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Mismatch Negativity auditory evoked potentials in adult musicians

Potencial evocado auditivo *Mismatch Negativity* em músicos adultos

Potencial evocado auditivo Mismatch Negativity en músicos adultos

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Abstract

Introduction: Mismatch Negativity (MMN) is an objective exam that does not depend on the subjects' task performance or attention. It is regularly used to study auditory processing relative to the automatic detection of auditory changes. **Objective:** To analyze the latencies and amplitudes of MMN in adult musicians and compare the results with those of the control group of normal hearing non-musicians. **Methods:** This is a cross sectional and comparative study. The sample consisted of 69 subjects, aged between 18 and 59 years, with 40 non-musician subjects (control group) and 29 musicians (study group) with at least 3 years of musical expertise, and ages over 18 years. All patients were assessed by peripheral auditory evaluation and MMN. **Results:** The mean latencies and amplitudes were 173.61 ms (±49.80) and 4.25µV (±3.60) in the control group, and 144.23 ms (±17.58) and 5.12µV (±2.73) in the study group. There was a significant difference between the groups per ear ($p<0.05$), and the mean latencies and amplitudes in the study group were 140.08 ms in the right ear and 148.37 ms in the left while the values of amplitude were 4.83µV in the right ear and 5.41µV in the left ear. **Conclusion:** The musicians presented better results for MMN, such as lower latency and greater amplitude, showing evidence of improved acoustic stimulus processing at the central level.

Keywords: Evoked Potentials Auditory; Electrophysiology; Music.

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LWN: research design, collection and analysis of the data, writing of the article.
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Resumo

Introdução: *Mismatch Negativity* (MMN) é um exame objetivo que não depende da realização de tarefas nem da atenção do sujeito. Tem sido utilizado para estudar o processamento auditivo relacionado à detecção automática de mudanças auditivas**. Objetivo**: Analisar latências e amplitudes do MMN em músicos adultos e comparar os resultados com um grupo controle de não músicos normouvintes. **Método:** Estudo transversal e comparativo. A amostra foi composta por 69 sujeitos, 40 sujeitos não músicos (grupo controle) e 29 sujeitos músicos (grupo estudo) todos com no mínimo três anos de experiência musical e idades superiores a 18 anos. Todos realizaram avaliação auditiva periférica e o MMN. **Resultados**: A média das latências e amplitudes do grupo controle foram, respectivamente, 173,61ms (±49.80) e 4,25µV (±3.60) e do grupo estudo foram, respectivamente, 144,23ms (±17.58) e 5,12µV (±2.73). Houve diferença estatisticamente significante entre os grupos por orelha (p<0,05), sendo a média das latências e amplitudes do grupo estudo de 140,08ms na orelha direita e 148,37ms na orelha esquerda, e 4,83µV na orelha direita e 5,41µV na orelha esquerda. **Conclusão**: O grupo de músicos apresentou melhores resultados, como menor latência e maior amplitude do MMN, evidenciando melhor processamento do estímulo acústico em nível central.

Palavras-chave: Potenciais evocados auditivos; Eletrofisiologia; Música.

Resumen

Introduccion: Mismatch Negativity (MMN) es un examen objetivo que no depende del desempeño de las tareas ni de la atención del sujeto. Se há utilizado para estudiar el procesamiento auditivo relacionado com la detección automática de câmbios auditivos. **Objetivo:** Analizar las latencias y amplitudes del MMN en músicos adultos y comparar los resultados con un grupo de control de músicos normales. **Metodos:** Estudio transversal y comparativo. La muestra estuvo compuesta por 69 sujetos, 40 sujetos no musicales (grupo de control) y 29 sujetos músicos (grupo de estudio) todos con al menos tres años de experiencia musical y mayores de 18 años. Todos se sometieron a evaluación de audición periférica y MMN. **Resultados:** El promedio de las latencias y amplitudes del grupo control fueron, respectivamente, 173.61ms (± 49.80) y 4.25µV (± 3.60) y del grupo de estudio, respectivamente, 144.23ms (± 17.58) y 5.12 µV (± 2,73). Hubo una diferencia estadísticamente significativa entre los grupos por oído (p <0.05) y el promedio de las latencias y amplitudes del grupo estudiado fue de 140.08ms en el oído derecho y 148.37ms en el oído izquierdo, y 4.83µV en el oído derecho y 5 .41 µV en el oído izquierdo. **Conclusión:** El grupo de músicos presentó mejores resultados, como menor latencia y mayor amplitud MMN, mostrando un mejor procesamiento del estímulo acústico a nivel central.

