The Journal of International Advanced Otology

J Int Adv Otol 2024; 20(3): 216–224 • DOI: 10.5152/iao.2024.231270

Original Article

P1–N1–P2 Cortical Auditory Evoked Potentials in Chronic Unilateral Acquired Conductive Hearing Loss in Adults

Abeir Osman Dabbous[1], Noha Ali Hosni[1], Alzahraa Al-Sayed Owais Emara[2], Adel Said El-Antably[3]

[1]Department of Otolaryngology, Audiological Medicine Professor of Audio-Vestibular Medicine, Audiology Unit, Kasr-Al-Ainy Faculty of Medicine, Cairo University, Egypt
[2]Department of Otolaryngology, Resident in the Audio-Vestibular Unit, Ain-Shams General Hospital, Ministry of Health, Cairo, Egypt
[3]Department of Otolaryngology, Assistant Professor of Otolaryngology, Kasr-Al-Ainy Faculty of Medicine, Cairo University, Egypt

ORCID iDs of the authors: A.O.D. 0000-0003-0288-077X, N.A.H. 0009-0001-0845-9954, A.A.O.E. 0009-0002-0864-7936, A.S.E. 0000-0002-3202-0407.

Cite this article as: Dabbous AO, Hosni NA, Emara AAO, El-Antably AS. P1-N1-P2 cortical auditory evoked potentials in chronic unilateral acquired conductive hearing loss in adults. *J Int Adv Otol.* 2024;20(3):216-224.

BACKGROUND: Chronic unilateral hearing loss causes imbalanced auditory input to the brain that triggers cortical reorganization. The effect of sensorineural hearing loss on the central auditory system (CAS) has been thoroughly studied, while there is a paucity of research on the effect of conductive hearing loss (CHL). The aim of this study was to assess the P1-N1-P2 cortical auditory evoked response potential (CAEP) in adult individuals with chronic acquired unilateral CHL.

METHODS: This study included 108 participants of both genders: 54 patients with unilateral chronic CHL who were compared to well-matched 54 controls. All were subjected to history-taking, otologic examination, basic audiological evaluation, and bone conduction N1-P2 CAEP.

RESULTS: The affected ears of the cases showed highly statistically significant shorter CAEPs N1, P2, N1-P2 latencies but not P1, and showed highly statistically significant larger N1, P2, N1P2, amplitude than the control group. Latencies decreased and amplitudes increased as the degree of CHL increased, but were not affected by patients' age, side, or duration of the CHL. Cases with tinnitus had statistically significant and worse results than those without tinnitus.

CONCLUSION: Unilateral chronic CHL might enhance neurocortical plasticity, with greater changes occurring at greater degrees of the CHL.

KEYWORDS: Auditory plasticity, chronic conductive hearing loss, cortical auditory evoked potential, cortical reorganization, tinnitus, unilateral

INTRODUCTION

Conductive hearing loss (CHL) may have many etiologies, all of which all result in the elevation of hearing thresholds. Otitis media raises the hearing thresholds by at least by 20 dB, and up to 50 dB in severe cases.[1] The effect of CHL on the central auditory nervous system and the resulting deficits have not thoroughly studied.[2]

The brain receives imbalanced auditory signals in cases of chronic unilateral hearing loss, resulting in cortical reorganization and modifications in brain networks involving sensory, conductive, and cognitive functions, including difficulties in localization and speech discrimination in noise, dysphoria, and restlessness.[3,4]

Cortical auditory evoked potentials (CAEPs) are long-latency responses occurring 50 to 300 ms after the onset of the stimulus. The CAEPs are exogenous potentials that are an obligatory product of stimulus characteristics. The CAEPs consist of: N1, the first negative voltage occurring at 90 to 150 ms (average 100 ms) after the stimulus, and is followed by P2, a positive wave occurring at between 160 and 200 ms. P1 is an earlier positive component at 40 to 50 ms appearing less consistently than N1 and P2. N2, a second negative component sometimes absent in normal subjects, follows P2 with a latency of 275 ms. In the mature CAEP and in adults, P1 and N2 Peaks are less prominent, and the response is dominated by N1 and P2.[5] The adult N1 and P2 waves appear to have

Corresponding author: Abeir Osman Dabbous, e-mail: abeirdabbous@kasralainy.edu.eg
Received: July 01, 2023 • **Revision requested:** December 04, 2023 • **Last revision received:** January 10, 2024 • **Accepted:** January 24, 2024 • **Publication Date:** May 23, 2024
Available online at www.advancedotology.org

multiple generators in the primary and secondary auditory cortex in Heschl's gyrus of both hemispheres. Although N1-P2 is affected by arousal level, it does not require cognitive processing.[6]

It has been proven in animals but inconsistently in humans that the central auditory system (CAS) undergoes structural and functional modifications affecting the auditory cortical response.[7,8] Recently, Parry et al,[9] showed results that provide direct evidence of increased neural response amplitude in the adult human auditory cortex. They showed significantly greater amplitudes of P1-N1 and N1-P2 in unilateral CHL cases than their controls.

Many researchers studied the effect of sensorineural hearing loss (SNHL) on the CAS, but as far as we are aware, there is only one research that assessed the effect of CHL on the CAS of humans, which needs to be thoroughly assessed for early intervention if necessary. The aim of the work was to study the adult N1-P2 CAEP in individuals having unilateral chronic acquired CHL, when stimulating the affected ear, and to correlate CAEP parameters (CAS), with the degree and duration of the CHL.

