



RESEARCH

EVALUATION OF AUDITORY LATE LATENCY RESPONSE IN OLDER ADULTS

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ABSTRACT

Introduction: To determine normal values of the latencies and amplitudes of auditory late latency responses for older adults and to investigate whether there was any difference between individuals in terms of the ear tested and gender.

Materials and Method: A total of 31 older adults (17 females and 14 males) between age of 65 to 85 years old participated. All were right-handed with normal hearing (pure-tone average \leq 25 decibels). The auditory late latency responses test was performed with 1 kilohertz tone burst stimuli at 70 dB normal hearing level. The mean latencies and amplitudes of the P1, N1, P2 and N2 waves were recorded. Gender and tested-ear effects were investigated.

Results: The mean latencies of the N1 and P2 waves in males were longer than in females for the right ears ($p < 0.05$). The mean latencies of the N1 and N2 waves were also longer in males than in females for the left ears ($p < 0.05$). In addition, the mean amplitudes of the P1- N1 and N1-P2 waves were smaller in males than in females for the left ears ($p < 0.05$).

Conclusion: This study has revealed normative values for auditory late latency responses in healthy older adults. The data belonging to the right and left ears have been provided. Furthermore, a difference has been observed between the genders in terms of latency (right N1 and P2; left N1 and N2) and amplitude (left P1- N1- and N1-P2) values.

Keywords: Evoked Potentials, Auditory; Aging; Hearing

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INTRODUCTION

Among the elderly population, the age group between 65 and 74 is classified as "young-old," the age group between 75 and 84 is classified as "old-old," and the age group that is 85 and above is classified as "oldest-old" (1). In the field of geriatric otology, there have been significant developments in determining the anatomical, physiological and audiological changes in the peripheral and central auditory pathways (2). The effects of changes in the peripheral auditory system in older adults can be seen throughout the central auditory system, including in the cochlear nucleus, the inferior colliculus, the medial geniculate body and the primary auditory cortex. In particular, auditory deprivation in the peripheral hearing organs disrupts the tonotopic organization of the auditory cortex (3, 4). These changes that occur during the transition from adulthood to the late stages of life have direct effects on the synaptic activity in the central auditory pathways, as well as neural production areas (5).

Auditory late latency responses (ALLR) are often used to evaluate changes in the central auditory system. The responses obtained with ALLR show voltage changes resulting from synchronized neural activity in the thalamo-cortical region of the central auditory system with the sound stimulus (6). Auditory evoked late latency response occurs 50 milliseconds (ms) after the delivery of a stimulus. P1, N1 and P2 cortical responses consist of a small positive wave (P1) and a large negative wave (N1), followed by a positive wave (P2). The N1 wave, also known as the N100, is negative and occurs approximately 100 ms after the stimulation (5).

The ALLR is used in evaluating high-level functions of the central auditory nervous system (CANS) and auditory processing, in recording the benefits of applied rehabilitation techniques (7) and in determining frequency-specific hearing sensitivity (8). The N1 and P2 waves are used to determine hear-

ing sensitivity in cases for whom a frequency-specific, non-behavioural measure is required (9). It is evident that the properties of waves are affected in neural pathologies related to the auditory cortex. Furthermore, the latency and amplitude parameters of ALLR waves change with aging (10).

The present study aimed to obtain reference values for the evaluation of auditory cortical functions among older adults by determining the normal latency and amplitude values of ALLR for this population, and to investigate whether there was any difference between the individuals in terms of their gender and the ear tested.

MATERIALS AND METHODS

This study was carried out in the Izmir Katip Celebi University, Ataturk Training and Research Hospital. The study was approved by Ankara Yildirim Beyazit University Ethics Committee (Date: 14/01/2021-Number: 04). Participants were informed about the study, and written informed consent was obtained from all of them. The study inclusion criteria were as follows: 1) Being between the ages of 65-85; 2) Having a normal otoscopic examination result; 3) Not having psychogenic or neurological disorders such as a cerebral tumor, schizophrenia, aphasia, multiple sclerosis or Parkinson's disease; 4) Having a pure-tone average (PTA) of ≤ 25 decibels (dB) hearing level (HL) at 500, 1000 and 2000 Hertz (Hz) for the right and left ears; 5) Not using hearing aids; 6) Being right-handed; and 7) Having speech discrimination scores of ≥ 80 percent.

