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Original Article

Artigo Original

Auditory pathway maturational study in small for gestational age preterm infants

Estudo maturacional da via auditiva em prematuros nascidos pequenos para a idade gestacional

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ABSTRACT

Purpose: To follow up the maturation of the auditory pathway in preterm infants small for gestational age (SGA), through the study of absolute and interpeak latencies of auditory brainstem response (ABR) in the first six months of age. **Methods:** This multicentric prospective cross-sectional and longitudinal study assessed 76 newborn infants, 35 SGA and 41 appropriate for gestational age (AGA), born between 33 and 36 weeks in the first evaluation. The ABR was carried out in three moments (neonatal period, three months and six months). Twenty-nine SGA and 33 AGA (62 infants), between 51 and 54 weeks (corrected age), returned for the second evaluation. In the third evaluation, 49 infants (23 SGA and 26 AGA), with age range from 63 to 65 weeks (corrected age), were assessed. The bilateral presence of Transient Evoked Otoacoustic Emissions and normal tympanogram were inclusion criteria. **Results:** It was found interaural symmetry in both groups. The comparison between the two groups throughout the three periods studied showed no significant differences in the ABR parameters, except for the latencies of wave III in the period between three and six months. As for the maturation with tone burst 0.5 and 1 kHz, it was found that the groups did not differ. **Conclusion:** The findings suggest that, in the premature infants, the maturational process of the auditory pathway occurs in a similar rate for SGA and AGA. These results also suggest that prematurity is a more relevant factor for the maturation of the auditory pathway than birth weight.

Keywords

Evoked Potentials
Brain Stem
Hearing
Hearing Disorders
Infant, Newborn
Infant, Premature

RESUMO

Objetivo: Acompanhar a maturação da via auditiva em recém-nascidos prematuros pequenos para a idade gestacional (PIG), por meio do estudo das latências absolutas e interpicos do potencial evocado auditivo de tronco encefálico (PEATE) nos primeiros seis meses de idade. **Métodos:** Estudo transversal e longitudinal prospectivo multicêntrico, que avaliou 76 recém-nascidos, 35 PIG e 41 adequados para a idade gestacional (AIG), nascidos entre 27 e 36 semanas de gestação na primeira avaliação. O PEATE foi realizado em três momentos (período neonatal, três meses e seis meses). Retornaram para a segunda avaliação 29 PIG e 33 AIG (62 lactentes), entre 51 e 54 semanas (idade corrigida). Na terceira, retornaram 49 lactentes (23 PIG e 26 AIG), com faixa etária de 63 a 65 semanas (idade corrigida). Foi critério de inclusão a presença bilateral de emissões otoacústicas evocadas por estímulo transiente e curva timpanométrica normal. **Resultados:** Verificou-se simetria interaural nos dois grupos. A comparação entre os dois grupos ao longo dos três períodos estudados não mostrou diferenças relevantes nos parâmetros do PEATE, exceto para as latências da onda III no período entre os três e seis meses. Quanto ao processo maturacional com *tone burst* 0,5 e 1 kHz, verificou-se que os grupos não se diferenciaram. **Conclusão:** Os resultados sugerem que, nos prematuros, o processo de maturação da via auditiva ocorre em tempo similar em PIG e AIG. Também sugerem que a prematuridade é um fator de maior relevância para a maturação da via auditiva que o fator peso ao nascer.

Descritores

Potenciais Evocados
Tronco Encefálico
Audição
Transtornos da Audição
Recém-Nascido
Prematuro

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INTRODUCTION

The multifactorial etiology of prematurity contributes to the possibility of several interoccurrences and serious sequelae. The combination of prematurity and intrauterine growth restriction (IUGR) is one of the main causes of morbidity and mortality[1,2]. Frequently, the condition of being born small for gestational age (SGA) is associated with IUGR and can cause alterations in neuropsychomotor development (including hearing and language skills)[1,3].

The auditory system goes through two stages of maturational development: the peripheral portion is ready in structure and size between the fifth and sixth month of gestation, whereas the structures in the central portion (in the brainstem), although present and functional at birth, continue to form synaptic connections and improve their efficiency during the first two years of life[4,5].

The maturation of auditory pathways at the brainstem can be assessed and monitored through changes in latency and amplitude, evidenced in responses of brainstem auditory evoked potentials (BAEPs), a recommended procedure to assess the integrity of central and peripheral auditory pathways in newborns (NBs) and infants[6].

