http://dx.doi.org/10.23925/2176-2724.2018v30i3p-585-594

ARTICLES

Long-latency auditory potential in children with typical development

Potencial evocado auditivo de longa latência em crianças com desenvolvimento típico

Potencial evocado auditivo de larga latencia en niños con desarrollo típico

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Abstract

Introduction: The Long Latency auditory evoked potential is used to evaluate the cortical processing of the acoustic information. Objective: To describe and compare the values of latency and amplitude of the Long Latency Evoked Potential in children. Also, to provide reference values. Material and Method: Quantitative and cross-sectional study. 20 individuals were evaluated with ages between 5:00 -9:11 with typical development. Evoked Potential was performed with the equipment Smart Ep (Intelligent Hearing Systems) with verbal stimuli using insert headphones. Wilcoxon test and Mann-Whitney test were used. Results: There were no statistical significant differences between latency values and components amplitude of this potential, considering variables of ear and gender. The following reference values for components latency and amplitude potential were obtained. Conclusion: By this study, it was possible to propose values of reference for the components of the potential into the sample, considering that no statistically significance difference was found in the variables studied.

Keywords: Electrophysiology; Evoked Potentials Auditory; Event-Related Potentials, P300; Child; Hearing.

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Authors' contributions:
AEHS, LF - idea, data collection, data analysis, writing
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Received: 10/12/2017
Accepted: 02/04/2018

Resumo

Introdução: O Potencial Evocado Auditivo de Longa Latência é utilizado para avaliar o processamento cortical da informação acústica. Objetivo: Descrever e comparar os valores de latência e amplitude do Potencial Evocado Auditivo de Longa Latência em crianças. Além disso, fornecer valores de referência. Material e Método: Estudo transversal e quantitativo, no qual foram avaliados 20 indivíduos com idade entre 5 e 9 anos e 11 meses, com desenvolvimento típico. Realizou-se tal potencial auditivo, com o equipamento Smart EP *(Intelligent Hearing Systems*), com estímulos verbais utilizando fones de inserção. Teste de *Wilcoxon* e teste de *Mann-Whitney* foram utilizados. Resultados: Não houve diferença estatisticamente significante em relação aos valores de latência e amplitude dos componentes deste potencial, considerando as variáveis orelha e gênero. Forneceram-se os valores de referência para latência e amplitude dos componentes deste potencial. Conclusão: A partir deste estudo foi possível propor valores de referência para os componentes deste potencial para a amostra estudada, considerando que não houve diferença estatisticamente significante para as variáveis estudadas.

Palavras-chave: Eletrofisiologia; Potenciais evocados auditivos; Potencial evocado P300; Crianças; Audição.

Resumen

Introducción: El Potencial Evocado Auditivo de Larga Latencia es usado para evaluar el procesamiento cortical de la información acústica. Objetivo: Describir y comparar los valores de latencia y amplitud del Potencial Evocado Auditivo de Larga Latencia en niños. Además, proporcionar valores de referencia. Material y método: Estudio transversal y cuantitativo, en el cual fueron evaluados 20 individuos con edad entre 5 a 9 años y 11 meses, con desarrollo típico. El potencial auditivo se evaluó con el equipo Smart EP(*Intelligent Hearing Systems*), con estímulos verbales utilizando auriculares de inserción. La prueba de *Wilcoxon* y la prueba de *Mann-Whitney*fueron utilizadas. Resultados: No hubo diferencia estadísticamente significativa en relación a los valores de latencia y amplitud de los componentes de este potencial, considerando las variables oreja y género. Se han proporcionado los valores de referencia para la latencia y la amplitud de los componentes de este potencial. Conclusión: A partir de este estudio fue posible proponer valores de referencia para los componentes de este potencial para la muestra estudiada, considerando que no hubo diferencia estadísticamente significativa para las variables estudiadas.

Palabras claves: Electrofisiología; Potenciales evocados auditivos; Potencial Evocado Evento P300; Niños; Audición.

Introduction

The Auditory evoked potentials (AEPs) investigate the integrity of central pathways, the maturational process and the dysfunctions that can be caused by pathologies. These potentials are sensitive to neuroelectrical changes, which occur in response to a sound stimulus[1]. From 1990s, the interest in studies with Long-Latency Auditory Evoked Potential (LLAEP) was increased. This potential is highlighted in research and clinical practice in individuals with auditory processing disorder (APD) and cognitive and language disorders, as they are less influenced by the physical properties of the stimuli and more influenced by the functional use that the subject makes of such stimulus [2,3,4,5,6,7]. Furthermore, it can be used for monitoring or as a biological marker of therapeutic process [8,9,10].

