Original Article

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Chronic tinnitus: analysis of clinical contributions from different audiological evalutions

Zumbido crônico: análise das contribuições clínicas de diferentes avaliações audiológicas

Hélinton Goulart Moreira[1], *Rúbia Soares Bruno*[2], *Sheila Jacques Oppitz*[2], *Milaine Dominici Sanfins*[3,4], *Michele Vargas Garcia*[5]

ABSTRACT

Purpose: To investigate whether there are differences in peripheral and central audiological findings between individuals with normal hearing thresholds with and without chronic tinnitus, and thereby understand which hearing tests are most important in this population. **Methods:** The sample was composed of convenience, including individuals from 18 to 59 years old, divided into two groups: Group 1 (G1) composed of subjects without complaints of chronic tinnitus, and Group 2 (G2) composed of individuals with chronic tinnitus. The evaluation consisted of the following procedures: Anamnesis, High-frequency audiometry (HFA), Transient Otoacoustic emissions (TOAEs), Auditory Brainstem Response (ABR)-click, Frequency Following Response (FFR), and Long Latency Auditory Evoked Potential (LLAEP)-speak. **Results:** G2 showed increased values for HFA, with significant differences. For both groups, TOAEs showed a predominance of responses. In ABR there were no statistically significant differences. In FFR, G1 obtained a greater amplitude of wave V and there was a greater absence in LLAEP of P1, N2, and P300 in G2. **Conclusion:** The HFA, the analysis of the wave V/I ratio in ABR, the FFR, and the LLAEP identified alterations in individuals with chronic tinnitus, demonstrating that such procedures are promising in the evaluation of this population.

Keywords: Tinnitus; Evoked potential; Hearing; Adult; Auditory cortex

RESUMO

Objetivo: Investigar se há diferenças nos achados audiológicos periféricos e centrais entre indivíduos com limiares auditivos normais com e sem zumbido crônico e, com isso, entender quais exames auditivos são importantes nessa população. **Métodos:** A amostra foi composta por conveniência, incluindo indivíduos de 18 a 59 anos, divididos em dois grupos: grupo 1 (G1), formado por sujeitos sem queixa de zumbido crônico e grupo 2 (G2), por indivíduos com zumbido crônico. A avaliação consistiu nos seguintes procedimentos: anamnese, audiometria de altas frequências (AAF), emissões otoacústicas transientes (EOAT), potencial evocado auditivo de tronco encefálico (PEATE)-clique, *frequency following response* (FFR) e o potencial evocado auditivo de longa latência (PEALL)-fala. **Resultados:** O G2 apresentou valores aumentados para a AFF, com diferenças significativas. Para ambos os grupos, a EOAT mostrou predominância de presença de respostas. No PEATE, não houve diferenças estatisticamente significativas. No FFR, o G1 obteve maior amplitude de onda V e houve maior ocorrência de ausências no PEALL dos potenciais P1, N2 e P300, no G2. **Conclusão**: A AAF, a análise da relação da onda V/I do PEATE, o FFR e o PEALL identificaram alterações nos indivíduos com zumbido crônico, demonstrando que tais procedimentos são promissores na avaliação dessa população.

Palavras-chave: Zumbido; Potenciais evocados; Audição; Adulto; Córtex auditivo

Study carried out at Curso de Fonoaudiologia, Departamento de Fonoaudiologia, Universidade Federal de Santa Maria – UFSM – Santa Maria (RS), Brasil.
[1]Curso de Fonoaudiologia, Universidade Federal de Santa Maria – UFSM – Santa Maria (RS), Brasil.
[2]Programa de Pós-graduação em Distúrbios da Comunicação Humana, Departamento de Fonoaudiologia, Universidade Federal de Santa Maria – UFSM – Santa Maria (RS), Brasil.
[3]Albert Einstein Ensino e Pesquisa, São Paulo (SP), Brasil.
[4]Centro de Eletrofisiologia e Neuroaudiologia Avançada, São Paulo (SP), Brasil.
[5]Departamento de Fonoaudiologia, Universidade Federal de Santa Maria – UFSM – Santa Maria (RS), Brasil.
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Corresponding author: Hélinton Goulart Moreira. E-mail: helintongoulart@hotmail.com
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INTRODUCTION

Tinnitus is a symptom caused by diverse underlying mechanisms and it manifests in many different ways[1]. In 2021, researchers put forward a chaos theory of chronic tinnitus based on dynamic and non-linear functioning of the human brain. It suggests that any change in the auditory system, even if very small, causes auditory deafferentation, which in turn produces generalized and diffuse changes in multiple brain areas and is ultimately experienced as unpleasant tinnitus[2]. In other words, neural deafferentation may result from any decrease in auditory inputs or an imbalance between excitation and inhibition, leading to a compensatory mechanism which results in an increas espontaneous and synchronous neural activity.

In the light of this concept of chronic tinnitus, it becomes necessary to investigate many different auditory and brain areas, and management methods based on current theories may not be effective[2]. Tinnitus is frequently present in individuals who have some type of hearing impairment, although there are frequent reports of its presence in people whose hearing thresholds are within the normal range[3].

