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Mismatch Negativity Occurrence with Verbal and Nonverbal Stimuli in Normal-Hearing Adults

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Abstract

Introduction The mismatch negativity (MMN) is a long-latency auditory evoked potential related to a passive elicited auditory event.

Objective To verify the occurrence of MMN with different stimuli, to describe reference values in normal-hearing adults with verbal and nonverbal stimuli and to compare them with each other, besides analyzing the latency, area, and amplitude regarding gender and between the ears.

Method Normal-hearing individuals, aged between 18 and 59 years old, participated in the study. As inclusion criterion in the study, all of them underwent tone threshold audiometry, logoaudiometry, tympanometry, and the Dichotic Sentence Identification (DSI) test, and later the MMN with 4 different stimuli, being 2 verbal (da/ta and ba/di) and 2 nonverbal stimuli (750/1,000Hz and 750/4,000Hz), which are considered stimuli with low and high contrast.

Results A total of 90 individuals composed the sample, being 39 males and 51 females, with an average age of 26.9 years old. In the analysis of the latency, amplitude, and area of the four stimuli between the ears, they were not considered statistically different. There was a significant difference between all of the stimuli in terms of latency, amplitude and area, with the highest latency found in da/ta, and the greatest amplitude and area in ba/di. Regarding gender, there was only difference in the latency of the da/ta stimulus.

Conclusion The da/ta and 750/1,000Hz stimuli elicited the most MMN in the population of normal-hearing adults. Among the genders, there was difference only regarding the latency of the verbal stimulus da/ta, and there was no difference between the ears.

Keywords
- auditory evoked potentials
- auditory cortex
- hearing
- adult
- electrophysiology

Introduction

The mismatch negativity (MMN) is a long-latency auditory evoked potential related to a passive elicited auditory event, that is, without the need to perform any task or attention of the individual to the sound stimulus, as it arises in an automatic way, represented by a negative wave or a valley.[1–3]

Mismatch negativity is generated when the individual automatically discriminates a sound change, in which the auditory system is based on memory traces of the regularity of a sound stimulus, and detects a change, regardless of his/her attention.[1,4,5] This potential can be realized with several types of stimuli, among them the nonverbal sound stimulus (tone burst), in which the stimuli differ in frequency, intensity or

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duration, or with verbal stimuli, using a syllabic set (consonant/vowel).[5]

Mismatch negativity is a useful exam to investigate neural mechanisms or to complement the audiological evaluation, thus it may also be valuable in the study of the auditory stimulus processing in the cortex[3] and to be used for monitoring and prognosis in auditory rehabilitation processes. However, in Brazil, for example, this potential has always remained within the scope of research and, until today, it has not been mentioned as being used in the clinical routine, demonstrating the need for further studies on registry parameters and normative or reference data in the different age groups for their variables, which are latency, amplitude, and area.

Therefore, it is justified to carry out the present study to obtain a comparative of MMN responses regarding latency, amplitude, and area, with different stimuli (verbal and nonverbal) in the adult population, in order to aggregate information that may contribute to the advancement in the use of this potential. In addition, it is justified to carry out the research on the SmartEP equipment (Intelligent Hearing Systems, Miami, FL, USA), which is used in many clinics and universities in Brazil, since few studies of this potential have been found in this equipment, being one with children and two with adults.[6–8]

Therefore, the objective of the present study is to verify the occurrence of MMN with different stimuli and to describe reference values in normal-hearing adults with verbal and nonverbal stimuli, and to compare them with each other, besides analyzing the latency, area, and amplitude regarding gender and between the ears.

Method

This was a cross-sectional, descriptive, quantitative study. It was sent to the Ethics and Research Committee on Human Subjects of the University in which the research was performed, being approved under the number CAAE 54827416.5.0000.5346.

All of the individuals invited to participate in the study were advised of their free and spontaneous participation, and were informed about the procedures, risks, benefits, and confidentiality of the research. After the acceptance, all of them signed a free and informed consent form, which included all the procedures to be performed. The present study followed the principles of beneficence established by Resolution 466/12.[9] The research procedures were performed individually at the audiology and electrophysiology outpatient clinic of a university hospital.

