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Auditory processing abilities in prematurely born children☆

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ABSTRACT

Aim

To compare the performance in temporal auditory ordering and resolution tests and the latency and amplitude in the records of middle latency auditory evoked potential and P3 of prematurely born children with the performance of full-term children undergoing the same assessment protocol.

Study design: Cross-sectional observational study.

Subjects: Fifty-two children, aged 8 to 10 years, participated in the study and were divided into two groups: study group: 16 prematurely born children, and control group: 36 born full-term, at low risk for developmental alteration and without scholastic or hearing difficulties.

Outcome measures: All subjects underwent ordering tests (Frequency and duration pattern tests) and temporal auditory resolution tests (Gaps in noise test) and had their middle-latency auditory evoked potential and P3 recorded by using an Intelligent Hearing System unit.

Results: Prematurely born children had worse performance in the temporal ordering and resolution tests as compared with children born full-term. With regard to middle-latency auditory evoked potential and P3, prematurely born children had higher mean values of latencies and poorer morphology, a statistical significance was evidenced for P3 in the right ear.

Conclusions: A prematurity effect was found in the temporal auditory processing measurements and in the P3.

1. Introduction

Premature birth is an important public health problem. Improvement in Pre-Term Care (PT) in Neonatal Intensive Care Units (NICU), resulting in better knowledge of the pathophysiology of neonatal morbidities, the use of antenatal corticosteroids and pulmonary surfactant; protective ventilation techniques, or less aggressive techniques; and in the recognition of the importance of early and aggressive nutrition, besides the valorization of human milk for these patients, have all led to an increasing number of survivors [1].

However, despite these unquestionable and evident advancements, preterm birth still impacts infant development, since several complications inherent in the very cause of early birth, the therapies necessary for survival and the need for medications with side effects such as diuretics, steroids, antibiotics, among others, may induce deleterious, sensory, and cognitive consequences [2,3]. Depending on their maturity and birth weight, the type and intensity of factors acting during the fetal period may put the premature infant at a higher risk of perinatal complications. Among the sequelae found are auditory changes. Speech and language delays and permanent hearing loss are more common among PTs when compared to those born full-term. Although speech and language delays are clearly linked to hearing loss, only a small percentage of prematurely born children have permanent hearing loss [4]. However, there is a possibility that language delay and learning may be associated with changes in auditory processing [5,6].

The interest in researching hearing abilities in prematurely born children is due to the high occurrence of auditory risk indicators in this population, encompassing very low birth weight, prolonged NICU stay, and the use of ototoxic medication. Children with a history of auditory risk at birth should have the development of their auditory system monitored [7]. The presence of these indicators appears to be related to reduced functioning of the auditory efferent pathway, with reduced inhibitory function in the cochlear mechanisms, which might affect auditory processing development [8–10]. Audiological assessment with the use objective assessment methods, with an emphasis on auditory evoked potentials, and behavioral auditory processing tests can be used as an index of auditory system development, speech perception, and auditory discrimination.

Abbreviations: PT, Pre-term; NICU, Neonatal Intensive Care Unit; GIN, Gaps in noise; MLAEP, middle latency auditory evoked potential

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Among the behavioral processing tests, those related to temporal auditory processing (temporal ordering and resolution) stand out. Temporal processing is one aspect of auditory behavior that has been related to speech perception in hearing children. More specifically, changes in temporal processing are associated with deficits in phonological processing, auditory discrimination, receptive language, and reading [11].

Aiming to increase the objectivity with which children with auditory processing disorders are assessed, it is recommended that electrophysiological parameters be used in addition to behavioral tests. Both middle- and long-latency auditory evoked potentials have been shown to be promising when related to auditory processing activities.

With this approach, the present study intends to contribute to the knowledge of the hearing abilities of premature children with indicators of risk at birth, assessing them in the age range of 8 to 10 years by means of electrophysiological and behavioral measurements.

This study aims to compare the performance in temporal auditory ordering and resolution tests and the latency and amplitude in the records of middle latency auditory evoked potential and P3 of prematurely born children with the performance of full-term children.

2. Patients and method

Approval for this study was granted by the local ethics committee (*277/09*). Informed written consent was obtained from the parent or legal guardian of each child evaluated in this study.