Recently, it has been recommended that detailed medical and audiological evaluations be done in individuals with chronic tinnitus as a first approach to improving treatments for tinnitus. The hope is that by understanding the physiological processes involved in the functioning of the peripheral and central auditory nervous systems, it may be possible to provide better clinical management[4].

In any audiological assessment, the possibility of deafferentation should be strongly considered[2]. Neural deafferentation, resulting from cochlear damage or subclinical synaptopathy, causes changes in brain neuroelectrical functioning, reorganization of the cortical tonotopic map, hyperactivity in the auditory cortex and thalamus, and increased neural synchrony, especially in areas connected to the auditory cortex[5].

The focus of this study is on the auditory system, looking to find diagnostic procedure(s) which have the greatest potential to assist in therapeutic management. The aim here was to compare peripheral and central audiological findings on individuals with normal hearing thresholds, with and without chronic tinnitus. We wanted to reinforce the idea that a more accurate diagnosis can be the basis for finding a better way of alleviating tinnitus symptoms[4].

METHODS

This was an analytical, longitudinal, and quantitative study. Subjects were selected by convenience from those who attended a teaching hospital in the south of Brazil from July 2017 to February 2018. The study was approved by the Ethics Committee in Research with Human Beings (CEP da Federal University of Santa Maria, nr 77611417.5.0000.5346).

The research followed the norms and guidelines of Resolution 466/12 of the National Health Council, and all individuals gave signed consent after being informed about the procedures, risks, and benefits.

Participants were enrolled at a clinical audiology outpatient clinic, scheduled via the Municipal Health Department of Santa Maria (RS) for an audiological assessment. A total of 151 individuals of both genders, aged between 18 and 59, were screened. Of these, 129 were excluded for the following reasons: 70 had sensorineural hearing loss; 23, mixed hearing loss; 4, conductive hearing loss; 11, hearing loss at an isolated frequency, and 21 with high-frequency hearing loss. They were excluded because we wanted to test only individuals with or without chronic tinnitus who had normal hearing (thresholds up to 25 dBHL[6]. This meant that the total sample consisted of 22 individuals.

Eligibility criteria

Subjects of both genders, with or without the perception of chronic tinnitus, were included in the study if they had auditory thresholds within the normal range of 0.25 to 8 kHz (up to 25 dBHL), type A tympanometric curves and bilateral contralateral stapedial acoustic reflexes, no history of self-reported or diagnosed neurological or psychiatric disease, and had had no continuous exposure to noise.

The participants were divided into two groups: group 1 (G1), composed of subjects without chronic tinnitus perception, and group 2 (G2), individuals who had had chronic tinnitus for at least 6 months; the tinnitus could be unilateral or bilateral but needed to have an annoyance score of at least 5 on the Visual Analogue Scale (VAS).

The testing protocol had two stages: a set of evaluation procedures (for initial screening) and research procedures (for data analysis). In total, testing took 3 hours.

Evaluation procedures

For screening, a basic audiological assessment was performed involving audiological anamnesis, visual inspection of the external acoustic meatus, pure tone audiometry, logoaudiometry, and acoustic immittance measurement.

To gauge tinnitus, a VAS scale was used – a line on a sheet of paper with the ends numbered from 0 to 10. One end of the line was marked "no ringing" and the other "worst ringing imaginable". The patient was asked to make a mark on the line corresponding to their present level of discomfort. In addition, a Tinnitus Handicap Inventory (THI) questionnaire was verbally addressed to the subject, with responses to 25 questions scored as: "yes" (4 points), "at times" (2 points), or "no" (0 points). The scores were added together to obtain a total score that characterized the severity of the tinnitus: negligible (0 to 16%), mild (18 to 36%), moderate (38 to 56%), severe (58 to 76%), or catastrophic (78 to 100%)[7,8].

Procedures

High frequency audiometry (HFA)

The thresholds of very high-pitched sounds were measured, taking in frequencies from 9 to 18 kHz at intensities up to the maximum of the equipment (110 dB). An Interacoustics

AS10 HF audiometer was used together with Koss headphones, according to the literature[9].

Transient-evoked otoacoustic emissions (TEOAEs)

TEOAEs were measured bilaterally using the Smart EP equipment from Intelligent Hearing Systems (IHS). The procedure was performed in an acoustically treated room using an 80 dB SPL click stimulus in the non-linear mode; 1024 stimuli were recorded in a window of 20 ms ensuring that artifacts were kept below 15%. The pass criterion was a signal-to-noise ratio greater than 3 dB at 3 of the 5 frequencies of 1, 1.5, 2, 3, and 4 kHz[10].

Electrophysiological assessment

For recording auditory evoked potentials, the two-channel Smart EP device was used. Average assessment time was 1.5 hours.

After cleaning the skin with exfoliating gel (Nuprep®), surface electrodes were attached on the scalp with Maxxi Fix® electrolytic paste and secured with adhesive tape, ensuring that the impedance between the electrodes was less than 3 kΩ. During the assessments, subjects were instructed to keep their eyes closed and stay still to reduce muscle artifacts. The light in the room was turned off to avoid electrical interference.