Adult subjects of both genders, aged between 18 and 59 years old, were invited to participate in the present study. Those who met the following eligibility criteria participated in the sample: auditory thresholds up to 25 dBnHL in frequencies from 250 to 8000 Hz bilaterally; at least 8 years of schooling; values of normality in the Dichotic Sentence Identification (DSI) test in the integration stage;[10] to not have external and middle ear alterations, identified by tympanometry; to not have a history of head trauma and/or stroke; to not present obvious neurological or psychiatric changes.

Each individual was evaluated individually in a single day. First, the procedures for the analysis of the eligibility criteria were performed, including audiological anamnesis, meatoscopy, tone threshold audiometry, logoaudiometry, and tympanometry, to identify the normality of auditory thresholds. The DSI test was then performed, which was used as a screening for possible alterations in auditory processing, since it evaluates the figure-background ability for verbal sounds.[10] For the DSI test, only the binaural integration stage was considered, and the normality criterion suggested by the literature was taken into account.[10]

Finally, and as the main research procedure, the subjects performed the MMN test, with the aid of the two-channel SmartEP equipment, using the oddball paradigm,[1,2,11] with probability of occurrence of the rare stimulus of 20%, that is, 150 rare stimuli out of a total of 750 averaged stimuli;[2,11,12] at a rate of 1.9 stimuli per second;[6] recording window of 512 milliseconds with 50 milliseconds prior to stimulation and binaural stimulation.

Four electrodes that accompanied the equipment were used, and they were positioned in the participants according to the norms of the International Electrode System 10-20, as follows: in the frontal region (Fz), the active electrode was placed; in the central region of the forehead (Fpz), the ground electrode was placed; and in the right and left mastoid, the reference electrodes were placed. The impedance was maintained at a level $\leq$ 3 kOhms. The Fz position for the active electrode was chosen because it was cited as one of the best positions to register MMN.[12,13]

Before the electrodes were positioned, the skin of the participants was cleaned in the aforementioned regions with the aid of gauze and of the Nuprep Skin Prep Gel (Weaver and Company, Aurora, CO, USA). Subsequently, for the placement of the electrodes, MaxxiFix (Carbogel, São Paulo, SP, Brazil) electrolytic paste was used, and they were fixed in the indicated regions with micropore tape.

During the examination, the subjects remained seated in a comfortable armchair and watched a subtitled movie without sound, which was transmitted by a computer. They were told to remain as quiet as possible and to pay attention only to the movie, trying to ignore the sound stimulus.[2,11,14,15] It was not possible to control the ocular movement during the exam, due to the unavailability of a larger number of electrodes in the equipment used. However, it was verified that there was no interference in the quality of the exam, since the number of artifacts was controlled.

The MMN was searched with four pairs of stimuli, two of which consisted of verbal stimuli, of which da/ta was considered a set of low contrast, and ba/di was considered a set of high contrast between the stimuli. In addition to these, 2 other nonverbal ones, of which the 750/1,000Hz stimuli were considered of low contrast, and the 750/4,000 Hz were considered of high contrast. In addition, there was also a difference in the duration of the stimuli, which were shorter for the nonverbal stimuli.

All of the the stimuli used were presented in alternating polarity and had durations of 5 milliseconds for 750 Hz; 10 milliseconds for 1,000 and 4,000 Hz; 114.8 milliseconds for the syllable /ba/; 206.2 milliseconds for /da/; 209.5 milliseconds for /di/, and 220.3 milliseconds for /ta/. According to the literature,[16,17] for the acquisition of a long latency potential, the duration of at least 30 milliseconds is required. However, in the present study, we also intended to identify how the MMN potential would be generated with short-term nonverbal stimuli.

The verbal stimuli were exposed at an intensity of 60 dBnHL, and the nonverbal stimuli were exposed at an intensity of 70 dBnHL. The potentials were picked up and viewed on the computer to which the equipment was coupled. The trace was filtered using a 1.0Hz low pass filter and a 30.0Hz high pass filter.[11]

For the marking of the MMN in the electrophysiological tracing, the most negative peak was considered[12,18–20] after the N1 valley,[11,21] obtained by the difference curve, subtracting the waves of response to the frequent stimulus of the curves of response to the rare stimulus.[2,6,20–23] In addition, only the valleys that were viewed in latency up to 300 milliseconds were taken into account,[23–25] considering that the sample was composed by normal-hearing adults.

