Contralateral suppression of transient evoked otoacoustic emissions in adolescents with and without tinnitus

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Contralateral suppression of transient evoked otoacoustic emissions in adolescents with and without Tinnitus

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Abstract

The severity of tinnitus has a high variability; it can potentially cause serious anxiety disorders and in some cases it can even lead to depression. Currently, one of the hypotheses of the genesis of tinnitus involves a deterioration in the functioning of medial olivocochlear system (MOCS). The functioning of the MOCS is evaluated through the contralateral suppression (CS) of transient evoked otoacoustic emissions (TEOAEs) by comparing the amplitudes without and with contralateral acoustic stimulation (CAS). The aim of the present study was to analyze the functioning of the MOCS in adolescents with and without tinnitus through the CS of the TEOAEs. A cross-sectional correlational descriptive study was carried out, involving 77 adolescents (n = 154 ears) with normal hearing with and without tinnitus, who underwent TEOAEs testing without and with CAS using white noise at 50 dB. The results evidenced that the adolescents without tinnitus showed higher global amplitude and higher amplitude in the frequencies 1000, 1500, 2000, and 3000 Hz, in both conditions without and with CAS, in comparison to the adolescents with tinnitus. This difference was statistically significant ($p<0.05$) in the 1000 Hz frequency and in the global amplitude, without and with CAS. In addition, the adolescents with tinnitus showed less difference between the global amplitudes in the conditions without and with CAS (suppression effect). These results suggest a possible relation between the functioning of the MOCS and the presence or absence of tinnitus, which could contribute to confirm the hypothesis of the involvement of the MOCS in the generation of tinnitus.

Keywords: tinnitus; medial olivocochlear system; contralateral suppression of transient evoked otoacoustic emissions; adolescents.

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1 Introduction

Tinnitus has been defined as the perception of sound in the absence of an external sound stimulus, which is not a disease in itself [1], but a symptom that can respond to various causes. The majority of the cases have been associated with hearing loss [2]. In the other cases, the occurrence of tinnitus has been associated with hearing loss induced by noise [3]. Nevertheless, tinnitus can also occur in patients with normal hearing thresholds [4]. Some people with troublesome tinnitus have audiometrically normal hearing; conversely, many people with hearing loss do not report tinnitus [5].

The mechanism of tinnitus generation in patients with normal audiograms in the conventional region (up to 8000 Hz) remains unclear [6].

The percentage of tinnitus patients without hearing impairment varies from only 8% for individuals with pure-tone thresholds up to frequency 8000 Hz ≤ 20 dB HL, to about 30% for patients with thresholds at frequencies 1000, 2000, 4000, and 6000 Hz ≤ 25 dB HL [7].

There are several hypotheses that attempt to explain the pathophysiology of tinnitus. These hypotheses are divided in two groups: cochlear mechanisms and non-cochlear mechanisms. The first group believes that the etiology of tinnitus is located in the cochlea isolated from the rest of the auditory pathway, while the second group emphasizes the retrocochlear and central aspects in regards to the generation and persistence of tinnitus, without excluding the role of the cochlea [2]. Taking into account the non-cochlear mechanisms, tinnitus has been defined by Jastreboff [8] as “the perception of sound that results exclusively from activity within the nervous system without any corresponding mechanical, vibratory activity within the cochlea, and not related to external stimulation of any kind”. Within the non-cochlear hypothesis is the one concerning "the participation of the medial olivocochlear system (MOCS)" [9].

This hypothesis states that one of the MOCS dysfunction may produce an alteration in the modulation of outer hair cells, causing an imbalance between hyperpolarization and depolarization, which causes an abnormal and exaggerated electrical activity that is misinterpreted by the central nervous system as a sound [9], [10].

Warr and Guinan [11] in 1978 showed that the MOCS originates in the brainstem, in the medial superior olivary complex, intersects at floor level of the fourth ventricle, and goes to the contralateral cochlea, and that it specifically innervate the bases of the outer hair cells of the organ of Corti.

Currently, studies of this pathway, the evaluation of its performance by contralateral suppression test (CS) of otoacoustic emissions (OAEs) and its possible relationship with the generation of

tinnitus are still being developed. This study can be applied in various types of OAEs, being the transient otoacoustic emissions (TEOAEs) one of the most studied ones.