For recording Auditory Brainstem Response (ABR) and frequency following responses (FFRs), the electrodes were positioned as follows: active electrode at Fz; ground electrode at Fpz; and reference electrode on the right and left mastoids[11]. For long latency auditory evoked potentials (LLAEPs), the electrodes were positioned as follows: Fz = ground electrode on the forehead; Cz = active electrode on the cranial vertex; and reference electrodes on the right and left mastoids. These positions are the most common in the literature[12]. The impedance between electrodes was less than 3 kΩ, the residual noise below 0.11 μV, and the signal/noise ratio >1.0. The maximum number of accepted artifacts was 10% of the total number of stimuli.

Auditory Brainstem Response(ABR)

Responses were elicited using a click stimulus of 80 dBnHL, of rarefied polarity, at a rate of 27.7/sec. Filtering was 0.1–3 kHz within a 12 ms window, and 2048 scans needed to be reproducible from two runs. The criterion for identifying the integrity of the auditory pathway was the presence of waves I, III, and V, as well as normal latency and interpeak intervals (within two standard deviations of the literature norms)[13]. Amplitude measurements were made from a positive peak to the next negative valley.

Frequency following responses (FFRs)

EEG responses were elicited using the syllable /da/ of 40 ms, alternating polarity, intensity 80 dB, rate of 10.9/sec applied only to the right ear[14]. Two scans with 3000 stimuli were performed, free of artifacts. The responses were added, giving a wave form composed of 6000 stimuli; in the same recording window, a filter of 100–2000 Hz was activated in the toolbar and applied to the resulting wave[15].

The evaluation of the FFR was performed in the time domain. Seven waves were identified: the first positive peak (V), followed by successive negative peaks (A, C, D, E, F, and O). The interpeak intervals were also calculated, which correspond to the wavelength of the fundamental frequency[15,16]. Also measured was the VA complex (the slope), which was calculated using the amplitudes and latencies of waves V and A; the slope is based on the formula: (amplitude of V – amplitude of A) divided by (latency of A – latency of V)[17].

Normative values from the Navigator Pro equipment[11] were considered. Although this equipment is different from the type we used, when we collected our data there were still no reference values for the IHS equipment. Nevertheless, the protocol we used was the same as the reference study and both sorts of equipment produce similar responses.

Long Latency Auditory Evoked Potential (LLAEP)

300 verbal stimuli were presented binaurally over insert earphones at an intensity of 80 ndBHL in the traditional oddball paradigm[18]. Stimuli were composed of the syllable /ba/, which was the frequent stimulus (80% of the time), and the syllable /di/, which was the rare stimulus (20% of the time). To begin, the examiner simulated the test orally, sounding out a sequence of /ba/ and /di/ in order for the subjects to understand the test. The individual was instructed to pay attention to the rare stimulus /di/, counting the number of them mentally. At the end, the examiner asked how many infrequent targets there were, and the number was compared to the total presented by the equipment, thus ensuring that the subject performed the activity correctly[19].

The stimulus rate was 1.1/sec, there were 300 sweeps, and filtering was 1–30 Hz in a time window of 510 ms. The latency (ms) and amplitude (μV) were obtained by identifying waves P1, N1, P2, N2, and P300[20,21]. After a run, if the P300 potential was absent, a few minutes rest were given and the exam repeated. In this way alertness and reliability could be ensured.

Data were placed in an Excel spreadsheet. Initially, the Shapiro–Wilk test was used to determine whether the sample distribution was normal or not. For statistical analyses, a Student *t*-test, paired Student *t*-test, and Chi-square test were used, with a significance level set at 5% ($p<0.05$).

RESULTS

The total sample group consisted of 22 individuals, 11 included in G1 and 11 in G2, representing 22 ears in each group and 44 ears in total. For G1, the mean age was 40.4 years, (range 27 to 57) while for G2 the average age was 44 years (range 26 to 59).

The distribution of the sample is shown in Table 1. The distribution was homogeneous between gender ($p = 0.183$) and age ($p = 0.43$) (Chart 1).

In G2, the time for which tinnitus had been perceived ranged from 8 months to 15 years (mean 4 years 6 months). In terms of

THI, tinnitus ranged from grade 1 (negligible) to 5 (catastrophic), with a mean of 3.09 (moderate). For the VAS, the minimum score was 7 and the maximum 10, with an average of 8.4.

Verbally, 63.6% reported whistle-type tinnitus and 36.4% waterfall-type tinnitus. Of these, 90.9% reported the sensation to be steady and 9.1% pulsatile, but all subjects reported that it was constantly present. For 63.6% of subjects, onset was sudden and for 36.4% it was gradual. In terms of location, 18.2% reported the location in both ears, with the right being worse; 45.5% reported in both ears, with the left being worse; and 9.1% reported "in the head". There were 18.2% who reported tinnitus in the right ear and 9.1% in the left.

