have been continually proven for neurological diagnosis testing (Musiek et al., 1994; Schwartz & Morris, 1991). The use of stimulus rate and frequency on ABR was clinically helpful to separate cochlear lesions from CN VIII nerve and brainstem lesions (Fowler & Noffsinger, 1983). Slow stimulus rates below 10/s can collect the greatest aggregate of CN VIII fibers and improve neural synchrony, whereas the latency shift between 20 and 50/s can be used for neurological diagnosis stressing synaptic efficiency (Schwartz & Morris, 1991;

Schwartz et al., 1994). When the stimulus rate increased from 9.7 to 49.7 and 59.7/s, patients with tumor showed a greater average wave V latency shift (Campbell & Abbas, 1987). In patients with multiple sclerosis, ABR was absent at stimulus rates greater than 25/s (Robinson & Rudge, 1977). ABR latencies increased and amplitudes decreased with increasing stimulus rates in both human newborns and adults. The wave V latency increases were larger for newborns than adults (Lasky, 1997). Although this present research does not suggest directly normative data for different developmental ages and various neurological lesions, it should be mentioned that this study strongly proposes the stimulus rate of 21/s as an optimal parameter which maximizes the amplitude of ABR waves. Although the use of other different rates may provide different criteria for quantitatively comparing the ABR amplitudes and latencies, the use of the optimal rate (21/s) can allow less time and a much secure method for ABR test compared to that of higher stimulus rates if properly set up.

There was another important factor affecting the results of our investigation regarding stimulus presentation levels. The present research presented all stimuli at 75 dB nHL with a masking level of 35 dB nHL. Generally, it has been reported that stimulus level is strongly associated with ABR amplitude and latency. Increasing stimulus levels decrease the latency of all waves and produces the steeper slope of the latency/intensity function (Sininger & Hyde, 2009). Furthermore, as hearing threshold approaches, the latencies of ABR wave tend to increase and are easier for visual detection of ABR waves. The significant differences between our current investigation and previous other studies may result from different presentation levels.

Another important factor affecting ABR response was gender in our study. Generally, the effect of stimulus rates on ABR latency and amplitude between female and male adults is distinct (Hall, 2007). The gender effect was found for wave I and III. In more detail, female adults have clearly shorter latency and larger amplitudes than those of male adults in ABR waves, which may come from different cochlear response times between female and male adults (Cha, 2004; Don et al., 1994; Watson, 1996). However, the present research showed that significant differences between female and male adults were found in both wave I and III amplitudes, and the amplitudes of wave I and III for female adults were smaller than those for male adults. Another significant difference between female and male adults was found in wave III latency, and the latency of wave III for female adults was longer than those for male adults. Furthermore, it is important to note that the amount of amplitude in wave V was larger than those of wave I and III in our investigation while that of wave III was smallest. This may indicate a relatively large instability of wave III as a function of stimulus rate. Therefore, it is prudent to use the wave III amplitude for ABRs in clinical applications.

Although our study provides the useful information of proper stimulus rates maximizing and enhancing the amplitudes and latencies of ABR waves, it should be mentioned that our study has some limitation on generalization and clinical application due to the small size of subjects, the selected subjects in the specific locations, the limited ranges of stimulus rate, and the different stimulus conditions from other studies. Therefore, future studies are needed to obtain more normative data from people with aging related hearing loss, noise induced hearing loss, and different abnormal hearing.