With regard to the amplitude marking, it was chosen to be done so based on the prestimulation line,[26] which was also the zero point of the amplitude, the limit where it was considered the maximum marking of the “height” of the valley, not exceeding for the positive part of the wave. The researchers of the present study understood that the amplitude of the valley refers to the negative part of the wave, not summed with the positive part. Thus, it was considered the measure of the latency point (most negative point), up to the prestimulation line. The valleys in the same latency of P1 or N1, or before N1, were not considered as MMN.

In relation to the area of the valley, it was realized that it is dependent on the amplitude, since it is registered in this equipment at the moment in which the amplitude measurement is made, demonstrating the whole size of the valley, since the wave fall begins (initial latency) to the final latency, being influenced by the duration of the potential to quantify its size. Therefore, in the present study, the variables studied were latency, amplitude, and valley area, as well as presence or absence of MMN with different sound stimuli.

In ►**Fig. 1**, there is a sample of how the registration and marking of the potential MMN with the da/ta stimulus was performed in a subject participating in the research.

The results were considered significant when $p \leq 0.05$, with 95% confidence interval (CI). The statistical tests used were the paired Student t-test for the comparison of the variables latency, amplitude, and area of the MMN with different stimuli, between the ears; the analysis of variance (ANOVA) test to compare the same MMN variables with different stimuli between the male and female genders, and the ANOVA test together with the Tukey multiple comparison (post hoc) test, to compare the mean values of latency, amplitude, and area between the different stimuli of the MMN.

Results

The present study included 90 subjects who met the eligibility criteria, aged between 18 and 56 years old, with a mean age of 26.9 years old, of whom 39 were males and 51 were females, and a comparison of the latency, amplitude, and area of each MMN stimulus between the ears of the participants was performed, as shown in ►**Table 1**. The results showed that, as there were only three significant comparisons between the ears in isolated cases, they were not considered statistically different, so the values were combined as mean.

Thus, it was considered that there was no difference in the comparison of the ears and the analysis were followed using the mean value of both ears. In this way, the four stimuli (two verbal and two non-verbal) were compared to verify the difference between the stimuli, regardinglatency, amplitude and area, as shown in ►**Tables 2**, **3** and **4**. Since we have observed the existence of a statistically significant mean difference between the stimuli in all of the variables, we used the Tukey multiple comparison (post hoc) test to compare the stimuli in pairs, and only the p-values of this analysis were shown at the end of each table.

Finally, as shown in ►**Table 5**, an analysis of the MMN was performed regarding gender, in a comparison made with latency, amplitude, and area. It can be observed that there was difference between the genders only in the latency of the da/ta stimulus, which was shown to be greater in the female gender. For the latency of the other stimuli, amplitude, and area, there was no difference between genders.

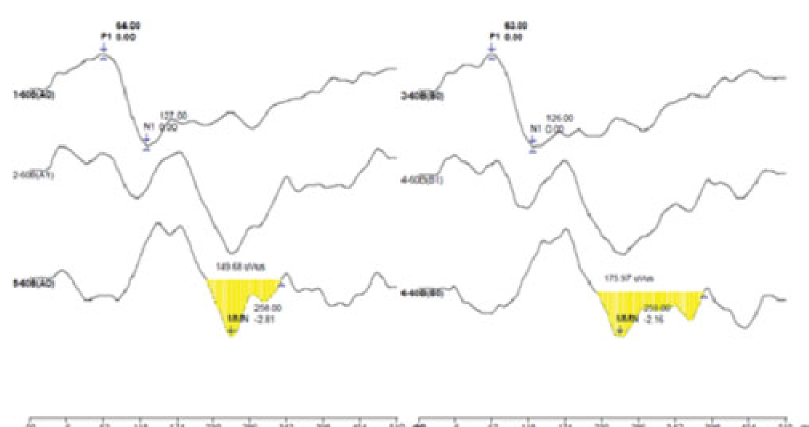

Fig. 1 Example of mismatch negativity marking elicited with verbal stimulus da/ta.