The components of the Long Latency Auditory Evoked Potentials (LLAEPs) are represented by sequential waves, classified according to polarity and with a certain latency value, being (P) positive and (N) negative. Potentials P1, N1, P2 and N2 are considered exogenous components, since they are influenced by the characteristics of the stimulus, such as intensity, duration and frequency and do not depend on the attentional state and voluntary activity of the individual. While the potential P3 is considered endogenous, since it depends on intrinsic events, such as the capacity for perception and cognition of the individual [1,11].

The generated sites from the LLAEPs encompass the auditory cortex region, specifically the structures arising from the thalamus-cortical and cortico-cortical auditory pathways, the primary auditory cortex and associative cortical areas. The potential P1, N1, P2, N2 are the components that bring the information of the acoustic arrival to the auditory cortex and the beginning of cortical auditory processing, showing if the acoustic signal was received properly. The P300 component demonstrates cognitive abilities responses, representing physiological phenomena involved in the process of attention, discrimination and auditory memory[1].

In the child population, it is essential to understand the functioning of cortical structures and to consider the maturational process in the implementation of the LLAEP; for this reason, the importance of tracing reference values in different age groups, methodologies and equipment. In this context, we did not find, in the literature, studies that report LLAEP reference values with verbal stimuli in typical Brazilian children, using SmartEpda IntelligentHearing Systems® (IHS) equipment using insertion earphones. In addition, as it is known, the latency and amplitude values of the LLAEP are influenced by both the acoustic stimulus and the intrinsic questions of the sample. Thus, studying the record of the LLAEP with the IHS equipment is interesting for the hearing evaluation clinic and for national scientific research.

In view of the above, the objective of this research was to describe and compare the latency and amplitude values of the LLAEP for verbal stimuli in children with typical development. In addition, provide reference values for upcoming research and clinical practice using the IHS equipment.

Methods

This study consists of a quantitative cross-sectional study, approved by the Ethics Research Committee of the Institution (under number 14804714.2.0000.5346). It met all the binding recommendations for research on human beings (Resolution No. 466/12).

For the sample composition, the following inclusion criteria were considered: 1) children aged 5 to 9 years and 11 months, of both genders, 2) tonal auditory thresholds within the normality patterns in both ears [12], 3) Type A tympanometric curve[13], 4) acoustic reflexes present at normal levels, 5) school development appropriate for age and 6) typical phonological acquisition.

The expected exclusion criteria were: 1) to present some associated pathology, history of hearing problems or other health problems, 2) alteration in auditory processing performed previously and 3) not collaborate to complete the evaluations listed in the present study.

53 individuals were invited to participate in the study. Of these, 16 did not attend for the examination and two did not allow the end of the evaluation. Thus, 35 individuals (66% of the initial sample) were considered, with 15 being excluded because they presented alterations in the phonological system, altered evaluation of immittanciometry and / or alteration in auditory processing. Thus, considering the eligibility criteria, the sample arrangement of the present study consisted of 20 individuals, five of whom were female and 13 were males, aged between 5 and 9 years and 11 months (mean age 7.45 years). It is emphasized that the excluded individuals received the necessary referrals.

The procedures performed for the composition of the sample group were: Anamnesis; Child language test - ABFW (phonology area) [14]; external auditory meatus inspection; Tonal threshold audiometry (TTA) [12]; Immittance measures [13]; Screening of auditory processing using the auditory processing test Pediatric speech intelligibility test adapted to Portuguese - *Pediatrics Speech Inteligibility* (PSI)[15] and the Auditory Function Scale questionnaire –*Scale of Auditory Behavior* (SAB)[16]. This screening was intended to rule out any auditory processing disorder (APD) -related alteration or complaint.

The equipment used for the audiological evaluation procedures were: KlinicWelch-Allyn brand clinical otoscope, Interacoustics brand AD629 audiometer, Interacoustics AT235 equipment, for tympanometric curve and acoustic reflex testing. The criterion of acoustic reflex threshold normality found between 70 and 90 dBNA was considered[13].

In the individuals that fulfilled all the eligibility criteria, Long Latency Auditory Potential was recorded and analyzed. For this purpose, the IntelligentHearing Systems (IHS) two-channel Smart EP module with disposable surface electrodes was used after cleaning the skin of the child with abrasive paste (Nuprep®). The active electrode was positioned in Cz (cranial vertex) and connected to channels A and B, at the positive input of the preamplifier. The reference electrodes were placed in positions M1 (right mastoid) M2 (left mastoid) and connected in channels A and B, at the negative input of the preamplifier, respectively. The ground electrode (Fpz) was positioned on the forehead. The impedance was maintained between 1-3 kohms and insert headphones were used.