Behavioral Hearing Test: Pure-tone and speech audiometry was performed using an AC-40 audiometer (Interacoustic AS, Assens, Denmark). Air-conduction hearing thresholds were measured at 250-8000 Hz using a TDH-39 earphone (Telephonics Co., Farmingdale, New York, U.S.A.). Bone conduction hearing thresholds were measured at 500-4000 Hz using a RadioEar B-71 bone vibrator (RadioEar Co., Middelfart, Denmark).



Evaluation of Auditory Late Latency Responses: The evaluations were performed using a Neurosoft device (Neuro-audio.net-1.0.104.1, Ivanovo, Russia). During the tests, the non-inverting electrodes were placed at the Fz region (F represents frontal; z represents midline), the inverting electrodes were placed on the mastoid region (left mastoid: M1; right mastoid: M2), and the ground electrodes were placed at the Fpz region (F represents frontal; p represents positive; z represents midline). A 0.1 Hz high-pass filter and a 35 Hz low-pass filter were used. The artifact rejection level was 100 microvolts (μV). A 1000 Hz, 70 dB normal hearing level (nHL) tone burst stimulus was delivered monaurally using ER-3A insert earphones. The stimulus duration was set as 50 ms, the rise-fall time was set as 10 ms, and the polarity rarefaction and rate as 0.5 Hz. The analysis time was 600 ms. The evaluations of ALLR were carried out while the individuals were watching a silent documentary video in a quiet room. The test subjects were sitting on a comfortable armchair and had their eyes open. Two traces were obtained in each presentation level. The amplitudes of ALLRs were determined with the peak-to-peak measure procedure. The peaks of the waves or the midpoint of broad peaks were marked. Tests were performed by the same audiologist to avoid differences in approaches among testers.

Statistical analysis:

The data analysis was performed using SPSS v. 24.0. In the descriptive analyses, categorical variables were presented as percentages and continuous variables as mean \pm standard deviation values. Variables that were not distributed normally were evaluated with non-parametric test (Mann-Whitney U), and normally distributed variables were evaluated with parametric test (independent sample t-test). Statistical significance was considered at $p < 0.05$.

RESULTS:

A total of 31 participants were included in our study. Of the patients, 14 (45.2%) were male and 17 (54.8%) were female. The mean ages of females and males were 72.35 ± 4.12 years and 73.71 ± 5.14 years, respectively. The mean PTA value of females were 17.94 ± 4.06 dB HL in the right ear and 15.49 ± 4.47 dB HL in the left ear. The mean PTA value of males were 21.54 ± 3.29 dB HL in the right ear and 21.42 ± 3.38 dB HL in the left ear (Figure 1).

Table 1 shows the mean values of ALLR (P1 latency, N1 latency, P2 latency, N2 latency, N1-P2 latency, P1-N1 amplitude, P2-N2 amplitude, and N1-P2 amplitude) for males and females. The results showed that the mean latencies of the N1 and P2 waves in males were longer than in females for the right ears ($p=0.036$, $p=0.013$ respectively). The mean latencies

