

# Characterization of Mismatch Negativity in children, adolescents and young adults

## Caracterização do *Mismatch Negativity* em crianças, adolescentes e adultos jovens

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### ABSTRACT

**Purpose:** To describe and analyze the latencies and amplitudes of mismatch negativity (MMN) according to ear, sex, and age group in children, adolescents, and young adults. **Methods:** This cross-sectional study included participants with normal hearing and typical development of both sexes. The sample comprised 260 children aged 9 to 11 years and 11 months, 110 adolescents aged 12 to 17 years and 11 months, and 110 young adults aged 18 to 29 years and 11 months. All participants underwent peripheral audiological assessment (otoscopy, acoustic immittance measures, pure-tone audiometry, and speech audiometry) and central auditory evaluation (brainstem auditory evoked potentials and mismatch negativity). **Results:** A negative correlation was observed between MMN latency and age group, indicating a decrease in latency with increasing age. No significant differences were found in MMN amplitudes across age groups, nor in MMN latencies and amplitudes between ears or sexes. **Conclusion:** The latencies and amplitudes of mismatch negativity were characterized in children, adolescents, and young adults. A reduction in MMN latency was observed with increasing age.

**Keywords:** Hearing; Evoked potentials; Auditory; Child; Adolescent; Adult

### RESUMO

**Objetivo:** descrever e analisar as latências e amplitudes do *Mismatch Negativity* entre orelhas, sexos e faixa etária de crianças, adolescentes e adultos jovens. **Métodos:** estudo transversal, do qual os participantes eram normo-ouvintes e com desenvolvimento típico, de ambos os sexos, sendo 260 crianças com idade entre 9 anos e 11 anos e 11 meses, 106 adolescentes entre 12 anos e 17 anos e 11 meses e 110 adultos jovens, entre 18 anos e 29 anos e 11 meses. Todos os sujeitos realizaram avaliação audiológica periférica (meatoscopia, medidas de imitância acústica, audiometria tonal limiar, audiometria vocal) e avaliação audiológica central (Potencial Evocado Auditivo de Tronco Encefálico e *Mismatch Negativity*). **Resultados:** Verificou-se correlação negativa de latências do *Mismatch Negativity* para a variável faixa etária, diminuídas à medida que houve aumento da idade dos sujeitos avaliados. Não foi constatada diferença significativa de amplitudes do *Mismatch Negativity* em relação à faixa etária, assim como nas latências e amplitudes entre as orelhas e os sexos. **Conclusão:** foi possível descrever as latências e amplitudes do *Mismatch Negativity* em crianças, adolescentes e adultos jovens. Verificou-se regressão de latências do *Mismatch Negativity* com o aumento da idade dos participantes.

**Palavras-chave:** Audição; Potenciais evocados auditivos; Criança; Adolescente; Adulto

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## INTRODUCTION

It is possible to measure the neural activity of the highest portion the auditory pathway through Long Latency Auditory Evoked Potentials (LLAEPs), which allow for an objective evaluation of the pathway, and which are being widely utilized in audiologic practice<sup>(1)</sup>. Among these, the *Mismatch Negativity* (MMN) stands out, as it's considered to be an electrophysiological test that represents the most accurate measure of auditory processing and auditory discrimination, which makes it relevant and promising<sup>(2,3)</sup>.

MMN is a negative component of Event-Related Potentials (ERPs)<sup>(1)</sup>. It occurs when the auditory system detects a change within a sequence of repeated acoustic stimuli, that is, it reflects the perception of rare stimuli among frequent stimuli<sup>(1,3)</sup>. Thus, it is considered a cognitive potential stimulus that essentially represents auditory discrimination, in addition to presenting an intrinsic relationship between attention, recognition and auditory memory skills<sup>(4,5)</sup>. The MMN generators are found in the temporofrontal cortex, with contributions from the thalamus and hippocampus, thus forming a complex of neural connections responsible for a large part of central auditory processing<sup>(6)</sup>. Its main advantage in comparison to other cortical electrophysiological tests lies in the fact that it is not influenced by the subject's attentional state and does not require their active participation, which makes it possible for it to be used on the evaluation of diverse populations and age groups<sup>(7,8)</sup>. Lastly, it is evident that MMN is an objective measure that reflects findings referring to auditory discrimination, being an auditory evoked potential (AEP) that provides sensorial responses of the auditory pathway.