Palabras clave: Potenciales evocados auditivos; Electrofisiología; Música.

Introduction

The perception of the environment is a multisensory experience and information from different systems is constantly integrated[1]. Hearing is the most important sense in human communication because it enables recognition of people by their vocal identity and perception of sound oscillations in their voices, in addition to other skills, e.g., differentiating frequencies, tones, intensities and duration of the varied sounds that make up a song, for example. For these competencies to be developed, the peripheral and central auditory systems need to be in full operation[2,3]. Thus, hearing assessment is essential to collect information about hearing functionality[4].

Hearing skills are essential, especially for musicians. Individuals need to develop these skills properly to be able to play or sing music harmonically, but impairments in the central auditory processing hinder the perception of stimuli and, consequently, the reproduction of music.[2,3].

Music has high cognitive and neuronal demands, and requires precise and exact synchronization of many simultaneous acoustic and auditory actions[5]. Among these actions, one of the most important is the control of acoustic parameters related to time, frequency and intensity; this way, musicians can develop and maintain better auditory discrimination and auditory memory skills[6]. Such skills can be assessed by means of long latency auditory evoked potentials[7].

Long latency auditory evoked potentials represent brain activity corresponding to specific auditory processes, and they are used to investigate the processing of auditory stimuli in the cerebral cortex[7-10]. One of the major potentials is Mismatch Negativity (MMN), which reflects the detection of auditory change, that is, it refers to an electrical brain response triggered by a discriminable change in some aspect of auditory stimulation, which appears regardless of the subject's attention[11].

According to the literature, MMN is identified at the point of greatest negativity, in the latency period between 100 and 250 ms, by subtracting the responses obtained for the frequent and the rare stimuli[9,11-13]. In MMN, latency is determined by the time it takes the central auditory system to distinguish rare stimuli from frequent stimuli, while amplitude is directly proportional to response magnitude[13].

One of the clinical applications of MMN is the study of dysfunctions of the central auditory system; it is an important instrument for investigation and objective assessment of detection and auditory discrimination ability, from the auditory nerve to the cerebral cortex. The main characteristic of MMN is non-dependence on task performance or subjects' attention to carry out the test[2,9,11,13].

Researchers have been using MMN to assess brain plasticity[8.9]. Recent studies[10.12] used MMN to evaluate the advantages of central auditory processing in musicians and non-musicians, and they found evidence that the ability of auditory discrimination is better in individuals with musical abilities.

Although there is scientific evidence proving better results in musicians, there is still no consensus over the use of protocols to determine MMN. This choice is made on the basis of the objectives of each particular study. Thus, research with different protocols is necessary to corroborate existing studies.

To contribute to the scientific literature on the findings of MMN, this study aimed to measure responses to the *Mismatch Negativity* test in normal-hearing adult musicians and compare them with the responses of non-musicians.

Method

This research was approved by the Research Ethics Committee of the Universidade Federal do Rio Grande do Sul (UFRGS), under protocol 2011039, fully respecting Resolution No. 466/12, which deals with research with human beings. The participants in this study were subjects that had signed an Informed Consent Form (ICF), which contained explanations about the goal and method of the study, the discomfort that the subjects might experience during the test, and the confidential handling of personal information.

This is an observational, cross-sectional and comparative study. The convenience sample was composed of females and males, aged over 18 years and a maximum of 59 years. To estimate the standardized effect size of 0.9 (moderate), a sample size of 28 subjects was calculated in each group. Significance level was set at 0.05 with power = 90% (Epilnfo - Statcal).

The inclusion criteria for the control group were individuals with normal hearing thresholds, aged between 18 and 30 years old, who had completed high school, with no history of dysfunction of the auditory system, that is, no otological pathologies or hearing complaints. Individuals with genetic impairments, history of neurological diseases, intellectual disability or other illnesses, and those who did not understand or were unable, for whatever reason, to carry out the procedures and complete the examination, were excluded from the study.

The inclusion criteria of the study group were professional musicians, with normal hearing thresholds in both ears, with a minimum musical expertise of three years, aged between 18 and 59 years and with no history of complaints of dysfunctions in the auditory system. Individuals were excluded from the study if they had genetic impairments, history of neurological diseases, intellectual disability or other illnesses, and if they did not understand or were unable, for whatever reason, to carry out the procedures and complete audiological evaluations.