MATERIAL AND METHODS

This study included a case group that included 54 ears of 54 adults with acquired unilateral CHL patients of at least one year duration, including cases having otitis media with effusion (OME), cases having otosclerosis, and others having chronic suppurative otitis media (CSOM), and 20 to 43 years old. The degree of the CHL was defined according to the air conduction pure tone hearing threshold level (HTL) average including the frequencies: 0.5kHz, 1kHz, 2kHz, and 4kHz (to include the Arabic language), with normal bone conduction hearing threshold level. Patients included were those coming to the Unit of the Audio-Vestibular Medicine for hearing testing. The control group included 54 right ears of 54 normal hearing healthy volunteer adult subjects (32 to 45 years old, gender-matched to the cases). This study was conducted from December 2019 to December 2020, after the Otorhinolaryngology Department's Medical Ethics Committee of Cairo University approval (Approval Number: MS-37; Date: September 7, 2019). All participants signed an informed consent. Exclusion criteria: individuals aged below 20 years and above 60 years; SNHL, mixed hearing loss, recent-onset CHL (<1year duration), bilateral CHL, any medical or neurological disease that may affect the auditory pathways (e.g., diabetes mellitus, hypertension). Testing included 1) history taking; 2) otologic evaluation; 3) audiometric testing in an Amplisilence model E Sound treated room, including i) pure tone audiometry using Madsen Itera II, audiometer (Otometrics, Denmark): Air conduction at octave intervals (frequency range from 250 to 8000 Hz), and bone conduction at octave intervals (frequency range from 500 to 4000 Hz); ii) speech audiometry including speech recognition threshold (SRT) and word discrimination score (WDS); iii) 226 Hz probe tone-tympanometry using Madsen Zodiac 901 middle ear analyzer (Otometrics, Denmark); iv) nasopharyngeal examination for the patients with unilateral type B tympanogram, to identify any nasal or nasopharyngeal changes; v) CAEP testing.

Electrode montage: high forehead (Cz) for the non-inverting electrode, the right or left mastoid (M1 and M2) for the inverting electrode, and the other mastoid for the ground electrode, with impedance kept below 5kΩ during testing. A 1 kHz tone burst stimulus, with 10-msec linear rise/fall times, 60-msec plateau time, and 80 ms duration, was presented via a bone transducer (B71) placed on the mastoid of the tested ear, at a rate of 1.1/s, at a level of 20 dBHL above the participant's bone conduction (BC) threshold. An insert earphone (EAR-3A10 Ω) was used for air conduction (AC) contralateral masking, with a narrow-band noise presented 30 dB higher than the level of the stimulus, following the protocol of Parry et al,[9] protocol, to exclude any response from the non-tested ear due to cross hearing. A total of 500 accepted sweeps were recorded, with a high pass filter (0.1 Hz) and a low pass filter (35 Hz). The artifact rejection level was set at 200 μV, while the subjects, as instructed, remained seated and alert, performing a quiet task such as reading. The parameters measured were N1 latency, P2 latency, and N1, P2 peak to peak amplitude.

Statistical Analysis

Data entry was done through Microsoft Excel 2013, and the Statistical Package for the Social Sciences (SPSS®), version 21.0, was used (IBM SPSS Corp.; Armonk, NY, USA). The arithmetic mean and standard deviation were calculated to describe quantitative data, while count and percent were used for qualitative data. Cross-tabulations were performed, and using the chi-square test or Fisher exact test was used when needed were performed to compare proportions of qualitative data. To compare normally distributed quantitative data, the independent *t*-test was used. The Pearson correlation coefficient (*r*) was used to compare normally distributed quantitative data. A *P*-value < .05 was considered statistically significant.

RESULTS

The CHL cases did not statistically significantly differ from their controls regarding gender but differed regarding age ($X^2 = 0.038$; $P = .845$): 31 (57.4%) of the cases were males, and 23 (42.6%) were females, compared to 32 (59.3%) and 22 (40.7%) of the controls. The cases showed a mean age of 30.56 ± 5.86 years (20-43 years), while that of the controls was 38.15 ± 3.71 years (32-45 years). The CHL cases showed a mean duration of 1.76 ± 0.53 years, (1.1 - 3.1 years). CHL was right-sided in 37/54 (68.5%) and left-sided in 17 (31.5%); CHL was mild in 21 (38.90%), and moderate in 33 (61.10%). The CHL was due to CSOM in 14 (25.9%), OME in 22 (40.7%), and otosclerosis in 18 (33.3%). In the affected ears, the mean air–bone gap (ABG) was: 27.22 ± 5.72 (15-40) dB; 27.29.17 ± 5.81 (20-40) dB; 29.17 ± 5.81 (20-40) dB and 28.24 ± 5.59 (20-40) dB at 0.5 kHz, 1 kHz, 2 kHz, and 4 kHz respectively. The mean audiogram for the affected ear of the cases is shown in Figure 1. Of those with intact tympanic membranes, 18 (45%) had type A tympanometry, and 22 (55%) had type B tympanometry, of which the Nasopharyngeal examination was free in 17/22 patients (77.3%) and showed pharyngitis in

MAIN POINTS

- Unilateral chronic conductive hearing loss (CHL) in adults might enhance neurocortical plasticity and increase central auditory gain, that was reflected in cortical auditory evoked potentials latencies, and amplitudes.
- The greater the degree of hearing loss, the more enhanced were these neurocortical plasticity changes.
- Tinnitus hindered these changes.
- Patients' age, duration, or side of the CHL had no effect on these changes.

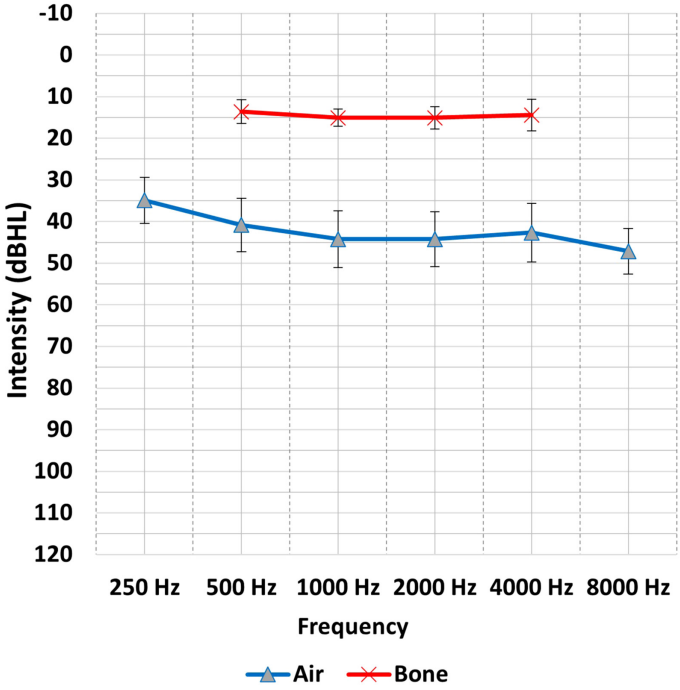

Figure 1. Mean and standard deviation of the air and bone conduction pure tone audiometric thresholds at different frequencies for the affected ear of the cases.

