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Comparison of maturational process of hearing threshold in early life between at-risk and low-risk preterm infants

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ABSTRACT

Aim: To detect any abnormality in the maturational process of hearing threshold during the early life in at-risk preterm infants.
Study design: The threshold of brainstem auditory evoked response was recorded and analyzed longitudinally from 30 to 42 weeks of postconceptional age in 357 at-risk infants born at 23–36 weeks of gestation. The results were compared with those in 82 low-risk infants born at 30–42 weeks at various postconceptional ages.
Results: From 31 to 42 weeks, the response threshold in the at-risk infants was consistently slightly higher than that in the low-risk infants. No statistically significant difference was found between the two groups of infants at any designated postconceptional ages. The threshold in the at-risk infants born at 23–29 weeks of gestation tended to be higher than those born at 30–36 weeks at various postconceptional ages, but the difference did not reach statistical significance. There was also no significant difference in the slope of BAER threshold-age function between the at-risk infants, irrespective of gestational ages, and the low-risk infants.
Conclusion: During the early life, hearing threshold in at-risk preterm, mainly very preterm, infants is marginally elevated, but the maturational process of the threshold is generally similar to that in low-risk infants, without notable abnormality.

1. Introduction

The organ of human Corti is near maturation at 25 weeks of gestation, and cochlear development continues at least into the third trimester [1]. Fetal blink-startle responses to vibro-acoustic stimulation are first elicited between 24 and 25 weeks of gestation and are present consistently after 28 weeks. From 26 weeks, fetal heart rate starts to change in response to vibro-acoustic stimulation. In terms of sensitivity and sound resolution the peripheral hearing system is already relatively mature by around 30 weeks. During the early life hearing threshold generally decreases with increasing age.

As a well-documented good objective estimate of peripheral auditory sensitivity, the threshold of brainstem auditory evoked response (BAER) has been widely used to assess peripheral hearing in infants and children [2–8]. The BAER can be recorded in preterm infants at as early as 26–28 weeks of gestation [5,9,10]. Shortly after birth, the threshold of BAER in preterm infants is higher than that in term infants, and then decreases with increasing age, from 30 to 40 dB nHL at 28 weeks to 10–20 dB at term date. After term, BAER threshold continuously decreases, though more slowly, up through several months to 1 year of age [11–13]. Our recent studies have shown that BAER threshold in preterm infants decreases from a mean 28 dB at 28 weeks of postconceptional age to around 13 dB at 42 weeks [5,8]. During the preterm period, the threshold changed at around 1 dB/week.

Hearing threshold in the infant can be affected by various unfavorable perinatal conditions or problems. Preterm infants who are born with unfavorable perinatal conditions or problems (i.e. at-risk preterm infants) are prone to hearing impairment, and their hearing threshold is often higher than normal infants [14–21]. To date, it remains unclear whether there is any abnormality in the maturational process of hearing threshold in at-risk preterm infants. To address this issue, on the basis of the data collected in the previous two studies [5,8], we recruited more infants, mainly those who did not have any major unfavorable perinatal conditions except for preterm birth (i.e. low-risk preterm infants) for normal maturation. Comparison of the early maturational process of BAER threshold was made between the at-risk and low-risk infants to define any differences and identify any abnormality in the at-risk infants. Comparison of the maturation was also made between the at-risk infants born at different gestations to examine whether the at-risk infants who are born at more preterm are more prone to maturational abnormality than those born at less preterm.

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2. Subjects and methods

2.1. Subjects

There were 357 at-risk preterm infants, ranging in gestation between 23 and 36 weeks. Most (n = 339) of these infants were from our previously two reported studies [5,8]. All had one or more associated unfavorable perinatal conditions or problems. The normal controls were 82 low-risk infants who did not have any major perinatal conditions or problems. It is known that preterm infants born at less than 30 weeks of gestation are often associated with significant perinatal conditions or problems. There are hardly any real low-risk infants. Thus, we recruited the low-risk or health infants from those who had a gestation of 30 weeks or greater (30–42 weeks); 43 from the John Radcliffe Hospital, University of Oxford, and 39 from the Children's Hospital of Fudan University. Informed consent was obtained from the parents before study entry.

The infants' data, including physiological parameters and testing occasions at each designated postconceptional age are given in Table 1. All infants were longitudinally studied from 30 to 42 weeks of postconceptional age. The threshold of BAER was obtained at 30, 31–32, 33–34, 35–36, 37–38, 39–40, and 41–42 weeks of postconceptional age to assess detailed age-related changes in the threshold from early preterm until late term. Based on the infants' clinical conditions and the availability of testing personnel, the infants were re-tested every 1–3 weeks. In total, 1170 BAER testing occasions were obtained at the designated postconceptional ages in the at-risk infants and 189 occasions in the low-risk infants.