First, a medical history interview was carried out to address general data such as: name, age, sex, educational level, presence of diseases, hand dominance, length of musical expertise, musical genre, instrument, length of training/weekly practice, among other data.

Then, the external auditory acoustic meatus was inspected. Afterwards, in a soundproof booth, pure tone air-conduction and bone-conduction audiometry (PTA) assessments were performed in the frequencies of 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz and in the frequencies of 500, 1000, 2000, 3000 and 4000 Hz, respectively. Davis and Silverman's (1970) classification was used[14].

Speech audiometry was performed by determining the Speech Recognition Percentage Index (SRPI) and then the Speech Recognition Threshold (SRT). SRPI was performed with 25 monosyllabic words, presented at a constant and comfortable intensity level (40 dBNA above the three-tone average value of the frequencies of 500, 1000 and 2000 Hz by air-conduction) in each ear; the patients were expected to repeat the words. SRT also used the initial intensity level of 40 dBNA above the three-tone average value by air-conduction. Such intensity was reduced until reaching the level at which the patients could understand and repeat 50% of the trisyllabic words presented. PTTA and speech audiometry were performed with a previously calibrated Inventis audiometer (Harp Inventis).

After PTTA had been completed, Acoustic Immitance Measurements (AIM) were performed with an AT235h Interacoustics Impedance Audiometer. Tympanometric curves were determined with a probe inserted into the patients' external auditory canal. Static and dynamic complacencies were investigated; the curve was drawn and described according to Jerger's classification (1970)[15]. During testing of ipsilateral and contralateral acoustic reflexes, the thresholds were investigated for frequencies of 500, 1000, 2000 and 4000 Hz in both ears.

After the basic peripheral hearing assessment, MMN testing was performed in an electrically and acoustically insulated room. For this test, the patients were seated in a comfortable chair with a headrest. The examiner cleansed the patients' skin with a prep gel (Nuprep®) and common gauze. Subsequently, silver electrodes were placed with an EEG conductive paste (Ten20®conductive) and adhesive tape. The ground electrode was placed on Fpz; the active electrode, on Fz; the electrode (M1) was placed on the left mastoid and (M2) was placed on the right mastoid and, finally, insertion earphones (*Earphone TONE™GOLD*) were worn in both ears. This test was performed using a *Contronic®* MASBE ATC Plus data acquisition system. Electrical impedance was less than 5Ω in each lead and the difference between the three electrodes did not exceed 2Ω.

After impedance measurement, electroencephalogram (EEG) scanning was performed to capture spontaneous brain electrical activity to check for artifacts that might affect the test results. The patients were instructed not to tension their limbs nor cross their legs or arms.

For MMN testing, several equal stimuli (frequent stimulus) were presented at short time intervals, alternated with stimuli that differed in frequency (rare stimulus). During this process, the patients were made to watch an interesting and quiet video on a tablet to divert their attention on the auditory stimuli that were presented.

For MMN recording, the auditory stimuli were presented monoaurally to accomplish one of the objectives of the study (to compare the right and the left ears), with frequency of 1000 Hz (50 cycles) for the frequent stimulus and 2000 Hz (50 cycles) for the rare stimulus, in an intensity between 70 dB and 80 dB, depending on acoustic comfort, as reported by the patients, with 1.8 stimuli per second. At least 150 mediations were used for the rare stimulus. The paradigm in use was 90% of frequent stimuli and 10% of rare ones, and polarity was alternated. During acquisition, full scale was 200 µV; high-pass filter = 1 Hz; low-pass filter = 20 Hz; time window = 500 ms, and tracing amplitude = 7 µV. For more reliable analyses, all electrophysiological records were analyzed by two evaluators, at different times. MMN recording protocol was based on another study that used the same equipment and investigated the same age group[9].

MMN was determined by subtracting the tracing corresponding to the frequent stimuli from the tracing corresponding to the rare stimuli. Latency marking was performed in the highest negativity found between 100 and 250 ms, after the N1 component. Amplitude was marked by considering the baseline (zero point) as the starting point until the greatest deflection, identified as MMN[11]. Figure 1 exemplifies MMN marking in a research subject.