CONCLUSIONS

This research investigated the effect of stimulus rate and gender on ABR latency and amplitude in different Korean young adults. When stimulus rates changed in five steps of 8, 16, 21, 32, and 64/s, significant differences in the latency and amplitude of wave I, III, and V were observed. Also, a gender effect was found on the latency of wave III and the amplitudes of wave I and III. As stimulus rates increased, the wave latency gradually increased in wave I, III, and V, whereas the amplitude of ABR waves inconsistently changed. The latency shift became longer in wave V than wave I and III. The amplitude of wave I, III, and V was greatest at a stimulus rate of 21/s and least at a stimulus rate of 32/s. These results indicated that the use of 21/s was feasible to maximize the ABR amplitude. From these results, comparison of different stimulus rates will provide helpful information in developing proper strategies that optimize and enhance ABR wave latencies and amplitudes in different gender groups, reducing the ABR test time in clinical applications, and establishing quantitatively normative database for clinical purposes. The limitations of this study are as follows. First, only small normal young adults ($N = 30$) participated to identify the optimal ABR response in different stimulus rates. Second, we could not compare different aging groups (e.g. children vs. elderly groups) and pathological conditions (normal vs. patient groups). Therefore, further investigation is warranted to include various age and pathological groups to enhance the validity and reliability in evaluating latencies and amplitudes of ABR waves.

ACKNOWLEDGEMENT

This study was supported by a research grant of Catholic University of Daegu.

REFERENCES

- Antonelli, A. R., Bellotto, R., & Grandori, F. (1987). Audiologic diagnosis of central versus eighth nerve and cochlear auditory impairment. *Audiology*, *26*(4), 209-226.
- American Speech-Language-Hearing Association (ASHA). (1998). The short latency auditory evoked potentials. Rockville, MD: Author.
- Campbell, K. C. & Abbas, P. J. (1987). The effect of stimulus repetition rate on the auditory brainstem response in tumor and nontumor patients. *Journal of Speech and Hearing Research*, *30*(4), 494-502.
- Cha, O. S. (2004). Auditory brainstem responses using the chained-sound stimuli protocol. Master thesis. Hallym University. Chuncheon.
- Chambers, R. D., Matties, M. L., & Griffiths, S. K. (1989). Correlations between various measures of head size and auditory brainstem response latencies. *Hearing Research*, *41*(2-3), 179-88.
- Choi, C-H. (2011). Preliminary study of therapeutic effect of a nitone-based antioxidant drug (HPN-07) on acute acoustic trauma. *Korean Journal of Communication Disorders*, *16*(2), 202-210.
- Choi, H. J. (2006). Auditory brainstem response (ABR) results in NICU. Master thesis. Kyungpook University. Daegu.
- Choi, H. Y., Lee, M. C., Jang, S. O., Oh, S. H., Kim, J. S., & Choi, J. H. (2004). The efficacy of automated distortion product otoacoustic emission and automated auditory brainstem responses in universal hearing screening. *Korean Journal of Otorhinolaryngology-Head and Neck Surgery*, *47*(1), 27-32.
- Don, M., Allen, A. R., & Starr, A. (1977). Effect of click rate on the latency of auditory brain stem responses in humans. *Annals of Otology, Rhinology, and Laryngology*, *86*, 186-195.
- Don, M., Ponton, C., Eggermont, J., & Masuda, A. (1994). Auditory brainstem response (ABR) peak amplitude variability reflects individual differences in cochlear response times. *Journal of the Acoustical Society of America*, *96*, 3476-3491.
- Fowler, C. & Noffsinger, D. (1983). Effects of stimulus repetition rate and frequency on the auditory brainstem response in normal, cochlear-implemented, and VIII nerve/brainstem-impaired subjects. *Journal of Speech and Hearing Research*, *26*(4), 560-567.
- Freeman, S., Sohmer, H., & Silver, S. (1991). The effect of stimulus repetition rate on the diagnostic efficacy of the auditory nerve-brain-stem evoked response. *Electroencephalography and Clinical Neurophysiology*, *78*(4), 284-290.
- Gerling, I. J. (1989). Interaction of stimulus parameters on the auditory brainstem response: A normal variant. *Ear and Hearing*, *10*(2), 117-123.
- Hall J. W. III (1992). Handbook of Auditory Evoked Responses (pp. 70-103). Boston, MA: Allyn and Bacon.
- Hall J. W. III (2007). *New Handbook of Auditory Evoked Responses* (pp. 171-211). Boston, MA: Allyn and Bacon.
- Hyde, M. L., Stephens, S. D. G., & Thornton, A. R. D. (1976). Stimulus repetition rate and early brainstem responses. *British Journal of Audiology*, *10*, 41-50.