2.2. Procedures of recording BAER and obtaining the threshold

The basic study procedures, approved by the Central Oxford Research Ethics Committee and the Ethics Committee of Children's Hospital of Fudan University, were the same as those previously reported [5,8]. BAER was recorded and analyzed using the Portable Evoked Potential System (Nicolet Biomedical Inc. Madison, WI, USA) in a quiet room without any other electrical equipment next to the nursery. The infants lay supine in a cot. Three gold-plated disk electrodes were placed at the middle forehead (positive), the ipsilateral earlobe (negative) and the contralateral earlobe (ground). Inter-electrode impedances were reduced to and maintained at 5 kΩ or less. The left ear was tested in all infants to keep the consistency in testing ear, avoiding the ear difference in BAER threshold (i.e. insure that estimates of population statistics were not biased by BAER difference between the two ears) and save recording time, which was the same as our previous BAER studies [5,8].

A TDH 39 headphone was comfortably placed over the ear with a great care to avoid pressing the ear canals. The acoustic stimuli were rarefaction clicks of 100 μs, delivered at a repetition rate of 21 per second monaurally through the headphone. Sweep duration was set as 12 ms. BAER recording was started after the infant fell asleep naturally. The evoked brain responses to 2048 clicks were amplified and filtered at 100–3000 Hz, and averaged for each run. Two runs of BAER recordings were made at each stimulus condition for reproducibility. During the recording, the position of the headphone was constantly monitored to avoid the headphone slipping off the position.

To determine the BAER threshold, click intensity was started at 60 dB normal hearing level (nHL) with 0 nHL referring to the average BAER threshold in young adults with normal hearing. Once BAER waves I, III, and V were clearly identified in the recorded BAER waveform, the intensity was then decreased to 40 dB nHL, and further decreased by 5–10 dB steps until no clear wave V was identified in the recorded waveform. The threshold was defined as the lowest intensity of the clicks that produced visible and reproducible wave V.

2.3. Data analysis

The data from the infants newly recruited and those previously reported [5,8] were pooled together for detailed analysis. The BAER threshold (mean and SD) obtained at each designated postconceptional age was compared between the at-risk and low-risk infants using analysis of variance to define any differences between them at the same postconceptional age. The at-risk infants born at less preterm (30–36 weeks of gestation) and those born at more preterm (23–29 weeks of gestation) were further, respectively, compared with the

Table 1
Demographic data of infants.

Postconceptional age / Gestation	30 w mean ± SD	31–32 w mean ± SD	33–34 w mean ± SD	35–36 w mean ± SD	37–38 w mean ± SD	39–40 w mean ± SD	41–42 w mean ± SD
Testing occasions							
Low-risk	14	20	32	36	26	34	27
At-risk 30–36 w	30	73	159	167	102	84	68
23–29 w	52	71	74	84	92	73	41
Gestation (w)							
Low-risk	30.5 ± 0.5	31.3 ± 0.5	32.5 ± 1.2	33.8 ± 1.5	35.7 ± 2.6	36.2 ± 3.4	37.1 ± 3.1
At-risk 30–36 w	30.3 ± 0.5	31.2 ± 0.8	31.7 ± 1.3**	32.6 ± 1.8**	33.1 ± 2.1***	33.4 ± 1.9***	33.2 ± 2.1***
23–29 w	27.5 ± 1.2***	27.6 ± 1.1***	27.3 ± 1.3***	27.3 ± 1.5***	27.6 ± 1.5***	27.6 ± 1.5***	27.5 ± 1.7***
Birthweight (g)							
Low-risk	1751 ± 119	1645 ± 211	1898 ± 344	2041 ± 408	2588 ± 793	2783 ± 977	3054 ± 861
At-risk 30–36 w	1570 ± 238*	1591 ± 308	1676 ± 334**	1726 ± 452**	1694 ± 434***	1740 ± 549***	1683 ± 406***
23–29 w	1217 ± 262***	1225 ± 240***	1145 ± 274***	1115 ± 243***	1075 ± 235***	1091 ± 292***	995 ± 268***
HC at testing (cm)							
Low-risk	29.0 ± 0.5	30.0 ± 1.5	30.9 ± 1.4	31.6 ± 2.0	33.3 ± 1.6	34.5 ± 2.1	35.1 ± 1.5
At-risk 30–36 w	28.9 ± 1.7	29.5 ± 1.8	30.4 ± 1.6	31.3 ± 1.6	32.2 ± 1.6	33.5 ± 1.7	34.9 ± 2.9
23–29 w	27.1 ± 1.5**	27.8 ± 2.1**	29.4 ± 2.0***	30.3 ± 1.7**	31.4 ± 2.4**	32.1 ± 3.1***	34.3 ± 2.3
Gender: M/F							
Low-risk	9/5	11/9	18/14	22/14	14/12	16/18	12/15
At-risk 30–36 w	18/12	41/32	75/84	92/75	55/47	38/46	40/28
23–29 w	29/23	40/31	40/34	49/35	49/43	39/34	22/19

w refers to week(s), HC refers to head circumference.
* $P < 0.05$,
** $P < 0.01$, and
*** $P < 0.001$ in analysis of variance for comparison between at-risk infants and low-risk infants.