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Influences of birthweight upon brainstem maturation as reflected by auditory brainstem response (ABR) evaluation

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Summary

The authors have studied auditory brainstem responses (ABR) in 49 preterm (Group A) and in 54 fullterm (Group B) newborns, classified according to the birthweight related to conceptional age, in order to verify the influences of this latter parameter upon ABR. In Group A newborns, 4 recording sessions were performed, while only 3 in Group B, to evaluate data obtained at the same extra-uterine age. The obtained data show that birthweight related to conceptional age seems to play a major role on the development of ABR, since no significant differences were detected between preterm and fullterm newborns, provided the birthweight was appropriate for conceptional age (ACA). On the contrary, small for conceptional age (SCA) newborns showed an abnormal ABR pattern at birth, which tended to normalize at the following recording sessions. The authors conclude that birthweight related to conceptional age represents an important factor in the development of auditory brainstem responses and that the audiological diagnosis has to be very cautious in SCA newborns, regardless if they are pre- or fullterm.

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Introduction

Auditory Brainstem Responses (ABR) are widely used in audiological and neurological pediatric practice [11,15,16]. A major field of application, however, is represented by the neurologic and auditory monitoring of the high-risk newborn [19]. Normative data in preterm newborns are rather difficult to ascertain due to technical and physiological factors [13,23], mainly linked to the influence of intra- and extra-uterine life and of birthweight upon brain maturation.

Since little has been related upon these points [8,11,19], the aim of the present paper is to study auditory maturational processes, as reflected by ABR, as a function of conceptional age and birthweight, in a population of preterm and of fullterm newborns.

It has to be clarified that conceptional age corresponds to the gestational age added to the extrauterine one. All newborns can be classified in 'preterm' (less than 37 weeks), 'at-term' (37–42 weeks), and 'post-term' (more than 42 weeks). Among the 3 groups, birthweight can be appropriate for conceptional age (ACA), small (SCA) or large (LCA). To allow such a classification, the appropriate birthweight for each week of gestation must be known. The most commonly used reference table is the Denver intrauterine weight curve, compiled by Lubchenco et al. [10]. Any infant whose birthweight is below the 10th centile is considered to be SCA, while those above the 90th centile are LCA.

Materials and Methods

ABR have been studied in a group of 49 preterm (Group A) and in a group of 285 fullterm (group B) newborns. Group A newborns, all born before the 37th week of conceptional age, showed a birthweight ACA in 38 cases, while in 11 it was SCA [10]. Newborns underwent a first recording session within the first 48 h of extra-uterine life, while a second, a 3rd and a 4th one were performed at the 42nd, 52nd and 64th week of conceptional age, respectively. With regard to Group B newborns, only 29 SCA and 25 ACA, randomly chosen, underwent the longitudinal ABR recording. A first session was performed within the first 48 h after birth (42nd week of conceptional age), a second and a 3rd one at the 52nd and 64th week of conceptional age, respectively. ABR was performed partly in the Neonatal Care Unit of the Hospital of Perugia, partly in the Audiological Laboratory of the E.N.T. Clinic of the University of Perugia. In the latter case, the infant was examined in an electrically shielded silent room. Signals were picked up by miniaturized (1.1 cm diameter) silver chloride Beckman electrodes positioned at the upper forehead (active) and at both mastoids (reference and ground), after having repeatedly cleaned the skin with alcohol to reduce interelectrode impedance to at least 5 kΩ. The employed stimuli were 2048 unfiltered alternating clicks, generated by rectangular electrical pulses of 0.1 ms duration and delivered monoaurally through a TDH 49 headphone at 70 dB nHL (normalized to the psychoacoustical threshold of 15 normally hearing subjects) intensity level, at 21 stim/s repetition rate. The signals were amplified (10^5) and filtered through an analogue bandpass filter (200–20000 Hz; −3 dB points down; 6 dB per octave slope). Analysis time was 10 ms and sampling time 10 μs. The obtained tracings were visualized on a Tektronix oscilloscope, recorded by means of a HP 7010/B recorder and stored on flexible diskettes (floppy disks) for further evaluations. Each test was performed at least 3 times to evaluate intraindividual variability. Identification of the responses was based upon their replicability and latency evaluation versus normative data [15].