Table 1 Comparison Between the Ears, Mean Values of all Subjects for Latency, Amplitude and Area in the Different Stimuli of the mismatch negativity

		Average	Median	SD	CV	Min	Max	N	CI	*p*-value[a]
Latency (ms)	da/ta RE	213.3	238.5	56.2	26%	100.0	299.0	78	12.5	0.240
	da/ta LE	210.6	230.0	56.7	27%	131.0	299.0	78	12.6	
	750/1,000 RE	186.9	177.0	45.2	24%	101.0	273.0	73	10.4	0.137
	750/1,000 LE	184.8	177.0	46.5	25%	100.0	298.0	73	10.7	
	ba/di RE	164.1	140.0	48.3	29%	120.0	249.0	17	23.0	0.311
	ba/di LE	161.6	139.0	48.6	30%	123.0	252.0	17	23.1	
	750/4,000 RE	179.0	166.0	41.8	23%	120.0	248.0	49	11.7	0.653
	750/4,000 LE	179.6	164.0	41.2	23%	119.0	249.0	49	11.5	
Amplitude (μV)	da/ta RE	−1.97	−1.85	−1.12	57%	−0.47	−7.58	78	0.25	0.206
	da/ta LE	−2.05	−1.79	−1.21	59%	−0.41	−8.26	78	0.27	
	750/1,000 RE	−1.22	−1.11	−0.58	48%	−0.37	−3.54	73	0.13	**0.011**
	750/1,000 LE	−1.36	−1.23	−0.66	49%	−0.34	−3.96	73	0.15	
	ba/di RE	−2.83	−2.60	−1.00	35%	−1.26	−4.65	17	0.47	**0.011**
	ba/di LE	−3.23	−3.25	−1.32	41%	−0.84	−5.58	17	0.63	
	750/4,000 RE	−1.44	−1.27	−0.71	50%	−0.37	−3.21	49	0.20	0.324
	750/4,000 LE	−1.50	−1.37	−0.66	44%	−0.34	−3.30	49	0.18	
Area (μVμs)	da/ta RE	111.3	97.0	81.8	73%	8.6	493.8	78	18.2	0.221
	da/ta LE	106.2	94.7	75.2	71%	8.5	423.3	78	16.7	
	750/1,000 RE	60.1	46.2	48.3	80%	5.7	220.2	73	11.1	0.869
	750/1,000 LE	59.6	43.5	51.1	86%	5.0	252.0	73	11.7	
	ba/di RE	152.2	150.7	66.1	43%	40.1	299.7	17	31.4	**0.014**
	ba/di LE	180.1	183.0	75.0	42%	55.6	369.8	17	35.6	
	750/4,000 RE	79.4	58.8	57.0	72%	10.1	232.1	49	15.9	0.692
	750/4,000 LE	81.2	61.8	54.7	67%	11.0	229.9	49	15.3	

Abbreviations: CI, confidence interval; CV, coefficient of variation; LE, left ear; Max, maximum; Min, minimum; N, number of subjects; RE, right ear; SD, standard deviation.
[a]Paired t-student test.

Discussion

In ►**Table 1**, there is a comparison between the ears with the different stimuli. Because there were only three significant comparisons between the ears in isolated cases, they were not considered statistically different, and therefore the union of the values occurred as an average. This fact was expected, considering that the cerebral hemispheres with specific electrodes were not evaluated, and the response capture was performed binaurally, which is allowed by the equipment.

The results of the current study agree with other authors[27] who also did not observe a difference in the responses of MMN elicited with nonverbal stimuli, between the ears, for both latency and amplitude in samples of normal-hearing adults. In relation to the area of the MMN, it is not much discussed in the studies, or few analyzes were made in this regard, as the case of a research that performed this measurement in the same equipment, but did not perform the comparison between the ears.[8]

In ►**Table 1**, it was still possible to observe that there was not the same number of subjects in each of the stimuli, because there was variability to elicit MMN according to the presented stimulus. Thus, it was found that the stimulus da/ta was the one that most elicited MMN, being present in 78 of the 90 subjects evaluated, followed by the stimulus of 750/1,000Hz, with 73 subjects, and by 750/4,000Hz, with 49 subjects. The stimulus that elicited least MMN was the verbal stimulus ba/di, which was visualized in only 17 of the 90 subjects.