2.1. Sampling

The calculation of the sample size considering a 95% confidence interval and a 3% error was performed at the Statistical Office of the Faculty of Medical Sciences of Santa Casa de São Paulo (FCMSCSP), and a sample of 36 subjects for each group was suggested.

To compose the control group of this research, 120 questionnaires regarding school complaints were sent to the elementary school teachers of a public school in the city of São Paulo. The teachers indicated the students, in the age group of 8 to 10 years of age, without any learning complaint. Next, 36 children were randomly selected, born at term, with low risk for developmental alteration and without school and hearing difficulties.

The selection of the children to participate in the study group of the present research was performed through the analysis of medical records at the High Risk Outpatient Clinic of Pediatrics of the Irmandade of Santa Casa of Misericórdia of Sao Paulo - University Hospital. Sixty-two charts of children aged 8 to 10 years were selected (those having no syndrome stigmata, neurological or psychiatric disorders), of which 43 children presented hearing risk factor at birth; hearing; were attending a public school in Sao Paulo city, presenting normal tonal and verbal audiometry. Of the 43 invited, only 16 agreed to participate in the research.

Thus, data were obtained from 52 children, paired by sex, between 8 and 10 years of age, whose tone auditory thresholds were within the normal range (with thresholds up to 25 dBHL in the sound frequencies from 250 to 8 kHz); had a tympanometric curve type A and contralateral stapedial acoustic reflexes (in the sound frequencies from 500 to 4000 Hz). Those participating in the study were divided into two groups:

2.2. Control group

Thirty-six children born full-term with no risk indicators for auditory changes, no auditory, scholastic or language complaints, enrolled in public schools in São Paulo's central region.

Table 1
Distribution of auditory risk indicators ($N = 16$).

Auditory risk indicator	N	(%)
Birth weight < 1500 g	8	50
Ototoxic medication > 7 days	8	50
Low Apgar	4	25
Mechanical ventilation > 5 days	2	12.5

2.3. Study group

Sixteen children receiving care at the hospital preterm follow-up clinic, with a history of prematurity, and having at least 1 risk indicator for hearing loss in the perinatal period. In this group, the mean birth weight was 1497 ± 379 g, and the mean gestational age was 32.2 ± 2.8 weeks. The risk factors for hearing loss considered in our evaluation were: low birth weight, use of ototoxic drugs (aminoglycosides and/or diuretics), Apgar score in first and/or fifth minutes < 6, and prolonged mechanical ventilation. Table 1 shows the distribution of these risk factors in the cohort evaluated.

In the anamnesis conducted with the parents/legal guardians of prematurely born children, scholastic difficulties were reported in 56% of cases. All children with altered tests had access to the auditory training program at the institution.

2.4. Procedures

All participants had their temporal auditory processing assessed and middle latency auditory evoked potential and P3 measured as described below.

2.4.1. Temporal auditory processing

The tests were performed by means of a Compact Disc recording, played on headphones by means of an Itera Madsen audiometer coupled to a Compact Disc player, in an acoustic booth, with an intensity of 50 dB SL.

1. Temporal ordering: Frequency and Duration Pattern Tests (AUDITEC), version for children, 3 binaurally presented tones, response naming (20 sequences each). The percentage of correct responses for each test was recorded.
2. Temporal Resolution: Gaps in Noise (GIN) test [12]: done monoaurally, training, test 1 in the first ear tested (32 sequences), test 2 in the second ear tested (32 sequences). In the GIN test, the stimuli are distributed among four test tracks and one training track. White-noise segments, six second each, are interspersed with random gaps (silence intervals). Gaps are randomized and have varying durations (2, 3, 4, 5, 6, 8, 10, 12, 15 and 20 ms). The training track was played before the beginning of the test, thus ensuring that the child understood the instructions.

Participants were instructed to push a response button upon hearing the gaps inserted in the noise. The gap detection threshold was recorded (identification of at least 4 gaps in six attempts). The ear being tested first was alternated, with approximately half of the children starting off with the right ear and half of them, with the left ear.