In the CS of the OAEs, it is necessary to perform two measurements of the amplitude of OAEs, one without contralateral acoustic stimulation (CAS) and the other with CAS; the difference between the two amplitudes is called suppression effect. In the case of an ear that does not present alterations, and that present an unscathed MOCS, the OAEs amplitude is reduced in the presence of acoustic stimulation. Therefore, the suppression effect is a phenomenon that occurs as a consequence of the normal functioning of the MOCS and its absence can be considered as a pathological finding that indicates an alteration of the system, which can be related to diverse dysfunctions, the presence of tinnitus being one of them [12].

Currently, the results based on the hypothesis of "the participation of the MOCS" are varied, so it is necessary to promote new researches that relate the CS of TEOAEs with the presence of tinnitus.

This research was conducted within a specific line of research for the study of MOCS and its diverse clinical and research applications in the framework of the program for the Conservation and Promotion of Hearing among Adolescents, implemented in CINTRA, Argentina.

The aim of the present study was to analyze the functioning of the MOCS in adolescents without and with tinnitus through the CS of the TEOAEs.

2 Methodology

A cross-sectional descriptive correlational study was carried out, involving 77 adolescents (n = 154 ears), aged 14 and 15, from two technical schools in the city of Córdoba, Argentina, who had received their parents' or tutors' informed written consent to participate in the study.

The inclusion criteria adopted for all adolescents (for both ears) were: normal otoscope exam, normal functioning of the middle ear, transient evoked otoacoustic emissions (TEOAEs) present and an audiometry in conventional and high frequency extended ranges within the parameters considered normal.

The presence of TEOAEs was determined by a whole reproducibility level ≥ 70% and signal-to-noise ratio (SNR) ≥ 6 dB SPL in three of the frequencies analyzed (1000, 1500, 2000, 3000, 4000) Hz .

The parameters considered normal in the audiometry in conventional range (250-8000) Hz and high frequency extended (8000-16000) Hz were hearing thresholds level ≤ 21 dB HTL at each frequency analyzed in both ranges.

The adolescents who had some hearing pathology at the time of the examination were excluded.

2.1 Audiological assessment

The audiological study was carried out in a utilitarian vehicle adapted as a mobile audiometric booth, complying with international ISO 82531-1:2010 [13] and national IRAM 4028-1:1992 [14] standards with regards to background sound levels of noise.

The audiological evaluations were performed in the morning after approximately 8 to 10 hours of auditory rest and lasted between 30 to 40 minutes per participant.

The audiological assessment consisted in:

- Auditory State Questionnaire, to learn about the medical history of the hearing and subjective report of tinnitus (presence or absence, frequency and duration).

- Otoscopic examination, to assess the condition of the ear canal and tympanic membrane.

- Tympanometry, to objectively determine the condition of the middle-ear.

- Standard audiometry in conventional and in extended high frequency ranges, to determine the hearing threshold level (HTL) in conventional frequencies (250-8000) Hz and extended range (8000-16000) Hz, using the bracketing method specified by the ISO 8253-1:2010 [13] standard. The test's signal level steps were fixed at 3 dB for HTL to be determined with greater precision than with traditional 5 dB steps.

The calibration was controlled 3 times a year: in the conventional range according to the ISO 389-1:1998 [15] and IRAM 4075:1995 [16] rules, using an artificial ear Brüel and Kjaer, type 415, equipped with a standard microphone, also Brüel and Kjaer type 4134, traceable to the reference standards of the European Community. In addition, a set of Sennheiser supra-aural earphones for both audiometric ranges calibrated according to ISO 389-8:2004 [17] standard was used. The application force of the headband (10.3 N) complies with the specifications of ISO 389-5:2006 [18] standard (10.0 N ± 1.0 N).

- Transient evoked otoacoustic emissions (TEOAEs): to detect mechanical cochlear status. The stimulus was a nonlinear click of 260 presentations with an intensity of 80 dB pk, the stimulus stability was maintained at ≥ 85% and the peak noise rejection level applied was 47.3 dB.

