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Developmental course of brain-stem auditory evoked potentials in the first days of full term infants

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Summary

Modifications of brain-stem acoustic evoked potentials (BAEPs) in the first 5 days of life of normal full-term infants are reported. BAEPs were recorded using rarefaction clicks at 70, 60, 40, 20 dB HL. Multiple linear regression analysis was performed to evaluate chronological and gestational age differences for all positive and negative peaks, interpeak latencies, amplitudes and amplitude ratios. The percentage of newborn infants with auditory threshold of 20 dB HL increased with the number of days. At all intensities the latency of PIII and PV decreased significantly between the 2nd and 3rd day, while the latency of PI decreased significantly between the 3rd and the 4th day; PIII and PV latencies decreased also between the 4th and the 5th day. The longer the period of gestation the longer was the PI latency recorded between the 2nd and 5th day after birth. The anatomical and physiological changes developing shortly after birth are probably responsible for the above findings. These changes most probably appear firstly in the cochlear and trapezoid nuclei and later on in the organ of Corti.

brain-stem auditory evoked potentials; newborn infants; auditory development; chronological, gestational age

Introduction

Various studies have investigated the auditory function of newborn infants, recording brain stem acoustic evoked potentials (BAEPs). These studies have shown in-

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tense changes in the BAEPs during extrauterine development, by comparing the potentials of premature and full-term infants [2,3,12,32–34]. The changes in BAEP morphology, latency and amplitude mainly occur during the first year of life [1,8,10,11,18,22,23,26,27].

These maturational processes are partly dependent on environmental stimulation. Gottlieb (1976) has pointed out that prenatal auditory stimulation is not crucial for a normal sensory development, but auditory experience after birth is crucial for later development of language and cognitive processes [9,37,39].

These modifications are genetically predetermined. It has been shown in female newborn infants and in adults that the latencies of the brain stem and cortical potentials are shorter than in males [4,19,20]. Premature infants of different gestational age, on whom BAEPs recordings were performed at various post-natal weeks of age, showed that functional auditory development is not modified by early exposure to stimulation; it occurs in gradual maturational stages quite similar to those of full-term infants [23].

Observing the trend of BAEPs recorded in a very large sample of subjects of various ages, ranging from birth to adulthood, Eggermont and Salamy [7] have recently shown that BAEP peripheral components follow a different maturation gradient from that of central components. According to these authors, the PI wave develops more rapidly over a fixed time period of approximately 5 weeks, whereas the PV wave develops over a longer fixed period. This development follows the trend of two exponential functions, the first of which has a duration similar to that of wave PI, whereas the second lasts for about 100 weeks.

Studies referring to BAEP modifications during the first days of life have yielded conflicting results regarding the percentage of recorded waves, the evolution of the auditory threshold for the PI and PV waves, and of the interpeak latencies (IPLs) [1,16,17,25,40]. Some authors attribute these phenomena principally to middle ear and cochlea modifications [5] while others consider that peripheral and central pathways are equally involved [23].

This paper confirms that BAEPs of newborn infants, (gestational age 38–41 weeks), change during the first days of life. It also contributes new evidence that these changes appear first at the central level rather than the peripheral level.

Subjects and Methods

Subjects

BAEPs were recorded from 80 normal newborn infants, 38 male and 42 female. The duration of pregnancy was defined according to the criteria of Dubowitz et al. [6]. The gestational age ranged from 38 to 41 weeks: for 17 of the infants it was 38 weeks; for 18 infants 39 weeks; for 36 infants 40 weeks and for 9 infants 41 weeks. Recordings were carried out between the 2nd and 5th day after birth: 10 newborn infants were 2 days old; 32 were 3 days old; 24 were 4 days old and 14 were 5 days old. The criteria for selecting the newborn infants for this study were based on the mother's history of pregnancy and the infant's state at birth. The mothers were between 20- and 38-years-old and had completed a normal pregnancy without any medication. They had a history of no more than two previous normal pregnancies and no more than one miscarriage before the 13th week of pregnancy; delivery had been normal and without intervention. The APGAR score of the newborn infants at the first and fifth minute was >8; birth weight was between 2800 and 3800 g. These had been vertex presentations and there had been an absence of perinatal and postnatal somatic or metabolic pathology; acoustic reactometry was positive.