Obtaining the procedure, the children were rested and were accommodated in a comfortable reclining chair. The individuals underwent for training with the stimuli presented in the exam, to better understand the exam, mainly because it is a pediatric population. Performing the examination, the child was on alert, silent and attentive to the acoustic stimuli and was instructed to pay attention only to rare stimuli, marking on paper every time they heard them. We considered the exams in which the child scored the percentage of 90 to 95% of the rare stimuli.

The frame 1 shows the stimulus parameters used to record the LLAEP of the present study. However, it should be noted that the parameters already adopted in previous studies with the same equipment [5,17,8,6,18].

Frame 1. Parameters of the stimulus used in recording long-latency auditory evoked potential in children with typical development

Module: *Smart EP*	***Intelligent Hearing Systems* (IHS)**
Frequent Stimuli	/Ba/
Rare Stimuli	/Di/
Number of Stimuli	300 (240 frequent and 60 rare)
Paradigm	Oddball
Phase	Rarefaction
Polarity	Alternating
Filters	100-3000 Hz
Gain	100.000
Window	512 ms
Transducer	ER-3ª
Intensity of Presentation	75 dBnHL
Acceptance Rate of Artifact	Up to 10% of the total stimuli presented
Reproducibility of tracings	No

Legend: μs; micro seconds; Hz: Hertz; ms; milliseconds

The verbal stimulus / Ba / x / Di / was used considering a study [18], in which the authors report that such speech contrast is considered the one of greater ease of perception and lower latency of P300.

Regarding the marking of the P3 wave, only the trace of the rare stimuli was considered. The highest peak and amplitude wave after the P1-N1-P2-N2 complex was scored. However, the P1-N1-P2-N2 complex was marked in the pattern of frequent stimuli. As a parameter of identification of these components, the data of McPherson (1996) [1] were used. The absolute latency of the components P1, N1, P2, N2 and P3 in milliseconds (ms) and the amplitude of P1-N1, P2-N2 and P3 in microvolts (μV) were determined considering the amplitude of the peak to the valley, following guidance in the IHS equipment manual itself.

All procedures were performed in a single session, but offered intervals between assessments for rest. The volunteers were able to understand the procedures.

The exams were analyzed by two trained judges with theoretical / practical knowledge in electrophysiology of hearing, especially LLAEP. The judges mark the components of this potential blindly, that is, performed the markings independently, in the printed record of the exams. Soon, after the researchers reproduced such markings in the respective examinations in the software of the equipment in question, obtaining the values of latency and amplitude with precision.

Wave latency and amplitude data were tabulated in an Excel spreadsheet for the statistical study. First, the concordance between the judges was analyzed. For this, the Wilcoxon test was used, once the data were paired, it was observed that there was no statistically significant difference between the judges, both in latency and in amplitude. Thus, it was decided to carry out the analyzis with average values between such markings.

Then, the variables ear and gender were analyzed, always considering latency values (P1, N1, P2, N2 and P3 in ms) and amplitude (P1-N1, P2-N2 and P3 in µV). The statistical model adopted included the Wilcoxon test and the Mann-Whitney test, and a significance level of 0.05 (5%) was defined for this study. In addition, all confidence intervals were constructed with 95% statistical confidence.

Results

Table 1 shows the comparison between the latency values, in milliseconds (ms), of the different components of the LLAEP, considering the variable "ear evaluated", using the Wilcoxon test. It is pointed out that the sample number was different in P1, since one of the subjects did not present this component.

The comparison between the amplitude values, in microvolt (µV), of the components P1-N1, P2-N2 and P3, considering the variable "ear evaluated" was also performed using the Wilcoxon test (Table 2).