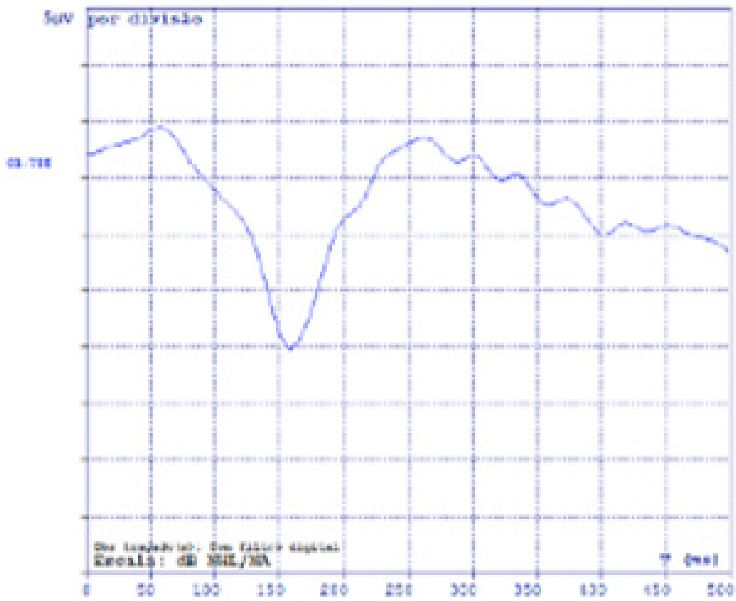

Figure 1. Example of the MMN potential in a subject of the present research.

The results were organized in the form of descriptive statistics, in which the categorical variables were represented by absolute and relative distributions, and the continuous variables, by mean, standard deviation and amplitude, with a study of data distribution by the *Kolmogorov-Smirnov* test.

The continuous variables between the control group and the study group were compared using *Student*'s t-test for independent groups (data with symmetric distribution) or the *Mann Whitney U* test (asymmetric data distribution). The data were analyzed in the software *Statistical Package for Social Sciences* version 20.0 (SPSS Inc., Chicago, IL, USA, 2008) for *Windows*, and the significance level of 5% was adopted for statistical decision criteria.

Results

Forty male and female subjects from the control group and 29 from the study group participated in this research, and most of them reported right-hand preference. Table 1 shows data from the characterization of the sample.

Table 1. Absolute and relative distribution for sex and hand preference; and measures of central tendency and variability for age

Variables	Control Group (n= 40)	Study Group (n= 29)
Age Mean ± SD [min-max]	22,38±2,94[18-29]	35,83±12,18[18-59]
Sex n(%)		
Females	20 (50%)	11 (37,93%)
Males	20 (50%)	18 (62,06%)
Hand preference		
Right-handed	37 (92,5%)	23 (79,31%)
Left-handed	3 (7,5%)	4 (13,79%)
Ambidextrous	0 (0%)	2 (6,89%)

Caption: SD= standard deviation

Table 2 shows the results for MMN latencies and amplitudes in both ears, from both groups. When comparing the averages of latencies and amplitudes between the ears in the same group, there was no statistically significant difference, indicating that RE and LE present similar latencies and amplitudes within the same group.

Table 2. Central tendency and variability measures for amplitude and latency of the right and left ear in each group

Variables	Control Group (n= 40)						Study Group (n= 29)					
	Mean	**SD**	**Mean**	**Min**	**Max**	**p-value**	**Mean**	**SD**	**Mean**	**Min**	**Max**	**p-value**
Latency RE	171.30	52.66	159	92	308	0.701§	140.08	19.41	137.91	106.38	179.54	0.189§
Latency LE	175.87	53.55	159	108	351		148.37	27.36	142.96	112.68	230.60	
Amplitude RE	-4.40	4.48	-3.00	-1.00	-23	0.688#	-4.83	2.96	-4.19	-1.41	-16.90	0.367#
Amplitude LE	-4.12	3.89	-2.00	-1.00	-20		-5.41	3.09	-4.92	-0.98	-13.99	

Caption: RE = right ear; LE = left ear; SD = standard deviation; Med = median; Min = minimum; Max = maximum; §Student's t-test; ##*Mann-Whitney* Test; significance level = p≤0.05

When comparing the mean latencies and MMN amplitudes between males and females in each group (Table 3), there was a statistically significant difference (p = 0.013) in the RE latencies of the control group. The mean latency of MMN of the RE in females was significantly lower when compared to that of males. For the other variables, there were no statistically significant differences.