In order to be familiarized with the mechanical behavior of the cochlea, it was evaluated with a click stimulus of 260 presentations, with an intensity of 80 dB SPL, in a nonlinear manner, with a rejection level of 47.3 dB SPL and a stimulus stability ≥ 85%. The studied frequencies were (1000, 1500, 2000, 3000, 4000) Hz. The TEOAEs were considered present in both ears when the reproducibility was ≥ 70 % and the signal to noise ratio (SNR) ≥ 6 dB SPL in at least 3 of the studied frequencies.

- Contralateral Suppression (CS) of TEOAEs, to analyze the suppression effect, for which the TEOAEs was repeated, this time with contralateral acoustic stimulation (CAS), using white noise at 50 dB that was generated by a digital audiometer. The suppression effect was considered when the difference between the global amplitude of the TEOAEs without and with acoustic stimulation was > 0 dB.

2.2 Audiological equipment

- An otoscope Heine Beta 100 model.
- An automatic middle ear “Minitymp” Kamplex MT10 Interacoustics analyser.
- A digital audiometer Madsen, model Orbiter 922 DH/1.
- A probe EAR TONE A3.
- A set of supra-aural earphones Sennheiser, model HDA 200.
- An Otodynamics Ltd DP ECHOPORT ILO 292 USB II.
- Two UGD TE y DPOAE Probes.
- An ILO V6 clinical OAE clinical analysis and data management software.

2.3 Statistics analysis

The data was analyzed using parametric and nonparametric statistical analysis considering the ear as unit. Student’s *t* test for independent samples was applied to analyze the amplitude per frequency and the global amplitude in the instances without and with CAS in adolescents with absence and presence of tinnitus. To analyze the differences of the suppressive effect, the Wilcoxon test was used in independent samples. In every case a significance level of 5% ($p<0.05$) was considered.

The statistical analyses were performed using InfoStat version 2015 Group InfoStat [19], FCA, Universidad Nacional de Córdoba, Argentina.

3 Results

The results obtained by the Auditory State Questionnaire showed that 64 % of adolescents had tinnitus (n=49) while 36 % had no tinnitus (n=28). In Figure 1 the distribution of the frequency of occurrence and duration of tinnitus in the evaluated adolescents is shown. Regarding the symptom’s frequency of occurrence, 85.71% reported an occasional appearance, 10.20% reported weekly occurrence and 4.08% daily occurrence. As for the duration, 73.46% claimed a duration of approximately 10 minutes, 20.41% a shorter than 10 minutes duration, and 6.12% indicated a duration that range between 10 minutes to an hour. This shows that most adolescents manifested an occasional frequency of occurrence and a duration of approximately 10 minutes.

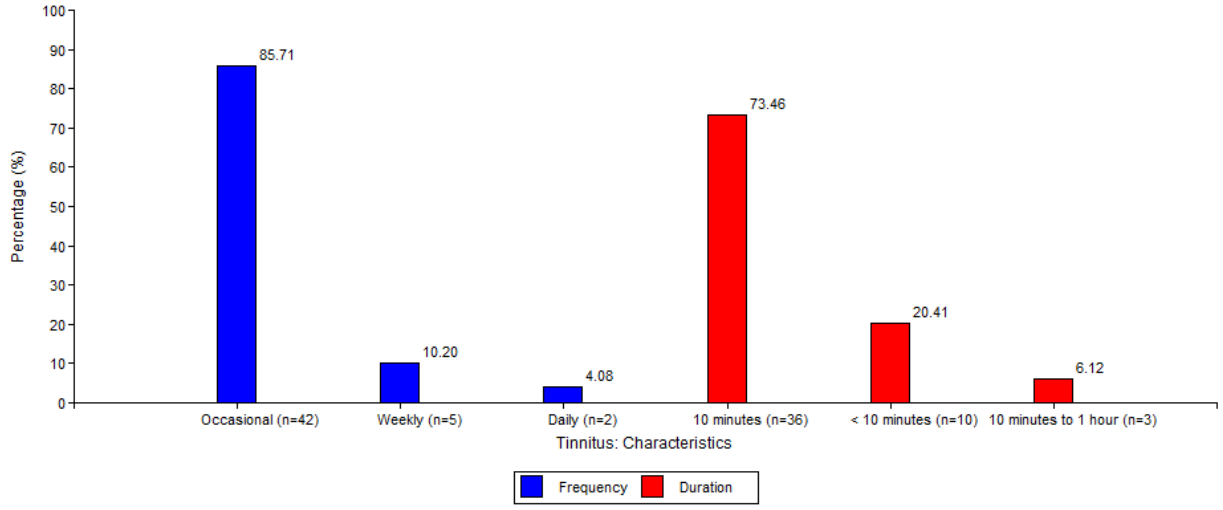

Figure 1: Distribution of the frequency of occurrence and duration of tinnitus in the adolescents

