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Original Article

Artigo Original

Longitudinal electrophysiological study of auditory pathway in small for gestational age infants

Estudo eletrofisiológico longitudinal da via auditiva em crianças nascidas a termo e pequenas para a idade gestacional

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Keywords

Evoked Potentials, Auditory, Brain Stem
Hearing
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ABSTRACT

Purpose: To follow the maturation of the auditory pathway of infants born small for gestational age term, by studying absolute and interpeak latencies of Auditory Brainstem Response (ABR) in the first six months of life. **Methods:** Multicentric prospective longitudinal study. The ABR was carried out in the neonatal period in 96 newborn infants, 49 small for gestational age (SGA) and 47 appropriate for gestational age (AGA). Of these, 77 infants (39 SGA and 38 AGA) returned for a second evaluation. In the third evaluation, 70 infants (35 SGA and 35 AGA) returned. **Results:** SGA and AGA did not present significant differences in the neonatal period and at three months of life. However, at six months, there was statistical significant difference between SGA and AGA groups for the latencies of wave III and interpeak I-III. Latencies of ABR waves decreased more rapidly in the first three months than the third to the sixth month of life for the SGA. AGA group showed progressive decrease in latency of ABR waves during the six months. **Conclusion:** The findings suggest that, for SGA infants, the maturational process of the auditory pathway occurs in different rate when compared to AGA infants. The SGA infants have faster maturation especially at the first three months of life, while in infants AGA, this process occurred in a constant and gradual way throughout the six months studied.

Descritores

Potenciais Evocados Auditivos do Tronco Encefálico
Audição
Transtornos da Audição
Recém-Nascido
Desenvolvimento Infantil

RESUMO

Objetivo: Acompanhar a maturação da via auditiva de lactentes nascidos a termo pequenos para a idade gestacional, por meio do estudo das latências absolutas e interpicos do Potencial Evocado Auditivo de Tronco Encefálico (PEATE) nos primeiros seis meses de vida. **Métodos:** Estudo multicêntrico prospectivo longitudinal. PEATE realizado no período neonatal em 96 recém-nascidos, 49 pequenos para a idade gestacional (PIG) e 47 adequados para a idade gestacional (AIG). Destes, 77 lactentes (39 PIG e 38 AIG) retornaram para a segunda avaliação. Na terceira avaliação, retornaram 70 lactentes (35 PIG e 35 AIG). **Resultados:** PIG e AIG não apresentaram diferenças significativas no período neonatal e aos três meses de vida. Aos seis meses, houve diferença estatística entre os grupos PIG e AIG para a onda III e interpico I-III. Latências das ondas do PEATE diminuíram mais rapidamente nos primeiros três meses que do terceiro para o sexto mês de vida para o grupo PIG. O grupo AIG mostrou diminuição progressiva da latência das ondas do PEATE durante os seis meses. **Conclusão:** Os resultados sugerem que a maturação da via auditiva nos PIG ocorre em ritmo diferente quando comparada aos AIG. Os PIG têm maturação mais rápida, especialmente nos três primeiros meses de vida; nas crianças AIG, esse processo ocorreu de modo constante e gradual ao longo dos seis meses estudados.

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INTRODUCTION

The newborns (NB) considered small for their gestational age (SGA) are 10% below the growth curve relating birth weight to the gestational age[1], being an indicator of intrauterine growth restriction (IUGR)[2].

The literature indicates that IUGR may cause deficiency of nutrients such as oxygen, proteins, fatty acids, and iron, essential for a proper neurological development, and it may culminate in impairments in the number of synapses, changes in the structure of the synapses, and/or affect the myelination of nerve fibers[3].

The degree of neurological impairment in the SGA infants depends on the time, the severity, and the duration of the insult in relation to the period of rapid brain growth[4]. The infants born in SGA terms, when compared to those born in the appropriate for gestational age (AGA) terms, present three times higher risk morbidity[5].

In face of these facts, the SGA infants (example of early malnutrition) are a study model for the effects that IUGR represents to neurodevelopment, including hearing and language[2,6].

The hearing monitoring, therefore, becomes fundamental, because the first 2 years, especially, the first 6 months of life, are critical for the development of oral language[7].