According to a research study, a child's small head circumference and short neural pathway length can be expressed by shorter I-V and III-V interpeak intervals of BAEPs. During prenatal period, an increase in speed of nerve conduction compensates the growth of the auditory pathways, causing the BAEP conduction time to decrease drastically. After birth, the speed of conduction compensates precisely the increased length of the pathways, thus stabilizing the BAEP conduction time[7].

Some authors attribute this curtailment to alterations in the morphological and functional development of the auditory nervous system[8]. It is reported in the literature that IUGR tends to bring about a scarcity of elements, such as oxygen, proteins, fatty acids, and iron, which are vital for an adequate neurological development. This scarcity increases the chances of brain alterations[9].

Considering that the first 6 months of life are fundamental for oral language development, auditory monitoring is indispensable[10]. It can be conducted through studies on the maturational process of brainstem auditory pathways, evidenced by BAEP responses.

Thus, the purpose of this study was to verify the maturational process of auditory pathways at the brainstem in premature infants who were born small for their gestational age.

METHODS

This is a prospective, longitudinal, cross-sectional, and multicentric study approved by the ethics committees of Universidade de São Paulo (CAPPesq HC-FMUSP Number 372/10), Hospital Universitário (Approval Report Number CEP-HU-USP 1009-10; SISNEP CAEE 0037.0.198.000-10), and Universidade Federal de São Paulo (Report Number 1235/11). The mothers and/or legal guardians that agreed to have their NBs participate in this research study signed the informed consent form. The NBs who comprised the convenience sample were born at the Hospital Universitário linked to Universidade de São Paulo (HU-USP) and at Hospital São Paulo linked to Universidade Federal de São Paulo (HSP-UNIFESP).

Even after the present study was completed, or in case we suspected a child had hearing impairments or alterations in the nerve conduction of sounds, hearing assessments and auditory development monitoring of the infants continued in the Audiology clinic of both institutions.

The infants were assessed from December 2010 to June 2012.

Initially, in the neonatal period, we assessed 76 preterm NBs allocated in two groups: Study Group, comprised of 35 SGA NBs (14 males and 21 females), and Control Group, comprised of 41 appropriate-for-gestational age (AGA) NBs (16 males and 25 females).

At 3 months of age, 62 infants returned for the second assessment. Of these, 29 belonged to the SGA group (12 males and 17 females) and 33 to the AGA group (13 males and 20 females).

Finally, 49 infants returned for the third assessment at 6 months of age. Of these, 23 belonged to the SGA group (9 males and 14 females) and 26 to the AGA group (12 males and 14 females).

The age range during the neonatal period varied from 27 weeks and 6 days to 36 weeks and 6 days. The adjusted age at the time of the examinations varied from 33 weeks and 2 days to 40 weeks and 3 days. In the second evaluation (at 3 months of age), the adjusted age varied from 51 weeks to 54 weeks and 3 days. Finally, in the third assessment (at 6 months of age), the adjusted age varied from 63 weeks and 2 days to 65 weeks and 3 days.

The eligibility criteria were indication that the NB was small-for-gestational-age in the SGA group, and appropriate-for-gestational-age in the AGA group. These criteria were based on the fetal growth reference curve used in the two institutions that participated in the study[11]. Information pertaining to weight adjustment at birth was obtained from the medical chart of the NBs.

We considered any NB whose gestational age at birth was up to 36 weeks and 6 days as preterm[12]. The other eligibility criteria were the bilateral presence of transient-evoked otoacoustic emissions (TEOAEs) and type-A tympanometric curves[13].

We excluded from the sample any NB who presented infectious risk for TORCHS (toxoplasmosis, rubella, cytomegalovirus, herpes, and syphilis), encephalopathy, craniofacial malformation, and conductive and/or cochlear alterations.

As the procedures adopted in this study, we read the medical charts of the NBs to collect data pertaining to the sample's eligibility criteria, anthropometric measurements, and gestational age, based on the date of the mother's last period and confirmed by ultrasonography.

After this, the NBs were summoned for the tests, which were conducted in the following order: inspection of the external acoustic meatus with a Welch Allyn otoscope, TEOAE test, and measurement of acoustic immittance to ensure the integrity of the cochlear function, more specifically of the external ciliate cells, and that the middle ear was not compromised. The same procedures were repeated in the two subsequent assessments (at 3 and 6 months of age).