These results were predictable due to the difference in contrast between the acoustic stimuli used in the present study. Thus, it was observed that the low-contrast stimuli

Table 2 Comparison of the Mean Latency Between the Different Stimuli of Mismatch Negativity

Latency	MMN da/ta	MMN 750/1,000	MMN ba/di	MMN 750/4,000
Average	211.9	185.8	162.9	179.3
Median	233.0	177.0	140.0	166.0
Standard deviation	56.3	45.7	47.7	41.3
CV	27%	25%	29%	23%
Min	100.0	100.0	120.0	119.0
Max	299.0	298.0	252.0	249.0
N	156	146	34	98
CI	8.8	7.4	16.0	8.2
p-value[a]	< 0.001			
p-value[b] 750/1,000	< 0.001	–	–	–
p-value[b] ba/di	< 0.001	0.068	–	–
p-value[b] 750/4,000	< 0.001	0.738	0.333	–

Abbreviations: CI, confidence interval; CV, coefficient of variation; Max, maximum; Min, minimum; MMN, mismatch negativity; N, number of ears.
[a]Analysis of variance test.
[b]Tukey multiple comparison (post hoc) test.

Table 3 Comparison of the Mean Amplitude Between the Different Mismatch Negativity Stimuli

Amplitude	MMN da/ta	MMN 750/1000	MMN ba/di	MMN 750/4000
Average	−2.01	−1.29	−3.03	−1.47
Median	−1.84	−1.20	−3.20	−1.31
Standard deviation	−1.16	−0.63	−1.17	−0.68
CV	58%	48%	39%	46%
Min	−0.41	−0.34	−0.84	−0.34
Max	−8.26	−3.96	−5.58	−3.30
N	156	146	34	98
CI	0.18	0.10	0.39	0.13
p-value[a]	< 0.001			
p-value[b] 750/1,000	< 0.001	–	–	–
p-value[b] ba/di	< 0.001	< 0.001	–	–
p-value[b] 750/4,000	< 0.001	0.464	< 0.001	–

Abbreviations: CI, confidence interval; CV, coefficient of variation; Max, maximum; Min, minimum; MMN, mismatch negativity; N, number of ears.
[a]Analysis of variance test.
[b]Tukey multiple comparison (post hoc) test.

Table 4 Comparison of the Mean of the Area Between the Different Mismatch Negativity Stimuli

Area	MMN da/ta	MMN 750/1,000	MMN ba/di	MMN 750/4,000
Average	108.8	59.9	166.2	80.3
Median	95.2	44.7	166.1	61.5
Standard Deviation	78.3	49.6	71.0	55.6
CV	72%	83%	43%	69%
Min	8.5	5.0	40.1	10.1
Max	493.8	252.0	369.8	232.1
N	156	146	34	98
CI	12.3	8.0	23.9	11.0
p-value[a]	< 0.001			
p-value[b] 750/1,000	< 0.001	–	–	–
p-value[b] ba/di	< 0.001	< 0.001	–	–
p-value[b] 750/4,000	0.004	0.072	< 0.001	–

Abbreviations: CI, confidence interval; CV, coefficient of variation; Max, maximum; Min, minimum; MMN, mismatch negativity; N, number of ears.
[a]Analysis of variance test.
[b]Tukey multiple comparison (post hoc) test.

presented a higher percentage of occurrences of the MMN potential, which is already indicated in the literature. However, the verbal stimulation with da/ta was the one with the best morphology and the highest number of occurrences, proving to be the best set of stimuli to elicit this potential among the four stimuli analyzed, and it may be influenced by the duration of the stimulus, which was longer than the low-contrast nonverbal stimulus.

It was also possible to observe that the short duration used in the nonverbal stimuli was able to elicit the potential, but that the stimuli with longer duration are probably better due to anatomophysiological issues. The present study reinforces the need to demonstrate the duration values of the stimuli in the work methodology, bringing clarity when exposing the characteristics of the stimuli, so that comparisons and analyzes can also be made regarding this characteristic of the stimuli.