The brainstem auditory evoked potential (BAEP) has been considered the gold standard in the diagnosis of the integrity of auditory pathway in neonates at risk of hearing impairment[8]. It enables monitoring of the maturation of the central auditory nervous system through changes in latency and amplitude that occur in the BAEP even before the behavioral changes become evident.

The objective of this study was to compare the BAEP results elicited by click and tone burst (TB) in the neonatal period, at 3 and 6 months of age in the SGA and AGA infants, and to verify whether the latencies of the waves obtained with TB serve as parameter for assessing the maturation of the central auditory nervous system.

Our hypothesis is that the maturation process of the hearing pathways in the SGA infants occurs at a different pace than that in the AGA infants, reaching, however, the same parameters established as normal for the AGA infants after 6 months of life.

METHODS

This multicentered study was initiated after the approval by the Ethics Committee in Research of the Universidade de São Paulo (CAPPesq HCFMUSP) under protocol no. 372/10, at the Hospital Universitário, registration CEP-HU/USP No 1009-10-SISNEP CAEE 0037.0.198.000-10, of the Universidade Federal de São Paulo, under protocol no. 1235/11. The mothers and/or legal guardians who agreed to the participation of their NB in this study have signed the informed consent.

The studied population comprised NB and infants from the city of São Paulo. The sample was of convenience for the children born at the Hospital Universitário associated to the Universidade de São Paulo (HU/USP) and from the Hospital São Paulo, associated to the Universidade Federal de São Paulo (HSP/UNIFESP).

Even after completion of this study or, in case any child presents suspected hearing impairment, or alteration in the nervous conduction of the acoustic stimulation, the hearing assessment and the auditory development monitoring were continued in the audiology clinics of both the institutions.

All infants were evaluated between December 2010 and June 2012.

It was a sample of convenience with a confidence interval of 95% and significance level of 5%.

In the neonatal period, 96 NB were evaluated and grouped into the study group (comprising 49 SGA NB, 20 males and 29 females) and the control group (comprising 47 AGA NB, 23 males and 24 females).

At 3 months of age, 77 infants returned for a second evaluation — 39 SGA infants (16 males and 23 females) and 38 AGA infants (18 males and 20 females).

At 6 months of age, 70 infants returned for a third assessment — 35 SGA infants (16 males and 19 females) and 35 AGA infants (17 males and 18 females).

The age range in the neonatal period varied from 37 to 41 weeks of gestation and, at the time of the assessment, it varied from 37 weeks and 1 day to 41 weeks and 2 days. In the second assessment (at 3 months of age), the corrected age ranged from 51 to 55 weeks and 1 day. Finally, in the third evaluation (at 6 months of age), the corrected age ranged from 63 weeks and 2 days to 64 weeks and 3 days.

The selection criteria were as follows:

- Presence of the indicator small for gestational age in the study group and appropriate for gestational age in the control group, both according to the reference curve for fetal growth adopted by both the institutions[1]. The data on weight adequacy at birth were extracted from the medical record charts of the NB.
- Bilateral presence of transient evoked otoacoustic emissions (TEOAEs) and type A tympanometric curve, according to the model by Margolis and Popelka[9] for all the evaluated groups.

NB who presented infection risk for TORCHS (toxoplasmosis, rubella, cytomegalovirus, herpes and syphilis), encephalopathy, craniofacial malformations, and conductive and/or cochlear alterations were excluded from the sample.

The procedure initially adopted for the study included extraction of data from the medical records of the NB, which was based on the selection criteria of the sample, anthropometric measures, and on their gestational age, and on the date of the last menstrual period and confirmed by ultrasonography.

Next, the NB who met the proposed criteria were invited to carry out the testing, which followed the given order: inspection of the external auditory canal for visualization of the tympanic membrane using a Welch Allyn otoscope; then, the TEOAE testing and acoustic immittance (tympanometry) to ensure the integrity of the cochlear function, more specifically of the outer hair cells, and the absence of middle ear impairment, respectively. The same procedures were repeated in both the subsequent evaluations (at 3 and 6 months of age).