Figure 1: The mean PTA value of males and females based on frequency

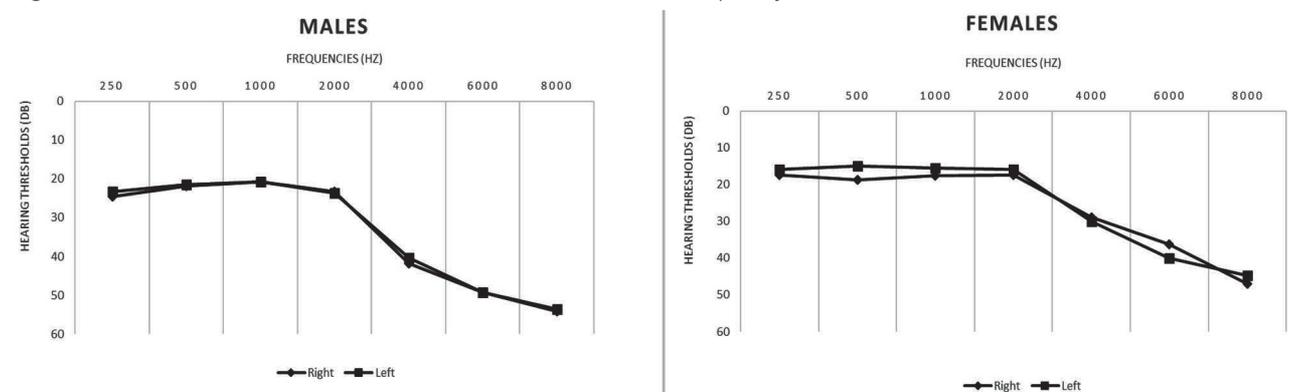


Table 1. Mean values of ALLR for males and females

		Latencies (ms) Mean ± SD (min - max)					Amplitudes (µv) Mean ± SD (min -max)			
		P ₁	N ₁	P ₂	N ₂	N ₁ - P ₂	P ₁ - N ₁	P ₂ - N ₂	N ₁ -P ₂	
Right	Males (n=14)	53.3 ± 4.3 (46.3–62.2)	107.4 ± 8.9 (93.9 -127.0)	211.9 ± 13.1 (181.2–228.9)	296.3 ± 26.5 (251.4–351.9)	104.5 ± 11.8 (83.3–124.4)	7.0 ± 1.8 (3.8–9.2)	2.7 ± 1.9 (0.7–7.8)	7.1 ± 1.9 (4.8–11.5)	
	Females (n=17)	50.1 ± 4.1 (42.3–58.2)	99.5 ± 8.4 (83.3–113.8)	196.7 ± 17.8 (169.3–232.8)	281.2 ± 15.8 (240.8 -305.6)	97.7 ± 17.5 (60.9–136.3)	8.0 ± 2.7 (3.7–14.7)	2.8 ± 1.6 (0.5–6.3)	7.8 ± 2.3 (4.3–12.6)	
	<i>p^a</i> (Z)	0.108 (-1.606)	*0.036 (-2.092)	*0.013 (-2.482)	0.071 (-1.807)	0.158 (-1.410)	0.565 (-0.576)	0.858 (-0.179)	0.382 (-0.874)	
Left	Males (n=14)	52.8 ± 4.9 (45.0–62.2)	108.5 ± 10.5 (86.0–121.7)	209.7 ± 11.5 (189.2–227.5)	293.6 ± 20.1 (263.3–332.1)	101.1 ± 12.5 (82.0–123.0)	5.7 ± 1.8 (2.7–8.5)	2.0 ± 1.6 (0.5–7.0)	5.8 ± 2.2 (3.2–11.1)	
	Females (n=17)	49.2 ± 4.5 (42.3–56.9)	101.1 ± 8.2 (87.3–115.1)	202.1 ± 15.5 (182.6–236.6)	271.4 ± 26.6 (188.4 –305.6)	100.8 ± 18.7 (71.4–146.8)	7.5 ± 1.9 (3.8–11.4)	2.2 ± 1.1 (0.5–4.4)	7.9 ± 2.4 (4.3–13.4)	
	<i>p^a</i> (Z)	0.063 (-1.858)	*0.020 (-2.327)	0.077 (-1.769)	*0.017 (-2.385)	0.735 (-0.338)	*0.035 (-2.106)	0.392 (-0.855)	*0.024 (-2.264)	

p < 0.05 was accepted as statistically significant. Statistically significant values are shown in italics and bold fonts.
a: *p*-value for Mann-Whitney U test

of the N1 and N2 waves were also longer in males than in females for the left ears (*p*=0.020, *p*=0.017 respectively). In addition, the mean amplitudes of the P1- N1 and N1-P2 waves were smaller in males than in females for the left ears (*p*=0.035, *p*=0.024 respectively).