As the obtained data, evaluated by means of the Kolmogorov–Smirnov one-sample test (Statistical Package for the Social Sciences) resulted to be normally distributed, the statistical evaluation was carried out by means of the Student's *t*-test and the linear regression analysis (package Statistical Analysis System). When a wave was absent, linear regression analysis was performed by taking into account abnormally high latency values (I 4 ms; III 7 ms; V 10 ms), which were not considered when calculating the mean values.

Results

Influence of birthweight within group A newborns (ACA vs SCA)

In the 38 ACA newborns, waves III and V were present at all recording sessions,

TABLE I

Mean values ± 1 SD of waves I, III and V latency values in preterm infants (Group A)

	Session	*Wave*	*n*	*Mean*	*S.D.*	*S.E.M.*	*P*
ACA	1st	I	36	2.33	0.21	0.03	
SCA	1st	I	–	–	–	–	–
ACA	2nd	I	38	2.05	0.13	0.02	
SCA	2nd	I	2	–	–	–	–
ACA	3rd	I	38	1.73	0.08	0.01	
SCA	3rd	I	8	1.89	0.11	0.04	0.0001
ACA	4th	I	38	1.66	0.06	0.01	
SCA	4th	I	11	1.81	0.19	0.04	0.0002
ACA	1st	III	36	5.28	0.27	0.05	
SCA	1st	III	–	–	–	–	–
ACA	2nd	III	38	4.90	0.20	0.04	
SCA	2nd	III	2	–	–	–	–
ACA	3rd	III	38	4.25	0.09	0.01	
SCA	3rd	III	8	4.47	0.24	0.08	0.0001
ACA	4th	III	38	4.06	0.10	0.02	
SCA	4th	III	11	4.32	0.21	0.06	0.0001
ACA	1st	V	36	7.54	0.23	0.04	
SCA	1st	V	–	–	–	–	
ACA	2nd	V	38	7.17	0.16	0.03	
SCA	2nd	V	2	–	–	–	–
ACA	3rd	V	38	6.70	0.11	0.02	
SCA	3rd	V	8	6.94	0.15	0.05	0.0001
ACA	4th	V	38	6.52	0.11	0.02	
SCA	4th	V	11	6.77	0.19	0.06	0.001

while wave I was absent in two at the first recording session. In 11 SCA ones all waves (I–V) were absent at the first recording session, waves III and V were present in two cases at the second, and all the waves were present in 8 cases at the third recording session. Mean values ± 1 SD of the latency values are reported in Table I. Only data concerning the 3rd and the 4th recording sessions could be compared, as in SCA newborns too many data are missing at birth. At the 52nd week a significant difference was present between the two groups (ACA and SCA) concerning wave I ($P \leqslant 0.0001$), III ($P \leqslant 0.0001$) and V ($P \leqslant 0.0001$) latency values. At the 64th week, a reduced but still significant difference was present. The linear regression analysis showed a significant ($t < 0.0001$) progressive reduction of the influences of the birthweight upon waves latency values with increasing age.

Influence of birthweight within group B newborns (ACA vs SCA)

In the 25 ACA newborns, a normal ABR waveform was detected in all cases except in two at the first and second recording sessions, while in all cases at the third one. Data referring to the last recording sessions (2nd and 3rd) are reduced in number as some children were lost at the follow-up. In the 29 SCA newborns, a normal waveform was observed in 18 at the first recording session, in 26 at the second and in all at the third one. Mean ± 1 SD of the latency values are reported in Table II. At the first recording session, a statistically significant difference was noted between ACA and SCA infants concerning waves I ($P \leqslant 0.005$) and V ($P \leqslant 0.05$) latency values. At the following recording sessions, no statistically

TABLE II

Mean values ± 1 SD of waves I, III and V latency values in fullterm infants (Group B)