Literature testifies to the extensive variety of possible clinical uses of MMN throughout the life cycle, in different developmental disorders and with different objectives<sup>(6)</sup>. In children and teenagers, research reveals findings of MMN in cases of developmental language disorder (DLD), phonological problems, aphasia, dyslexia, learning difficulties, autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), central auditory processing disorders (CAPD), hearing loss, recurrent otitis, psychosis, among others<sup>(6,9-11)</sup>. In adults, most studies investigated MMN in cases of central auditory processing disorders, such as Multiple Sclerosis and Amyotrophic Lateral Sclerosis, as a neurophysiological marker and, in psychiatric disorders, as a biomarker for hearing disorders in schizophrenia<sup>(1,4,6,12)</sup>.

Depending on the objective to be evaluated, it is possible to trigger MMN with a variety of stimulation, such as tonal and verbal auditory stimuli and their elementary variations, mainly frequency, duration and phonemic differences<sup>(3)</sup>. The commonly used analysis of MMN occurs through the observation of latency, which represents the time that the rare stimulus takes to be differentiated from the frequent stimulus, and the wave amplitude, which demonstrates the greater or lesser capacity of the auditory system to differentiate the auditory stimuli presented and reflects the number of neurons activated by the auditory stimuli as well as the efficacy of neural functions. Under these conditions, when prolonged latency and amplitude attenuation are observed, clinical changes are objectively evidenced, with a highlight on their contribution to the patient's auditory monitoring<sup>(7,9)</sup>.

Research reports that, in general, MMN presents latencies between 150 and 200 ms<sup>(4,13,14)</sup>, 150 and 250 ms<sup>(7)</sup>, 150 and 350 ms<sup>(15,16)</sup> highlighting great variability in the responses proposed as the normality standard. In the same way, it is also worth highlighting that the measures are influenced by the tonal or speech stimuli. Regarding amplitude, they report values lower than 2  $\mu\text{V}$ <sup>(4)</sup> or around 5  $\mu\text{V}$ <sup>(15,16)</sup>. Some studies with adolescents have indicated that there is stability in the latencies and amplitudes of the MMN<sup>(17)</sup>, however, other authors report that neurophysiological processes continue to develop in this age group and can influence latency, which suggests that MMN must be evaluated considering the influence of the patient's age<sup>(18)</sup>.

It is worth noting that most scientific research points out that, due to the great variability of responses considering technical characteristics like records, protocols, equipment and analyses, or biological characteristics such as the evaluated individual's age, there is no defined standard of normality for MMN measurements, which represents a limitation to its use in clinical practice<sup>(9)</sup>.

Besides that, it is observed that a large part of the studies aims to investigate individuals diagnosed with neurological, psychiatric or phonoaudiological alterations, revealing a gap in comparison to recent research that evaluated normal hearing individuals, with no auditory complaints and typical development. Considering the relevance of MMN in the evaluation of cortical auditory responses and the need to investigate the values of latency and amplitude throughout the lifecycle, large scale studies such as this one are necessary to verify these data and validate results obtained in a standardized fashion<sup>(1,9)</sup>.

Thus, this study has the general objective of characterizing the MMN findings in normal-hearing and typically developing children, adolescents and young adults and, specifically, to describe and analyze the MMN latency and amplitude values, in response to the *tone burst* stimulus, comparing the data between ears, sexes and age group.

## METHODS

This study was approved by the Research Ethics Committee of the Federal University of Rio Grande do Sul – CEP/UFRGS, under the Certificate of Presentation for Ethical Appreciation (CAAE) number 55977316.8.0000.5334. The Free and Informed Consent Form was accepted and signed by the young adult participants and by the guardians of the children and adolescents, who consented to their participation through the Free and Clarified Assent Term. Both documents contained the objectives of the study, the steps to be taken, their risks and benefits.