2.4.2. Middle latency auditory evoked potential and P3

Auditory evoked potentials were assessed by using the two-channel Intelligent Hearing System Smart EP (USB Jr. Platform). The subjects were seated in a slightly reclined chair and instructed to remain relaxed, albeit on the alert. After the skin was cleaned with an abrasive paste, the electrodes were placed with the help of an electrolyte paste in accordance with the protocol for each potential test to be performed, as described below. The stimuli were delivered by means of insertion phones ER-3A. The tests were performed in an acoustically and electrically treated room. The electrical impedance was kept at less than five kohms.

The markings registered by an experienced examiner and two judges were all in agreement. They judges were not aware about the group into which the students had been allocated in the study.

2.4.3. Middle-latency auditory evoked potential (MLAEP)

The five electrodes were placed at the mastoids (M1 and M2), right and left temporal lobes (C3 and C4), and forehead (Fz, ground).

The stimuli were clicks presented in monaural mode, at a rate of 9.9 clicks per second, and with an intensity of 70 dB HL, by ER3 insertion phones. Altogether, 1024 scans were performed and the recording window used was 115 ms. The latencies of the Na and Pa components and the amplitudes Na-Pa were registered at positions C3M1, C3M2, C4M1 and C4M2.

2.4.4. P3

The four electrodes were placed at the vertex (Cz, active), mastoids of the right and left ears (M1 and M2, reference), and forehead (Fz, ground). To record the P3, two hundred sweeps were recorded using 1000 Hz tone-burst for the frequent tone versus 2000 Hz for the rare tone stimuli having 20 ms plateau and 5 ms rise/fall times. The stimuli were presented in an oddball paradigm with 80 and 20% occurrence probability, respectively. The intensity of the stimuli was 70 dBHL 800 ms analysis time; 0.5 to 30 Hz filter; 160 microvolt sensitivity; alternating polarity; and a stimulus presentation rate of 1.10 stimuli per second. Patients were instructed to mentally count the rare stimuli. The response obtained for the rare stimuli will exhibit a positive peak at around 300 ms, and therefore labeled the P3. The latency of the P3 peak was registered.

2.4.5. Data analysis

The examiners were blinded when interpreting the data.

The Mann-Whitney test and the Student's *t*-test were used in the statistical analysis. The descriptive level was emphasized in all tests, with a significance level of 0.05 (or 5%) being used for rejecting the null hypothesis.

3. Results

The study had 36 participants in the control group and another 16 in the study group. These statistics indicate that the age distributions in the two groups are similar.

In analyzing the results from the duration and frequency pattern (Fig. 1) tests, a significant correlation ($p = 0.01$ and $p = 0.04$, respectively) can be observed in the comparison between the groups, with the control group showing a better performance with regard to the tests conducted.

Table 2
Detection threshold of silence intervals (ms) in the temporal resolution test, Gap in noise (GIN), according to group and ear.

Threshold (ms)	Right ear		Left ear	
	Control	Study	Control	Study
Mean	5.5	6.8	5.3	7.0
Median	5.5	6.0	5.0	6.0
Standard deviation	1.05	1.7	1.2	2.0
p-Value	0.02		0.01	

In the GIN test analysis (Table 2), with regard to the detection thresholds of silence intervals, differences between the groups were observed for both ears, and lower thresholds for both the right ($p = 0.02$) and the left ear ($p = 0.01$) were found in the control group.

The P3 latency analysis showed lower latency values for the control group in both ears, but with a statistically significant difference only for the right ear (Table 3). It should be noted that all children could be assessed for P3 but this response was absent in two children in the study group.

In the MLAEP analysis, the latencies of the Na and Pa components and the Na-Pa amplitudes at the C3M1, C3M2, C4M1 and C4M2 positions were compared, and no significant differences were observed between the groups, despite the fact that the morphology of the tracings was poorer in the group of prematurely born children.

For the analysis of the Pa component, the non-parametric test at the C4M1 and C3M2 positions and the *t*-test at the C3M1 and C4M2 positions were used; no significant differences were observed between the groups.

In analyzing the amplitude, no statistically significant difference was found between the groups with respect to electrode positions (Table 4).

4. Discussion

Prematurely born children, besides being exposed to adverse health situations that may affect brain development, are also deprived of the intrauterine sound environment early on. The consequences of atypical perinatal acoustic exposure on auditory and brain development are still unknown [13].