	Session	*Wave*	*n*	*Mean*	*S.D.*	*S.E.M.*	*P*
ACA	1st	I	25	1.99	0.15	0.03	
SCA	1st	I	18	2.12	0.12	0.03	0.005
ACA	2nd	I	13	1.84	0.26	0.07	
SCA	2nd	I	26	1.92	0.17	0.03	N.S.
ACA	3rd	I	5	1.96	0.19	0.09	
SCA	3rd	I	29	1.74	0.09	0.02	N.S.
ACA	1st	III	25	4.87	0.30	0.06	
SCA	1st	III	18	4.56	0.30	0.07	N.S.
ACA	2nd	III	13	4.48	0.26	0.07	
SCA	2nd	III	26	4.40	0.37	0.07	N.S.
ACA	3rd	III	5	4.12	0.24	0.10	
SCA	3rd	III	29	4.16	0.29	0.05	N.S.
ACA	1st	V	25	7.12	0.22	0.04	
SCA	1st	V	18	7.29	0.30	0.06	0.05
ACA	2nd	V	13	6.80	0.34	0.09	
SCA	2nd	V	26	6.92	0.28	0.06	N.S.
ACA	3rd	V	5	6.48	0.24	0.06	
SCA	3rd	V	29	6.58	0.31	0.06	N.S.

TABLE III

Mean values ± 1 SD of waves I, III and V latency values in ACA newborns

	Session	Wave	n	Mean	S.D.	S.E.M.	P
Group A	2nd	I	38	2.05	0.13	0.03	
Group B	1st	I	25	1.99	0.15	0.04	N.S.
Group A	3rd	I	38	1.73	0.08	0.01	N.S.
Group B	2nd	I	13	1.84	0.26	0.07	
Group A	4th	I	38	1.66	0.06	0.01	N.S.
Group B	3rd	I	5	1.96	0.19	0.09	
Group A	2nd	III	38	4.90	0.20	0.03	N.S.
Group B	1st	III	25	4.87	0.30	0.06	
Group A	3rd	III	38	4.25	0.09	0.01	N.S.
Group B	2nd	III	13	4.48	0.26	0.07	
Group A	4th	III	38	4.06	0.10	0.02	N.S.
Group B	3rd	III	5	4.12	0.24	0.10	
Group A	2nd	V	38	7.17	0.16	0.26	N.S.
Group B	1st	V	25	7.12	0.22	0.04	
Group A	3rd	V	38	6.70	0.11	0.02	N.S.
Group B	2nd	V	13	6.80	0.34	0.09	
Group A	4th	V	38	6.52	0.11	0.02	N.S.
Group B	3rd	V	5	6.48	0.24	0.11	

significant differences could be detected. The linear regression analysis showed a significant ($t < 0.0001$) progressive reduction of the influences of birthweight upon waves latency values with increasing age.

TABLE IV

Mean values ± 1 SD of waves I, III and V latency values in SCA newborns

	Session	Wave	n	Mean	S.D.	S.E.M.	P
Group A	2nd	I	2	–	–	–	
Group B	1st	I	18	2.12	0.12	0.03	–
Group A	3rd	I	8	1.89	0.11	0.04	
Group B	2nd	I	26	1.92	0.17	0.03	N.S.
Group A	4th	I	11	1.81	0.19	0.06	
Group B	3rd	I	29	1.74	0.09	0.02	N.S.
Group A	2nd	III	2	–	–	–	
Group B	1st	III	18	4.56	0.30	0.07	–
Group A	3rd	III	8	4.47	0.24	0.08	
Group B	2nd	III	26	4.40	0.37	0.07	N.S.
Group A	4th	III	11	4.32	0.21	0.06	
Group B	3rd	III	29	4.16	0.29	0.05	N.S.
Group A	2nd	V	2	–	–	–	
Group B	1st	V	18	7.29	0.30	0.06	–
Group A	3rd	V	8	6.70	0.11	0.02	
Group B	2nd	V	26	6.92	0.28	0.06	N.S.
Group A	4th	V	11	6.52	0.11	0.02	
Group B	3rd	V	29	6.58	0.31	0.06	N.S.