Recording procedure

The infants were tested in a quiet room where they lay in cribs during spontaneous sleep after their meal. The non-stimulated ear rested on a pillow. An earphone (TDH 39) encased in a rubber support (MX/41 AR) was placed over the stimulated ear. Stimuli were 9/s, 0.1 ms rarefaction clicks. Single-ear stimulation was carried out at intensities of 70, 60, 40, and 20 dB HL (equal to 100, 90, 70, and 50 dB peSPL).

Ag/AgCl electrodes were attached with collodion to the vertex and to each mastoid. The inter-electrode impedance was always lower than 3 kΩ. The EEG was amplified (gain 4 × 10 000) using a handpass of 160–3000 Hz (12 dB/octave slope) and averaged using a sweep of 10 ms. Two averages of 2048 stimuli were obtained from each ear, recording from Cz to the ipsilateral (Mi) and contralateral (Ci) mastoids. The EEG was monitored on an oscilloscope and the recording was interrupted each time noticeable artefacts were present on the EEG. The test lasted for approx. 1.5 h. The recording was suspended if the baby woke up.

BAEPs measurement

All positive and negative peaks, as identified by Jewett and Williston [13], of the ipsilateral and contralateral responses were measured. Components were identified by superimposing the first and the second averages of the responses from both ears, recorded at the same intensity. The BAEPs obtained from decreasing intensities were compared.

The following criteria were adopted for measuring the positive and the negative components. Wave PI was identified as the first positive peak after 1.3 ms. If several peaks appeared within 0.7 ms, PI latency was taken to be the mean of all peaks of equivalent amplitude during that period. In doubtful cases, especially at intensities lower than 70 dB, a comparison of ipsilateral and contralateral responses allowed the identification of wave I. The same rule was adopted for waves PIII and PV. Wave PII was measured both as a hump on the descending limb of PI and as a separate peak. The wide negativity that distinctly separated the positive waves PI and PII from the subsequent components was designated as NII. Wave PIII was measured as the first positive peak after NII. NIII latency was measured as a negative peak on the descending limb of PIII and not over 0.8 ms. In those cases in which PIV and PV were clearly distinct, wave NIV latency was evaluated. PV was defined as the widest positive peak after the NIII trough, recorded ipsilaterally and contralaterally and constantly present at all intensities. Wave NV latency was measured at the end of the descending limb of PV, but not more than 1.0 ms later than PV. Peak-to-peak amplitudes were measured between positive and following negative peaks.

Statistical analysis

For each day of life, the means and standard deviations (S.D.) of peak latencies, IPLs, amplitudes and amplitude ratios (AR) of the BAEPs were calculated, together with the percentage of newborn infants with an auditory threshold below 20 dB HL.

In order to test whether the BAEPs were affected by the chronological, gestational or conceptional (i.e. chronological + gestational) age, a multiple linear regression analysis (MLRA) was carried out. Since it was assumed that changes in BAEPs during the first days of life would happen quickly and linearly, it was considered that linear regression might appropriately describe the age-related BAEP changes. The significance of linear regression was evaluated by means of F value and the significance of the individual regression coefficients by means of Student's t-test. The ± signs of the regression coefficients revealed the direction of the regression. Regression analysis was performed separately on each intensity and on all intensities combined.

The days of life were grouped into 3 intervals (2nd + 3rd day, interval 1; 3rd + 4th day, interval 2; 4th + 5th day, interval 3); Student's t-test for independent variables and MLRA were performed for each interval to evaluate in which interval BAEP changes were most significant. A further t-test for paired data was carried out to evaluate reliability among the averages.

Results

The percentage of newborn infants with an auditory threshold of less than 20 dB HL increased as age increased. On the 2nd day, (first day of recordings) only 54% of the ears tested showed a threshold of less than 20 dB HL, whilst on the 3rd and 4th day the percentages increased to 70% and 82%, respectively.

At 70 dB HL, the percentage of the BAEP waves recorded varied with time from birth. On the 2nd day, PI was observed in 94% recordings; PIII and PV in 88%. These three waves were observed in all infants tested from the 3rd day onwards. NII was present in all infants from the 2nd day. The numbers showing NIII increased from 77% on the 2nd day to 94% on the 3rd day and to 100% on the 5th day. Those showing NV increased from 88% on the 2nd day to 98% on the third and 100% on the 5th day. There were no significant differences between the first and second averages at any given intensity for any peak.