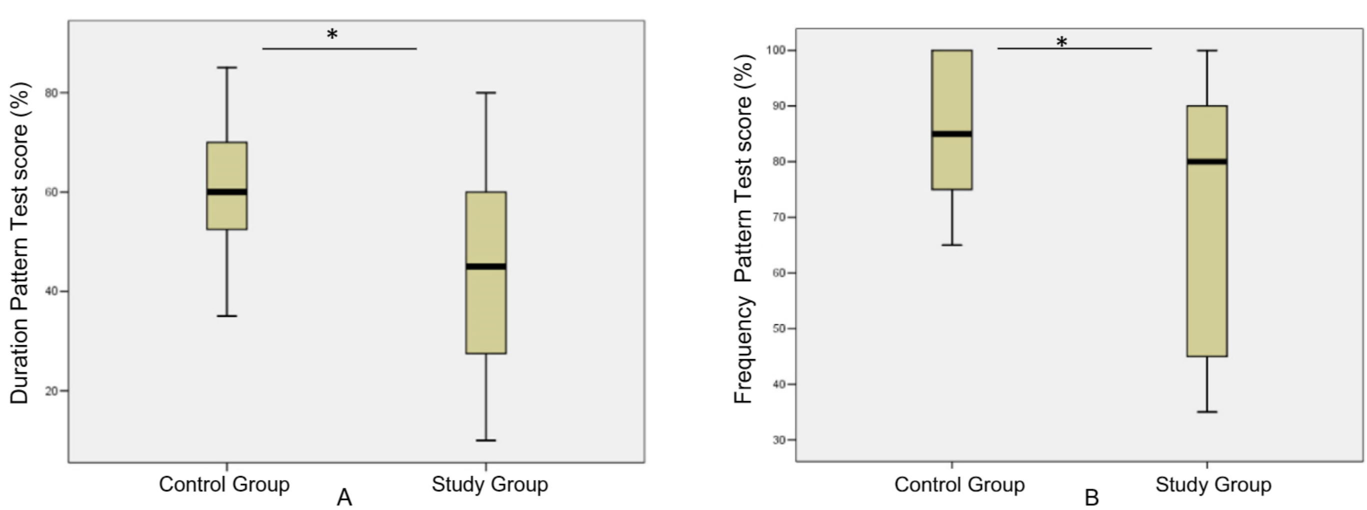

Fig. 1. Box-plots for the duration (A) and frequency (B) pattern test score (%) according to group (*$p < 0.05$).

Table 3
Latency, in the Long-latency Auditory Evoked Potential-P3 (ms), according to group and ear.

	P3 right ear		P3 left ear	
	Control	Study	Control	Study
Mean	318.8	336.7	331.1	338.0
Median	319	335.0	319.0	339.0
Standard deviation	27.9	29.6	39.1	35.2
p-Value	0.04		0.43	

Table 4
Comparison of the Na and Pa latency (ms) and the Na-Pa amplitude (μV) of the MLAEP according to ear and group for C3M1, C4M1, C3M2 and C4M2.

			Mean	*p-Value*
C3M1-left ear	Na	Control	18.86	0.787
		Study	19.79	
	Pa	Control	32.53	0.219
		Study	34.31	
	Na-Pa	Control	1.21	0.232
		Study	1.18	
C4M1-left ear	Na	Control	19.35	0.657
		Study	19.57	
	Pa	Control	33.26	0.364
		Study	33.95	
	Na-Pa	Control	1.39	0.443
		Study	1.27	
C3M2-right ear	Na	Control	19.42	0.520
		Study	18.41	
	Pa	Control	32.18	0.127
		Study	34.31	
	Na-Pa	Control	1.41	0.363
		Study	1.20	
C4M2-right ear	Na	Control	19.38	0.661
		Study	19.36	
	Pa	Control	32.91	0.503
		Study	33.52	
	Na-Pa	Control	1.12	0.679
		Study	1.14	

In this study, the results of the behavioral tests for evaluating the temporal auditory processing (ordering and resolution) evidenced the group effect, with the group of prematurely born children having an impaired performance being when compared to the group of children of the same age group but born full-term. This result is in agreement with the literature, which also reports poorer temporal resolution performance of preschool children born preterm [14]. Other studies have reported that prematurely born children with central auditory processing disorder had a poorer overall performance in the battery of auditory processing diagnostic assessment tests, with a larger number of altered tests, which is suggestive of a more global dysfunction of the central auditory nervous system [5].