At USP, to capture the TEOAEs, a cochlear emission analyzer ILO 92 (Otodynamics®, London), with two channels, incorporating the results of the ILO 88, Version 5.61, was used; the B-Type ILO OAE probe, wrapped in a soft olive, was used to transmit the stimulus. The eliciting stimulus was a kind of nonlinear click, with an intensity between 78 and 83 dBpeSPL, in quickscreen mode. The presence of answers was considered by means of a signal-to-noise relation of 3 dB at 1 or 1.5 kHz and 6 dB at 2, 3, and 4 kHz, with a 50% higher reproducibility and a 70% higher stability. In the case of presence of answers, the test was interrupted after 80 accepted stimuli, whereas in the case of their absence, the test continued until reaching 260 stimuli (proposed by the equipment), in which case the NB would be excluded from the sample and forwarded to an otorhinolaryngologist for evaluation and posterior audiological follow-up.

At UNIFESP, a portable automatic equipment, AccuscreenPRO (GN Otometrics®), was used. In this last one, to achieve the "PASS" criterion in the TEOAEs testing, the equipment was calibrated by the manufacturer for the automatic analysis of the responses, according to the following parameters: evaluation by binomial statistics; nonlinear click stimuli in a sequence with a velocity of 60 Hz and intensity of 70–84 dB SPL (45–60 dBHL, with self-calibration depending on the volume of the auditory canal); frequency spectrum of 1.4–4 kHz; artifact lower than 20%. When these parameters were met, "PASS" was registered by the equipment.

The measures of acoustic impedance encompassed tympanometry with probe sound of 1 kHz, conducted using a middle ear analyzer (model AT 235-H) from Interacoustics, in both the institutions participating in the study.

To carry out the BAEP, the infant remained in the crib or on their mother's lap, in natural sleep state.

In order to capture the BAEP, the clinical/diagnostic equipment, Smart-EP, by Intelligent Hearing Systems®, was used by both the institutions participating in the study. The preparation of all NB for the BAEP testing was as follows: previous skin cleansing with abrasive paste and the fixation of Meditrace-200 disposable pediatric electrodes from Kendal®, in the frontal region (Fpz) and in the right and left mastoid ones (M_2 and M_1), according to the International Electrode System (IES 10-20 standard)[10]. The acoustic stimulus was presented by a pair of ER-3A insert earphones, eliciting the responses. The electrode impedance was kept below 3 kΩ.

The click with rarefied polarity acoustic stimulus was monoaurally presented at 80 dBnHL for the evaluation of the auditory pathway integrity, at a presentation speed of 27.7 clicks per second, duration of 0.1 ms, high-pass filters of 100 Hz, and low-pass ones of 1.500 Hz, with a total of 2,048 stimuli. The recording window used was of 12 ms.

In the sequence, the same procedure was executed, using acoustic TB stimuli in a Blackman envelope, without plateau, with duration of 8,000 and 4,000 μs at 0.5 and 1 kHz, respectively, at a repetition rate of 39.1 Hz, totaling 2,048 stimuli of condensed polarity. A window of 25 ms, a high-pass filter of 30 Hz, and a low-pass one of 1.500 Hz were used at all frequencies. The stimulus was presented monoaurally at an intensity of 80 dBnHL.

The BAEP was captured twice in each ear, to obtain the reproducibility of the waves and to ensure, then, the presence of the response.

For the analysis of the BAEP to click stimulus, the absolute latencies of waves I, III, and V, and the interpeak intervals I–III, III–V, and I–V at 80 dBnHL were measured in the three assessments conducted (neonatal period, at 3 and 6 months of post-conceptual age).

Similarly, for the analysis of the BAEP responses to the TB stimulus, the absolute latency of wave V at 80 dBnHL was measured in the three assessments conducted with each child.

The statistical analysis consisted, initially, of data description through the averages and standard deviations of each studied group. Then, all the measures of right and left ears of each individual were compared using the paired up Student's *t*-test. The comparison of the averages between the groups was done using the analysis of variance (ANOVA) test.

For the analysis of the maturation process of the BAEP waves, in the first place, each child of each group was compared to themselves in the first three stages studied. Afterward, for comparison between the SGA and AGA groups, the approximate matching of the corrected age (about 2 weeks of interval) was sought. Finally, to analyze the maturation process of the ABR waves, the Turkey test was used for the comparative analysis, two by two, in the three studied stages (neonatal period, and at 3 and 6 months of age).