Table I shows the means and S.D. of the BAEP components at 70 dB HL recorded at each day of life. Figure 1 shows the BAEPs recorded at different intensities on the 2nd, 3rd, 4th and 5th day of life in four newborn infants.

When MLRA was performed on all the data combined for all intensities it showed that gestational age had a statistically significant effect on PI latency only (t = 2.13, P <0.05). The greater the gestational age the longer the PI latency. The amplitudes of waves IV and V were significantly smaller in infants of higher, gestational age (wave IV: t = −3.36, P <0.01; wave V: t = −2.84, P <0.01). Positive and negative IPLs were not affected by gestational age. MLRAs performed separately for each intensity showed that the effect of gestational age was significant only at 70 dB HL; the latencies of PI, PII, PIV, NIII and NV were significantly longer when the gestational age was higher (PI: t = 2.81, P <0.01; PII: t = 2.54, P <0.05; PIV: t = 2.59, P <0.05; NIII: t = 2.82, P <0.01; NIV: t = 2.33, P <0.05).

MLRA also showed that chronological age had a statistically significant effect on

TABLE I

Means and standard deviations (S.D.) of the latencies of positive and negative peaks, amplitudes and ratio values of BAEPs recorded at 70 dB HL from normal fullterm infants.

		PI	PII	PIII	PIV	PV
2nd day	X	1.57	2.65	4.56	5.77	6.89
	S.D.	0.16	0.15	0.34	0.36	0.44
	n	30	30	29	23	29
3rd day	X	1.61	2.66	4.35	5.67	6.72
	S.D.	0.13	0.20	0.26	0.22	0.30
	n	88	73	86	67	81
4th day	X	1.51	2.63	4.80	5.57	6.64
	S.D.	0.09	0.27	0.20	0.27	0.27
	n	51	46	51	45	46
5th day	X	1.48	2.59	4.19	5.40	6.46
	S.D.	0.14	0.22	0.22	0.22	0.15
	n	30	26	30	21	29
		NI	NII	NIII	NIV	NV
2nd day	X	2.25	3.47	5.12	6.31	7.77
	S.D.	0.20	0.26	0.27	0.43	0.38
	n	30	31	27	25	29
3rd day	X	2.27	3.40	5.08	6.19	7.59
	S.D.	0.18	0.23	0.23	0.23	0.28
	n	81	89	82	60	74
4th day	X	2.15	3.28	4.29	6.11	7.45
	S.D.	0.19	0.25	0.23	0.26	0.32
	n	49	52	50	43	43
5th day	X	2.24	3.35	4.78	5.86	7.29
	S.D.	0.24	0.17	0.22	0.16	0.26
	n	28	30	28	18	26
		AI	AIII	AV	AR V/I	
2nd day	X	0.19	0.12	0.18	1.07	
	S.D.	0.10	0.04	0.05	0.52	
	n	30	27	29	29	
3rd day	X	0.17	0.17	0.21	1.39	
	S.D.	0.06	0.07	0.08	0.92	
	n	81	82	74	67	
4th day	X	0.22	0.15	0.20	0.95	
	S.D.	0.06	0.05	0.04	0.33	
	n	49	50	41	40	
5th day	X	0.25	0.18	0.21	0.89	
	S.D.	0.07	0.08	0.07	0.15	
	n	28	28	26	25	