At Universidade de São Paulo, we used a dual-channel cochlear emissions analyzer ILO92 (Otodynamics®, London), with the resources available in the ILO88 version 5.61, which enabled us to register the TEOAE with a B-Type ILO OAE Probe catheter with a soft olive-shaped tip. We used a nonlinear click eliciting stimulus at an intensity between 78 and 83 dB peSPL on the QuickScreen mode. The presence of responses was considered based on a signal-to-noise ratio of 3 dB at 1 or 1.5 kHz, and 6 dB at 2, 3, and 4 kHz, with a reproducibility value higher than 50% and stability over 70%. In case we detected any responses, the exam was interrupted after 80 accepted stimuli; in case they were absent, we carried on with the examination until the 260 stimuli suggested by the equipment were reached. In case of absence of responses, the NB was excluded from the sample and referred to an otorhinolaryngologist for evaluation and audiologic treatment.

At Universidade Federal de São Paulo, we used a portable, automatic GN Otometrics® AccuscreenPRO machine. To detect the “PASS” mark when registering the TEOAE, the manufacturer calibrated the machine to automatically analyze the responses following these parameters: evaluation by binomial statistics; nonlinear click stimuli in sequences at a speed of 60 Hz and intensity of 70–84 dB SPL (45–60 dB HL, with autocalibration depending on the volume in the ear canal); frequency range between 1.4 and 4 kHz; and artifact below 20%. Whenever these parameters were obtained, the machine registered “PASS.”

In both participating institutions, the acoustic immittance was measured by means of a tympanometry with a 1-kHz probe tone released by a middle ear analyzer (Interacoustics, model 235-H).

During the conduction of the BAEP, the infant was in a crib or on his/her mother’s lap, sleeping naturally.

To capture the BAEPs, we used a clinical/diagnostic Intelligent Hearing Systems® machine (model Smart-EP), in both participating institutions. The NBs were prepared for the BAEPs as follows: their skin was previously cleaned with abrasive paste, and we attached disposable Kendall Medi-Trace® 200 pediatric electrodes on their frontal region (Fpz) and on the right and left mastoids (M_2 and M_1) in accordance with the guidelines of the IES 10-20 standard (International Electrode System)[14]. The acoustic stimulus was presented through in-ear earphones (model ER-3A), which elicited the responses. The impedance of the electrodes was maintained below 3 kΩ.

The acoustic stimulus used was of the rarefying, click type, presented monaurally at 80 dB nHL, for evaluation of the integrity of the auditory pathway. For a total of 2,048 stimuli, 27.7 clicks were presented per second with a duration of 0.1 ms, 100-Hz high-pass filters, and 1,500-Hz low-pass filters to avoid excessive artifacts[5]. The recording lasted 12 ms.

After this step, the same procedure was conducted with a tone burst (TB) acoustic stimulus presented in a Blackman envelope, without plateaus, with a duration of 8,000 μs and 4,000 μs at the frequencies of 0.5 and 1 kHz, respectively, and repetition rate of 39.1 Hz, totalizing 2,048 stimuli of condensed polarity. We used a window of 25 ms, a 30-Hz high-pass filter, and a 1,500-Hz low-pass filter in all frequencies. The stimulus was presented monaurally at an intensity of 80 dB nHL.

The BAEP was captured twice in each ear with the purpose of obtaining the reproducibility of the waves and guaranteeing the presence of responses.

For the analysis of the BAEP responses with click stimuli, we measured the absolute latencies of the waves I, III, and V and the interpeak intervals I-III, III-V, and I-V at 80 dB nHL in the three evaluations conducted (neonatal period, at 3 months, and at 6 months of postconceptual age).

Likewise, for the analysis of the BAEP responses with TB stimuli, we measured the absolute latency of wave V at 80 dB nHL in the three evaluations conducted.

The results of each evaluation were registered and given to the mother or legal guardian along with a brief explanation about auditory and language development.

The analysis of the results began with a description of the averages and standard deviations of each group studied. We later compared all the measurements of the right and left ears of each individual through paired Student’s *t*-test. We compared the averages between the groups using the analysis of variance. Tukey’s test was used in the comparative two-by-two analysis in the three periods studied, namely neonatal period to 3 months (NB to 3m), between 3 and 6 months (3m and 6m), and between the neonatal period to 6 months (NB to 6m).

In the analysis of the maturational process of the BAEP waves, each child was first compared to him/herself in the three periods studied. To compare the SGA and AGA groups, we conducted an approximate pairing by adjusted age (about 2 weeks of interval). Finally, we analyzed the maturational process based on BAEP parameters.

In the statistical data analysis, we used a confidence interval of 95% and a significance level of 5%. The statistically significant values were marked with an asterisk (*) and the tendency to significance with two asterisks (**).