5/22 patients (22.7%). Tympanoplasty was then done in 9/14 CSOM patients (64.3%). Ten out of the 54 patients were on the waiting list for different surgeries. Table 1 shows the demographic information of the participants (n = 54).

Figures 2 and 3 show an example for CAEPs: P1, N1, P2, N1P2, trace for the tested ear of a control subject, and the CHL ear of a case respectively in this study. The CHL ears of the cases showed highly statistically significant shorter BC- CAEPs N1, P2, and N1-P2 latencies

Table 1. The Demographic Information of the Participants (n = 54)

Gender: (Male/Female) n ratio	31/23 (1:1.5)
Age (years) mean, SD, min-max.	30.56 ± 5.859 (20-43)
Duration of CHL (years) mean, SD, min-max.	1.76 ± 0.53 (1.1-1.3)
Cause of CHL: (CSOM/OME/Otosclerosis) n %	14/22/18 (25.9/40.7/33.3)
Degree of hearing impairment: (mild/moderate) n ratio	21/33 (1:1.57)
Ear discharge n %	12 (22.20%)
Ear operations n %	9 (16.70%)
Tinnitus n %	27 (50%)
Vertigo n %	9 (16.70%)

CHL, conductive hearing loss; CSOM, chronic suppurative otitis media; OME, otitis media with effusion.

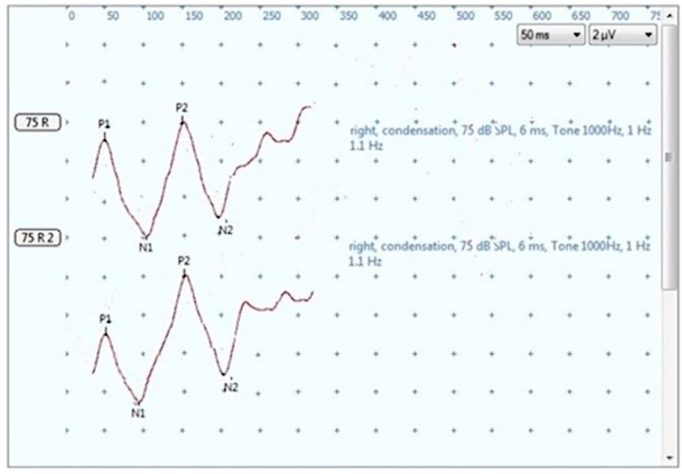

Figure 2. An example trace for CAEPs: P1, N1, P2, N1P2, for the tested ear of one of the controls in this study (male, 23 years old, right ear).

but not P1 and a statistically significantly larger N1, P2, N1-P2 amplitude (Table 2) than the tested ears of the control group. Cases with tinnitus: 27 (50%) had statistically significant smaller amplitude and delayed latency of CAEP except the P1 latency and the N1 P2 latency difference than those without tinnitus: 27 (50%). There was no right/left side difference in the cases regarding CAEP amplitude or latency.

Table 3 shows the Pearson correlation coefficient (r) between the CAEP latency and amplitude with the AC hearing threshold and with the ABG at different frequencies, as well as with the SRT, WDS, CHL ear and with CHL duration, and cases' age. A statistically significant moderate negative correlation was found between the affected ear AC hearing threshold at 500 and 4000Hz and both N1 and P2 latency. Additionally, a strong statistically significant negative correlation was found between the affected ear AC hearing threshold at 1000 and 2000Hz and both N1 and P2 latency. Furthermore, a statistically significant strong positive correlation was found between the affected ear AC hearing threshold at 1000, 2000, and 4000Hz and N1, P2, and N1-P2 amplitude. There was also a moderate positive correlation between the affected ear AC hearing threshold at 500 and all amplitudes, as well as between the AC threshold of hearing at 4000 and CAEPs N1 amplitude.

A statistically significant strong negative correlation was found between the affected ear ABG at 1000, 2000, and 4000 Hz and both

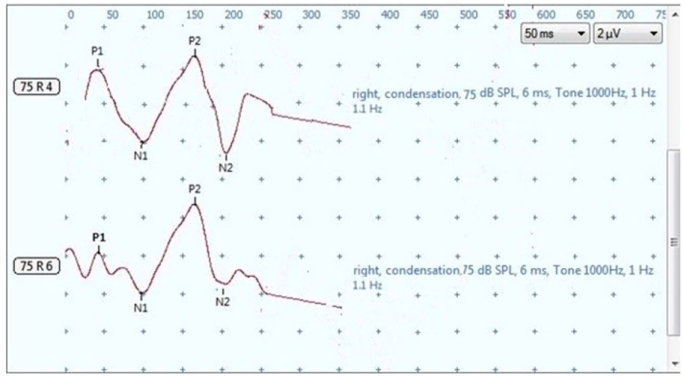

Figure 3. An example for CAEPs: P1, N1, P2, N1P2, trace for the affected ear of one of the cases in this study (male, 40 years old, right ear).