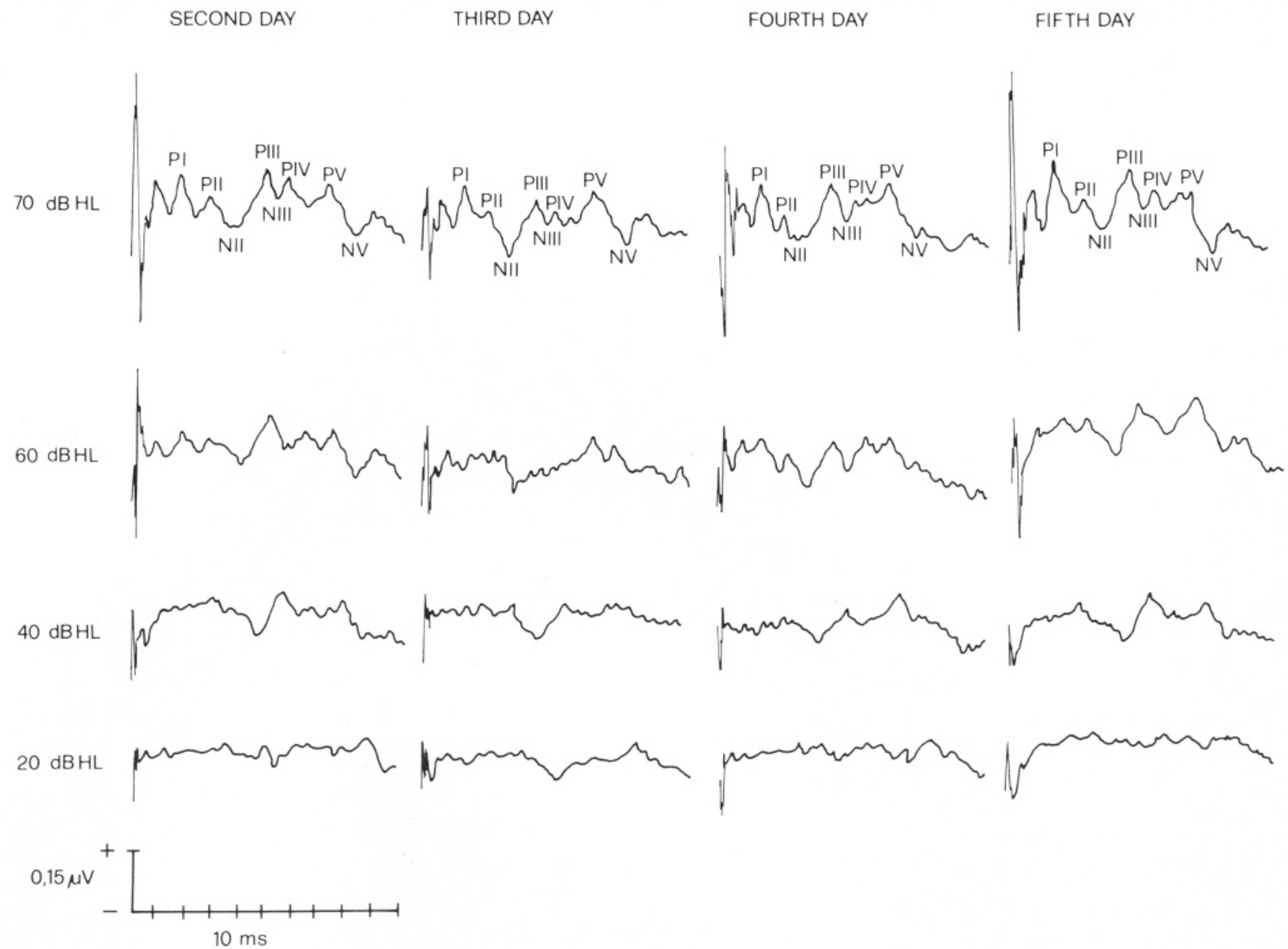

Fig. 1. Brain stem acoustic evoked potentials of four full-term infants recorded between the 2nd and 5th day after birth.

the latencies of all positive and negative components of BAEPs, except NI; absolute latencies decreased with age. The IPLs which decreased significantly as chronological age increased were: PI-PIII, PI-PV, PII-PV, NI-NIII and NI-NV. Only the amplitude of PI increased significantly with age. A further consequence was that the AR, V/I, decreased significantly. Table II shows a summary of MLRA on all the data combined for all intensities related to chronological age.

When the effect of chronological age on BAEP latencies, IPLs and amplitudes were evaluated separately for each intensity and each time interval, it was observed that some BAEP components showed a different developmental trend depending on the day of recording and stimulus intensity. At 70 dB HL, PIII, PV and NV latencies decreased significantly between the 2nd and 3rd day of life (interval 1). PI latency decreased significantly between the 3rd and 4th day (interval 2). PIII and PV latencies significantly decreased between the 4th and 5th day (interval 3). Table III shows a summary of MLRA on the BAEP latencies at 70 dB HL related to different time intervals. At 60 and 40 dB HL the results were similar to those at 70 dB HL: PV latency decreased significantly during interval 1, (60 dB HL: $t = -2.23$, $P < 0.05$)

TABLE II

Summary of multiple linear regression analysis of all components at all intensities in fullterm newborn infants. For each component, the *F* value, regression coefficient and *t* value are shown.