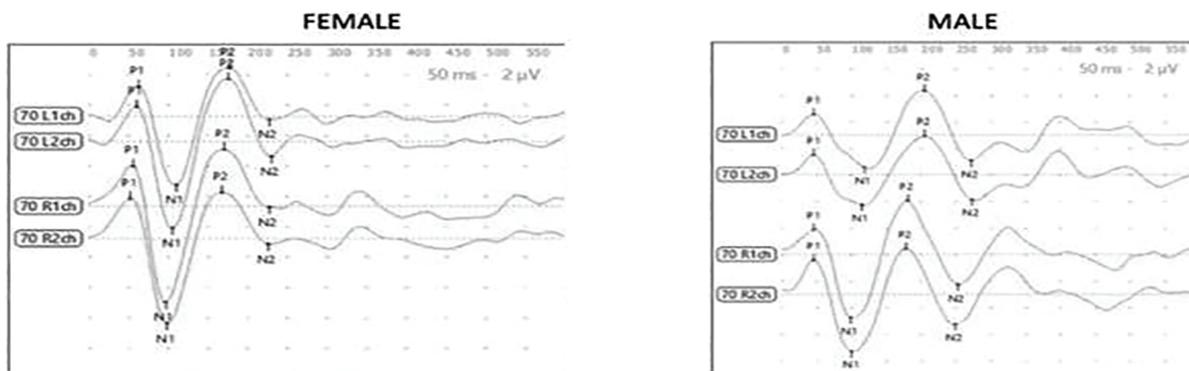
The mean values of ALLR for the whole group are presented in Table 2. The results showed no significant difference (for all analyzes, *p* > 0.05).

A sample waveform of ALLR for males and females is presented in Figure 2.

DISCUSSION:

This study evaluated ALLR, one of the auditory evoked potentials, in older adults and estimated normative values in this regard. Auditory evoked potentials are the potentials recorded in the cortex, which is the highest level of auditory pathway, using

Figure 2. Sample waveform of ALLR for males and females



**Table 2:** Mean values of ALLR for the whole group

All group (n=31)	Latencies (ms) Mean \pm SD (min - max)					Amplitudes (μ v) Mean \pm SD (min -max)		
	P ₁	N ₁	P ₂	N ₂	N ₁ - P ₂	P ₁ - N ₁	P ₂ - N ₂	N ₁ -P ₂
Right	51.5 \pm 4.4 (42.3–62.2)	103.0 \pm 9.4 (83.3–127.0)	203.6 \pm 17.4 (169.3–232.8)	288.0 \pm 22.3 (240.8–351.9)	100.8 \pm 15.3 (60.9–136.3)	7.6 \pm 2.3 (3.7–14.7)	2.8 \pm 1.7 (0.5–7.8)	7.5 \pm 2.1 (4.3–12.6)
Left	50.8 \pm 4.9 (42.3–62.2)	104.4 \pm 9.9 (86.0–121.7)	205.5 \pm 14.2 (182.6–236.6)	281.5 \pm 26.0 (188.4–332.1)	101.0 \pm 15.9 (71.4–146.8)	6.7 \pm 2.0 (2.7–11.4)	2.1 \pm 1.3 (0.5–7.0)	7.0 \pm 2.5 (3.2–13.4)
p^b (t)	0.544 (0.610)	0.571 (-0.569)	0.623 (-0.494)	0.294 (1.059)	0.960 (-0.050)	0.124 (1.561)	0.128 (1.543)	0.397 (0.852)

p < 0.05 was accepted as statistically significant. Statistically significant values are shown in italics

b: p-value for independent samples t test

auditory stimulation. They provide remarkable information regarding the development of the auditory system, perception, discrimination, cognitive functions, and the benefits of auditory habilitation/rehabilitation. Electrophysiological evaluation of these potentials is quite fast, less tiring, and very valuable in terms of the information it provides. Normative values for auditory cortical responses are of great importance in clinical audiology applications. There are many studies evaluating ALLR in older adults. These studies often compare patients with various pathologies, such as hearing loss, tinnitus, cognitive disorders, and diabetes, with control groups (11-17). The findings of the present study were compared with the results of the control groups in these previous studies. But first, relevant studies on ALLR waveforms in older adults were reviewed.

In the literature, there are studies proving prolongation in N1 and P2 latencies in older adults (18). Some researchers have noted the effects of aging on ALLR as the prolongation of latencies and the reduction of amplitudes (19). Some studies have also reported that N1 latency is not affected by age (20). The presence of accompanying age-related hearing loss affects ALLR more, causing both prolonged latencies and increased amplitudes (11).