All the tests were two tailed. All the analyses were calculated with the statistical software STATA®, version 10.0.

RESULTS

In this study, we used two methodologies to analyze the results: cross-sectional data analysis in the first part and longitudinal analysis in the second part.

In the cross-sectional study, we analyzed the absolute latencies of the waves I, III, and V, as well as the I-III, III-V, and I-V interpeak intervals (click), and latency of the wave V (TB) in each group.

No statistical differences were evidenced between the ears in both groups. We decided, therefore, to group the values obtained in the right and left ears in the subsequent analyses. The comparison was thus maintained between the SGA and AGA groups.

The comparative analysis of the BAEP waves in the neonatal period shows that the groups did not differ significantly when compared to each other.

At 3 months, the AGA and SGA groups differed only in relation to the III-V interpeak interval (Table 1).

Table 1. Comparative study of the averages of the parameters of brainstem auditory evoked potentials in small-for-gestational-age and appropriate-for-gestational-age infants at 3 months

Infants	SGA (n=29)		AGA (n=33)		p-value
BAEP	Mean (ms)	SD	Mean (ms)	SD	
Wave I	1.74	0.18	1.75	0.11	0.890
Wave III	4.45	0.24	4.43	0.31	0.719
Wave V	6.58	0.39	6.69	0.27	0.176
I-III Ipi	2.63	0.35	2.64	0.16	0.860
III-V Ipi	2.13	0.23	2.27	0.22	**0.018***
I-V Ipi	4.74	0.62	4.91	0.22	0.130
0.5-kHz TB	8.47	0.86	8.50	0.87	0.921
1-kHz TB	8.46	0.57	8.35	0.75	0.532

*Statistical significance (p≤0.05) – ANOVA

Caption: SGA = small for gestational age; AGA = appropriate for gestational age; BAEP = brainstem auditory evoked potential; SD = standard deviation; Ipi = interpeak interval; TB = tone burst

The comparative study of the absolute latencies of the BAEP waves between the groups at 6 months evidenced differences only in regard to the III-V interpeak interval, with a shorter latency in the SGA in relation to the AGA group (Table 2).

Table 2. Comparative study of the averages of the parameters of brainstem auditory evoked potentials in small-for-gestational-age and appropriate-for-gestational-age infants at 6 months

Infants	SGA (n=23)		AGA (n=26)		p-value
BAEP	Mean (ms)	SD	Mean (ms)	SD	
Wave I	1.71	0.10	1.72	0.09	0.506
Wave III	4.31	0.23	4.29	0.19	0.753
Wave V	6.34	0.30	6.40	0.27	0.473
I-III Ipi	2.60	0.24	2.56	0.19	0.592
III-V Ipi	2.04	0.13	2.13	0.16	**0.035***
I-V Ipi	4.64	0.29	4.68	0.22	0.527
0.5-kHz TB	7.86	0.62	8.13	0.85	0.239
1-kHz TB	8.10	0.70	8.27	0.40	0.324

*Statistical significance (p≤0.05) – ANOVA

Caption: SGA = small for gestational age; AGA = appropriate for gestational age; BAEP = brainstem auditory evoked potential; SD = standard deviation; Ipi = interpeak interval; TB = tone burst

The two-by-two comparative analysis between the periods studied in the AGA infants showed differences in the latencies of wave I only in regard to the NB to 3m period (p<0.01); in regard to the waves III and V, and III-V interpeak interval, we found differences in the three periods. When comparing the interpeak intervals, we verified differences pertaining to I-III and I-V between NB to 3m and NB to 6m (p<0.01) periods. When comparing by TB, the differences found at 0.5 kHz occurred from NB to 6m (p<0.01) period, and from 3m to 6m period at 1 kHz.

Regarding the SGA infants, the two-by-two comparison for wave I and the I-III interpeak interval showed statistical relevance between NB to 3m (p<0.05) and NB to 6m (p<0.01) periods. Concerning the waves III and V, and interpeaks III-V and I-V, statistical relevance was found in the three periods (p<0.01). When the eliciting stimulus used was TB, the differences verified at 0.5 kHz occurred from NB to 6m (p<0.01). At 1 kHz, they occurred from NB to 6 cm (p<0.01), and 3m to 6m (p<0.05).

The results of the evolutionary study of the averages of the latencies of BAEPs in the SGA and AGA groups over the course of 6 months are shown in Figure 1.

We also analyzed the speed of maturation of each BAEP parameter, expressed through a decrease in the latency that occurred between each period analyzed, with the purpose of showing this process more clearly.