Table 3. Measures of central tendency and variability for amplitude and latency between males and females and in each group

Variables	Group	Sex	Mean	SD	Median	Minimum	Maximum	p-value
Latency RE	CG	Fem	151.09	41.12	153.68	92.5	242.61	0.013§
		Male	191.46	56.05	171.34	112.68	308.21	
	SG	Male	144.64	19.11	146.11	106.38	179.54	0.107§
		Fem	132.63	18.32	136.65	106.38	163.14	
Latency LE	CG	Fem	162.65	41.13	158	108	262	0.120§
		Male	189.10	61.86	174	116	351	
	SG	Male	155.11	29.93	149.26	116.47	230.60	0.090§
		Fem	137.34	18.91	132.87	112.68	173.23	
Amplitude RE	CG	Fem	-4.08	3.19	-3.03	-1.00	-14.97	0.516#
		Male	-4.74	5.55	-2.16	-1.00	-23.27	
	SG	Male	-4.87	3.48	-4.12	-1.41	-16.90	0.653#
		Fem	-4.76	1.97	-4.72	-2.39	-7.74	
Amplitude LE	CG	Fem	-4.45	4.47	-3.00	-1.00	-20	0.669#
		Male	-3.80	3.28	-2.00	-1.00	-12	
	SG	Male	-5.44	3.41	-4.96	-0.98	-13.99	0.822#
		Fem	-5.37	2.63	-4.92	-1.66	-11.43	

Caption: RE = right ear; LE = left ear; fem = females; male = males; CG = control group; SG = study group; §Student's t-test; #*Mann-Whitney* Test; significance level = p≤0.05

Table 4 shows a comparison of the latency and amplitude averages between the groups per ear. There was a statistically significant difference in latency between groups regarding the RE and the LE, and between groups for amplitude of the LE.

Table 4. Measures of central tendency and variability for amplitude and latency and comparison between groups by ear

		Mean	SD	Median	Minimum	Maximum	p-value
Latency RE	CG	171.30	52.66	159	92	308	0.003§
	SG	140.08	19.41	137.91	106.38	179.54	
Latency LE	CG	175.87	53.55	159	108	351	0.014§
	SG	148.37	27.36	142.96	112.68	230.60	
Amplitude RE	CG	-4.40	4.48	-3.00	-1.00	-23	0.054#.
	SG	-4.83	2.96	-4.19	-1.41	-16.90	
Amplitude LE	CG	-4.12	3.89	-2.00	-1.00	-20	0.045#.
	SG	-5.41	5.41	-4.92	-0.98	-13.99	

Caption: RE = right ear; LE = left ear; SD = standard deviation; Med = median; SG = Study Group; §Student's t-test; #*Mann-Whitney* Test; significance level = p≤0.05

When comparing the average values of latencies and amplitudes of both ears between the control group and the study group (Table 5), the values showed a statistically significant difference, both for latency and amplitude.

Table 5. Measures of central tendency and variability for amplitude and latency in both ears and comparison between groups

		Mean	SD	Median	Minimum	Maximum	p-value
Latency	CG	173.61	49.80	158.72	107.01	329.65	0.003§
	SG	144.23	17.58	144.85	111.42	175.42	
Amplitude	CG	-4.25	3.60	-2.52	-1	-14.61	0.035#.
	SG	-5.12	2.73	-4.54	-1.51	-15.44	

Caption: CG = control group; SG = study group; §Student's t-test; #*Mann-Whitney* Test; significance level = p≤0.05

There was no statistically significant correlation between length of musical expertise and latency and amplitude of MMN (Table 6), both for the length of expertise (years) and for the weekly practice (hours) variables.

Table 6. Correlation between length of expertise in years and hours of weekly practice with latency and amplitude

	Length of expertise (years)	Weekly practice (hours)
Latency	0.056*	0.922*
Amplitude	0.358*	0.809*

Caption: * *Pearson* Correlation; significance level = p≤0.05

Discussion

This study showed that the musicians presented better results in MMN. Such results corroborate those of other studies involving long latency auditory evoked potentials[16-18], which also showed that musicians have better responses to hearing skills. This fact is justified by structural and functional changes relative to neuroplasticity, owing to long-term musical training[18].