Influence of conceptional age

In ACA newborns, both preterm and fullterm, no significant changes in ABR wave latency could be observed at the same conceptional age. In fact, in group A the values concerning the second, 3rd and 4th recording sessions are almost superimposable to those referring to the corresponding sessions (1–3) of group B. In some cases, group A subjects showed reduced latency values compared to the corresponding group B ones (Table III). When considering SCA newborns, a slight but not statistically significant difference of latency values between group A and group B newborns could be observed concerning all waves. Although reduced, this difference was still present at the last recording session (64th conceptional week) (Table IV).

Discussion

Evidences exist in the experimental animal and in humans that ABR wave latency values and overall waveform are strictly related to maturational processes at the end organ and brainstem pathway levels [9,17,18,21]. In fact, it has been shown that ABR is often difficult to record before the 28th week of conceptional age even at high stimulus intensities, while at this age potentials appear at 55–60 dB HL [12,22]. According to Salamy [19], only the 50% of newborns below 30 weeks of age show responses at 60 dB stimuli, while they become clearly evident two weeks later. These results are in agreement with Eggermont [3] and Galambos [4], who state that after the 30th week of gestational age, middle ear, end organ and brainstem neuronal pathways are already sufficiently mature, these processes taking place in a caudo-rostral direction [1,6,7,20].

Our data show that at birth ABR peaks are absent in all the SCA preterm newborns in response to 70 dB nHL clicks, while their occurrence progressively increases at the following recording sessions. Also in 11/29 SCA fullterm newborns the occurrence of ABR peaks is significantly reduced at birth, while it is almost normal in ACA newborns, both pre- and fullterm. ABR peak latency values and overall waveform differences between ACA and SCA newborns tend to decrease with increasing conceptional age and, at the 64th week, the differences are greatly reduced. As all the newborns who presented an absence of the ABR pattern were SCA, regardless they were pre- or fullterm, we can state, in agreement with Morgon and Salle [14], that birthweight in relation to conceptional age represents a major factor in the genesis of the ABR pattern.

In ACA preterm newborns, in fact, ABR waveform was almost superimposable to that observed in ACA fullterm ones, and underwent the same maturational changes, except in some cases in whom the normalization occurred later. To explain that no significant differences can be observed between pre- and fullterm ACA newborns at the same conceptional age, as previously shown also by Chiarenza et al. [2], it must be remembered that the neurologic maturation follows precise predetermined steps [24], which can not be modified by preterm birth.

No definite evidence concerning the mechanisms underlying birthweight influences upon brainstem maturation as reflected by ABR parameters are reported in the literature, although they are probably due to a delay in myelination.

It can finally be suggested that the audiological diagnosis has to be very cautious in SCA newborns, and that a careful follow-up is mandatory up to 7–8 months of extra-uterine life, in order to prevent false positive results.

References

1 Beiser, M., Himelfarb, M.Z., Gold, S. and Shannon, E., Maturation of auditory brainstem potentials in neonates and infants, Int. J. Pediat. Otorhinolaryngol., 9 (1985) 69–76.

2 Chiarenza, G.A, D'Ambrosio, G.M., Bindelli, D.R., Moro, F. and Diasio, G., Brainstem acoustic evoked potential in preterm and fullterm newborns. In G.A. Chiarenza and D. Papakostopoulos (Eds.), Clinical Applications of Cerebral Evoked Potentials, Excerpta Medica, Amsterdam, 1982, pp. 363–376.

3 Eggermont, J.J., Physiology of the developing auditory system. In S.E. Treub and B. Schneider (Eds.), Auditory Development in Infancy, Plenum, New York, 1985, pp. 21–45.

4 Galambos, R., Maturation of auditory evoked potentials. In G.A. Chiarenza and D. Papakostopoulos (Eds.), Clinical Applications of Cerebral Evoked Potentials, Excerpta Medica, Amsterdam, 1982, pp. 323–343.