After the inferential analysis was carried out, no statistically significant difference between the suppressive effect and the hearing thresholds of the right and left ear was found, and thus no differentiation between them was made in subsequent analysis. The results of the TEOAEs without and with CAS are shown in Tables 1, 2 and 3.

Table 1, which refers to the TEOAEs without CAS, shows that the mean amplitude of each frequency evaluated was higher in the group with absence of tinnitus, with the exception of the 4000 Hz frequency. A significant effect of the presence of tinnitus in the 1000 Hz frequency without CAS was observed.

Table 1: Mean of amplitude difference per frequency in the TEOAEs without CAS between ears with absence and presence of tinnitus

Frequencies [Hz]	Absence of tinnitus [n]	Presence of tinnitus [n]	Mean Absence of tinnitus [dB SPL]	Mean Presence of tinnitus [dB SPL]	Differences [dB SPL]	*t*-value	Significance p-value [p<0,05]
1000	56	98	8.29	5.52	2.77	3.04	**0.0028**
1500	56	98	8.77	8.04	0.73	0.89	0.3774
2000	56	98	6.36	5.00	1.36	1.70	0.0907
3000	56	98	3.79	2.95	0.84	0.95	0.3444
4000	56	98	1.13	1.51	-0.38	-0.46	0.6471

Table 2, which refers to the TEOAEs with CAS, shows that the mean amplitude of each frequency was higher in the group with absence of tinnitus, with the exception of frequency 4000 Hz. At the

same time, similar to the results found without CAS, a significant effect of the presence of tinnitus in frequency 1000 Hz with CAS was observed.

Table 2: Mean of amplitude difference per frequency in the TEOAEs with CAS between ears with absence and presence of tinnitus

Frequencies [Hz]	Absence of tinnitus [n]	Presence of tinnitus [n]	Mean Absence of tinnitus [dB SPL]	Mean Presence of tinnitus [dB SPL]	Differences [dB SPL]	*t*-value	Significance p-value [p<0,05]
1000	56	98	7.10	4.85	2.25	2.60	**0.0102**
1500	56	98	7.83	6.95	0.88	1.08	0.2798
2000	56	98	5.42	4.03	1.39	1.81	0.0718
3000	56	98	3.05	2.01	1.04	1.17	0.2433
4000	56	98	0.52	0.96	-0.44	-0.52	0.6032

Table 3, which refers to the global amplitude of the TEOAEs in conditions without and with CAS**,** the results show significant differences between both groups (with presence and absence of tinnitus) in the conditions without and with CAS. In comparison to the group with tinnitus, the global amplitude was higher in the group without tinnitus.

Table 3 Mean of global amplitude difference in the TEOAEs in conditions without and with CAS between ears with absence and presence of tinnitus

Global amplitude	Absence of tinnitus [n]	Presence of tinnitus [n]	Mean Absence of tinnitus [dB SPL]	Mean Presence of tinnitus [dB SPL]	Differences [dB SPL]	*t*-value	Significance p-value [p<0,05]
Without CAS	56	98	14.54	13.01	1.53	2.19	**0.0302**
With CAS	56	98	13.51	12.22	1.29	1.99	**0.0489**

In addition, the results obtained from the CS of the TEOAEs showed that the suppression effect was > 0 dB in both groups. However, the group with absence of tinnitus got a higher value of the suppression effect (1.03 dB SPL) than the group with presence of tinnitus (0.79 dB SPL), although the difference between both values was not statistically significant (p>0.05).

4 Discussion and conclusions

Currently, due to the heterogeneity of the hypotheses regarding mechanisms of the generation of tinnitus, researches that contribute to evaluate the MOCS by CS of TEOAES and its possible relationship with the generation of tinnitus are necessary.