In ►**Table 2**, the data indicate that the stimuli that have more subtle differences between them are the most difficult to be discriminated, and with this occurs the increase in latency. This demonstrates a delay in the discrimination of the sounds in relation to the stimuli with higher contrast that are easier to be discriminated, as in the case of the ba/di stimulus, which presented the lowest latency.

In the present study, it was possible to observe that the marking of the MMN became doubtful when done in tracings generated by stimuli of greater contrast, as in the case of ba/di and of 750/4,000Hz, since for both verbal and nonverbal stimuli there was the presence of 2 negative valleys in the majority of the subjects, and the first one was usually in very early latency – before N1 or next to it – and the second was generally in latency after 300 milliseconds (usually ~ 400 milliseconds), which meant that many valleys were not

Table 5 Comparison of Latency, Amplitude, and Area Between Genders in Different Mismatch Negativity Stimuli

		Gender	Average	Median	SD	CV	Min	Max	N	CI	*p*-value[a]
Latency (ms)	da/ta	F	220.0	245.0	55.6	25%	131.0	299.0	92	11.4	**0.030**
	da/ta	M	200.5	182.0	55.5	28%	100.0	299.0	67	13.3	
	750/ 1,000	F	190.5	178.0	47.1	25%	100.0	298.0	82	10.2	0.195
	750/ 1,000	M	180.7	171.0	43.1	24%	115.0	264.0	66	10.4	
	ba/di	F	147.4	135.5	37.7	26%	120.0	242.0	16	18.5	0.688
	ba/di	M	178.3	145.0	50.3	28%	124.0	252.0	21	21.5	
	750/ 4,000	F	186.7	169.5	44.7	24%	119.0	249.0	60	11.3	0.110
	750/ 4,000	M	173.4	171.5	36.4	21%	123.0	245.0	44	10.8	
Amplitude (μV)	da/ta	F	−2.13	−2.13	−1.01	47%	−0.41	−4.81	92	0.21	0.083
	da/ta	M	−1.80	−1.56	−1.32	73%	−0.47	−8.26	67	0.32	
	750/ 1,000	F	−1.24	−1.11	−0.64	51%	−0.34	−3.96	82	0.14	0.345
	750/ 1,000	M	−1.34	−1.20	−0.62	46%	−0.37	−2.77	66	0.15	
	ba/di	F	−3.21	−3.44	−1.03	32%	−1.39	−5.26	16	0.51	0.269
	ba/di	M	−2.76	−2.79	−1.28	46%	−0.84	−5.58	21	0.55	
	750/ 4,000	F	−1.44	−1.37	−0.63	44%	−0.34	−2.89	60	0.16	0.922
	750/ 4,000	M	−1.45	−1.27	−0.74	51%	−0.44	−3.30	44	0.22	
Area (μVμs)	da/ta	F	112.6	96.1	72.9	65%	8.5	331.0	92	14.9	0.317
	da/ta	M	99.9	83.6	85.3	85%	12.3	493.8	67	20.4	
	750/ 1,000	F	57.8	42.0	49.9	86%	5.0	252.0	82	10.8	0.696
	750/ 1,000	M	61.0	48.1	49.3	81%	5.7	244.4	66	11.9	
	ba/di	F	171.4	180.5	57.4	33%	68.3	269.5	16	28.1	0.210
	ba/di	M	156.5	150.7	85.3	54%	21.3	369.8	21	36.5	
	750/ 4,000	F	75.0	58.4	52.7	70%	10.1	232.1	60	13.3	0.564
	750/ 4,000	M	81.4	61.9	58.8	72%	7.7	205.9	44	17.4	

Note: CI, confidence interval; CV, coefficient of variation; F, female; Gen., gender; M, male; Max, maximum; Mi., minimum; N, number of ears; SD, standard deviation.
[a]Analysis of variance test.

termed as MMN. Therefore, there was a large number of absences of MMN with these stimuli. The valleys marked in the present study were those that fit within the latency stipulated in the methodology, even if in the tracing there was the presence of another negative valley. It is believed that because these were high-contrast stimuli, it was easier for most subjects to pay attention to the test, influencing the uptake of MMN and making another representation of the discrimination of stimuli that may not be the MMN, or even if it were superimposed on the N1.[15] The report of the presence of two negative valleys has already been made by other researchers;[25] however, this was observed in children, demonstrating that this fact occurs when the auditory pathway is not yet fully mature, which is believed not to be the case in the present study, generating even more doubts in the marking of these stimuli.