Table 1. Comparison of latency (ms) values between right ear and left ear for different components of Long-Latency Auditory Evoked Potential in children with typical development (n = 20)

Latency		Mean	Median	Standard Deviation	Q1	Q3	N	IC	P value
P1	RE	89,6	90	12,2	83	96	19	5,5	0,129
	RL	91,6	90	11,2	84	99	19	5,1	
N1	RE	135,4	138	13,7	126	142	20	6,0	0,099
	RL	137,6	140	12,4	128	143	20	5,4	
P2	RE	180,7	178	16,1	169	193	20	7,1	0,234
	RL	177,7	178	16,6	171	185	20	7,3	
N2	RE	239,2	249	30,1	235	253	20	13,2	0,913
	RL	240,2	248	24,7	238	253	20	10,8	
P3	RE	347,1	353	48,7	336	377	20	21,4	0,601
	RL	347,4	354	47,9	338	381	20	21,0	

Wilcoxon Test
Legend: OD: right ear; OE: left ear; Q1: 1st quartile; Q3: 3rd quartile; N: sample number; CI: confidence interval.

Table 2. Comparison of amplitude (µV) values between right ear and left ear for different components of Long-Latency Auditory Evoked Potential in children with typical development (n = 20)

Amplitude		Mean	Median	Standard Deviation	Q1	Q3	N	IC	p value
P1-N1	OD	5,14	5,27	2,07	3,66	5,91	19	0,93	0,376
	OE	5,85	4,81	3,08	4,11	6,51	19	1,39	
P2-N2	OD	6,93	5,80	3,80	4,71	8,13	20	1,67	0,247
	OE	6,97	6,48	3,76	5,11	6,98	20	1,65	
P3	OD	7,17	6,23	3,19	4,78	9,18	20	1,40	0,117
	OE	7,72	6,98	3,16	5,89	9,20	20	1,38	

Wilcoxon Test
Legend: RE right ear, LE left ear, Q1 1st quartile, Q3 3rd quartile, N sample number, Q3 3rd quartile and CI confidence interval

As there is no statistically significant difference between the ears, it was decided to analyze the influence of gender on the different components of the LLAEP considering the average between the ears. In this case, the Mann-Whitney test was used and no statistically significant difference was observed between the genders. Figure 2 shows the latency values (ms) of P1, N1, P2, N2 and P3 among genders, while in figure 3 the values of amplitude (µV) of P1-N1, P2-N2 and P3 were compared.

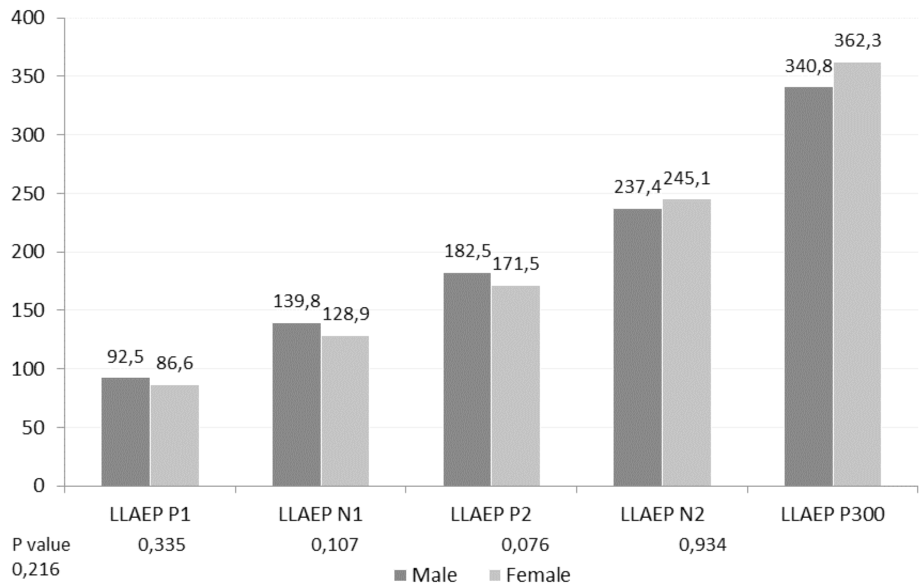

Figure 1. Comparison of latency (ms) values between male and female genders for the different components of the Long Latency Auditory Evoked Potential in children with typical development (n = 20)