The results were obtained by comparing both groups with the purpose of verifying in which group maturation occurred more distinctly.

The latency of wave I decreased in the AGA and SGA groups. It did not differentiate the groups significantly in the three periods studied.

Regarding the evolution of wave III, both groups differed only in the period from 3m to 6m. However, considering the variation that occurred from NB to 3m and NB to 6m, we verified that it was not relevant.

The results evidenced a marked reduction in the latency of wave V in the first 6 months of life in both the groups, without statistical relevance.

Concerning the I-III, III-V, and I-V interpeak intervals, the groups did not differ in the three periods evaluated.

In regard to the maturational process shown by wave V with a TB stimulus at 0.5 and 1 kHz, we verified that, once again, there was no difference between the groups.

Figure 2 shows the reduction of the latency averages verified over the course of 6 months.

DISCUSSION

In this study, our purpose was to follow the development of premature SGA infants during the first 6 months of their lives, for verifying if it occurs in a similar manner to the development of children whose gestation did not suffer interoccurrences, and to provide, whenever necessary, quick and early interventions. Initially, we aimed at verifying whether auditory development occurred simultaneously in the right and left ears.

The results of this study evidence a symmetry between the ears in the SGA and AGA groups when the eliciting stimulus was of the click type. These results differ from those of a study in which the authors concluded that auditory functioning is asymmetrical, with a slight advantage to the right ear. According to them, BAEP responses have higher amplitudes of wave V and shorter latencies in the right ear[15].

On the other hand, the results of our study agree with current studies in which the authors concluded that maturation along the central auditory pathway occurs simultaneously in both ears[16–18] when the eliciting stimulus is of the click type.

It is also in agreement with other authors who found a strong correlation between the ears both for the click and the TB stimulus at 0.5 kHz, as well as with others who did not find interaural differences in the BAEPs with TB stimuli at various frequencies[19–21].

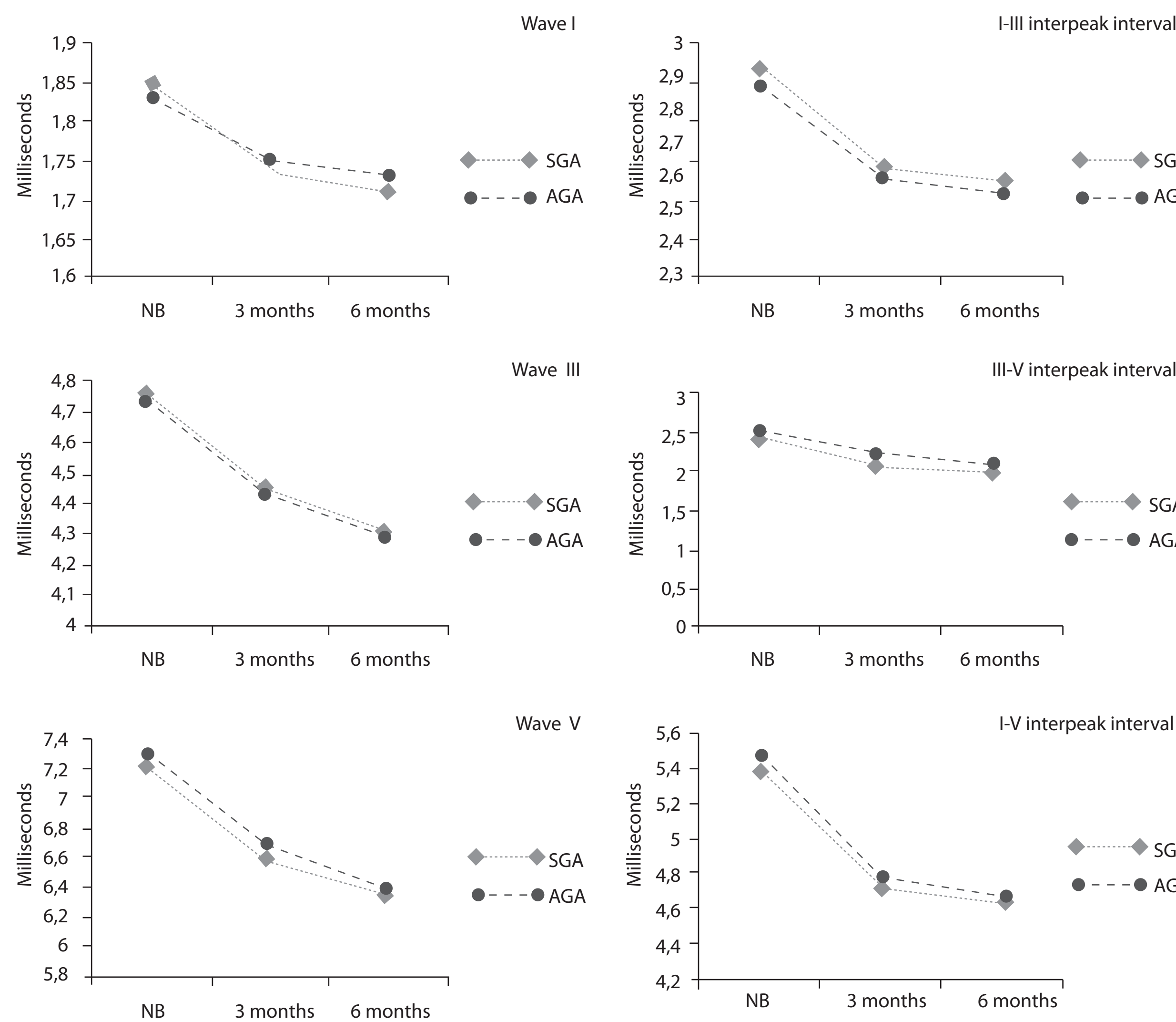
In this study, when we compared the groups in the neonatal period, the absolute latencies and the interpeak intervals obtained did not differentiate them in regard to weight adjustment. This led us to conclude that preterm SGA and AGA infants behave in the same way when it comes to hearing. The I-V interpeak interval was shorter in the SGA than in the AGA group.