Table 2. Comparison Between the Affected Ears of the Cases Group and the Tested Ears of the Control Group Regarding Bone Conduction CAEPs: P1, N1, P2, N1P2, Latency and P1, N1, P2, N1-P2, Amplitude

Bone Conduction CAEPs	Cases Group Affected Ears				Controls Tested Ears				*t*-value	*P*
	Mean	SD	*Min*	*Max*	Mean	SD	*Min*	*Max*		
P1 Latency (ms)	48.13	1.19	45.9	50.23	48.54	1.14	45.9	50.23	1.79	.075
N1 Latency (ms)	76.69	2.34	72.22	79.85	87.4	2.08	85.22	98.71	25.11	<.001*
P2 Latency (ms)	155.77	2.6	150.42	159.86	177.45	1.49	174.3	179.8	53.18	<.001*
N1-P2 Latency (ms)	79.07	1.25	76.27	82.67	90.05	2.03	81.09	94.27	33.82	<.001*
N1 amplitude (uv)	4.15	0.42	3.3	4.9	3.24	0.07	3.1	3.35	-15.59	<.001*
P2 amplitude (uv)	5.21	0.43	4.5	6	3.89	0.07	3.8	4.21	-22.00	<.001*
N1-P2 amplitude (uv)	9.35	0.83	7.9	10.7	7.13	0.11	6.93	7.45	-19.6	<.001*
P1 Latency (ms)	48.13	1.19	45.9	50.23	48.54	1.14	45.9	50.23	1.79	.075

CAEPs, cortical auditory evoked potentials.
*$P < .05$ (statistically significant).

Table 3. Pearson correlation coefficient (*r*) between the CAEP latencies and Amplitudes with the air conduction hearing threshold, the air–bone gap at different frequencies, the Speech reception threshold, word discrimination score in the affected ear and with the duration of the conductive hearing loss and age of the cases

Frequency:			Bone Conduction CAEPs						
			Latency				Amplitude		
			P1	N1	P2	N1-P2	N1	P2	N1 P2
Affected (CHL) ear air conduction hearing threshold	250 Hz	*r*	0.035	−0.012	−0.039	−0.058	0.158	0.138	0.153
		P	.804	.933	.782	.677	.253	.319	.269
	500 Hz	*r*	0.008	−0.556	−0.469	0.064	0.624	0.64	0.654
		P	.956	.000*	.000*	.643	.000*	.000*	.000*
	1000 Hz	*r*	−0.024	−0.81	−0.813	−0.172	0.793	0.823	0.836
		P	.864	.000*	.000*	.214	.000*	.000*	.000*
	2000 Hz	*r*	−0.044	−0.788	−0.768	−0.12	0.742	0.762	0.778
		P	.754	.000*	.000*	.389	.000*	.000*	.000*
	4000 Hz	*r*	−0.06	−0.64	−0.663	−0.18	0.642	0.718	0.705
		P	.67	.000*	.000*	.192	.000*	.000*	.000*
	8000 Hz	*r*	−0.151	−0.145	−0.139	−0.019	0.045	0.166	0.11
		P	.279	.296	.315	.894	.747	.231	.428
Affected (CHL) ear air–bone gap	500 Hz	*r*	−0.04	−0.599	−0.561	−0.044	0.661	0.727	0.718
		P	.775	.000*	.000*	.75	.000*	.000*	.000*
	1000 Hz	*r*	−0.104	−0.831	−0.817	−0.14	0.797	0.868	0.862
		P	.459	.000*	.000*	.311	.000*	.000*	.000*
	2000 Hz	*r*	−0.104	−0.831	−0.817	−0.14	0.797	0.868	0.862
		P	.459	.000*	.000*	.311	.000*	.000*	.000*
	4000 Hz	*r*	−0.06	−0.841	−0.808	−0.103	0.779	0.842	0.839
		P	.668	.000*	.000*	.458	.000*	.000*	.000*
age		*r*	0.178	−0.058	−0.047	0.011	−0.186	−0.054	−0.123
		P	.203	.676	.736	.936	.179	.699	.377
Duration of CHL		*r*	0.09	−0.012	0.037	0.099	0.006	−0.017	−0.006
		P	.521	.929	.792	.475	.965	.902	.966
SRT in the affected ear		*r*	−0.099	−0.84	−0.77	−0.029	0.851	0.832	0.87
		P	.479	.000*	.000*	.837	.000*	.000*	.000*
WDS in the affected ear		*r*	0.08	0.796	0.784	0.139	−0.834	−0.825	−0.858
		P	.569	.000*	.000*	.316	.000*	.000*	.000*

CAEP, cortical auditory evoked potentials; CHL, conductive hearing loss; SRT, speech reception threshold; WDS, word discrimination score.*
*$P < .05$ (statistically significant).

Table 4. Comparison Between cases with a Mild and Cases with a Moderate Degree of CHL Regarding their Amplitude and Latency of CAEP.

Bone Conduction CAEPs:	Cases with Mild Degree of CHL				Cases with Moderate Degree of CHL				*t*-value	*P*
	Mean	SD	*Min*	*Max*	Mean	SD	*Min*	*Max*		
P1 Latency (ms)	48.38	1.21	45.90	49.77	47.97	1.16	45.97	50.23	1.250	.215
N1 Latency (ms)	78.78	0.89	76.13	79.85	75.36	1.97	72.22	77.73	8.700	<.001*
P2 Latency (ms)	158.04	1.24	155.24	159.86	154.32	2.16	150.42	156.83	8.030	<.001*
N1-P2 Latency	79.25	1.05	77.73	81.04	78.96	1.37	76.27	82.67	0.830	.406
N1 amplitude (uv)	3.70	0.24	3.30	4.10	4.43	0.21	4.00	4.90	−11.58	<.001*
P2 amplitude (uv)	4.79	0.25	4.50	5.40	5.47	0.29	5.00	6.00	−8.90	<.001*
N1-P2 amplitude (uv)	8.49	0.43	7.90	9.50	9.90	0.47	9.20	10.70	−11.19	<.001*

CAEP, cortical auditory evoked potentials; CHL, conductive hearing loss.*P < .05
*P < .05 (statistically significant).

N1 and P2 latencies, while a moderate negative correlation was found at 500 Hz. A statistically significant strong positive correlation was found between the affected ear ABG at 1000, 2000, and 4000 Hz and N1, P2, and N1-P2 amplitude, while a moderate positive correlation was found regarding N1 amplitude and ABG at 500 Hz.

A statistically significant strong negative correlation was found between neither the cases N1 and P2 latencies and the SRT and WDS in the affected ear. A statistically significant strong positive correlation was found between the cases' amplitude of N1, P2, N1-P2 and the SRT and WDS in the affected ear.