The auditory temporal resolution can be defined as the ability to detect time intervals between sound stimuli or the shortest time interval an individual can discriminate between two audible signals [11]. Time resolution is considered a fundamental skill in the auditory perception of verbal and non-verbal sounds, in the perception of music, rhythm and punctuation, and in the discrimination of frequency, duration and phonemes. Although the relations among changes in auditory processing, language disorders and learning disorders are complex, comorbidities are frequent, and many of these children have alterations in temporal processing [15,16]. Children with impaired temporal resolution are more prone to have learning difficulties than children with normal temporal resolution [17].

In the present study, no significant differences were found in the MLAEPs between the groups studied, consistent with the literature, where there was no agreement between the MLAEP results and the temporal pattern tests administered, even though MLAEPs appear to be useful in verifying the effects of auditory training [23]. In our study, although there was no statistical difference between the groups, the group of prematurely born children had poorer morphology of the tracings.

Another important finding of this study was the group effect on the latency of the P3. Prematurely born children had higher latencies in the right ear as compared to children in the control group. P3 is an auditory evoked potential referred to as endogenous potential because it reflects the functional use that the subject makes of the auditory stimulus, being highly dependent on the cognitive abilities, auditory attention and discrimination being among them. It is an cortical response as it depicts the electrical brain activity related to auditory stimuli. They are neurophysiological correlates of cortical sound discrimination and sound processing and can be used to document the plasticity in auditory system development. The P3 depends on the maturation of central structures, and latencies are expected to decrease with age, whereas increases in latency P3 can be considered a sign of late maturation of the precortical or cortical sound transmission or cortical sound processing [18]. Dupin [19] also showed the group effect on the P3 component prematurely born and full-term children evaluated at the age of 5 years. The P3 recordings provide an objective assessment of the central auditory nervous system. Despite the fact that they are present in children, P3 has a reduced amplitude and increased latency, with full maturation occurring around adolescence [20]. Thus, during the typical development occurring over the course of the school years, a reduction in latency, an increase in amplitude and improvement in the morphology of P3 recordings are expected to be observed, due to the maturation of the auditory pathways. In the literature, children with complaints of learning difficulties had higher P3 wave latency values than did the children in the group with no complaints [21,22]. In addition to the differences between groups being marked by P3 wave latency, only in the group of prematurely born children was this potential absent. The absence of the P3 wave is reported to be associated with school complaints and impaired attention and memory skills [21,22].

In our study, complaints of scholastic difficulties in the group of prematurely born children amounted to 56%. This raises the hypothesis that the poorer temporal resolution and P3 observed on prematurely born children may be a factor promoting the greater learning difficulties exhibited by these children. Longitudinal and transversal follow-up studies of prematurely born children showed a greater occurrence of scholastic difficulties as compared to children born full-term [24,25]. The survival of these infants imposes the challenge of returning a child to their families and to society who is fully capable of developing their affective, cognitive and productive potentials.

A limitation of our study is the relatively small sample size. Besides, further studies could address the hearing abilities in premature and full-term children: with and without learning problems and also with and without auditory risk factors, to verify the impact of these issues on the processing of sound stimuli contributing to scholastic concerns.

In the present study, prematurity and its effects can be seen to have a significant impact on temporal auditory processing measurements, both on ordering and temporal resolution, and on the long-latency auditory evoked potential P3. The present data seem to be indicating a possible recommendation for auditory processing evaluations at around 8–10 years of age in children who were born premature and have an auditory risk factor. Although the group of prematurely born children showed clear evidence of the need to undergo central auditory processing assessment and, therefore, when indicated, have access to auditory training, no child had had this opportunity until the time of the study. Both the diagnosis of central auditory processing disorders and the access to auditory training are still major challenges.

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Conflict of interest

The authors have no potential conflicts of interest to disclose.

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