In another study, the researchers observed preterm SGA and AGA infants during the neonatal period and verified that, in the AGA group, the latencies of BAEP waves and the I-V interpeak interval decreased constantly and gradually up until the age equivalent to a full term. In the same period, the SGA group evidenced a I-V interpeak interval significantly shorter than that of the SGA in all postconceptual ages, which reflects accelerated neurological maturation or an alteration in neural function. The authors concluded that detailed follow-ups of these individuals are necessary to determine whether the onset of alterations in brainstem development in preterm SGA infants are correlated to late neural deficiency[8].

In a recent study, the authors observed the auditory behavior of the preterm SGA infants by comparing them to the AGA infants in the neonatal period. They did not find any relevant differences in regard to BAEP responses. The authors concluded that the SGA condition did not prove to be a risk for retrocochlear alterations[18].

At 3 months, the AGA and SGA groups differed in regard to the III-V interpeak interval, with shorter latencies in the SGA group and longer latencies in the AGA group.

This difference was also observed at 6 months, which can denote a few concomitant phenomena, namely accelerated maturation possibly due to a rapid increase in axonal myelin density in the brainstem[22], expressed through shorter latencies of wave



Caption: NB = newborn; SGA = small for gestational age; AGA = appropriate for gestational age

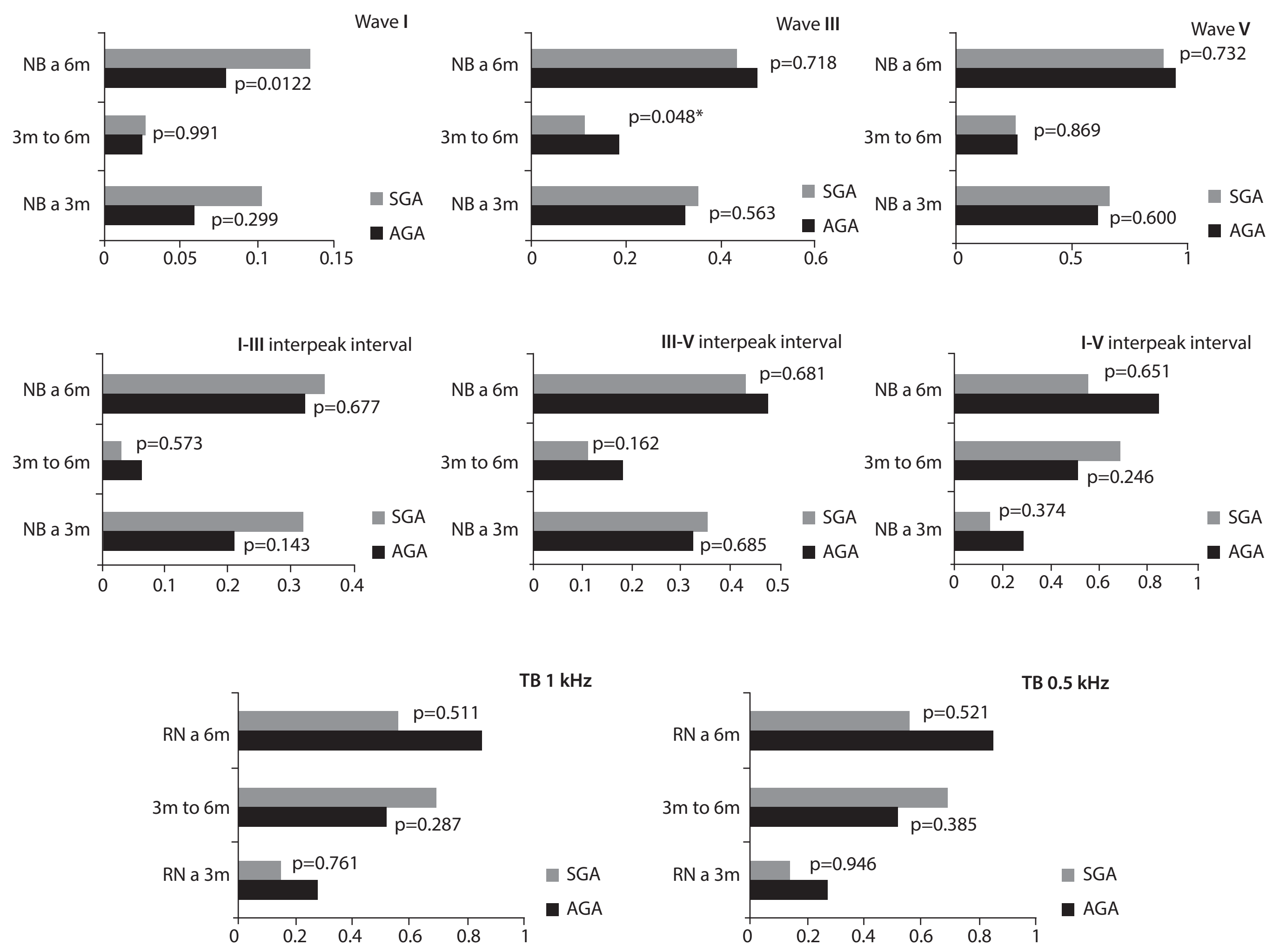
Figure 1. Evolutionary study of the averages of the latency of the waves of the brainstem auditory evoked potentials in appropriate-for-gestational-age and small-for-gestational-age infants over the course of 6 months

V and/or less time dispended for nerve conduction because of the shorter length of nerve fibers of the auditory pathway in the brainstem in the most rostral region of the SGA infants[7,22]. It can also be due to alterations in synaptic function[8], considering that, at 3 months, the auditory pathway station responsible for generating wave III showed longer latencies in the SGA group than in the AGA group, while the latency of wave V was shorter, apparently contradicting the order of maturation of the auditory pathway. This relation continued at 6 months, which leads us to hypothesize that, although not significant, this difference can point to late dysfunctions or development alterations.