Table 4 shows the comparison between cases with a mild and cases with a moderate degree of CHL regarding their amplitude and latency of CAEP. Table 5 shows the comparison between cases with and without tinnitus regarding the bone conduction CAEPs latency and amplitude. A comparison among different etiologies of CHL regarding bone conduction CAEPs latency and amplitude is shown in Table 6.

The age of CSOM: 33.43 ± 5.60 years, OME: 25.91 ± 4.514 years, otosclerosis: 34 ± 3.25 years, with a statistically significant difference between the OME and CSOM patients' groups regarding age (P = 0.000), and between the OME and otosclerosis patients' groups regarding age (P = .000). The duration of CHL was 1.94 ± 0.57 years, 1.48 ± 0.28 years, 1.98 ± 0.59 years in CSOM, OME, and otosclerosis respectively, with a statistically significant difference found between the duration of CHL in OME and CSOM patients (P = .007), and between the duration of CHL in OME and otosclerosis patients (P = .002). However, no statistically significant correlation was found between either the cases' age or the duration of CHL duration and CAEP latencies or amplitude.

Table 5. Comparison Between Cases With and Without Tinnitus Regarding the Bone Conduction Cortical Auditory Evoked Potentials Latency and Amplitude

Bone Conduction CAEPs:	Cases Without Tinnitus (N = 27)		Cases With Tinnitus (N = 27)		*t*-value	*P*
	Mean	SD	Mean	SD		
P1 latency (ms)	47.94	1.21	48.32	1.16	−1.16	.251
N1 latency (ms)	75.98	1.72	77.40	2.68	−2.30	.026*
P2 latency (ms)	154.97	1.90	156.57	2.97	−2.35	.023*
N1-P2 latency (ms)	78.98	1.36	79.17	1.15	−0.54	.589
N1 amplitude (uv)	4.35	0.18	3.94	0.49	4.04	<.001*
P2 amplitude (uv)	5.38	0.29	5.03	0.49	3.22	.002*
N1-P2 amplitude (uv)	9.73	0.43	8.97	0.95	3.77	.001*

CAEP, cortical auditory evoked potentials.
*P < .05 (statistically significant).

All CSOM and the majority of the OME cases (19/22 = 86.4%) had moderate CHL, while all the otosclerosis cases had mild CHL. This distribution was statistically significant (X^2 = 43.098; P = .000). Chronic suppurative otitis media cases showed a statistically significant shorter N1 latency and P2 latency and larger N1, P2 amplitudes compared to OME cases, who in turn showed a significant shorter N1, P2 latencies and greater N1, P2 amplitudes than those of the otosclerosis cases. Cases with mild CHL had statistically significant delayed N1 latency and P2 latency and smaller amplitudes of N1 and P2 than cases with moderate CHL.

DISCUSSION

Conductive Hearing Loss and Cortical Auditory Evoked Potentials

The present study showed that CHL enhances neurocortical plasticity: reflected in the statistically significant shorter BC CAEPs N1, P2, and N1-P2 latencies, and larger BC N1 amplitude, P2 amplitude, N1-P2 amplitude in the CHL ears compared to the control group ears. This could be due to reduced auditory input from the CHL ear that resulted in decreased central auditory inhibition, leading to increased gain centrally as a neural adaptation mechanism.

However, P1 was still comparable to the controls. P1, which originates from the primary auditory cortex, gets enhanced in response to short-term auditory deprivation as was previously shown.[9] However, the minimal duration in the current study was one year, which may explain this result.

Parry et al,[10] were the first study to reveal an alteration in the cortical response in adults having unilateral chronic CHL depriving the ear of sensory stimulation. They found that the CHL group showed statistically significantly larger mean P1-N1-P2 amplitudes than their well-matched controls. They explained the reason for this change to be 'homeostatic plasticity,[11] which is a neural adaptation through

Table 6. Comparison Among the Different Etiologies of Conductive Hearing Loss in the Cases Group Regarding Bone Conduction Cortical Auditory Evoked Potentials Latency and Amplitude

		Bone Conduction CAEPs						
		Latency (ms):				Amplitude (uv):		
		P1	N1	P2	N1-P2	N1	P2	N1 P2
CSOM (n = 14)	Mean	48.12	73.22	152.14	78.92	4.62	5.76	10.39
	SD	1.18	0.72	1.48	1.92	0.14	0.13	0.20
	Min	45.97	72.22	150.42	76.27	4.40	5.50	10.10
	Max	50.23	74.47	154.89	82.67	4.90	6.00	10.70
OME (n = 22)	Mean	47.87	76.96	155.94	78.98	4.26	5.26	9.52
	SD	1.22	0.60	0.58	0.83	0.14	0.17	0.23
	Min	45.97	76.10	155.09	77.52	4.00	5.00	9.00
	Max	49.73	77.90	156.83	80.06	4.50	5.50	10.00
Otosclerosis (n = 18)	Mean	48.45	79.07	158.37	79.31	3.64	4.71	8.35
	SD	1.15	0.50	0.95	1.07	0.20	0.13	0.24
	Min	45.90	78.28	157.27	77.73	3.30	4.50	7.90
	Max	49.77	79.85	159.86	81.04	3.90	5.00	8.90
*F***		1.160	370.943	154.097	0.474	145.110	208.086	330.577
P		.322	.000*	.000*	.625	.000*	.000*	.000*
Post hoc test	*Latency (ms)*			*Amplitude (uv)*				
	N1	*P2*	*N1*	*P2*	*N1 P2*			
OME: CSOM	0.000*	0.000*	0.000*	0.000*	0.000*			
OME: Otosclerosis	0.000*	0.000*	0.000*	0.000*	0.000*			
CSOM: Otosclerosis	0.000*	0.000*	0.000*	0.000*	0.000*			

CAEP, cortical auditory evoked potentials; CSOM, chronic suppurative otitis media; OME, otitis media with effusion.
*$P < .05$ (statistically significant).
**F of ANOVA

regulation of neuronal excitability and synaptic efficiency for cortical activity stabilization in response to changes in auditory experience instead of neural or cochlear pathology. Results of the current study are in accordance with their study.