Regarding the variability of latency and amplitude of the ears in each group, Table 2 shows that, when the average values of latencies and amplitudes are compared between the ears in the same group, there was no statistically significant difference, indicating that the RE and the LE present similar latencies and amplitudes, within the same group. These results corroborate those in the literature[9,21] and, especially, the findings of a study involving adult and elderly subjects[21] in which the authors reported no differences between latencies and amplitudes in the RE and the LE.

When MMN latency and amplitude averages were compared between males and females and in each group separately (Table 3), there was a statistically significant difference (p = 0.013) in the RE latencies of the control group, which showed lower values of RE latency in females, when compared to males. The results of the present study are in line with the literature, which describes lower latency values for females[6,9]. A previous study[22] reported that women have better responses to discrimination of phonemic contrasts. Therefore, it can be inferred that women may present better responses to different acoustic stimuli[8]. Other studies have also reported differences between males and females in cognitive electrophysiological assessments, such as MMN[2,9,23], and these differences can be justified by the temporal acoustic changes that occur in the presentation of stimuli, with females having better hearing discrimination skills. Differences between men and women can be explained by neurophysiological variations, and verbal language skills are more favorable to women, who have greater sensitivity in the temporal spectrum and in the auditory discrimination of phonemic contrasts.[2,9,23].

Regarding the comparison of latencies per ear, between the groups (Table 4), this study showed a statistically significant difference in both ears (p = 0.003 and p = 0.014), with MMN latency being lower in the SG. There were also differences for amplitude in the LE between the groups (p = 0.045), with the amplitude being greater for the SG. Although the results of this comparison between the groups are specified by ear, they corroborate the scientific literature[3,6,24], which shows better responses in musicians. These results can be justified by the fact that long-term musical auditory training provides agility and greater ease in the identification of acoustic changes.

The main findings of the study sample are shown in Table 5. In this table, the initial hypothesis can be confirmed, that is, the group of musicians presented better responses than the group of non-musicians, in the comparison of both the latency averages (p = 0.003) and the amplitude averages (p = 0.035). A previous study[3] used musical stimuli presented in conditions of low uncertainty (predictable changes) and high uncertainty (unpredictable changes) to elicit MMN in musicians and non-musicians. The researchers showed that for the condition of low uncertainty, the subjects with musical training showed better results, that is, the central auditory system could easily identify the changes that occurred in the stimulus presented. This fact can justify the better MMN responses obtained in the present study, since the stimuli presented (1000 and 2000 Hz) can be classified as of low uncertainty, that is, there is a predictability for the central auditory system to identify stimuli, since the rare stimulus presented is the same throughout the exam.

There are several reasons that justify better responses in musicians, such as innate genetic predisposition, brain plasticity, increase in cognitive skills as a result of auditory training, increase in the number of neurons involved, greater brain area involved, and greater brain activity during sound discrimination[2,25-28].

A previous study[29] conducted with magnetoencephalography found that musicians and non-musicians use different neural processes, and classify the sense of responding in the same way, but it was found that their responses were different, i.e., musicians responded better. Another study with musicians[30] showed that latencies are lower when the stimuli are deviated from the rhythm and different from the frequent ones. Another study reported that jazz musicians have better responses than musicians who play other music genres because of the complexity of alternating tones, which are very different and sudden[26]. These findings from other studies, with other types of procedures, show that, in fact, musicians have differentiated hearing skills in comparison to normal non-musician listeners. This finding proves the initial hypothesis of this study, using the MMN auditory evoked potential in musicians.

It was also found that the musicians' minimum and maximum latency values were within the range estimated as a MMN recording pattern, with values ranging between 100 ms and 250 ms [2,9,11,21].

Table 6 shows the data on length of expertise and weekly practice. In this study, it was found that regardless of length of expertise (years) or weekly practice (hours), there were no differences between latencies and amplitudes in the study group. These findings differ from those reported in the literature[3.25-28]. One of the hypotheses is that the studies of the literature used a shorter length of musical expertise than the one of the present study. Thus, the subjects' auditory musical training may have had greater influence on their responses.

In general, in the results of the present study, the musicians showed better responses, that is, lower latencies and greater amplitudes of MMN. Based on these data, it can be inferred that musical stimuli, in the long term, improve the functionality of the central auditory system, allowing efficient identification of acoustic changes, which are related to temporal auditory processing.

Conclusion

Based on the results of the present study, there were differences between musicians and non-musicians, with lower latency values and greater amplitudes of the MMN potential for individuals with musical expertise.

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