The possibility of late dysfunctions in the SGA population reinforces some suggestions by authors pertaining to monitoring these children during the critical period of language acquisition[18,23,24].

The evolutionary study of the SGA and AGA infants evidenced a maturational process over the course of 6 months at the cost of a marked reduction in the latencies in the first 3 months, a fact that led us to consider that, especially in the first 3 months of life, premature infants present an accelerated maturation that later continues gradually. According to a renown study in the literature, in children, shorter head circumferences and shorter neural pathway lengths can be expressed through shorter I-V and III-V interpeak intervals[7]. However, other authors credit this to the influence of prenatal factors, such as IUGR, over the functional development of the nervous system; these factors, they argue, are responsible for early brainstem "maturation," evidenced in the first weeks of life. This "maturation" could be the result of a prenatal rupture of processes such as neogenesis, neuronal migration, elaboration of dendritic cells, and synaptogenesis, among others. Neuropathological studies conducted with premature children with severe IUGR revealed an immature distribution of small and little differentiated neurons[8,25].

Upon observing the maturation of each BAEP response separately, we verified that the maturation of wave I occurred mainly in the first 3 months of life, especially in the SGA group,



Caption: SGA = small for gestational age; AGA = appropriate for gestational age; TB = tone burst

Figure 2. Average of reduction in the absolute latencies and interpeak intervals in the three periods evaluated

which showed the most marked decrease in latency, although it was not significant. Wave I varied the least when compared to the other BAEP parameters, which points to the fact that it is practically mature at birth, and this corroborates other findings in the literature[26]. The fact that wave I is generated in the cochlear nerve, thus setting the speed for peripheral conduction, justifies its period of early maturation[5].