5 Galambos, S.C. and Galambos, R., Brain stem response audiometry in newborn hearing. Arch. Otolaryngol., 105 (1979) 86–90.

6 Goldstein, J.J., Krumholz, A., Feflix, J.K., Shannon, D. and Carr, R.F., Brainstem evoked response in neonates, Am. J. Obstet. Gynecol., 135 (1979) 622–628.

7 Hecox, K., Electrophysiological correlates of human auditory development. In L.B. Cohen and P. Salapateck (Eds.), Infant Perception: From Sensation to Cognition, Academic Press, New York, 1975, pp. 151–191.

8 Hecox, K. and Galambos, R., Brainstem evoked response in human infants and adults, Arch. Otolaryngol., 99 (1974) 30–33.

9 Krumholz, A., Felix, J.K., Goldstein, P.J. and McKenzie, E., Maturation of the brainstem auditory evoked potential in premature infants, Electroenceph. Clin. Neurophysiol., 62 (1985) 124–134.

10 Lubchenco, L.O., Hansman, C., Dressler, M. and Boyd, E., Intrauterine growth as estimated from liveborn birthweight data at 24 to 42 weeks gestation, Pediatrics, 32 (1963) 793–796.

11 Maurizi, M., Ottaviani, F. and Paludetti, G., Potenziali evocati uditivi e maturazione delle vie uditive troncoencefaliche. In B. Calogero and G. Cervellera (Eds.), Fisiopatologia e Clinica delle Vie Uditive del Troncoencefalo, Pozzi, Rome, 1985, pp. 156–184.

12 Mjøen, S., ABR in pediatric audiology, Scand. Audiol., Suppl. 13 (1981) 141–142.

13 Mjøen, S. and Qvigstad, E., Auditory brainstem response in neonates during the first 48 hours after birth, Scand. Audiol., 12 (1983) 43–45.

14 Morgon, A. and Salle, B., A study of brain stem evoked responses in prematures, Acta Otolaryngol., 89 (1980) 370–375.

15 Paludetti, G., Maurizi, M., Ottaviani, F. and Rosignoli, M., Reference values and characteristics of brain stem audiometry in neonates and children, Scand. Audiol., 10 (1981) 177–186.

16 Prosser, S., Arslan, E., Conti, G. and Michelini, S., Evaluation of the monoaurally evoked responses in diagnosis of sensori-neural hearing loss, Scand. Audiol., 12 (1983) 103–106.

17 Roberts, J.L., Davis, H., Phon, G.L., Reicher, T.J., Sturtevant, E. and Marshall, R.E., Auditory brainstem responses in preterm neonates: maturation and follow-up, J. Pediat., 101 (1982) 257–263.

18 Rotteveel, J.J., Colon, E.J., Notermans, S.L.H., Stoelinga, G.B.A. and Visco, Y.M., The central auditory conduction at term data and three months after birth, Scand. Audiol., 14 (1985) 179–186.

19 Salamy, A., Maturation of the auditory brainstem response from birth to early childhood, J. Clin. Neurophysiol., 1 (1984) 293–329.

20 Salamy, A., McKean, C. and Buda, F., Maturational changes in auditory transmission as reflected in human brain stem potentials, Brain Res., 96 (1975) 361–366.
21 Salamy, A., Eldredge, L. and Wakeley, A., Maturation of contralateral brainstem responses in preterm infants, Electroenceph. Clin. Neurophysiol., 62 (1985) 117–123.
22 Starr, A., Amlie, R.N., Martin, W.H. and Sanders, S., Development of auditory function in human infants revealed by auditory brainstem potentials, Pediatrics, 60 (1977) 831–839.
23 Stockard, J.E., Stockard, J.J. and Cohen, R.W., Auditory brainstem response variability in infants, Ear Hear., 4 (1983) 11–23.
24 St. Anne Dargassies, J., Neurological maturation of the premature infant of 28 to 41 weeks' gestational age. In F. Falkner (Ed.), Human Development, W.B. Saunders, Philadelphia, 1964, pp. 306–325.