Chart 1. Statistical analysis of the sample considering the variables gender and age between the groups

Variables	G1	G2	*p*-value
Number of ears	22	22	
Age	40.4	44	0.43
Gender (number)			
Male	6	2	0.183
Female	5	9	

Subtitle: G1 = group 1 = individuals without chronic tinnitus; G2 = group 2 = individuals with chronic tinnitus

Examining the high frequency audiometry (HFA), comparisons between the groups were made in terms of right and left ears (44 ears in all) (Table 1).

TEOAEs were present in both groups, and had similar magnitudes, with no significant differences ($p = 0.138$) (Table 2).

ABR showed similar latencies and amplitudes between the groups, and in all comparisons there were no significant differences between them (Table 3).

For the FFRs, latencies, interpeak intervals, and amplitudes between groups showed generally similar responses, with only one significant difference (V amplitude, $p = 0.041$) (Table 4).

For LLAEPs, G1 presented better findings for the latency of the P300 component ($p = 0.003$) and no difference in the comparison of amplitudes (Table 5).

In the analysis of the presence/absence of LLAEP waves, there were significant differences ($p < 0.05$) for 3 of the 5 variables (Chart 2).

Figure 1 shows examples of traces of the ABR illustrating the greater response amplitudes for wave V in G2 (Figure 1).

Figure 2 illustrates how the FFR has higher latencies for components V and A in G2 (Figure 2).

Figure 3 shows how the LLAEP in G2 had longer latencies for the P1 and N1 components as well as a greater amplitude for P300 (Figure 3).

Table 1. Comparison between groups for high frequency audiometry for both ears

HFA dBSPL	Group	*n*	Average	Median	Mín	Max	SD	CI (95%)	*p*-value
9 kHz	G1	22	13.86	15.00	0.00	20.00	5.96	(4.58; 8.52)	0.001*
	G2	22	22.95	22.50	5.00	45.00	10.43	(8.02; 14.90)	
10 kHz	G1	22	16.59	15.00	5.00	25.00	6.25	(4.80; 8.92)	0.002*
	G2	22	25.45	25.00	10.00	50.00	11.12	(8.55; 15.88)	
11 kHz	G1	22	12.05	12.50	0.00	25.00	9.59	(7.38; 13.71)	<0.001*
	G2	22	27.50	27.50	10.00	50.00	9.35	(7.19; 13.36)	
12 kHz	G1	22	10.91	5.00	0.00	35.00	11.30	(8.69; 16.14)	<0.001*
	G2	22	31.36	30.00	15.00	55.00	10.82	(8.32; 15.46)	
13 kHz	G1	22	16.14	12.50	0.00	40.00	12.24	(9.41; 17.49)	<0.001*
	G2	22	42.27	45.00	20.00	75.00	13.95	(10.73; 19.93)	
14 kHz	G1	22	28.18	30.00	5.00	45.00	10.86	(8.35; 15.52)	<0.001*
	G2	22	53.86	52.50	20.00	90.00	21.15	(16.27; 30.22)	
15 kHz	G1	22	32.50	32.50	10.00	55.00	14.62	(11.24; 20.89)	<0.001*
	G2	22	59.77	57.50	10.00	100.00	24.42	(18.78; 34.89)	
16 kHz	G1	22	38.86	37.50	10.00	60.00	16.03	(12.33; 22.90)	<0.001*
	G2	22	68.86	72.50	10.00	100.00	25.82	(19.86; 36.89)	
17 kHz	G1	22	50.68	50.00	10.00	90.00	18.34	(14.11; 26.21)	0.001*
	G2	22	75.45	82.50	25.00	105.00	24.92	(19.17; 35.61)	
18 kHz	G1	22	61.36	60.00	5.00	90.00	21.83	(16.79; 31.19)	0.023*
	G2	22	77.27	77.50	20.00	105.00	22.98	(17.67; 32.83)	

*Statistically significant values ($p \leq 0.05$)

Subtitle: HFA = high frequency audiometry; G1 = group 1 = individuals without chronic tinnitus; G2 = group 2 = individuals with chronic tinnitus; *n* = number of ears (total=44 ears); Min = minimum; Max = maximum; CI = confidence interval; dB = decibel; dBSPL = decibel sound pressure level; SD = standard deviation

Table 2. Comparison of groups in relation to the presence of transient otoacoustic emissions

		Group 1		Group 2		Total		*p*-value
		n	%	n	%	N	%	
TOAE	No	0	0%	4	18%	4	9%	0.138
	Yes	22	100%	18	82%	40	91%	

Subtitle: TOAE = transient otoacoustic emissions; No = absence of transient otoacoustic emissions; Yes = presence of transient otoacoustic emissions; *n* = number of ears; G1 = group 1 = individuals without chronic tinnitus; G2 = individuals with chronic tinnitus

Table 3. Comparison between groups for brainstem auditory evoked potential latencies in both ears