All the test were bicaudados and all the analysis was calculated using the STATA® statistical software, version 10.0.

RESULTS

Initially, the absolute latencies of waves I, III, and V and the interpeak intervals I–III, III–V, and I–V (click) and the latency of wave V, elicited by tone TB in each group, were analyzed, in an attempt to characterize the ABR for the click and TB stimuli at 80 dBnHL in the studied population.

The data obtained in the SGA and AGA NB for each of the ABR parameters, preliminarily, were analyzed separately for each ear.

Statistically, one may verify the absence of relevant differences between right and left ears in both the groups.

Thus, the obtained values for the right and left ears were grouped for the subsequent analysis, maintaining the comparison between the SGA and AGA groups.

The results described next show that the SGA and AGA NB did not significantly differentiate from each other in the neonatal period (Table 1), and occurring likewise at 3 months of age (Table 2). However, at 6 months of age, the comparative analysis of the ABR parameters for the SGA and AGA groups showed differences in the absolute latency of wave III, as well as in the interpeak interval I–III. In the analysis of the ABR parameters, when the elicited stimulus was TB, there were no differences (Table 3).

Next, it was attempted to analyze the behavior of the maturation process of the parameters for the ABR by group, through the comparison of the average values of the waves' latency, in the neonatal period, and at 3 and 6 months of age.

From the results of the AGA group (Table 4), it may be verified that there was a significant decrease of the latencies of each ABR wave by click acquisition, occurring the same in the acquisition by TB in 0.5 and 1 kHz. According to the Tukey test (comparison two by two), regarding the maturation of waves I, III, and V, as well as the interpeak intervals I–III, III–V, and I–V, the difference occurred in the three periods: NB at 3 months of age (3m), 3m to 6 months of age (6m), and NB to 6m — p<0.01. Statistically, there was a significant decrease in the absolute latencies of the BAEP wave V with TB in the NB at 6m at 0.5 and 1 kHz (p<0.01).

The evolutionary behavior of the BAEP parameter for the SGA group (Table 5) showed a significant decrease of the absolute latencies of each ABR wave. The same occurred to the interpeak intervals I–III, III–V, and I–V in all the periods studied. There was a significant decrease in the absolute latency in the ABR wave V with TB at 1 kHz and a tendency at 0.5 kHz.

In the comparison two by two, regarding waves I, III, and V and the interpeak interval I–III, significant differences were observed between the periods of NB to 3m and between NB to 6m (p<0.01), with no difference between 3m and 6m. The interpeak intervals III–V and I–V showed differences within all three periods (p<0.01).

The difference was observed only in the period from NB to 6m (p<0.01) at both TB evaluated frequencies.

Finally, Figure 1 shows the reduction in the latencies for each ABR parameter separately, allowing the visualization of

Table 1. Comparison of the averages of the parameters of brainstem auditory evoked potential (click and tone burst) in newborns small for their gestational age and appropriate for their gestational age

NB	SGA (n=49)		AGA (n=47)		p-value
ABR	Mean (ms)	SD	Mean (ms)	SD	
Wave I	1.82	0.17	1.80	0.14	0.543
Wave III	4.65	0.26	4.61	0.25	0.433
Wave V	7.02	0.36	6.95	0.29	0.334
IPI I–III	2.82	0.23	2.80	0.23	0.543
IPI III–V	2.37	0.29	2.34	0.24	0.526
IPI I–V	5.19	0.36	5.10	0.39	0.233
TB 0.5 kHz	8.50	0.78	8.56	0.79	0.706
TB 1 kHz	8.62	0.78	8.50	0.80	0.454

Statistical significance (p≤0.05); ANOVA test

Caption: NB = Newborn; SGA = small for gestational age; AGA = appropriate for gestational age; ABR = auditory brainstem response; SD = standard deviation; IPI = interpeak interval; TB = tone burst

Table 2. Comparison of the averages of the parameters of brainstem auditory evoked potential (click and tone burst) at 3 months of age