This is a cross-sectional, observational, contemporary and individual research composed of female and male sex individuals. The groups were made up of children, aged between 7 and 11 years and 11 months old; adolescents, between 12 and 17 years and 11 months old; young adults, between 18 and 29 years and 11 months old. The age group was defined through the criteria of neural maturation, which establishes itself at the age of 7, and due to the risk of identification of presbycusis starting at the age of 30, which led to the inclusion of adults up to 29 years and 11 months old<sup>(5)</sup>. Data collection was carried out at the Center for Studies and Research in Hearing Electrophysiology and Neuroaudiology at the Federal University of Rio Grande do Sul (UFRGS).

The study refers to a convenience sampling, in which the children and teenagers were students from public schools which obtained a partnership with an extension project implemented and carried out by UFRGS, under the coordination of the supervisor of this research. The adults who participated received an invitation, which was publicized on social media and through posters distributed at UFRGS. To estimate the standardized effect size of 0.8 (moderate), a sample size of 257 children, 106 teenagers and 110 young adults was calculated. A significance level of 0.05 with 90% power was accepted (*Epi Info – Statcalc*).

The following inclusion criteria were adopted: to be between 7 and 29 years and 11 months old; to present auditory thresholds within the limits of normality in the peripheral auditory evaluation and bilaterally normal Brainstem Auditory Evoked Potential (BAEP), as a measure of objective evaluation of integrity of the auditory pathway up to the brainstem; to present as result of the measurement of acoustic immittance: type A tympanometric curve and presence of contralateral and ipsilateral reflexes in all tested frequencies and in both ears; children and teenagers with typical development (considering information gathered through anamnesis regarding to the alert signals to alterations in the development and to the child development milestones up to 5 years of age), with no auditory complaints, no diagnosis of otological pathologies (recurrent otitis, sensation of tinnitus or diagnosis of auditory system dysfunction), with all the cited items being verified through anamnesis; to not make use of continuous medications and had regular school performance, which would be testified by proving that they hadn't failed two consecutive bimesters previous to the participation on the study; adults with complete secondary education.

Subjects that presented some auditory alteration diagnosed during the procedures taken, besides those who did not take or complete the proposed procedures were excluded; subjects with a history or complaint of otological pathologies, including recurrent otitis, sensation of tinnitus or diagnosis of auditory system dysfunction; subjects with a clinical history or diagnosis of genetic syndromes, neurological alterations, disorders in neurodevelopment or other pathologies and clinical history of delay on the development of acquisition of the milestones of cognitive and motor development.

The selected participants underwent the following steps:

- Anamnesis: elaborated by the researchers themselves, which covered general data such as name, age, sex, school performance for children and teenagers, level of education for young adults, history or presence of any otological complaints, other pathologies and general state of health. In this stage, those responsible for the children and adolescents participated.
- Meatoscopy: the external auditory canals were inspected with a Welch Allyn otoscope (Welch Allyn Inc., Skaneateles Falls, NY, USA), to rule out the presence of earwax and/or foreign bodies. If the presence of alterations was verified in meatoscopy, the individual would be referred for otorhinolaryngological evaluation.
- Acoustic Immittance Measurements: this exam was carried out to check the functioning of the middle ear. For tympanometry, the Impedance Audiometer AT235h equipment (Interacoustics, Middelfart, Denmark) was used, with a 226 Hz probe. The static and dynamic compliances were checked and the tympanometric curve was drawn. The only accepted answer was the type A

curve with compliance of 0.3 to 1.6 ml and peak of -100 to +100 daPa<sup>(19)</sup>. The ipsilateral and contralateral acoustic reflex thresholds were investigated, with a 226 Hz probe inserted into the external auditory canal and through the earphone, at frequencies 500, 1000, 2000 and 4000 Hz, in both ears.

The tonal and vocal audiometry tests were done in an acoustically treated cabin, with a Harp Inventis audiometer (Inventis S.R.L, Padua, Italy).