To the best of our knowledge, there is no more research on adults to compare with. On the other hand, although Sanfins et al,[12] found that females with bilateral OME showed prolonged P2 latency and N2 latency than their controls, but this was not demonstrated in unilateral OME 6 years and under. This was probably because P2 can differentiate the occurrence of either ipsilateral stimulation or contralateral stimulation,[13] while acoustic perception is represented by N1.[13] The importance of P2 resides in that it reflects the number of activated auditory neurons as a result of stimulation.[12]

Maruthy and Mannarukrishnaiah,[14] showed that children who had a history of OME showed a prolonged CAEP component waves P1, N1, P2, N2. But children 3 years old showed shorter latencies than controls.[13] While Colella-Santos et al,[15] showed that children who had a history of OME showed a prolonged CAEP last 2 waves (P2, N2). Shaffer,[16] showed that N1 and P2 latencies were prolonged only in active OME than either children who had a history of OME or who had just a few occurrences of OME. But Sanfins et al,[12] found that those with recurrent OME caused chronic damage to the CANS resulting in auditory deprivation. Cortical reorganization was demonstrated by Maruthy and Mannarukrishnaiah,[14] who showed the increased central gain phenomenon as a compensatory mechanism to lower auditory system lesion[17], reflected by earlier CAEP latencies[14], with prolonged I-III and I–V interpeak intervals in auditory brainstem response.[14]

The 2 deoxy-glucose uptake, which measures the metabolic activity of the major ascending pathways from the stimulated ear, showed a marked decrease in both neonatal and adult gerbils with CHL and cochlear ablation. However, the CANS effects in CHL in adults were different and significantly less than CHL in the young or the cochlear ablation in adults.[18] Also, using magnetic resonance imaging enhanced by Mn2+, younger mice with unilateral CHL showed more effect on neural activity than older mice.[19] However, Cañete et al,[20] did not find speech sounds elicited CAEPs differences between children with unilateral congenital aural atresia compared to controls.

Studies of young adult mice with chronic CHL induced by tympanic membrane TM removal, and others due to chronic otitis media, showed that auditory deprivation, per se, damages the afferent and efferent pathways, especially the terminals of the lateral olivocochlear to the inner hair cells, in the same manner as known to be happening by hearing loss due to noise or aging. Part of the long-lasting disturbances in human CANS processing after chronic middle ear diseases can originate from the cochlea.[21]

Rodents developed audiogenic seizures reflecting a reduction in central inhibition as a consequence of sound deprivation after CHL due to damage to the tympanic membrane. This effect of an extreme increase in central nervous system activity is not found in CHL in children after OME.[22]

Normal-hearing adult listeners who have had unilateral CHL by using earplugs for a prolonged time have resulted in partial reversible sound deprivation and could be measured by the acoustic reflex threshold. This effect was bilateral and due to increased central auditory gain.[23]

The auditory system plasticity does not remain always the same throughout life. There are times when the auditory system is more sensitive to the surrounding environment and sound inputs.[24,25] But there are many developmental periods during which the central auditory system functional organization can be affected by auditory experience, and this adaptive plasticity only exerts its influence at a critical time. By training adult animals, the cortical auditory representation can be altered.[26]

Effect of the Side and Degree of Conductive Hearing Loss on Neurocortical Plasticity

In the current study, there were no significant differences in affecting neurocortical plasticity, which is in agreement with Sanfins et al[11] In the current study, there were greater neuro cortical plastic changes with increased AC hearing threshold, SRT, and the ABG reflecting a greater amount of CHL.

Xu et al,[2] showed that mild to moderate CHL can cause functional changes in the auditory cortex in the form of an increase in short-term synaptic depression, postsynaptic potential latency, and a decrease in action potential adaptation, and changes in the postsynaptic potentials with an increase in the latency of spikes.

Conductive hearing loss caused by ear occlusion resulted in the modification of synaptic properties at the beginning of the auditory pathway through size reduction and increased ability to neurotransmitter release.[27] This results in faster depletion of the synapses, which reduces the resolution at central parts of the auditory nerve, affecting the perception. Conductive hearing loss may result in changes similar to these in higher levels of the auditory pathway, sharing in behavioral disturbances.[28]

Effect of Patient's Age, Duration and Etiology of Conductive Hearing Loss on Cortical Auditory Evoked Potentials

In the present study, although the cases' mean age was statistically significantly younger than their controls, the eldest of the controls was 43 years and of the cases was 45 years, which was not assumed to affect the CAEP response. Moreover, no significant correlation was found between either CAEP latency or amplitude of the controls with their age, nor between the cases' CAEP latency or amplitude with their age as well as CHL duration. However, the duration range varied from 1.1 to 3.1 years only, which was not wide enough to allow studying the effect of prolonged hearing loss duration. This needs further studies using a bigger duration range for each etiology of CHL to assess its effect. However, the enhanced CAEP response despite this short duration and the greater effect with the greater degree of hearing loss may reflect that the amount of auditory deprivation per se and not the deprivation time was the factor that reflexly causes cortical reorganization and shows a positive effect on the cortical auditory activity. This was previously shown by Li et al,[28] and Morita et al,[29] in cases of idiopathic sudden sensorineural hearing loss, where the resultant partial asymmetrical hearing loss, of sudden onset, resulted in enhanced cortical auditory evoked responses.

Buran et al,[30] stated that juvenile-onset CHL in animals resulted in impairment of frequency modulation detection more than adult-onset CHL of the same sensory deprivation duration. But unilateral CHL can result in auditory cortex effects that can or cannot be age dependent. Adult-onset hearing loss is accompanied by weaker inhibition possibly due to changes in the amount and release of GABA.[31] These findings can differentiate the period of onset of hearing loss and can explain the effect of CHL on auditory perception in adults.[31] Vanderauwera et al,[32] also concluded that unilateral hearing loss is a complex condition regarding the auditory deprivation mechanism and adaptive central plasticity.