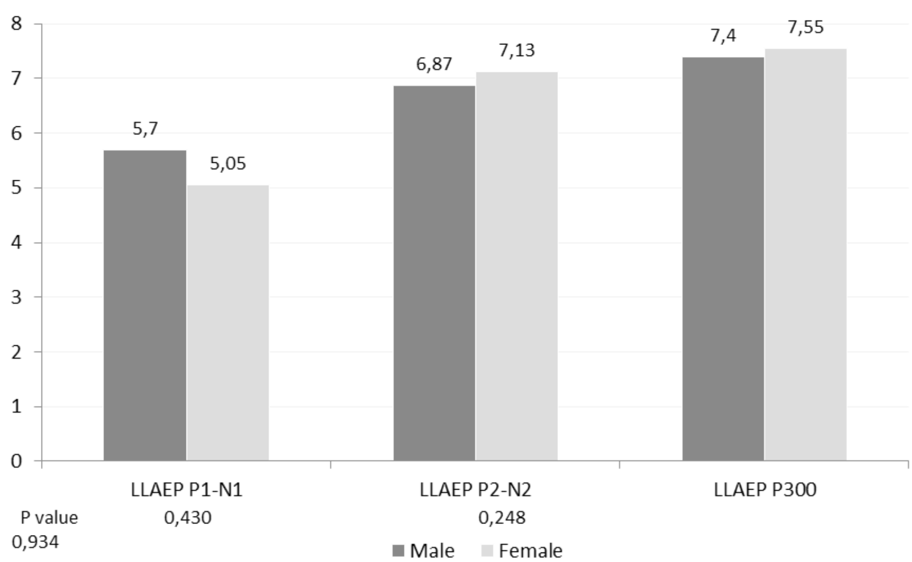

Figure 2. Comparison of the amplitude values (µV) between the male and female genders for the different components of the Long Latency Auditory Evoked Potential in children with typical development (n = 20)

It can be observed that there was no statistically significant difference regarding the latency and amplitude of the LLAEP components when comparing male gender and female gender.

After these analyzes, LLAEP reference values with verbal stimuli for children with typical development, ages 5 to 9 years and 11 months, could be established using Intelligent Hearing Systems (IHS) Smart EP equipment. As a way of visualizing such data, a graph was elaborated in which the average values of the different LLAEP components, in the present study, are compared with the classical theoretical reference. The variables "ear evaluated" and "gender" were not considered, since, as previously shown, no statistically significant difference was found between them.

Table 3. Comparison of the latency reference values (ms) of the components of the Long Latency Auditory Evoked Potential of the present study with the classical theoretical reference

Latency	Mean in this study	McPherson (1996)
P1	90,6	54-75
N1	136,5	83-135
P2	179,2	137-194
N2	239,7	200-280
P3	347,25	241-396

Table 4. Reference values of the amplitude (µV) of P1-N1, P2-N2, P3 of the present study (n = 20)

	Amplitude
P1-N1	5,49
P2-N2	6,95
P3	7,44

Discussion

Regarding the latency values of the LLAEP components (P1, N1, P2, N2 and P3) with verbal stimulus, considering the ear variable evaluated, no statistically significant difference was observed between the right and left ears (Table 1). Other researches also confirm the maturational process equivalence between the right and left sides in the pediatric population [3,4,5] and adult[19,18,20], both for verbal and nonverbal stimuli [19]. In this way, it is inferred that the maturation of the auditory pathway is similar between the ears, that is, the development of the auditory abilities occurs synchronously between both.

One fact that was evidenced in the present study was the value of standard deviation in relation to the latency of the P3 component in both ears. It is believed that this difference occurs because P3 is an endogenous component, that is, it requires the voluntary action of the individual[1]. Thus, the responses may be influenced by attentional processes, it should be noted that a difference was observed in the enthusiasm and involvement in the individuals of the sample collected during the exam.

So, some individuals were more involved and consequently more attentive to the exam.In literature we also observed a higher standard deviation in the latency variable of the P3 component[21,22,6,17,23,24].

In the amplitude values analysis of P1-N1, P2-N2 and P3, considering the ear variable evaluated, there were no statistically significant differences between the right and left side. This finding corroborates other studies that also evaluated the amplitude of these complexes and did not observe such difference [5,6]. It is observed that the amplitude values are little studied and cited in the literature. However, it is known that the amplitude is related to the magnitude of the synaptic activity involved during the perceptual processing of the acoustic stimuli[1,5], and the LLAEP amplitude study can bring more contributions to the understanding of cortical auditory processing.

When comparing the latency and amplitude values of the LLAEP components between the male and female gender, there was no statistically significant difference between them (Figure 2 and 3). Studies also indicate that this difference is not found [2,5,25,24]. Authors who studied the comparison between the genders with different fixations of the electrodes also did not find statistically significant difference [25,24]. When searching the difference between genders comparing the components P1, N1 and P2, recorded through the use of earphones and speaker box, no such difference was observed [5]. In view of the above, it is stated that the maturational process of the central auditory system occurs in a similar way between the male and female genders[2]. In this way, it is understood that the reference values described in this research can be used for both genders.