Infants	SGA (n=39)		AGA (n=38)		p-value
ABR	Mean (ms)	SD	Mean (ms)	SD	
Wave I	1.73	0.10	1.74	0.08	0.747
Wave III	4.37	0.21	4.34	0.14	0.439
Wave V	6.56	0.30	6.52	0.21	0.468
IPI I–III	2.64	0.19	2.60	0.15	0.362
IPI III–V	2.19	0.17	2.19	0.17	0.858
IPI I–V	4.84	0.30	4.79	0.24	0.395
TB 0.5 kHz	8.24	0.72	8.32	0.61	0.598
TB 1 kHz	8.27	0.46	8.11	0.37	0.550

Statistical significance (p≤0.05); ANOVA test

Caption: SGA = small for gestational age; AGA = appropriate for gestational age; ABR = auditory brainstem response; SD = standard deviation; IPI = interpeak interval; TB = tone burst

Table 3. Comparison of the averages of the parameters of brainstem auditory evoked potential (click and tone burst) at 6 months of age

Infants	SGA (n=35)		AGA (n=35)		p-value
ABR	Mean (ms)	SD	Mean (ms)	SD	
Wave I	1.71	0.11	1.69	0.09	0.441
Wave III	4.31	0.19	4.20	0.17	0.019*
Wave V	6.33	0.29	6.30	0.25	0.657
IPI I–III	2.65	0.35	2.50	0.16	0.021*
IPI III–V	2.07	0.18	2.09	0.14	0.647
IPI I–V	4.64	0.25	4.60	0.23	0.541
TB 0.5 kHz	8.27	0.73	8.11	0.62	0.372
TB 1 kHz	8.30	0.48	8.17	0.45	0.321

Statistical significance (p≤0.05); ANOVA test

Caption: SGA = small for gestational age; AGA = appropriate for gestational age; ABR = auditory brainstem response; SD = standard deviation; IPI = interpeak interval; TB= tone burst

Table 4. Averages of the latencies of brainstem auditory evoked potential in appropriate for gestational age infants

AGA/Term	NB (n=47)		3m (n=38)		6m (n=35)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Wave I	1.80	0.15	1.73	0.09	1.69	0.10	<0.0001*
Wave III	4.61	0.26	4.34	0.15	4.20	0.19	<0.0001*
Wave V	6.88	0.18	6.52	0.21	6.30	0.25	<0.0001*
IPI I–III	2.80	0.24	2.60	0.17	2.50	0.18	<0.0001*
IPI III–V	2.32	0.26	2.19	0.18	2.08	0.16	<0.0001*
IPI I–V	5.10	0.45	4.79	0.25	4.60	0.23	<0.0001*
TB 0.5 kHz	8.55	0.81	8.32	0.71	8.14	0.65	0.003*
TB 1 kHz	8.50	0.83	8.28	0.62	8.13	0.5	0.007*

Statistical significance (p≤0.05); ANOVA test

Caption: AGA = appropriate for gestational age; NB = newborn; 3m = 3 months; 6m = 6 months; SD = standard deviation; IPI = interpeak interval; TB = tone burst

Table 5. Averages of the latencies of brainstem auditory evoked potential in small for gestational age infants

SGA/Term	NB (n=49)		3m (n=39)		6m (n=35)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Wave I	1.82	0.17	1.73	0.10	1.71	0.12	<0.0001*
Wave III	4.65	0.26	4.37	0.22	4.31	0.20	<0.0001*
Wave V	7.02	0.37	6.56	0.30	6.33	0.23	<0.0001*
IPI I–III	2.82	0.24	2.64	0.21	2.65	0.25	0.0000*
IPI III–V	2.37	0.30	2.19	0.18	2.07	0.21	<0.0001*
IPI I–V	5.19	0.37	4.84	0.30	4.64	0.26	<0.0001*
TB 0.5 kHz	8.50	0.83	8.24	0.84	8.27	0.84	0.096
TB 1 kHz	8.62	0.82	8.38	0.65	8.27	0.57	0.008*

Statistical significance (p≤0.05); ANOVA test

Caption: SGA = small for gestational age; NB = newborn; 3m = 3 months; 6m = 6 months; SD = standard deviation; IPI = interpeak interval; TB = tone burst the pace at which the maturation took place in each site generator of waves, when comparing the two groups.