ABR	Variables	Groups	N	Average	Median	Mín	Máx	SD	CI (95%)	*p*-value
ms	wave I	G1	22	1.57	1.55	1.4	1.8	0.1	(0.07; 0.14)	0.791
		G2	20	1.57	1.55	1.4	1.75	0.09	(0.07; 0.13)	
	wave III	G1	22	3.75	3.80	3.45	4	0.2	(0.15; 0.28)	0.338
		G2	22	3.8	3.79	3.5	4.2	0.18	(0.13; 0.25)	
	Wave V	G1	22	5.68	5.69	5.35	5.98	0.2	(0.15; 0.28)	0.835
		G2	22	5.69	5.74	5.33	5.95	0.2	(0.15; 0.28)	
	I–III	G1	22	2.17	2.14	1.75	2.55	0.23	(0.17; 0.32)	0.385
		G2	19	2.23	2.23	1.9	2.65	0.17	(0.12; 0.25)	
	III–V	G1	22	1.93	1.95	1.5	2.25	0.14	(0.10; 0.20)	0.399
		G2	22	1.89	1.89	1.7	2.25	0.13	(0.09; 0.18)	
	I–V	G1	22	4.1	4.10	3.72	4.45	0.2	(0.15; 0.28)	0.713
		G2	19	4.13	4.18	3.73	4.4	0.2	(0.15; 0.30)	
µV	amp I	G1	22	0.3	0.29	0.11	0.63	0.11	(0.08; 0.16)	0.182
		G2	22	0.25	0.24	0.07	0.45	0.11	(0.08; 0.15)	
	amp V	G1	22	0.47	0.48	0.24	0.77	0.14	(0.11; 0.20)	0.802
		G2	22	0.46	0.48	0.24	0.74	0.14	(0.10; 0.20)	
	ratio V/I	G1	22	1.77	1.58	0.57	4.27	0.8	(0.61; 1.14)	0.179
		G2	22	2.14	2.00	0.62	4.43	0.99	(0.76; 1.42)	

Subtitle: ABR = Auditory Brainstem Response; G1 = group 1 = individuals without chronic tinnitus; G2 = group 2 = individuals with chronic tinnitus; ms = milliseconds; µV = microvolts; *n* = number of ears (total = 44 ears); SD = standard deviation; Min = minimum values; Max = maximum values; CI = confidence interval

Table 4. Comparison of latencies, interpeak intervals, and frequency following response amplitudes between groups

	FFR		Average	Median	SD	Min	Max	*N*	CI	*p*-value
ms	V	G1	6.08	6.25	0.71	4.5	6.88	11	0.42	0.079
		G2	6.89	6.63	1.24	5.88	10.25	10	0.77	
	A	G1	8.2	7.88	1.18	6.38	10.88	11	0.7	0.377
		G2	8.67	8.32	1.18	7.5	11.75	10	0.73	
	C	G1	17.16	17.38	1.13	14.88	19	11	0.67	0.935
		G2	17.21	17.38	1.42	15.25	20.13	11	0.84	
	D	G1	22.62	22.63	1.68	18.5	25.25	11	0.99	0.377
		G2	23.33	22.63	1.66	21.5	26.63	8	1.15	
	E	G1	31.48	31.38	1.5	29	33.38	11	0.89	0.377
		G2	31.98	31.94	0.91	30.75	33.25	10	0.56	
	F	G1	39.83	39.88	0.82	38.88	41.5	11	0.48	0.184
		G2	40.39	39.94	1.03	39.38	42	10	0.64	
	O	G1	48.5	48.75	0.88	47.38	50.5	11	0.52	0.306
		G2	49.15	48.5	1.75	47.87	53.38	9	1.14	
	Slope	G1	0.184	0.184	0.1	0.041	0.38	11	0.059	0.717
		G2	0.169	0.16	0.067	0.06	0.302	9	0.044	
	V–A	G1	2.12	1.63	1.08	1.25	4.63	11	0.64	0.374
		G2	1.77	1.63	0.51	1.25	2.87	10	0.32	
	A–C	G1	8.96	9.62	1.86	5.37	11.5	11	1.1	0.744
		G2	8.74	8.63	1.16	7.25	10.38	10	0.72	
	C–D	G1	5.72	5.25	2.15	2.12	8.5	11	1.27	0.896
		G2	5.59	5.37	2.15	2.5	8.13	8	1.49	
	D–E	G1	8.55	8.5	2.5	5.62	14.12	11	1.48	0.85
		G2	8.36	8.87	1.38	5.25	9.37	8	0.95	
	E–F	G1	8.35	8.38	1.48	6.5	11.13	11	0.87	0.903
		G2	8.41	8.38	0.45	7.75	9.13	10	0.28	
	F–O	G1	8.44	8	0.93	7.25	10.5	11	0.55	0.717
		G2	8.62	8.31	1.31	7.12	12.13	10	0.81	
	V–O	G1	42.42	42.12	1.37	41.12	45.5	11	0.81	0.206
		G2	41.52	41.74	1.71	37.75	44.12	9	1.12	
µV	V	G1	0.214	0.19	0.064	0.1	0.3	11	0.038	0.041*
		G2	0.138	0.11	0.09	0.05	0.34	9	0.059	

*Statistically significant values ($p \leq 0.05$)

Subtitle: FFR = frequency following response; G1 = group 1 = individuals without chronic tinnitus; G2 = group 2 = individuals with chronic tinnitus; ms = milliseconds; µV= microvolts; SD = standard deviation; Min = minimum values; Max = maximum values; *N* = number of individuals; CI = confidence interval

Table 4. Continued...