This study described latency reference values for the components P1, N1, P2, N2 and P3 and amplitude of P1-N1, P2-N2 and P3, with verbal stimulus.

The mean values of latency found for these components are shown in Table 3. For the pediatric population, in the age range of 3 to 12 years, classical literature highlights[1] the following latency values: 54-75 ms for P1; 83-135 ms for N1; 137 - 194 ms for P2; 200 - 280 ms for N2 and 241 and 396 ms for P3. In the comparison of the latency values of the LLAEP exogenous and endogenous components between the present study and the classic literature it is verified a higher latency of P1 and N1 in the present study. It is believed that this difference is justified because the present research is carried out with verbal stimulus and the classical one with tonal stimulus. The verbal stimulus is considered more complex when compared to the tonal stimulus; in addition, it has a longer duration[21]. Therefore, the processing of acoustic information takes a longer time when verbal stimuli are used[6]. It should be pointed out that different researchers observed that even when there was no statistically significant difference, there was an increase in the mean latencies and a decrease in the amplitude in the LLAEP trajectories, by purchasing the record of this potential with verbal and nonverbal stimuli in adult individuals with thresholds within normality [19,5].

Another reason for such finding would be the modifications during the maturational process of the central auditory system. The study that served as the basis for the aforementioned comparison-[1]describes values for the population up to 12 years, while the present study up to 9 years and 11 months. In this way, the difference between such data is also justified. Still in relation to maturation of the auditory pathway, other authors performed the LLAEP in children at three moments in the nine-month period. The researchers observed stability of the N1 and N2 components and reduced latency of P1, P2 and P3 with verbal stimuli throughout the assessments. These results indicate maturational change of the central nervous system (CNS) in child development[6]. It should be noted that the components P1, N1 and P2 undergo changes in the maturational process until the second decade of life[1,2], thus demonstrating a reduction in latency and an increase in amplitude considering the age range[2] .

Two studies were found whose samples were with pediatric population, which used the same equipment of the present research and presented similar methodology. In the free field evaluation, the observed values were between 96.67 and 104.83 ms for P1; 144.25 and 150.7ms for N1; 181.7 and 194.28ms for P2; 247.55 and 251.93ms for N2 and 283.5 and 300.47ms for P3[6].

In the findings comparison of the present study, which was performed with insertion phone, and those of the research cited previously[6], lower latencies of P1, N1, P2 and N2 and higher latency of P3 were observed in the present study with the use of an insertion. This difference is probably justified by the difference of the transducer used for LLAEP record. In another study[5], the authors searched for latency and amplitude values of P1, N1 and P2 in children aged 4 to 12 years, comparing the use of the insert headphone and speaker with verbal stimulus, with no difference significant in relation to the latency and amplitude values of the components with different transducers. It was found that the latency values found in the mentioned study[5] were higher than the values of the present study, it is emphasized that both were realized with insertion phones and with verbal stimuli.

The mean amplitude values of P1-N1, P2-N2 and P3 were also investigated (Table 4). Other authors also studied mean values of amplitude for the pediatric population in the IHS equipment and showed values of P1-N1 and P2-N2 compatible with the present study[6]. However, these authors find larger amplitude values for P3. Smaller values of P3 amplitude found in the present study are justified because the age of the study sample was from 5 to 9 years and 11 months, and the study cited above evaluated children from 6 to 13 years. The hypothesis for this difference is that the amplitude values of P3 try to increase during the maturational process of the central auditory system[1,6].

Other investigations with the pediatric population are found in the literature, where latency and amplitude values of the LLAEP components are reported in audiologically normal children[5,6] and / or children with pathologies[3,4,26,27,28]. However, the present research shows a proposal of reference values for the recording and analysis of the LLAEP, with verbal stimuli and insert headphones, in the IHS Smart EP equipment of typical children aged 5 to 9 years and 11 months.

It should be noted that the LLAEP reliability has been previously investigated[26,29] and this procedure brings relevant information about central auditory processing of acoustic stimuli. In addition, this evaluation instrument assumes a place of importance both in the clinical practice of evaluation of hearing disorders and in the scientific research related to the Electrophysiology of hearing.

Conclusion

The obtained results allow concluding that there is no statistically significant difference in relation to the latency values of the components P1, N1, P2, N2 and P3 and amplitude of P1-N1, P2-N2 and P3 for verbal stimulus, considering the variables "ear" and "gender." It was possible to propose reference values for the components of LLAEP in children with typical development, for verbal stimulation. Since the latency and amplitude values provided by this research were close to the classic data.

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