The adolescents in the sample were between the ages of 14 and 15, all them with normal hearing; however, a group of them showed the presence of tinnitus in different frequencies of occurrence and duration, while the other group did not showed this symptom at all. Most of the adolescents with tinnitus manifested that the frequency of occurrence was occasional and that the duration of it was of approximately of 10 minutes.

In the present study, the analysis of the amplitude per frequency of the TEOAEs without and with CAS, showed a higher response in the group of adolescents without tinnitus in the frequencies 1000, 1500, 2000 and 3000 Hz, which shows a statistically significant difference in the 1000 Hz frequency. In a study conducted by Cruz Fernandes y Momensohn dos Santos [20], the suppressive effect of the CS of TEOAEs in a group of subjects with tinnitus compared with a control group was studied. The results showed a statistically significant difference only in 1000 Hz frequency in the left ear of the subjects of the group with tinnitus compared to the control group. On the other hand, Geven et al. [9] used the CS of TEOAEs and their result showed suppression in the tinnitus group and in the control group, except for 2000 and 2800 Hz frequency bands in the right ear, where subjects with tinnitus showed less pronounced suppression. The researchers concluded that the suppression of TEOAEs seems equally effective in patients with tinnitus than in healthy patients, and that it is still possible to consider that the MOCS plays a role in the cause of tinnitus.

In the analysis of amplitude per frequency of the TEOAEs without and with CAS, it is necessary to highlight the 4000 Hz frequency because it is the only one in which lower values were found for the group without tinnitus in comparison to the one with tinnitus. This is why for future researches it is recommendable to particularly examine the 4000 Hz frequency as it is can be susceptible to change by the influence of noise exposure, also to contribute with others studies in order to achieve a more specific analysis in relation to the tone in which tinnitus is perceived.

As for the response of the TEOAEs in instances without and with CAS, the analysis of the mean global amplitude showed higher values in the group without tinnitus than on the one with tinnitus. The difference in both instances was statistically significant, which proves a higher response of the outer hair cells in the presence of sound stimulation in adolescents without tinnitus. These results resemble the ones obtained in previous researches. One of which was conducted by Mor and Azevedo [21] who compared the results of the TEOAEs and the functioning of the MOCS in two groups: one without tinnitus and the other with tinnitus. They obtained a non-statistically significant difference between the two groups in terms of the amplitude response of the TEOAEs and suppression effect. However, their results showed that the global response levels of the TEOAEs of the ears without tinnitus were significantly higher and that the functioning of the MOCS was more efficient.

As for the suppressive effect, although the difference found between the group without tinnitus and the one with tinnitus was not statistically significant, the observed trend is that the magnitude

of the suppressive effect was lower in the group with tinnitus. The research conducted by Riga et al. [22] using DPOAEs suppression have shown that contralateral auditory stimulation is less effective in patients with tinnitus given that after the presentation of CAS, the response level of the DPOAEs of the subjects with tinnitus was intensified and a less intense suppression effect was registered. This constitutes another point of interest to consider and analyze in future studies.

The results obtained in the present study suggest a possible relation between the functioning of the MOCS and the presence or absence of tinnitus, which could contribute to the hypothesis of the involvement of the MOCS in the generation of tinnitus. All things considered, it is still necessary to promote further studies in order to continue researching on the CS of TEOAEs and its relationship with tinnitus, taking into consideration that currently in Argentina there is no background information regarding this area of knowledge.

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References

[1] Sumitrajit, D.; James, W. H. Otoacoustic emissions: Principles, procedures and protocols. Plural Publishing, San Diego (USA), 1st edition, 2011.

[2] Baguley, D. M. Mechanisms of tinnitus. *British Medical Bulletin*, Vol 63(1), 2002, pp 195-212.

[3] Axelsson, A. Causes of tinnitus. Proceedings IV International Tinnitus Seminar, Bordeaux, France, August, pp 275–277, 1990. In print book.

[4] Chéry-Croze, S.; Moulin, A.; Collet, L.; Morgon, A. Is the test of medial efferent system function a relevant investigation in tinnitus?, *British Journal of Audiology*, Vol 28, 1994, pp 13-25.