The wave latencies I, III, and V and the ABR interpeak interval I–III showed a rapid decrease in the first 3 months, stabilizing from 3m to 6m in the SGA group. However, the interpeak intervals III–V and I–V presented a gradual decrease throughout all the studied periods. The latencies of wave V, obtained by TB 0.5 kHz, revealed a maturation process also through latency decrease in the first 3 months, unlike what happened when the eliciting TB stimulus was 1 kHz, where the reduction occurred gradually until 6 months of age.

However, the AGA group showed constant and gradual maturation, observed through progressive decrease of the latency of all ABR waves elicited by click and TB, during the 6 months (Figure 1).

DISCUSSION

There are many challenges NB and SGA infants pose toward professionals committed to understanding how their systems respond to the aggressions suffered during intrauterine life and how, and for how long, these aggressions will affect their lives.

The following discussion was hampered by the scarcity of works addressing the maturation process of the auditory pathway in the SGA population, the focus of this study. Added to that is the fact that, in the studies found, the objectives, as well as the equipment and methodology used (acquisition speed, earphones, stimuli polarity, etc.), were quite varied.

The results of this study showed that there was no asymmetry between ears in the SGA and AGA groups when the eliciting ABR stimulus was the click. Such results diverge from studies that found, in ABR responses, higher amplitudes of wave V and shorter latency of waves in the right ears of small children. According to the authors, the brainstem responses would support the Idea that, in general, there is a favoring of the right ear in sound processing along the auditory pathway(11).

However, the results of this study are in line with the ones in current literature, which concluded that the maturation process throughout the central auditory pathways occurs simultaneously in both ears(12–18).

In the neonatal period, the characterization and comparison of the AGA and SGA groups (Table 1) did not show differences between them, leading to the conclusion that both of them behave likewise, from the auditory point of view, in agreement to studies that also did not find relevant differences as to weight adequacy(18,19). It diverges, however, from the study that evaluated the maturation of the ABR responses in SGA NB, when compared to the AGA ones. The authors observed a significant delay in the onset of waves III and V, and the interpeak interval I–V of SGA infants, suggesting an alteration of the auditory pathway in the brainstem(20).

Therefore, in the neonatal period, the weight adequacy variable did not influence the results, once that SGA and AGA NBs did not differ.

At 3 months of age, the comparison between the AGA and SGA groups showed that they did not differ, for both the click and the TB (Table 2). Thus, this study agrees with the authors who referred to a significantly delayed response to the auditory stimulation by TB (0.5, 1, 2, 4, 6, and 8 kHz) in SGA term when compared to the auditory response of AGA infants born at term(21).

At 6 months of age, the AGA and SGA infants (Table 3) differed from themselves in relation to the wave latency III and the interpeak interval I–III, which was not presented in the previous months. No studies in the literature that could support these findings were found, so they are believed to be suggestive of a late dysfunction of the auditory nervous system until the entrance in brainstem, which may be either temporary or permanent. Such malfunction may have been originated still in intrauterine life and manifested later on.

Literature alerts us to the fact that the degree of neurological impairments in SGA infants depends on the time, the severity, and the duration of the distress in relation to the rapid growth period of the brain, and that the gestational age of the child must be taken into account: the SGA may manifest several features of premature children, for having remained in distress for longer time(2,4,22). A comparative study carried out between the SGA and AGA infants concluded that the former presented a three times higher risk of morbidity than the latter ones(5).