- Jang, J. W., Lee, G. S., Song, D. G., Kim, S. H., Kim, W. D., & Lee, S.G. (2007). Usefulness of auditory brainstem response as early predictor of kernicterus in early breast-feeding jaundice. *Korean Journal of Pediatrics*, 50(9), 848-854.
- Jang, K-H. (2014). Effect of gender and stimulus rates on auditory evoked responses. Master thesis. Catholic University of Daegu. Gyeongsan.
- Jiang, Z. D., Wu, Y. Y., & Zhang, L. (1991). Amplitude change with click rate in human brainstem auditory-evoked response. *Audiology*, 30, 173-182.
- Jo, Y. H. (2013). Auditory brainstem response in newborns with hyperbilirubinemia. Master thesis. Hanyang University. Seoul.
- Jung, W. H. (2007). Automated algorithm of automated auditory brainstem response for neonates. Master thesis. Yonsei University. Seoul.
- Kim, H. J. & Lim, H. J. (1992). The effect of the test parameters upon the brainstem evoked response audiometry in normal persons. *Korean Journal of Otorhinolaryngology-Head and Neck Surgery*, 35(1), 34-42.
- Kim, H. M., Go, T.S., Kim, G. S., Lee, M. S., & Kim, K. H. (1995). Auditory brainstem responses in premature and fullterm infants. *Korean Journal of Pediatrics*, 38(8), 1036-1045.
- Kim, J. H. & Kim, J. S. (2002). Clinical application of bone conduction auditory brainstem responses to tone burst. *Korean Journal of Communication Disorders*, 7(3), 160-178.
- Kim, J. S., Lee, M. S., Lee, J. H., Park, M. S., Lee, J. H., Kim, M. S., et al. (1999). Brainstem evoked potentials to tone burst in normally hearing adults. *Korean Journal of Audiology*, 3(1), 56-62.
- Kim, S. C. (2007). Development of template for automatic interpretation of the auditory brainstem response in the infant. Ph.D. dissertation. Yonsei University. Seoul.
- Klein, A. J., Alvaqrez, E. D., & Cowburn, C. A. (1992). The effects of stimulus rate on detectability of the auditory brainstem response in infants. *Ear and Hearing*, 13(6), 401-405.
- Krizman, J., Skoe, E., & Kraus, N. (2010). Stimulus rate and subcortical auditory processing of speech. *Audiology and Neurootology*, 15(5), 332-342.
- Lasky, R. E. (1997). Rate and adaptation effects on the auditory evoked brainstem response in human newborns and adults. *Hearing Research*, 111(1-2), 165-176.
- Lee, M. S. (2000). Brainstem evoked potentials to tone burst in normally hearing adults. Master thesis. Hallym University. Chuncheon.
- Lee, O. Y., Nam, B. H., Park, Y. H., Lee, S. H., & Park, C. I. (2002). Effect of Salicylate on DPOAEs and ABRs in guinea pigs. *Korean Journal of Otorhinolaryngology-Head and Neck Surgery*, 45(7), 646-650.
- Lee, K. S. & Baek, M. K. (1983). Normal ranges of auditory brainstem response in Korean. *Korean Journal of Otorhinolaryngology-Head and Neck Surgery*, 26(2), 217-225.
- Leung, S-M., Slaven, A., Thornton, A. R. D., & Brickley, G. J. (1998). The use of high stimulus rate auditory brainstem response in the estimation of hearing threshold. *Hearing Research*, 123(1-2), 201-205.
- Lightfoot, G., Sininger, Y., Burkard, R., & Ludwig, A. (2007). Stimulus repetition rate and the reference levels for clicks and short tone bursts: A warning to audiologists, researchers, calibration laboratories, and equipment manufacturers. *American Journal of*