In the current study, CSOM cases showed a statistically significant shorter latency of N1 and of P2, as well as greater N1 and P2 amplitudes than OME cases, who in turn showed a significant shorter latency of N1 and of P2, as well as greater N1 and P2 amplitudes than otosclerosis cases. This might be related to the severity of the CHL, not age or duration of the CHL because although the OME cases showed a statistically significant shorter CHL duration and younger age compared to each of the CSOM and otosclerosis cases, age and CHL duration in this study were not found to be correlated with CAEP latencies or amplitudes. Moreover, all CSOM and the majority of the OME cases had moderate CHL, while all the otosclerosis cases had mild CHL. Hearing loss degree in this study was correlated with CAEP N1 and P2 latencies and amplitudes, so we assumed that the earlier latencies and greater amplitudes were due to the greater degrees of hearing loss. The greater effect of CSOM than OME on neuroplasticity needs to be further explored.

Effect of Tinnitus on Cortical Auditory Evoked Potentials

In the present study, cases with tinnitus had a statistically significant delayed latency of CAEP except for the P1 Latency and the N1 P2 latency difference and had a significantly smaller amplitude than those without tinnitus. So, it seems that the presence of tinnitus-related central neuronal activity hinders other neuroplastic cortical changes induced as a result of chronic peripheral hearing loss. Tinnitus, which may or may not be accompanied by hearing loss, may result from hyperactivity in the auditory cortex and overamplification of spontaneous neural activity. While peripheral hearing loss results in cortical reorganization and increased neural gain and may or may not be accompanied with tinnitus.

Zeng[33] reported that there are 2 potential mechanisms allowing the central system to compensate for reduced peripheral input: Increasing central noise or increasing central gain. An additive central noise, which compensates for elevated hearing thresholds like those seen in traditional hearing loss, is more likely to induce tinnitus than hyperacusis.

Wang et al,[34] reported that tinnitus can be generated anywhere in the auditory pathway, from the ear canal to the auditory cortex. Adaptive changes related to tinnitus in CAS (neural plasticity)[35] result

in the maintenance of this phantom perception. These are maladaptive neuroplastic changes which begin at the cochlear nucleus and proceed to the auditory cortex and other brain areas, including an increase in the spontaneous firing rates and an increase in synchrony among CAS neurons[36] or a decrease in central inhibition through the efferent auditory pathway [37,38]

To sum up, reduced auditory input from the CHL ear results in a decreased auditory input that can decrease central auditory inhibition, leading to increased central auditory gain, which is reflected in an enhanced BC CAEPs response.

Unilateral chronic conductive hearing loss in adults might enhance neurocortical plasticity and increase central auditory gain, reflected in the statistically significant shorter bone conduction CAEPs N1, P2, and N1-P2 latencies, and larger bone conduction N1, P2, N1-P2 amplitudes in the CHL ears of cases compared to their controls. These changes are enhanced by the greater degrees of hearing loss but hindered by the presence of tinnitus and are not affected by the age, duration, or side of the CHL.

Further studies are needed to assess the effect of tinnitus on neuroplasticity and to compare between bilateral and unilateral CHL, and between SNHL and CHL, and among different etiologies and durations of CHL.

Ethics Committee Approval: This study was approved by This study was approved by Ethics committee of Faculty of Medicine, Cairo University (Approval Number: MS-37; Date: September 7, 2019).

Informed Consent: Informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.O.D.; Design – A.O.D.; Supervision – A.O.D., A.S.E., N.A.H.; Resources – A.A.O.E.; Materials – A.A.O.E.; Data Collection and/or Processing – A.A.O.E.; Analysis and/or Interpretation – A.A.O.E., A.O.D., A.S.E., N.A.H.; Literature Search – A.A.O.E.; Writing – A.O.D., A.A.O.E.; Critical Review – A.O.D., A.S.E., N.A.H.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declare that this study received no financial support.