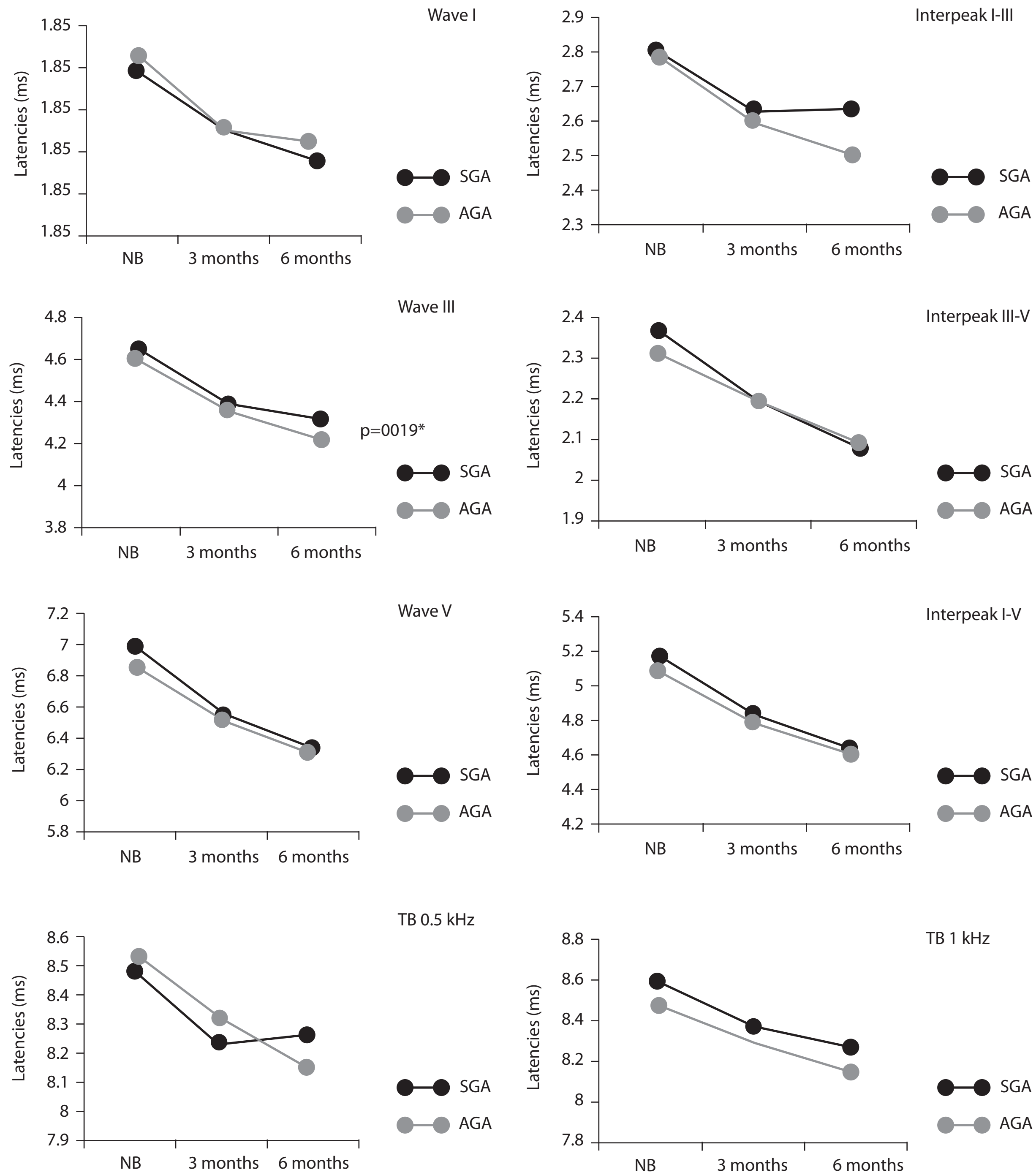
One cannot state whether the differences presented in the SGA population in relation to the AGA remained at 6 months of age, because the study did not follow the groups thereafter. The possibility of evidencing a late dysfunction, such as the one presented, reinforces the conclusion by some author that such delays may occur in multiple development areas. Thus, these authors suggest that neurobehavioral competences of children with very low birth weight should be evaluated at least once and monitored during the first 2 or 3 years of age, a critical period for language acquisition(18,23–25).

According to the results obtained for the AGA group (Table 4 and Figure 1), it was noted that it has gradually evolved during the 6 months, without presenting periods of greater acceleration nor deceleration in maturation pace. The ABR with TB also offered assistance in the visualization of this process in both the evaluated frequencies.

Nevertheless, in the SGA infants (Table 5 and Figure 1), the maturation process was evidenced during the 6 months of age, at the expenses of accentuated maturation in the first 3 months, because no significant differences were observed in the intermediary period.

According to literature data, the phases of greater vulnerability to irreversible neurological lesions are between 15 and 20 weeks of gestation and between 30 weeks and 2 years of age, being a moment associated to myelination, axonal and dendritic growth, and stabilization of synaptic connections(4). Similarly, the maturation of the brainstem is due the myelination and synaptic plasticity of the auditory experience(26).