[5] Baguley, D.; McFerran, D.; Hall, D. Tinnitus. *The Lancet*, Vol 382(9904), 2013, pp 1600-1607.

[6] Fabijańska, A.; Smurzyński, J.; Hatzopoulos, S.; Kochanek, K.; Bartnik, G.; Raj-Koziak, D.; Mazzoli, M.; Skarżyński, P. H.; Jędrzejczak, W. W.; Szkiełkowska, A.; Skarżyński, H. The relationship between distortion product otoacoustic emissions and extended high-frequency audiometry in tinnitus patients. Part 1: normally hearing patients with unilateral tinnitus. *Medical Science Monitor*. Vol 18 (12), 2012, pp CR765-70.

[7] Vernon, J. A; Meikle M. B. Tinnitus masking. In: Tyler R (ed.), Tinnitus Handbook, Thomson Learning, NY (USA), 2000, pp 313-356.

[8] Jastreboff, P. J. Tinnitus as a phantom perception: Theories and clinical implications. In Mechanisms of tinnitus, J. A. Vernon; A. R. Moller (eds.), Needham Heights, M. A; Allyn; Bacon, 1995, pp 73-93.

[9] Geven, L. I.; de Kleine, E.; Free, R. H.; Van Dijk, P. Contralateral suppression of otoacoustic emissions in tinnitus patients. *Otology and Neurotology,* Vol 32, 2011, pp 315-321.

[10] Puel, J. L.; Guitton, M. J. Salicylate-induced tinnitus: molecular mechanisms and modulation by anxiety. *Progress in Brain Research*, Vol 166, 2007, pp 141-146.

[11] Warr, W.B.; Guinan, J. J., Jr. Efferent innervation of organ of Corti: two separate systems, *Brain Research,* Vol 173, 1978, pp 15-155.

[12] Hinalaf M. Supresión contralateral de otoemisiones acústicas y pruebas audiológicas subjetivas en la detección temprana de hipoacusias no ocupacionales en la adolescencia. PhD Thesis. Universidad Nacional de Córdoba, Argentina, 2013.

[13] ISO 8253-1. Acoustics-Audiometric test methods-Part 1: Pure-tone air and bone conduction audiometry. International Organization for Standardization, 2010.

[14] IRAM 4028-1. Tone audiometry. Basic test methods. Argentine Institute of Standardization and Certification, 1992.

[15] ISO 389-1. Acoustics-Reference zero for the calibration of audiometric equipment-Part 1: Reference equivalent threshold sound pressure levels for pure tones and supra-aural earphones. International Organization for Standardization, 1998.

[16] IRAM 4075. Electroacoustic. Audiometer. Argentine Institute of Standardization and Certification, 1995.

[17] ISO 389-8. Acoustics-Reference zero for the calibration of audiometric equipment-Part 8: Reference equivalent threshold sound pressure levels for pure tones and circumaural earphones. International Organization for Standardization, 2004.

[18] ISO 389-5. Acoustics-Reference zero for the calibration of audiometric equipment-Part 5: Reference equivalent threshold sound pressure levels for pure tones in the frequency range 8 kHz to 16 kHz. International Organization for Standardization, 2006.

[19] Di Rienzo, J. A.; Casanoves, F.; Balzarini, M. G.; Gonzalez L.; Tablada, M.; Robledo, C. W. InfoStat versión 2015. Grupo InfoStat, FCA, Universidad Nacional de Córdoba, Argentina. URL http://www.infostat.com.ar

[20] Cruz Fernandes, L.; Momensohn dos Santos, T. M. Zumbido e audição normal: estudo da supressão das emissões otoacústicas transientes. *Brazilian Journal of Otorhinolaryngology,* Vol 75, 2009, pp 414-419.

[21] Mor R.; Azevedo Frasson de M. Emissões otoacústicas e sistema olivococlear medial: pacientes com zumbido sem perda auditiva. *Pró-Fono Revista de Atualização Científica,* Vol 17, 2005, pp 283-292.

[22] Riga, M.; Papadas, T.; Werner, J. A.; Dalchow, C. V. A clinical study of the efferent auditory system in patients with normal hearing who have acute tinnitus. *Otology and Neurotology,* Vol 28, 2007, pp 185-190.