- Audiology*, 16(2), 94-95.
- Musiek, F. E., Borenstein, S. P., Hall III, J. W., & Schwaber, M. K. (1994). Auditory brainstem response: Neurodiagnostic and intraoperative applications (pp. 351-374). In: J. Katz (4th ed.). *Handbook of Clinical Audiology*. Baltimore, MD: Williams & Wilkins.
- Palludetti, G., Maurizi, M., & Ottaviani, F. (1983). Effects of stimulus repetition rate on the auditory brainstem response (ABR). *American Journal of Otolaryngology*, 4(3), 226-234.
- Park, S. Y., Sin, J. W., & Choi, J. H. (2010). Diagnostic value of the ABR latency in the acoustic neuroma. *Clinical and Experimental Otorhinolaryngology*, 21(1), 46-49.
- Parthasarathy, T. K., Borgsmiller, P., & Cohan, B. (1998). Effects of repetition rate, phase, and frequency on the auditory brainstem response in neonates and adults. *Journal of American Academy of Audiology*, 9, 134-140.
- Picton, T. W., Stapells, D. R., & Campbell, K. B. (1981). Auditory evoked potentials from the human cochlea and brainstem. *The Journal of Otolaryngology. Suppl.*, 10, 1-41.
- Ponton, C. W., Moore, J. K., & Eggermont, J. J. (1996). Auditory brainstem response generation by parallel pathways: Differential maturation of axonal conduction time and synaptic transmission. *Ear and Hearing*, 17, 402-410.
- Rhee, C-K., He, P., Jung, J. Y., Ahn, J-C., Chung, P-S., & Suh, M-W. (2012). Effect of low-level laser therapy on cochlear hair cell recovery after gentamicin-induced ototoxicity. *Lasers in Medical Science*, 27, 987-992.
- Robinson, K. & Rudge, P. (1977). Abnormalities of the auditory evoked potentials in patients with multiple sclerosis. *Brain*, 100, 19-40.
- Santos, M. A., Munhoz, M. S., Peixoto, M. A., & Silva, C. S. (2004). High click stimulus repetition rate in the auditory evoked potentials in multiple sclerosis patients with normal MRI. Does it improve diagnosis? *Revue de laryngologie-otologie-rhinologie (Bord)*, 125(3), 151-155.
- Schwartz, D. & Morris, M. (1991). Strategies for optimizing the detection of neuropathology from the auditory brainstem response. In: J. T. Jacobson, & J. L. Northern (Ed.). *Diagnostic Audiology*. Austin, TX: Pro-Ed.
- Schwartz, D.M., Morris, M. D., & Jacobson, J. T. (1994). The normal auditory brainstem response and its variants (pp. 123-153). In: J. T. Jacobson JT (Ed.). *Principles and applications in auditory evoked potentials*. Boston, MA: Allyn and Bacon.
- Seo, J-H., Jeon, E-J., Park, Y-S., Kim, J. E., Kim, D-H., Nam, I-C., et al. (2012). Correlation of threshold of click-evoked auditory brainstem response with pure-tone threshold average in various formulas. *Korean Journal of Otorhinolaryngology-Head and Neck Surgery*, 55(12), 764-770.
- Sininger, Y. S. & Hyde, M. L. (2009). Auditory brainstem response in audiometric threshold prediction. In: J. Katz, L. Medwetsky, R. Burkard, & L. Hood (6th ed.). *Handbook of Clinical Audiology* (pp. 293-321). Baltimore, MD: Lippincott Williams & Wilkins.
- Suzuki, T., Kobayashi, K., & Takagi, N. (1986). Effects of stimulus repetition rate on slow and fast components of auditory brain-stem responses. *Electroencephalography and Clinical Neurophysiology*, 65(2), 150-156.
- Watson, D. (1996). The effects of cochlear hearing

loss, age and sex on the auditory brainstem response. *Audiology*, 35(5), 246-58.

Woo, H. Y., Kim, J. T., & Kwon, D. H. (1995). Auditory brainstem evoked response in normal adults. *Inje Medical Journal*, 16(2), 231-239.

Yagi, T. & Kaga, K. (1979). The effect of the click repetition rate on the latency of the auditory evoked brainstem response and its clinical use for a neurological diagnosis. *Archives of Otorhinolaryngology*, 222(2), 91-97.