- Pure Tone Audiometry (PTA): hearing thresholds were investigated in both ears via air, carried out with the use of supra-aural headphones at frequencies of 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz and, via bone, at frequencies of 500, 1000, 2000, 3000, 4000 Hz. Normal hearing thresholds in both ears were considered below or equal to 15 dBHL for children and adolescents, and below or equal to 25 dBHL for adults<sup>(20,21)</sup>.
- Vocal Audiometry: in the Percentage Speech Recognition Index (SRI) survey, 25 monosyllabic words were presented in each ear at a fixed and comfortable intensity (40 dBHL above the tritonal average value of the frequencies of 500, 1000 and 2000 Hz of the airway), for the subject to repeat them correctly. A percentage of correct answers of 92 to 100% was considered a normal response. In the Speech Recognition Threshold (SRT) test, the initial intensity used was also 40 dBHL above the tritonal airway average, which was reduced until reaching the intensity level at which the individual repeated 50% of the trisyllabic words presented<sup>(22)</sup>.
- Brainstem Auditory Evoked Potential (BAEP): this test was performed with the goal of verifying the integrity of the auditory pathway and ensure that the auditory stimulus was conducted to the brainstem region. The click stimulus was presented separately to the right and left ears, at a speed of 27.7 stimuli per second, with 2,048 *sweeps* measured at an intensity of 80 dBHL. A recording window of 12 ms, high-pass filter of 100 Hz and low-pass of 3,000 Hz, stimulus duration of 100 µsec and rarefied polarity were used. To ensure wave reproducibility, two tracings were taken from each ear. The absolute latencies of the BAEP click waves should be within expected values, close to: wave I = 1.54 ms, wave III = 3.69 ms and wave V = 5.54 ms; as for interpeak intervals, the expected values are close to: I-III = 2.14 ms maximum, III-V = 1.86 ms maximum, I-V = 4.00 ms maximum<sup>(23)</sup>.
- *Mismatch Negativity* (MMN): for the examination, the individual was positioned in a comfortable chair with head support. The examiner cleaned the skin with Nuprep® exfoliant (Weaver and Company, Aurora, CO, USA) and common gauze. Soon after, silver electrodes were placed with Ten20® electrolytic paste (Weaver and Company, Aurora, CO, USA) and surgical Micropore tape (3M, St. Paul, MN, USA). The ground electrode was placed on the forehead and the active electrode on (Cz), close to the scalp; the electrode (M1) was placed on the right mastoid and (M2) on the left mastoid and, finally, the Earphone TONE™GOLD 3A / 5A (Contronic, Pelotas, RS, Brazil) insert headphones were placed in both ears. The BAEP and MMN exams were carried

out in an acoustically and electrically treated room and the equipment of brand MASBE ATC Plus (Contronic, Pelotas, RS, Brazil) was used.

The electrical impedance was less than  $5\Omega$  in each lead and the difference between the three electrodes did not exceed  $2\Omega$ . After checking the impedance, the electroencephalogram (EEG) was scanned to capture spontaneous cerebral electrical activity, to check for artifacts that could interfere with the examination. Subjects were instructed not to tense their limbs and not to cross their legs or arms.

To record the MMN, in relation to the parameters used, the auditory stimuli were presented monaurally, in both ears, in short time intervals between each other (ms), with frequency variation, being 1000 Hz (50 cycles) for the frequent stimulus and 2000 Hz (50 cycles) for the rare stimulus, at an intensity of 80 dBHL. 750 stimuli were presented, aiming to acquire at least 150 rare stimuli, the possibility of occurrence of which is 20% of the total stimuli, with an 80/20 paradigm and alternating polarity. During acquisition, the full scale was 200  $\mu\text{V}$ , high-pass filter of 1 Hz, low-pass filter of 20 Hz, temporal window of 500 ms and trace amplitude of up to 7.5  $\mu\text{V}$ <sup>(24)</sup>.

In relation to the criteria used for analysis, the MMN latency was marked at the lowest peak of maximum amplitude from 150 ms, after N1 peak, considering the difference (*mismatch*) between the responses of the frequent and rare stimulus, visualized in individual traces<sup>(25)</sup>. It is worth noting that for the analysis of the MMN records, two judges from the area of audiology with knowledge and previous experience in hearing electrophysiology analyzed the recordings, and for each wave three collections were carried out to verify replicability.

During this process, individuals were conditioned to watch a silent video of their choice on the tablet, with the intention of diverting attention to the auditory stimuli that were presented. No instructions or additional information about the auditory stimuli were reported. The exam had a total duration of 20 minutes, with 10 minutes being necessary to evaluate each ear with the three acquisitions required to identify reproducibility.