ALLR has been investigated among older adults in several studies (10-14,16, 21-23). Table 3 systematically summarizes these studies and the results of

the present study. The present study determined normal ALLR values among older adults and investigated the presence of a difference between the individuals in terms of gender and the tested ear. None of the previous studies compare and estimate normative data for ALLR in older adults based on gender and the tested ear. In fact, the gender and dominant ear of the subjects may affect electrophysiological evaluation. In a guideline for using human event-related potentials, it is recommended that the investigator report the genders of the subjects in groups and ensure that any group effects are not confounded with gender distribution difference in groups (24). In addition, in a study conducted on children with autism who were given auditory training, it was shown that the P1 and N1 amplitudes in the dominant and non-dominant ears may be different (25). Gender, dominant ear, age and many other unspecified factors may affect the waveforms of the ALLR. In this context, to our current knowledge, this is the first study to investigate normative data for ALLR in older adults.

The results of the present study showed that the latencies of the N1 and P2 waves were longer in the right ears of males than in females ($p=0.036$ and $p=0.013$, respectively). Similarly, the latencies of the N1 and N2 waves were longer in the left ear in males ($p=0.020$ and $p=0.017$, respectively). There was no significant difference between genders in terms of

amplitudes in the right ears, whereas N1-P1 and N1-P2 amplitudes were higher in the left ears of females than in males ($p=0.035$ and $p=0.024$, respectively) (Table 1). Longer latencies in males provide valuable evidence to support the notion that gender differences should be considered when evaluating ALLR in older adults. Furthermore, detection of higher amplitudes in the left ears and in females was primarily associated with being right-handed; however, comparison of the right and left ears in the whole group (Table 2) did not show statistically significant difference, suggesting that this difference was related to gender and not to the ear tested. Since these values were not evaluated according to gender in previous studies, a comparison could not be made; however, this is another evidence that gender differences should be considered when evaluating ALLR in older adults.

In a study by Coser et al. (2007), the mean latency of the N1 wave was reported to be 100 ms in older adults aged 60-80 years who had difficulty in understanding speech despite reporting no hearing loss during the auditory test (12). No separate calculations were made for latency values regarding the differences in gender and tested ear side. Furthermore, 80 dBNA sound level was used in the tests (Table 3). In the present study, the mean latency of the N1 wave was found to be 103.0 ± 9.4 ms for the right ears and 104.4 ± 9.9 ms for the left ears. While Coser et al. (12) reported the mean latency of the P2 wave to be 176 ms (Table 3), this value was 203.6 ± 17.4 ms for the right ears and 205.5 ± 14.2 ms for the left ears in the present study (Table 2). The longer P2 latency in the present study was thought to be due to the difference in electrode placement between test applications and the use of a lower sound level.

In a study by O'Brien et al. (23), in which ALLRs of older adult musicians and non-musicians were compared, the test performed by placing the non-inverting electrode in Fz and at 75 dB sound pressure

level (SPL) was similar to the present research protocol. However, gender and the tested side were not evaluated separately in this study. They reported the mean latencies to be 61 ms for P1, 109 ms for N1, and 174 ms for P2 (Table 3). In the present study, the mean latency of the P1 wave was shorter. While the mean latency of the N1 wave was similar to the study by O'Brien et al., (23) the mean latency of the P2 wave was longer.

In a study by Lister et al. (14) aiming to identify individuals with possible cognitive impairment, ALLR latencies of 17 older adults in the cognitively normal control group were 39.2 ± 7.3 ms for P1, 94.8 ± 8.6 ms for N1, and 207.8 ± 19.2 ms for P2 (Table 3). The mean latency of the P2 wave reported by the authors was observed to be similar to the value obtained in the present study. However, the P1 and N1 latencies in males and females were longer in the present study. We believe that this is due to the use of a pure tone sound at level of 85 dB SPL in their study (compared to use of a tone-burst at level of 70 dB nHL in our study).

In a systematic review, Tome et al. (2015) presented normative data of N1 and N2 for different age groups (10). Data for older adults were presented similarly to our study, but excluding gender and ear side, as well as P1 and P2 waveforms. On the other hand, the presence of similar N1 and N2 features in both studies indicates the consistency of the normative data for ALLR.