FFR		Average	Median	SD	Min	Max	*N*	CI	*p*-value
A	G1	-0.133	0.11	0.083	-0.01	-0.32	11	0.049	0.511
	G2	-0.157	0.16	0.082	-0.01	-0.29	10	0.051	
C	G1	-0.136	0.13	0.073	-0.01	-0.27	11	0.043	0.708
	G2	-0.15	0.11	0.094	-0.03	-0.3	11	0.056	
D	G1	-0.119	0.09	0.098	-0.03	-0.31	11	0.058	0.97
	G2	-0.118	0.14	0.073	-0.01	-0.19	8	0.05	
E	G1	-0.195	0.2	0.088	-0.01	-0.33	11	0.052	0.152
	G2	-0.249	0.23	0.075	-0.17	-0.43	10	0.046	
F	G1	-0.196	0.19	0.069	-0.08	-0.28	11	0.041	0.735
	G2	-0.232	0.22	0.124	-0.09	-0.48	10	0.077	
O	G1	-0.123	0.08	0.13	-0.02	-0.47	11	0.077	0.293
	G2	-0.176	0.17	0.09	-0.04	-0.35	10	0.056	

*Statistically significant values ($p \leq 0.05$)

Subtitle: FFR = frequency following response; G1 = group 1 = individuals without chronic tinnitus; G2 = group 2 = individuals with chronic tinnitus; ms = milliseconds; µV= microvolts; SD = standard deviation; Min = minimum values; Max = maximum values; *N* = number of individuals; CI = confidence interval

Table 5. Comparison of groups for latencies (ms) and amplitudes (µV) in both ears in the long-latency auditory evoked potential

LLAEP	Variable	Group	*n*	Average	Median	Mín	Máx	SD	CI (95%)	*p*-value
ms	P1	G1	22	53.55	52	50	67	4.64	(3.56; 6.62)	0.141
		G2	12	56.5	52.5	50	67	6.76	(4.79; 11.48)	
	N1	G1	22	100.45	98.5	80	116	9.54	(7.34; 13.63)	0.529
		G2	22	102.23	102	86	121	8.96	(6.89; 12.80)	
	P2	G1	22	183.32	181.5	153	222	19.37	(14.90; 27.68)	0.312
		G2	22	189.64	189.5	153	217	21.49	(16.53; 30.71)	
	N2	G1	22	257.77	257.5	212	297	26.58	(20.44; 37.98)	0.734
		G2	15	253.67	268	192	302	46.32	(33.91; 73.05)	
	P3	G1	22	312.14	315.5	253	371	33.52	(25.78; 47.90)	0.003*
		G2	12	307.33	319.5	229	355	39.93	(28.28; 67.79)	
µV	P1–N1	G1	22	4.89	4.96	2.23	7.9	1.83	(1.40; 2.61)	0.061
		G2	8	6.64	6.25	3.63	10.97	2.97	(1.96; 6.04)	
	N1–P2	G1	22	7.89	7.82	3.05	13.36	3.25	(2.50; 4.64)	0.699
		G2	17	8.3	6.88	4.1	14.9	3.27	(2.43; 4.98)	
	P2–N2	G1	22	5.03	4.82	1.37	7.49	1.34	(1.02; 1.91)	0.913
		G2	13	4.94	4.05	1.01	11.17	3.52	(2.52; 5.80)	
	P3	G1	22	6.02	4.45	3.01	14.4	3.3	(2.54; 4.72)	0.246
		G2	11	7.87	5.56	3	20.42	5.73	(4.00; 10.05)	

*Statistically significant values ($p \leq 0.05$)

Subtitle: LLAEP = long latency auditory evoked potential; G1 = group 1 = individuals without chronic tinnitus; G2 = group 2 = individuals with chronic tinnitus; µV = microvolts; Min = minimum; Max: maximum; CI = confidence interval; SD = standard deviation; ms = milliseconds; *n* = number of ears (total = 44 ears)

Chart 2. Relationship between groups for the absence/presence of long-latency auditory evoked potentials in both ears

LLAEP (ms)		G1		G2		Total		*p*-value
		n	%	*n*	%	*n*	%	
P1	Absence	0	0%	10	45%	10	22.72%	<0.001*
	Presence	22	100%	12	55%	34	72.27%	
N1	Absence	0	0%	0	0%	0	0%	NA
	Presence	22	100%	22	100%	44	100%	
P2	Absence	0	0%	0	0%	0	0%	NA
	Presence	22	100%	22	100%	44	100%	
N2	Absence	0	0%	7	31.81%	7	15.90%	0.003*
	Presence	22	100%	15	68.18%	37	84.09%	
P3	Absence	0	0%	10	45%	10	22.72%	<0.001*
	Presence	22	100%	12	55%	34	72.27%	

*Statistically significant values ($p \leq 0.05$)