Regarding nonverbal stimuli, the current study was in line with the study by Sanju et al,[8] since in both studies no significant difference was found for latency in two sets of stimuli with low and high contrast. The results were also in agreement with the study by Bishop et al,[28] which used verbal and nonverbal stimuli that differed in contrast and verified that the greater contrast elicited an earlier MMN. The authors compared the ba/bi to ba/da stimulus, and 1,000/ 2,000Hz to 1,000/1,030Hz. However, it did not corroborate the fact that the MMNs with verbal stimuli were more precocious, if compared with the da/ta.

The aforementioned study[28] also noted the presence of a second negative peak. However, unlike the present study, they observed it in all stimuli (with low and high contrast), and with similar latencies between them (around 300 to 600 milliseconds), being considered as Late Discriminative Negativity. The authors of the study claim that this component should not be considered as a late manifestation of MMN. Instead, they suggest that this peak may be reflecting additional processing of auditory stimuli that occurs when the characteristics of the stimulus are difficult to be detected, or by the effects of age, when the listener has less experience with such stimuli. However, it is added that this fact occurred in the present study only in the stimuli with high contrast, which would be considered the easiest ones, and in a sample considered experienced in the detection of the presented stimuli, since they are all adults. Without having other justifications so far for this fact to occur, it is understood that the use of this stimulus would not be the most adequate to elicit MMN.

In the latency analysis, it was observed that the coefficient of variation (CV) was low ($< 50\%$), which allows us to say that the data are homogeneous in each of the stimuli (►**Table 2**). The mean latency found in verbal and nonverbal stimuli was observed where the MMN valley is traditionally found. Thus, it can be said that the latency variation in most of the stimuli was compatible with 100 to 250 milliseconds, as already demonstrated in many studies,[4,5,20,28–32] and also for the da/ ta stimuli, compatible with what has been referenced by other authors,[33] who suggest a variation from 150 to 275 milliseconds.

In relation to the amplitude, the verbal stimuli showed to be greater, with emphasis on the ba/di stimulus that presented the greatest amplitude, followed by the da/ta stimulus (►**Table 3**). However, it is worth noting that this analysis was done by ear, with the ba/di stimulus being analyzed based on 34 ears, and the da/ta stimulus being analyzed based on 156 ears. This difference in the number of ears evaluated may have influenced the results, evidencing greater amplitude for ba/di, considering that few ears were evaluated in relation to the other stimuli, which does not allow the data to be so reliable. Thus, it is believed that the sample size contributed to this result, due to the fact that the majority of the individuals did not elicit MMN with this stimulus. In addition, the MMN may overlap the N1, which also has its amplitude increased by this increase of contrast.[15]

Other authors[34] also showed greater amplitude with the increase of differences between tones; however, this was observed with nonverbal stimuli, on which they believe that the amplitude increase corresponded due to an improvement in the discrimination as a result of increasing the difference between the two tones, which is translated into the conscious perception of change by the individual. This fact occurred in another research[20] performed with verbal stimuli that differed with contrasts of easy, medium, and difficult discrimination, for which the authors also found a greater amplitude when the difference between the stimuli increased. They point out that this fact could perhaps be explained by the influence of the overlap of the N1 potential in these cases of great magnitude of difference between stimuli, because they are perceived earlier.

The amplitude values found in the current study corroborate those already observed in the study by Takegata et al,[26] regarding nonverbal stimuli. For verbal stimuli, the present research presented higher values. However, other authors showed an even larger average amplitude.[27]

When evaluating illiterate individuals, and after 1 year of study, Schaadt et al observed an increase in the amplitude with verbal stimulation after literacy.[32] However, the results were lower than those found in the present study, probably because the current sample had at least 8 years of schooling, which may have contributed to the amplitude being greater than that presented in the aforementioned study.

Another study by, Choudhury et al, also observed an increase in the amplitude in the condition paying attention to the stimulus, when it presented a smaller Inter-stimulus Interval (greater difficulty of discrimination).[25] Based on this, it can be thought that the greater amplitude that occurred in the current study, which was in the ba/di stimulus, may have been influenced by the attention that individuals could have paid at the moment they were submitted to this stimulus,even though they are easy to discriminate, given the great contrast between them and because they are speech stimuli, which are more noticeable.