The SGA group showed the most accelerated rhythm of reduction of wave III latency in all periods analyzed, especially between 3 and 6 months. Perhaps this reduction was responsible for the differences presented in the III-V interpeak interval between the SGA and AGA groups at 3 and 6 months. In a previous study, the authors concluded that prematurity has more influence over the maturation process of wave III than weight, due to the characteristics that involve this physiological process[27].

The latencies of wave V were greatly reduced in the SGA and AGA groups in the first 3 months of life, with marked variation up until 6 months. This reduction was more expressive in relation to waves I and III, as they varied 0.135 and 0.481 ms, respectively, in the SGA group, whereas wave V varied 0.894 ms in the same period (NB to 6m). This piece of evidence confirms that the maturation of the auditory pathway along the brainstem occurs in a caudorostral manner, which suggests a relation with the process of myelination of nerve fibers along the auditory pathway, a probable factor of constant reduction of the latencies of BAEP waves III and V observed during the perinatal period[27].

We observed the same behavior in the latencies of the I-III, III-V, and I-V interpeak intervals as a possible direct consequence of the degree of myelination of nerve fibers, and of the speed of sound transmission from a given generating spot to another, in accordance with other findings in the literature[27].

The maturational process of wave V, acquired with BAEP and TB stimuli, was seen in both frequencies used. This is in agreement with other studies that reported that the latency of wave V with a TB stimulus decreases significantly until 61 weeks of postconceptual age, thus indicating the occurrence of maturation at the same speed in both frequencies[19].

Finally, considering prematurity first, along with low weight, we agree with other authors on the fact that delays in the development of the SGA infants frequently occur in several development areas (motor, attention, memory, adaptation, visual, and auditory)[24,28]. The authors in question suggest that the neurobehavioral abilities of children with low birth weight must be assessed at least once and monitored during the first 2 or 3 years of life. These evaluations enable pediatricians and caretakers to identify eventual development alterations during early childhood and to refer the children to rehabilitation services before school, thus increasing their chances of academic success.

FINAL CONSIDERATIONS

The phases of greater vulnerability for acquiring irreversible neurological lesions are concentrated between 15 and 20 weeks of gestation, and between 30 weeks of gestation and 2 years of age, a moment associated with myelination, axonal, and dendritic growth, and stabilization of synaptic connections[29]. In this scenario, IUGR, along with prematurity, is an important risk factor for neurodevelopment, especially in developing countries[1,2].

An aspect that may have interfered with the analysis of the results in the present study was that we did not subdivide the group with preterm NB, even though some were classified as extremely premature, others as having low weight, and others as late preterm. This fact probably hindered a more precise evaluation of the moment when the SGA and AGA infants differed in regard to the maturational process. Because some preterm infants were in the NICU, it seems clear that some of them were in proper conditions to be assessed only a few weeks after their birth, when several interoccurrences had already happened.

Another factor that must be taken into consideration is that, the younger the preterm infant's gestational age, the longer the time of extrauterine sound exposure to which he/she was submitted in the NICU, even before the first BAEP assessment. It is reported in the literature that brainstem nuclei have a synaptic plasticity that can be influenced by auditory experience, and that they are able to "learn" synaptically by means of collateral axons and dendritic germination, leading to changes in the mechanisms of neural response. Therefore, once a fetal and neonatal brainstem is capable of perceiving sounds, it becomes increasingly more sensitive to them as exposure is repeated[30].

Finally, because the SGA infants are a heterogeneous population per se and an example of extremely early malnutrition, morphological and physiological deficits to neural development can be caused by the latter. Moreover, the aspects that converge to cause minimal neurological dysfunctions also inflict great damage to their auditory processing of speech sounds. And, taking into consideration that, although not at risk for deafness, the SGA children are at risk for altered auditory abilities, all these factors indicate that they must be followed and treated professionally.

CONCLUSION

Preterm AGA and SGA infants undergo accelerated maturation, especially in the first 3 months, therefore experiencing a period of recuperation (catch-up) from the point of view of hearing.

The influence of prematurity in the maturational process of the central auditory nervous system is greater than the influence of weight at birth.

**RGA participated in data collection and manuscript elaboration; EMAD and RG wrote the manuscript; AAF conducted statistical data analysis; MFA co-supervised the study and supervised manuscript elaboration; CGM supervised the study and manuscript writing.*

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