Subtitle: LLAEP = long latency auditory evoked potential; G1 = group 1 = individuals without chronic tinnitus; G2 = group 2= individuals with chronic tinnitus; ms = milliseconds; *n* = number of ears; NA = not applicable

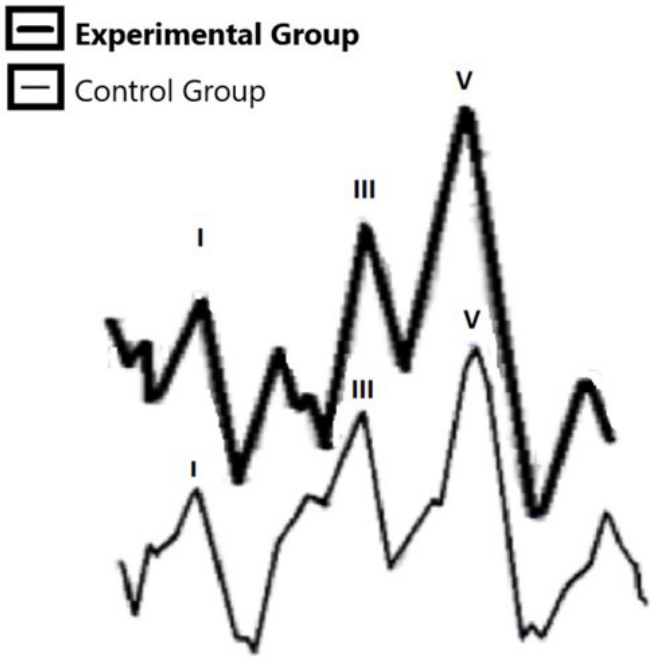

Figure 1. Traces of the brainstem auditory evoked potential for group 1 (control group) and group 2 (experimental group)

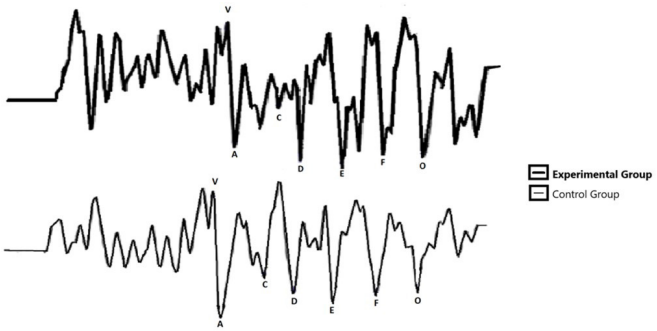

Figure 2. Traces of the frequency following response for group 1 (control group) and group 2 (experimental group)

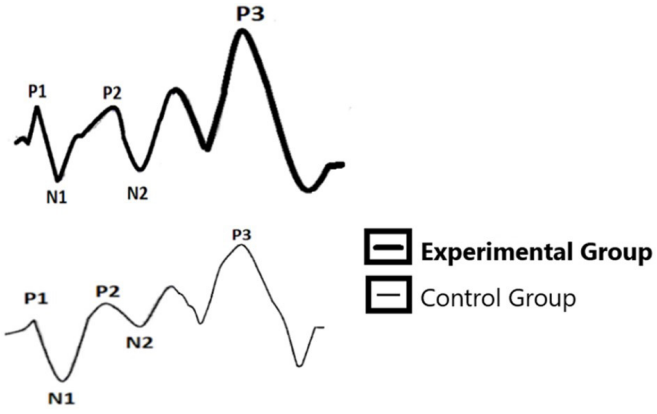

Figure 3. Traces of the long latency auditory evoked potential for group 1 (experimental group) and group 2 (control group)

DISCUSSION

The subject of the present study is in complete agreement with the current literature, highlighting the need to set common criteria for evaluating tinnitus. Common standards will allow for a more adequate clinical management and perhaps, eventually, total cure of tinnitus[22].

High frequency audiometry (HFA) has shown lower thresholds (better hearing) in G1 compared to G2. The findings agree with researchers[23] who have studied the relevance of HFA in individuals with tinnitus and normal auditory thresholds. This study has found that HFA provides additional useful information in this population, suggesting that subjects with tinnitus tend to have alterations in the basal region of the cochlea. Thus, the increase in auditory thresholds at high frequencies may be the cause of the perception of chronic tinnitus, perhaps due to an auditory deafferentation mechanism[24].

The work described in (24) emphasizes the importance of high thresholds at high frequencies in subjects with chronic tinnitus but with preserved peripheral auditory acuity up to 8 kHz, suggesting that this test could be an important addition to a battery of assessments for diagnosis of tinnitus. HFA provides additional useful clinical information, since it is correlated with the laterality, frequency, and severity of tinnitus[23].

For TOAEs (Table 2), we found no responses in only two subjects, demonstrating the similarity between the groups in terms of outer hair cell function. This finding differs from another study[24], which found differences in TOAEs and DPOAEs between subjects with and without tinnitus. However, perhaps these differences are due to the different type of analysis performed – one in which the response amplitude was measured but not the presence or absence, which was performed here. We suggest that the amplitude of responses of outer hair cells is smaller in individuals with chronic tinnitus, although this reduction does not inhibit the presence of responses in the frequency band assessed by TEOAEs. We have found that the higher frequency regions, analyzed through DPOAEs, increase their response amplitude so as to compensate for the neural reduction at the level of the VIII cranial nerve[24].