The aforementioned authors suggest that attention plays an important role in the development and refinement of neural auditory processing mechanisms, inducing a recruitment of more neural resources and greater neural synchrony, increasing the amplitude of the potential. Considering the stimulus with the second largest amplitude, the da/ta, on the basis of the mentioned study, it can be said that it presented one of the largest amplitudes because it is a stimulus with greater difficulty of discrimination, since it has a small contrast. Thus, what is perceived in these two sets of stimuli used in the present study is that the processing of verbal stimuli requires greater neural synchrony to respond to the stimuli due to their linguistic load, thus generating greater amplitudes, independently of having higher or lower contrast.

Regarding the amplitude of nonverbal stimuli, another study[8] also found no significant difference for low- and high-contrast stimuli, and the means found were higher than those of the present study. However, the stimuli used had much lower contrasts than those used in the present study.

In relation to the MMN valley area (►**Table 4**), it is possible to observe that its value was proportional to the amplitude, since the larger the potential size, the greater the amplitude and the valley area. Therefore, it is observed that the highest area value belonged to the ba/di stimulus, which was the one that presented the greatest amplitude, and so on.

In a study that was also performed on the SmartEP[8] equipment, the authors analyzed the area in non-verbal stimuli of different contrasts, and values higher than those found in the present study were observed, since the amplitudes had also been referred to as larger. The other studies[6,7] which also searched the MMN in the SmartEP equipment, did not analyze this variable, making it difficult to compare their values.

In the analysis performed to compare the responses of the MMN to gender (►**Table 5**), it can be observed that there was difference only in the latency of the da/ta stimulus, which was shown to be higher in the female gender. These findings corroborate with a study[35] that also did not show any difference between genders for latency and amplitude with nonverbal stimuli.

However, it contradicts other findings,[4] which found lower latencies and higher amplitudes in women for stimuli that differed in frequency, although they did not perform gender analysis. And yet another study,[27] which also showed a difference between genders regarding latency, being higher for men.For amplitude, no significant difference was found, as occurred in the current study.

These differences, observed in the amplitude, in the latency and in the area of MMN, may suggest that the characteristics of each population, such as culture, schooling, attention and other nonauditory factors, can influence the responses received, as well as the different equipment used, which leads us to believe that the reference values for a population should be based on both the type of stimulus that will be used and its contrast, as well as on the results of the local population itself, and for an adequate equipment, to obtain more reliable data. The difference in the acoustic pattern of verbal and nonverbal stimuli also suggests that the processing of the two types of stimuli by the central auditory nervous system occurs differently.[19]

The paradigm used is another factor that can interfere in the latency and amplitude of the MMN.Differences between stimuli[11,19] and also the environmental conditions at the place of registration and the time the subject was exposed to the exam[15] may also interfere.

Thus, the differences between verbal and nonverbal stimuli, as well as the differences according to the contrasts of the stimuli in the population of normal-hearing adults, were evident. In general, the mean latency was compatible with what is already described in the literature, with the amplitude being somewhat lower than the average of the other studies. Perhaps the mode of marking the amplitude chosen in the present study may have contributed to this result. However, further studies with this potential are suggested to clarify some remaining doubts about it, which are not discussed in most of the articles, as it is the case in the area, and the presence of other negative valleys in the resulting wave that may confuse the marking of the MMN.

Conclusion

It was possible to perform MMN on the SmartEP equipment in normal-hearing adults and to describe reference values for verbal and nonverbal stimuli of different contrasts, which showed differences between them in terms of latency, amplitude, and area.

The da/ta and 750/1,000Hz stimuli were the ones that elicited the most MMNs in the population of normal-hearing adults. Among the genders, there was difference only regarding the latency of the verbal stimulus da/ta, and there was no difference between the ears.

Contribution of Authors
Brückmann M. was responsible for data collection, data tabulation, statistical analysis and manuscript preparation. Garcia M. V. was responsible for the advisement and revision of the manuscript.

Conflicts of Interests
The authors have no conflicts of interests to declare.

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