Chronological age	PI	PII	PIII	PIV	PV
F value	627.39[a]	277.20[a]	355.69[a]	83.90[a]	339.55[a]
r	−0.025	−0.022	−0.055	−0.082	−0.071
t	−2.93[a]	−2.04[a]	−4.92[a]	−5.68[a]	−5.76[a]
	NI	NII	NIII	NIV	NV
F value	338.25[a]	458.13[a]	265.96[a]	85.06[a]	247.28[a]
r	−0.010	−0.044	−0.068	−0.086	−0.064
t	−0.92	−4.48[a]	−4.90[a]	−5.60[a]	−4.75[a]
IPL:	PI−PIII	PI−PIV	PII−PV	NI−NIII	NI−NV
F value	6.45[a]	12.14[a]	3.79[a]	3.67[a]	5.11[a]
r	−0.032	−0.045	−0.053	−0.053	−0.058
t	−3.10[a]	−3.97[a]	−4.08[a]	−3.79[a]	−3.94[a]
	AI	AIII	AV	ARV/I	
F value	36.38[a]	16.75[a]	18.14[a]	6.84[a]	
r	−0.007	0.000	0.002	−0.060	
t	3.23[a]	−0.10	1.032	−2.12[a]	

[a] $P < 0.01$
[b] $P < 0.05$

TABLE III

Summary of multiple linear regression analysis of BAEP latencies for the 70 dB HL level at different time intervals. For each component the *F* value, regression coefficient and *t* value are shown.

Interval		PI	PIII	PV	NIII	NV
One	*F* value	1.62	13.21[a]	7.17[a]	0.58	7.13[a]
	r	0.035	−0.201	−0.184	−0.037	−0.170
	t	1.27	−3.63[a]	−2.67[a]	−0.76	−2.67[a]
Two	*F* value	10.90[a]	3.55[b]	1.87	14.14[a]	9.82[a]
	r	−0.101	−0.046	−0.080	−0.151	−0.128
	t	−4.66[a]	−1.07	−1.46	−3.79[a]	−2.33[b]
Three	*F* value	1.52	2.91	3.35	3.78	4.05
	r	−0.041	−0.134	−0.200	−0.110	−0.109
	t	−1.30	−2.11[b]	−2.55[b]	−1.56	−1.11

[a] $P < 0.01$
[b] $P < 0.05$

and during interval 2 at 40 dB HL ($t = -3.26$, $P < 0.01$); PI latency decreased significantly during interval 2 (60 dB HL: $t = -2.61$, $P < 0.01$; 40 dB HL: $t = -2.61$, $P < 0.01$), as did NV latency during the interval 2 (60 dB HL: $t = -1.98$, $P < 0.05$; 40 dB HL: $t = -3.39$, $p < 0.01$). At 20 dB HL, MLRA showed that all positive and negative latencies decreased significantly during interval 2.

At 70 dB HL, IPLs PI-PIII, PI-PV, PII-PIII, PII-PV, NII-NV and NIII-NV decreased significantly during interval 1. This significant decrease was present at 60 and 40 dB HL only for PI-PV (60 dB HL: $t = -2.56$, $P < 0.05$; 40 dB HL: $t = -3.27$, $P < 0.01$). During interval 3 only the IPLs PI-PV, PII-PV and NI-NIII decreased significantly (Table IV). The amplitude of PI increased significantly only during interval 2 and only at 70 dB HL ($t = 3.69$, $P < 0.01$), and the amplitude of PIII increased significantly during interval 1 at 70 dB HL ($t = 2.75$, $p < 0.01$). Conceptional age had no significant effect on BAEP latency, amplitude or IPL.

TABLE IV

Summary of multiple linear regression analysis of BAEP IPLs for the 70 dB HL level at different time intervals. For each component the *F* value, regression coefficient and *t* value are shown.