The stipulated stages of the assessments were carried out in a single session, even with the possibility of return. Breaks between the tests were provided for rest.

The results were organized in the form of descriptive statistics. The Kolmogorov-Smirnov test was used to assess data normality. The T-student test was used to compare mean

latency and amplitude values between age groups, sexes and ears. Statistical analyses were performed using the Statistical Product Service Solutions (SPSS) program version 25.0 (IBM Corp., Armonk, NY, USA). The significance level adopted was 5% ( $p < 0.05$ ) and all confidence intervals were constructed with 95% statistical confidence.

To ensure agreement and greater reliability of the MMN analyses, the Kappa Agreement Coefficient test was performed<sup>(26)</sup>. The correlation between the strength of agreement and the Kappa value was interpreted based on the scale:  $< 0.00$  (poor), 0.00-0.20 (negligible), 0.21-0.40 (weak), 0.41-0.60 (moderate), 0.61-0.80 (substantial), and 0.81- 1.00 (almost perfect). The interpretation of the Interclass Correlation Coefficient (I) was based on the following classification: I value  $< 0.4$  (poor correlation strength), I between 0.4 - 0.75 (satisfactory correlation strength) and I  $> 0,75$  (excellent correlation strength)<sup>(27)</sup>.

## RESULTS

The total sample was composed of 480 participants, from both sexes, with ages between 7 and 30 years old. Table 1 presents the characterization data of the sample.

Table 2 presents the results of the latency values (ms) and amplitudes ( $\mu\text{V}$ ) of MMN, where the data was stratified by age group (children, teenagers, young adults).

There was a negative correlation between the latency values (ms) of the MMN for the age group variable, decreasing as age increased. There was no statistically significant difference in amplitudes ( $\mu\text{V}$ ) among the age group studied.

In the comparative analysis between the participants' right ear and left ear (Table 3), no statistically significant difference was found in the MMN latency (ms) and amplitude ( $\mu\text{V}$ ) values in any of the age groups studied. Likewise, in the analysis between female and male sexes, no statistically significant difference was found in the values of latencies (ms) and amplitudes ( $\mu\text{V}$ ) in the age groups studied. Therefore, it was decided to group the MMN values in relation to ears and sexes.

As for the analysis of the *Mismatch Negativity* (MMN) components, there was excellent agreement between judges (Kappa 0.86). It was possible to obtain a score of 0.82 in the interclass correlation coefficient, resulting in an almost perfect correlation.

**Table 1.** Sample characterization

| Age (n)       | Female | Male | Average age   |
|---------------|--------|------|---------------|
|               |        |      | Mean $\pm$ SD |
| 7 (n= 52)     | 26     | 26   |               |
| 8 (n= 52)     | 26     | 26   |               |
| 9 (n= 52)     | 26     | 26   |               |
| 10 (n= 52)    | 26     | 26   |               |
| 11 (n= 52)    | 26     | 26   |               |
| 12-15 (n=55)  | 28     | 27   | 14 $\pm$ 1.9  |
| 16-18 (n=55)  | 27     | 28   | 17 $\pm$ 1.8  |
| 19-25 (n=55)  | 28     | 27   | 22 $\pm$ 4.5  |
| 25-30 (n= 55) | 28     | 27   | 27 $\pm$ 4.8  |

**Subtitle:** n = number of subjects in the sample; SD = standard deviation

**Table 2.** Mismatch Negativity latency and amplitude results in relation to age group

| Age (n)       | MMN            |                |
|---------------|----------------|----------------|
|               | Latency (ms)   | Amplitude (µV) |
|               | Mean ± SD      | Mean ± SD      |
| 7 (n= 52)     | 212.71 ± 33.57 | 3.81 ± 0.83    |
| 8 (n= 52)     | 189.52 ± 31.94 | 3.85 ± 0.52    |
| 9 (n= 52)     | 181.73 ± 28.71 | 3.73 ± 0.50    |
| 10 (n= 52)    | 176.42 ± 21.83 | 3.96 ± 0.74    |
| 11 (n= 52)    | 163.17 ± 21.47 | 3.98 ± 0.61    |
| 12-15 (n=55)  | 159.82 ± 20.22 | 3.87 ± 0.48    |
| 16-18 (n=55)  | 156.35 ± 19.45 | 3.27 ± 0.53    |
| 19-25 (n=55)  | 154.35 ± 19.33 | 3.85 ± 0.68    |
| 25-30 (n= 55) | 153.35 ± 16.21 | 3.76 ± 0.64    |