The present study has several strengths. Firstly, although there have been previous studies evaluating ALLR in older adults, the difference between genders has not been investigated in these studies. The present study is more comprehensive in showing the difference in ALLR by gender among older adults. Furthermore, the data of the right and left ears were analyzed separately. In our literature search, we found only one systematic review presenting normative data for ALLR in older adults;

**Table 3:** Systematic presentation of studies examining ALLR in older adults

First author (year)	N	Age	Stimulus	P1		N1		P2		N2		
				Latans (ms)	Amplitude (μ V)	Latans (ms)	Amplitude (μ V)	Latans (ms)	Amplitude (μ V)	Latans (ms)	Amplitude (μ V)	
Cranford 1991	40	20-80 (10=60-80)	NA	NA	NA	97	NA	187	NA	NA	NA	
Tremblay 2003	10	61-79	Speech	NA	Similar to young group	Prolonged	Similar to young group	Delayed	NA	NA	NA	
Coser 2007	19	60-80	Tonebursts	NA	NA	100 \pm 90	NA	176 \pm 25	NA	NA	NA	
Kim 2012	8	60-76	Tone (quite)	NA	NA	111 \pm 11.87	4.62 \pm 2.74	187.5 \pm 21.75	NA	NA	NA	
			Tone (noise)	NA	NA	140.57 \pm 18.54	3.57 \pm 1.11	210.57 \pm 13.44	NA	NA	NA	
O'Brien 2015	8	55-70	Harmonictone	65 \pm 8	2.02 \pm 1.1	104 \pm 10	-0.02 \pm 0.95	171 \pm 15	2.0 \pm 1.4	NA	NA	
Tome 2015	307	61-85	deviant	NA	NA	99.6 \pm 9.1	6.8 \pm 5.0	NA	NA	238.3 \pm 26.9	2.3 \pm 2.0	
Lister 2016	17	Mean 72.8	Pure tone	39.2 \pm 7.3	1.4 \pm 1.0	94.8 \pm 86	-4.1 \pm 1.7	207 \pm 19.2	3.7 \pm 1.9	NA	NA	
			Speech	41.0 \pm 6.2	1.5 \pm 0.9	95.5 \pm 9.8	-3.9 \pm 1.6	201.1 \pm 10.8	3.8 \pm 1.9	NA	NA	
Konrad 2017	71	26-71	Tone bursts	NA	NA	112	NA	111	NA	NA	NA	
Gurkan 2020	57	65-88	Speech	36.12 \pm 9.22	2.24 \pm 1.92	90.74 \pm 9.22	-6.37 \pm 2.72	185.67 \pm 19.13	4.90 \pm 2.39	NA	NA	
Our study	31	65-85	Tone-bursts	R	51.5 \pm 4.4 (42.3–62.2)	7.6 \pm 2.3 (3.7–14.7)	103.0 \pm 9.4 (83.3–127.0)	7.5 \pm 2.1 (4.3–12.6)	203.6 \pm 17.4 (169.3–232.8)	2.8 \pm 1.7 (0.5–7.8)	288.0 \pm 22.3 (240.8–351.9)	NA
				L	50.8 \pm 4.9 (42.3–62.2)	6.7 \pm 2.0 (2.7–11.4)	104.4 \pm 9.9 (86.0–121.7)	7.0 \pm 2.5 (3.2–13.4)	205.5 \pm 14.2 (182.6–236.6)	2.1 \pm 1.3 (0.5–7.0)	281.5 \pm 26.0 (188.4–332.1)	NA

NA: Not Available

however, this systematic review only included data on N1 and N2 waves. In the present study, normative data for both latency and amplitudes of the N1, N2, P1, and P2 waves were presented with a sufficient sample size. We believe that our study will make a significant contribution to the literature and will shed light on further research on this subject.

Despite these strengths, the study has several limitations. The cognitive status of the individuals participating in the study could not be evaluated objectively. Furthermore, the pure tone was preferred as an auditory stimulus. Speech sounds could

also be used as auditory stimuli, and both stimuli could have been compared. We recommend that these factors be considered in future studies.

In the present study, the normative data for ALLR in older adults indicate that the latencies of the N1 and P2 waves in the right ear and N1 and N2 waves in the left ear were longer in males than in females. Additionally, P1-N1 and N1-P2 amplitudes in the left ear were found to be greater in females than in males. Knowing the effect of gender on ALLR in older adults will provide clinically accurate assessment of these patient groups.

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