Having a proper diet is essential for the individual from the moment of conception, because it is through it that nutrients (oxygen, iron, protein, fatty acids, etc.) that are essential to a full neurological development are metabolized by the organism. It seems evident, therefore, that children deprived from such nutrients during their intrauterine formation are susceptible to higher occurrence of minimal neurological disorders (attention



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

Figure 1. Averages of the latencies of the parameters of brainstem auditory evoked potential in appropriate for gestational age infants and small for gestational age infants

deficit, hyperactivity, and/or school underperformance), possibly due to changes in the neural function[3].

The maturation process of wave V, acquired in the ABR with TB, was visualized at the two frequencies used. The data that agreed with the study referring that the latency of wave V of TB decreased significantly until 61 weeks of post-conceptual age, indicating the occurrence of maturation[16]. However, the use of TB for such a purpose was not as true to the use of click, once a gradual decrease only in the latency of wave V was observed. It is noteworthy that the TB did not allow the clear visualization of waves I and III, a fact that affects the evaluation and monitoring of the auditory pathway in its full extension to the lateral lemniscus and inferior colliculus, in the brainstem.

Thus, this study suggests that the stimulus by specific frequency (TB) is used especially for the detection of electrophysiological thresholds, as recommended by the current literature[14,27], with the use of the click stimulus to monitor the maturation of the auditory pathway.

FINAL CONSIDERATIONS

The balanced set of genetic information contained in cells, the contribution of fundamental substrates for the metabolism of energy, and hormonal influence result in adequate fetal growth.

The SGA infants are pose a challenge to public health, because of their heterogeneity, caused by the occurrence of aggravations in different periods of intrauterine life, with different duration and intensity and, therefore, with prognosis as to their growth and development. The degree of impairment is related to time, duration, and severity of the distress. It may be inferred, thus, the prolonged lack of essential elements for proper brain development may have culminated in a greater loss in the number of synapses, in changes in the synaptic junction structure or affected nerve fibers myelination. Such damage will inevitably incur possible damage to neurodevelopment, including hearing and language[2,4,22].

The integrity of the auditory system is essential for language development, for each child must be able to pay attention, to detect, to discriminate, to locate sounds, to memorize, and to integrate auditory experiences to recognize and understand the spoken language[28].

Considering that the process required for the perception of spoken language has a substantially automatic and independent basis of superior cognitive elements, that is, it would occur largely in the brainstem, a lesion of the auditory pathways would, then, be responsible for numerous difficulties in understanding the spoken language[29].

Finally, to, in fact, meet the most basic foundations of infant's hearing health, and because it cannot be categorically stated which child will present disorders of this nature, the results of this study agree with those of Campos[30] as to the need to create public policies to guide parents and to disseminate strategies. Such simple care steps contributed to the improvement and/or stimulation of hearing development since birth. It is also believed that such a measure would diminish a lot its cost and impact on society, besides bringing undeniable benefits to the quality of global communication of this population.

This study suggests, therefore, that SGA infants are considered to be at risk of developing hearing alterations/dysfunctions, not regarding hearing accuracy itself, but regarding the quality of processing the acoustic information. It is then emphasized that, when performing the neonatal hearing triage, these children are sent to, at least, one electrophysiological assessment, auditorily monitored, until the age of 3.

CONCLUSION

The results of this study corroborate our initial hypothesis, because the maturation process of the auditory pathways in SGA infants occurred at different speeds when compared to the AGA infants. That is because the SGA ones were accelerated until 3 months, stabilizing at 6 months of age, whereas the AGA infants showed gradual maturation throughout the studied period.

The TB stimulus evidenced the maturation process throughout the 6 months studied, best at 1 kHz; at 0.5 kHz, this process was not observed so clearly. However, the TB stimulus did not substitute the click when the objective is to observe the maturation process throughout the central auditory nervous system.

**RGA was responsible for the Project, for the outline of the study and data collection and tabulation, and for the elaboration of the manuscript; EMAD supervised the information regarding the medical portion of the study at USP; RG supervised the information regarding the medical portion of the study at UNIFESP; AAF was responsible for the data statistical analysis; MFA and CGM were responsible for the overall orientation of the stages of the manuscript's writing and elaboration.*

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