Subtitle: MMN = Mismatch Negativity; n = number of subjects in the sample; SD = standard deviation; ms = millisecond; µV = microvolt

**Table 3.** Mismatch Negativity latency and amplitude results in relation to age group and ears

| Age (n)       | MMN             |                 |                   |                   |       |
|---------------|-----------------|-----------------|-------------------|-------------------|-------|
|               | Latency (ms) RE | Latency (ms) LE | Amplitude (µV) RE | Amplitude (µV) LE | p     |
|               | Mean ± SD       | Mean ± SD       | Mean ± SD         | Mean ± SD         |       |
| 7 (n= 52)     | 211.43± 30.22   | 213.24 ± 34.61  | 3.69 ± 0.72       | 3.92 ± 0.91       | 0.143 |
| 8 (n= 52)     | 191.47 ± 30.72  | 186.61 ± 32.39  | 3.88 ± 0.55       | 3.79± 0.54        | 0.162 |
| 9 (n= 52)     | 181.95 ± 29.33  | 180.82 ± 28.97  | 3.71 ± 0.55       | 3.74 ± 0.53       | 0.149 |
| 10 (n= 52)    | 175.83 ± 21.77  | 176.12 ± 21.71  | 3.91 ± 0.65       | 3.99 ± 0.68       | 0.173 |
| 11 (n= 52)    | 164.22 ± 21.32  | 162.23 ± 21.40  | 3.82 ± 0.65       | 3.99 ± 0.72       | 0.165 |
| 12-15 (n=55)  | 160.54 ± 20.12  | 159.25 ± 20,53  | 3.86 ± 0.52       | 3.88 ± 0.49       | 0.124 |
| 16-18 (n=55)  | 155.27 ± 19.92  | 157.34 ± 19.31  | 3.34 ± 0.57       | 3.26 ± 0,55       | 0.178 |
| 19-25 (n=55)  | 153.98 ± 19.35  | 154.87 ± 19.41  | 3.72 ± 0.66       | 3.84 ± 0.71       | 0.173 |
| 25-30 (n= 55) | 153.26 ± 16.10  | 152.56 ± 17.33  | 3.68 ± 0.71       | 3.79 ± 0.55       | 0.182 |

t-Student test

p≤0,05 significant

Subtitle: MMN = Mismatch Negativity; RE = right ear; LE = left ear; n = number of subjects in the sample; SD = standard deviation; ms = millisecond; µV = microvolt

## DISCUSSION

The results found confirm those of other research which refer to MMN latency response to the *tone burst* stimulus between 150 and 250 ms in normal hearing children with typical development<sup>(14,16,24)</sup> and latency of 150 and 290 ms in normal hearing teenagers and young adults<sup>(5,16,28)</sup>. It was observed that the amplitudes of MMN weren't different between the age groups, being inferior or equal to 5 µV as ratified in other studies<sup>(5,16,28)</sup>.

It is evident, however, that in the teenager age group, considering the age between 12 and 17 years and 11 months old, there is research that presents a decrease in MMN latency in teenagers in comparison to children, probably due to a neural maturation effect<sup>(14,16,18,29)</sup>.

Furthermore, as far as latency is concerned, a negative correlation of that parameter was verified in the age group analysis, indicating that, with the increase of age, there is a reduction of the MMN latency values. It is understood that the more rostral the evaluated structure in the auditory pathway is, the greater the response latency until the stimulus reaches the central auditory pathways will be. Therefore, it is fundamental that there be integrity and synchrony of the auditory pathway so that the information is duly comprehended and, for that reason, the BAEP test was applied in advance in all individuals. However, in accordance with the maturational process, the sensorial experiences of the central nervous system (CNS)

strengthen and, thus, the tendency is to obtain a faster and more precise response from the whole central auditory pathway. So, the decrease of the latency of MMN in adults, when compared to children, may be related to myelination and the increase of the efficiency and synchronization of synapses<sup>(16,27-29)</sup>.