In view of the above, it is suggested that, whenever possible, experimenters use both methods to measure OAEs – that is analyse not only the amplitude of responses but also their presence or absence. Understanding cochlear mechanics is important, since small changes in sensory input from the cochlea can result in a larger compensatory increase in neural amplification of the auditory system, the end result of which is chronic tinnitus[2,25]. However, in this context, it is worth mentioning a recent study[26] which suggested that tinnitus is not always initiated in the cochlea, and that therefore diagnostic and therapeutic strategies should focus on the central auditory nervous system, limbic system, and autonomous nervous system.

A recent survey showed that the ratio of wave V/I amplitude in ABR can serve as a reliable metric to objectively identify tinnitus, as well as to monitor neuroplastic changes in the auditory pathway over time[27]. The present research supports this approach, since, in our ABR analysis, an increase in the V/I ratio was observed only in subjects with chronic tinnitus. This finding is in line with the central gain theory, in which, when similar wave I values are observed between groups, increases in the V/I wave ratio reflect reduced output of the auditory nerve. This is turn may cause neural amplification at the brainstem

level. This finding contributes to the characterization of tinnitus as a neuroplasticity disorder[27-29].

In the FFR, the responses were similar between the groups, with one point of difference. It is noteworthy that G2 had higher latencies compared to G1, especially in the VA complex, demonstrating that subjects with tinnitus have greater difficulty decoding the rapid temporal changes inherent to consonants[30]. This supports the compensatory hypothesis, in which some aspects of auditory processing recover due to progressive compensatory plasticity at higher stages of the central auditory pathway. Compensation is observed only at higher levels of the auditory pathway, where acoustic signal processing takes place[31,32].

In the FFR, it was possible to register seven wave amplitudes, with a significantly greater difference in the amplitude of wave V in G1 compared to G2. In this sense, it is possible to observe that individuals with tinnitus have maladaptive subcortical plasticity, in addition to impairment to the cognitive functions of attention and memory. Therefore, these individuals may have problems processing speech in difficult listening situations, since processing requires all levels of attentional capacity, and may be impaired after the development of tinnitus[33].

Two recent systematic reviews highlighted P300 as a potential biomarker for subjective tinnitus, justifying that the symptom causes inhibition of attention to external stimuli, resulting from changes in auditory and cognitive functioning[2,34,35]. Therefore, this leads to the hypothesis that cortical dysfunction is linked to the thalamus, so that the LLAEP might help in correlating tinnitus with neurobiological alterations.

Cortical dysfunctions linked to the thalamus contribute to the perception of tinnitus, since they can impair inhibitory blocking mechanisms. In typical auditory functioning, the tinnitus signal is canceled at the thalamic level by an inhibitory feedback loop which originates in the paralimbic structures. However, as observed in the present study, the impairment of blocking can interrupt the inhibition of the signal at the thalamic level, resulting in the retransmission of the signal to the auditory cortex and be perceived as tinnitus[26].

At the same time, when the absence or presence of LLAEP components was analysed here, individuals with tinnitus had a much higher number of absences. This demonstrates that the changes are not restricted just to the auditory regions, but there are modifications to subcortical routes as well, so that tinnitus involves a network of structures in non-auditory areas, including temporoparietal, prefrontal, and limbic regions[36,37]. In this sense, neuroplastic changes begin at the brainstem level and proceed to the upper stages of the auditory pathway. Thus, these changes can cause impairments in speech decoding, in attention, and in memory, explaining the absence of the cognitive potential (P300) which depends on these aspects for its elicitation.

The findings of the present study have shown that tinnitus, even if generated peripherally, causes neurobiological changes in the central auditory pathway. In this sense, chronic tinnitus can be characterized as a neuroplasticity disorder, explained by chaos theory. Because brain function is non-linear and dynamic, small changes in sensory input can cause large and irregular changes in general brain function. This manifests as a functional impairment in the processing of acoustic information, as well as in cognition, negatively impacting the subjects' quality of life[2].

The findings of this research confirm current evidence derived from the assessment of patients with chronic tinnitus who have normal thresholds up to 8 kHz. It is important that hearing professionals understand how multiple evaluations, with rapid testing, open the way for providing a better diagnosis and ultimately, perhaps, remission of the condition[4].

Study Limitation

In addition to the small number of samples, it was not possible to perform frequency analyses in the FFR on the Smart EP equipment, due to the unavailability of the BioMark™ program. This work also highlights a need to characterize such procedures in individuals with tinnitus who have also suffered COVID-19, as these subjects my react differently to those tested here.

CONCLUSION

Using HFA, analysis of the wave V/I ratio in ABR, the FFR, and the LLAEP, we could detect alterations in individuals with chronic tinnitus. Our findings have shown that such procedures are promising tools in evaluating subjects with tinnitus.

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