Interval		PI-PIII	PI-PV	PII-PIII	PII-PV	NI-NIII	NI-NV	NIII-NV
One	*F*	15.41[a]	15.04[a]	20.42[a]	10.54[a]	0.12	13.85[a]	6.21[b]
	r	−0.214	−0.233	−0.233	−0.217	−0.017	−0.218	−0.129
	t	−3.92[a]	−3.87[a]	−4.51	−3.24[a]	−0.36	−3.72[a]	−2.49[a]
Two	*F*	3.16[b]	1.16	0.58	0.23	5.80[a]	5.44[a]	1.93
	r	0.044	0.024	−0.010	−0.036	−0.075	0.005	0.054
	t	1.016	0.47	−0.21	−0.60	−1.69	0.09	1.93
Three	*F*	1.24	2.04	4.76	3.15	13.53[a]	6.37[a]	1.20
	r	−0.083	−0.153	−0.125	−0.184	−0.152	−0.139	0.054
	t	−1.47	−2.01[b]	−1.62	−2.06[b]	−2.47[b]	−1.26	0.60

[a] $P < 0.05$
[b] $P < 0.01$

Discussion

Other authors [5,23,28,29] have previously observed that the auditory threshold of premature and full-term newborn infants, recorded at different post-natal stages, decreases with age. In our study, the percentage of infants with an auditory threshold of less than 20 dB HL increases progressively from 54% on the 2nd day to 82% on the 4th day. The NII wave was the only one which was present in all newborns from birth. The positive and negative wave latencies, along with their respective IPLs, decrease as age increases. These observations agree with those studies reporting similar percentages of PI in full-term infants during the first hours and weeks of life [1,16,25]. A statistically significant decrease in the latencies of PIII, PV and NV at higher intensities was observed from the second day onwards; a decrease in the latency of PI was observed at all intensities, but only from the 3rd day onwards. Thus it appears that, at birth, changes in BAEPs occur primarily at a central level particularly in the cochlear and trapezoid nuclei; the studies in man by Moller et al. [21] suggest that these structures generate wave PIII and wave PV, respectively. The earlier decrease in latencies of the waves originating in the central structures and the increase in amplitude of PIII in human newborn infants confirm the findings of several electrophysiological studies conducted in animals, which show that the central auditory system has the potential capacity for specific functioning before the development of the peripheral system [24]. The subsequent decrease in PI latency is probably due to developmental factors affecting the receptor system. Studies of animal neonates confirm that the peripheral system develops through at least two general paths, one mechanical and one neurohormonal [31]. Genetic and perinatal effects influence these two general paths [15]. At birth there are secretory fluids in the middle ear, but these drain away after a short time [28,33–35]. The organ of Corti is similar to that of the adult in the foetus at 26 weeks; but its functioning depends upon the presence after birth of the thyroid hormones which control the development of the tectorial membrane, the opening of the Corti canal and the maturation of the pillar cells [30,38]. The combined action of mechanical and neurohormonal factors, and possibly of other as yet unidentified factors could be responsible for the decrease of PI latencies and for the increase in amplitude at 70 dB HL after the 3rd day of life.

The changes of PIII, PV, and NV waves during the first 5 days of life cannot be attributed to the myelinization process, it is too slow and is in any event 95% present at birth in the three levels of the auditory pathways [14]. Animal studies of prenatal development of the auditory system show that ganglion fibres penetrate both the cerebral and cochlear levels, and influence the development of both the outer and the central parts of the auditory system [36]. The synapses appear in the foetus at 6–7 months, but the maximum period of histological differentiation coincides with the beginning of auditory function [24].

Once the interaction between the central and peripheral nervous systems has been established, there is a refinement of hearing capacity. On the 3rd day after birth, there is a statistically significant reduction of all wave latencies, even at 20 dB HL, and a further reduction of PIII and PV latencies at 70 dB HL after the 4th day. These observations are consistent with BAEP changes found in infants of higher gestational age: these infants show increased latencies of PI, PII, PIV, NIII, NIV and NV at 70 dB HL, and a reduced amplitude of IV and V waves at all intensities. These peripheral and central effects may be attributed to the physiological sensory deprivation to which the foetus is subjected during pregnancy.

BAEP recordings in full-term infants, repeated at intervals of a few hours during the first days of life, add to the information on interactive phenomena which occur immediately after birth, and support the notion of a concurrent peripheral and central maturation, with emphasis initially on the central pathways. Even during the first days of life a characteristic and varied trend could be detected in a wide range of BAEP parameters. The constant presence after birth of some waves, such as NII, could be of clinical relevance. These normative data are also useful in providing values for those newborn infants at risk in intensive care.

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