Regarding the analysis between ears, studies also did not find statistically significant differences when comparing MMN latencies and amplitudes<sup>(5,14-16)</sup>. Based on these findings, it is inferred that there is a similar and simultaneous development of the auditory skills tested in the MMN, between the right ear and the left ear, ergo, the synchrony between the information received by each side.

In what concerns the analysis of the sexes, some studies reveal that there is a difference in MMN results between the sexes, with increased latencies for the male sex and larger amplitudes for the female sex<sup>(5,14)</sup>, demonstrating that there is an important neurophysiological difference between the sexes, in which women are more favored compared to men in terms of discrimination and auditory processing. This hypothesis was not found in the results presented and is in line with other studies<sup>(15,16)</sup>. Therefore, it is understood that the MMN latency and amplitude values obtained in the present research can be used for both sexes.

The MMN findings are in accordance with what scientific literature reports in what concerns the recording protocol used. On the present research, the traditional paradigm (Oddball) was used, as it is the most commonly applied, with tonal stimuli and

frequency variation; the frequent stimulus of 1,000 Hz and the rare stimulus of 2,000 Hz were used. Latencies below 300 ms were observed when the tones presented were more distinct and were associated to the central comparison process between the deviant stimulus and the standard stimulus, influenced by the capacity of discrimination between these stimuli<sup>(30)</sup>. Amplitudes of up to 5 $\mu$ V were also observed when the stimulus differed in only one domain, in this case, the frequency<sup>(30)</sup>.

It is recommended to avoid differences greater than 10% between the stimuli, so that there is no overlap of the P3 potential in the responses<sup>(7)</sup>. However, in this study, a difference greater than 10% was used and the overlap of the P3 potential was not observed. Other research that used similar parameters, with differences greater than 10% between stimuli, report similar values of latency and amplitude, which allows the observation of the influence of the acquisition protocol in MMN responses<sup>(5,14-16,30)</sup>.

In general, it was observed that the greater variability in the analyzed parameters of MMN concerns the evaluation protocol utilized. Verbal stimuli tend to augment the latency, as well as low tonal stimuli, in all age groups. For children, it is estimated that the amplitude in responses is greater at school age, being the opposite observed in elderly people, with the reduction of the amplitude<sup>(1,14,24,30)</sup>. This way, it is suggested that the examiner selects the stimulation they find most adequate for their objectives and verify what latency and amplitude values were reported for that protocol.

It is important to note that scientific literature preconizes the need for research that verify the MMN findings in greater samples, with stratified age group, due to the high level of variation in the protocols, stimuli and methodologies of MMN, which represent a difficulty in defining standardized data of this potential<sup>(9,30)</sup>. Considering that, it is emphasized that the results of this study allow the audiologists, clinicians and researchers of the hearing electrophysiology field, to obtain normative reference values for the *tone burst* stimulus of MMN in an ample sample, stratified in different age groups.

Regarding the limitations of this research, it is considered that the age group could be expanded by evaluating adults over the age of 30. In view of this, it is suggested that future research characterize the MMN findings in samples with a larger age group. In the same manner, the absence of procedures to evaluate school and cognitive performance, as well as behavioral evaluation of the auditory processing are considered limitations of the study.

The present research described the values of latencies and amplitudes of MMN in normal-hearing children, adolescents and young adults with typical development, with duly established equipment, parameters and analyses. The contribution of this study is centered on the possibility of presenting normative reference values, which may contribute to the evaluation with the *tone burst* stimulus and, also, for future scientific research with populations of different diagnoses, aiming to establish a comparison parameter. Furthermore, it should be noted that MMN proves to be a useful, promising tool with wide possibilities for clinical application.

## CONCLUSION

It was possible to describe and analyze the latencies and amplitudes of the MMN with the *tone burst* stimulus in normal-hearing children, adolescents and young adults. It is concluded

that there was a negative correlation of MMN latencies for the variable age group, decreasing as age increased. There was no statistically significant difference in MMN amplitudes for the studied age group, as well as in MMN latencies and amplitudes between ears and sexes.

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