REFERENCES

1. Roberts J, Hunter L, Gravel J, et al. Otitis media, hearing loss, and language learning: controversies and current research. *J Dev Behav Pediatr*. 2004;25(2):110-122. [CrossRef]
2. Xu H, Kotak VC, Sanes DH. Conductive hearing loss disrupts synaptic and spike adaptation in developing auditory cortex. *J Neurosci*. 2007;27(35): 9417-9426. [CrossRef]
3. Firszt JB, Reeder RM, Holden LK. Unilateral hearing loss: understanding speech recognition and localization variability-implications for cochlear implant candidacy. *Ear Hear*. 2017;38(2):159-173. [CrossRef]
4. Shah J, Pham GN, Zhang J, et al. Evaluating diagnostic yield of computed tomography (CT) and magnetic resonance imaging (MRI) in pediatric unilateral sensorineural hearing loss. *Int J Pediatr Otorhinolaryngol*. 2018;115: 41-44. [CrossRef]
5. Hall III JW. Auditory late responses (ALRs) historical perspective, in: Hall III JW. *eHandbook of Auditory Evoked Responses, Chapter 11 (Kindle Locations:15218-15219)*.2015, Kindle file.
6. Lightfoot G. *The N1-P2 cortical auditory evoked potential in threshold estimation. Insights in practice for clinical audiology*; 2010. https://www.audiologyonline.com/articles/n1-p2-cortical-auditory-evoked-851
7. Syka J. Plastic changes in the central auditory system after hearing loss, restoration of function, and during learning. *Physiol Rev*. 2002;82(3):601-636. [CrossRef]
8. Hine J, Thornton R, Davis A, Debener S. Does long-term unilateral deafness change auditory evoked potential asymmetries? *Clin Neurophysiol*. 2008;119(3):576-586. [CrossRef]
9. Brotherton H, Plack CJ, Maslin M, Schaette R, Munro KJ. Pump up the volume: could excessive neural gain explain tinnitus and hyperacusis? *Audiol Neurootol*. 2015;20(4):273-282. [CrossRef]
10. Parry LV, Maslin MRD, Schaette R, Moore DR, Munro KJ. Increased auditory cortex neural response amplitude in adults with chronic unilateral conductive hearing impairment. *Hear Res*. 2019;372:10-16. [CrossRef]
11. Turrigiano GG. Homeostatic plasticity in neuronal networks: the more things change, the more they stay the same. *Trends Neurosci*. 1999;22(5):221-227. [CrossRef]
12. Sanfins MD, Donadon C, Borges LR, Skarżyński PH, Colella-Santos MF. Long-term effects of unilateral and bilateral otitis media and myringotomy on long-latency verbal and non-verbal auditory-evoked potentials. *Int Arch Otorhinolaryngol*. 2020;24(4):e413-e422. [CrossRef]
13. Baumann SB, Rogers RL, Papanicolaou AC, Saydjari CL. Intersession replicability of dipole parameters from three components of the auditory evoked magnetic field. *Brain Topogr*. 1990;3(2):311-319. [CrossRef]
14. Maruthy S, Mannarukrishnaiah J. Effect of early onset otitis media on brainstem and cortical auditory processing. *Behav Brain Funct*. 2008;4:17. [CrossRef]
15. Colella-Santos MF, Donadon C, Sanfins MD, Borges LR. Otitis media: long-term effect on central auditory nervous system. *BioMed Res Int*. 2019;2019:8930904. [CrossRef]
16. Shaffer EK. Auditory evoked potentials in children with and without otitis media. Tejas - Texas. *J Audiol Speech Pathol*. 1999;XXIII:10-20.
17. Salvi RJ, Wang J, Ding D, Stecker N, Arnold S. Auditory deprivation of the central auditory system resulting from selective inner hair cell loss: animal model of auditory neuropathy. *Scand Audiol Suppl*. 1999;51:1-12.
18. Tucci DL, Cant NB, Durham D. Conductive hearing loss results in a decrease in central auditory system activity in the young gerbil. *Laryngoscope*. 1999;109(9):1359-1371. [CrossRef]
19. Yu X, Wadghiri YZ, Sanes DH, Turnbull DH. In vivo auditory brain mapping in mice with Mn-enhanced MRI. *Nat Neurosci*. 2005;8(7):961-968. [CrossRef]
20. Cañete OM, Purdy SC, Brown CRS, Neeff M, Thorne PR. Behavioural performance and self-report measures in children with unilateral hearing loss due to congenital aural atresia. *Auris Nasus Larynx*. 2021;48(1):65-74. [CrossRef]
21. Liberman MC, Liberman LD, Maison SF. Chronic conductive hearing loss leads to cochlear degeneration. *PLoS One*. 2015;10(11):1423-1441. [CrossRef]
22. Lauer AM, Dent ML, Sun W, Xu-Friedman MA. Effects of non-traumatic noise and conductive hearing loss on auditory system function. *Neuroscience*. 2019;407:182-191. [CrossRef]
23. Munro KJ, Turtle C, Schaette R. Plasticity and modified loudness following short-term unilateral deprivation: evidence of multiple gain mechanisms within the auditory system. *J Acoust Soc Am*. 2014;135(1):315-322. [CrossRef]
24. Takesian AE, Kotak VC, Sanes DH. Developmental hearing loss disrupts synaptic: implications for auditory processing. *Future Neurol*. 2009;4(3):331-349. [CrossRef]
25. Kral A. Auditory critical periods: a review from system's perspective. *Neuroscience*. 2013;247:117-133. [CrossRef]
26. Polley DB, Steinberg EE, Merzenich MM. Perceptual learning directs auditory cortical map reorganization through top-down influences. *J Neurosci*. 2006;26(18):4970-4982. [CrossRef]

27. Zhuang X, Sun W, Xu-Friedman MA. Changes in Properties of Auditory Nerve Synapses following Conductive HEARing Loss. *J Neurosci*. 2017;;37(2):323-332. [CrossRef]
28. Li LP, Shiao AS, Chen LF, et al. Healthy-side dominance of middle- and long-latency neuromagnetic fields in idiopathic sudden sensorineural hearing loss. *Eur J Neurosci*. 2006;24(3):937-946. [CrossRef]
29. Morita T, Hiraumi H, Fujiki N, et al. A recovery from enhancement of activation in auditory cortex of patients with idiopathic sudden sensorineural hearing loss. *Neurosci Res*. 2007;58(1):6-11. [CrossRef]
30. Buran BN, Sarro EC, Manno FA, Kang R, Caras ML, Sanes DH. A sensitive period for the impact of hearing loss on auditory perception. *J Neurosci*. 2014;34(6):2276-2284. [CrossRef]
31. Caspary DM, Ling L, Turner JG, Hughes LF. Inhibitory neurotransmission, plasticity, and aging in the mammalian central auditory system. *J Exp Biol*. 2008;211(11):1781-1791. [CrossRef]
32. Vanderauwera J, Hellemans E, Verhaert N. Research insights on neural effects of auditory deprivation and restoration in unilateral hearing loss: A systematic review. *J Clin Med*. 2020;9(3):812. [CrossRef]
33. Zeng FG. Tinnitus and hyperacusis: central noise, gain and variance. *Curr Opin Physiol*. 2020;18:123-129. [CrossRef]
34. Wang K, Tang D, Ma J, Sun S. Auditory neural plasticity in tinnitus mechanisms and management. *Neural Plast*. 2020;2020:7438461. [CrossRef]
35. Henry JA, Roberts LE, Caspary DM, Theodoroff SM, Salvi RJ. Underlying mechanisms of tinnitus: review and clinical implications. *J Am Acad Audiol*. 2014;25(1):5-22; quiz 126. [CrossRef]
36. Shore SE, Roberts LE, Langguth B. Maladaptive plasticity in tinnitus--triggers, mechanisms, and treatment. *Nat Rev Neurol*. 2016;12(3):150-160. [CrossRef]
37. Caspary DM, Llano DA. Auditory thalamic circuits and GABAA receptor function: putative mechanisms in tinnitus pathology. *Hear Res*. 2017;349:197-207. [CrossRef]
38. Riga M, Katotomichelakis M, Danielides V. The potential role of the medial olivocochlear bundle in the generation of tinnitus: controversies and weaknesses in the existing clinical studies. *Otol Neurotol*. 2015;36(2):201-208. [CrossRef]