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Neural conduction impairment in the auditory brainstem and the prevalence in term babies in neonatal intensive care unit

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HIGHLIGHTS

- Term babies in neonatal intensive care unit (NICU) are at high risk of brain damage and neurological impairment.
- The present study found that neural conduction in the auditory brainstem was impaired in NICU term babies, which occurred in one-third babies.
- NICU term babies are at risk of the impairment and the high rates in maximum length sequence brainstem auditory evoked response enhance early detection of the impairment.

ABSTRACT

Objective: To detect neural conduction abnormality in the auditory brainstem in term babies in the neonatal intensive care unit (NICU), determine prevalence of the abnormality, and assess if maximum length sequence (MLS) technique improves early detection of the abnormality.
Methods: One hundred and six term babies were recruited, and studied by recording and analysing MLS brainstem auditory evoked response (BAER). Interpeak intervals were analysed in detail, which were then compared with those in normal term babies.
Results: Wave V latency and I–V and III–V intervals in MLS BAER were increased in the NICU term babies at all click rates 91-910/s, particularly at 455 and 910/s ($p < 0.05$–0.001). No major abnormalities were found in wave I and III latencies and I–III interval. The abnormal increase in I–V and III–V intervals were seen in significantly more cases at 455 and 910/s in MLS BAER than at 21/s in conventional BAER ($\boldsymbol{X}^2 = 10.92$–13.88, all $p < 0.01$). As a whole, 38 (35.8%) of the NICU babies had abnormal III–V and/or I–V intervals in MLS BAER, which was significantly more than 13 (12.2%) in conventional BAER ($X^2 = 16.14$, $p < 0.01$).
Conclusion: There is neural conduction impairment in the auditory brainstem in NICU term babies, which occurs in one-third of these babies.
Significance: Term babies in NICU are at risk of neural conduction impairment in the auditory brainstem. High click rates in MLS BAER enhance early detection of the impairment.

1. Introduction

The neonatal brain is known to be at risk of damage as a result of various perinatal problems that directly or indirectly affect the immature brain. Studies using the brainstem auditory evoked response (BAER), an objective test to assess the functional integrity of the brainstem and auditory pathway, has shown that the neonatal brainstem is susceptible to some unfavourable perinatal conditions, typically hypoxia–ischemia, or asphyxia, and hyperbilirubinemia (Hall III, 2007; Wilkinson and Jiang, 2006). Conventional BAER, i.e. the BAER obtained using conventional averaging techniques, has relative high false negative results, and cannot effectively detect some neuropathology (Majnemer and Rosenblatt, 1996, 2000; Wilkinson and Jiang, 2006). Since early 1980's, the maximum length sequence (MLS) has been developed to study the auditory evoked responses to increase understanding of the functional integrity of the auditory system (Bell et al., 2006; Jiang, 2012; Jirsa, 2001; Lasky, 1997; Nagle and Musiek, 2009). More recently, the MLS technique has been

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introduced to study the BAER in babies with perinatal problems. These studies have proven that the MLS technique enhances detection of some neuropathology in the neonatal brain, typically hypoxia–ischemia (Jiang, 2012; Jiang and Chen, 2014; Jiang et al., 2003, 2005, 2010; Wilkinson et al., 2007).

Newborn babies, including term babies, who are admitted to the neonatal intensive care unit (NICU) have various problems or complications, some of which may damage the immature brain, typically hypoxia–ischemia, hyperbilirubinemia, and meningitis (Majnemer and Rosenblatt, 1996, 2000; Wilkinson and Jiang, 2006). Prompt detection of neonatal brain damage and understanding of prevalence of the damage is of great importance for early intervention and proper management to protect the immature brain and reduce any damage. Previous MLS BAER studies revealed that there is functional impairment of the brainstem in term babies after perinatal hypoxia–ischemia (Jiang et al., 2003, 2010). It is of interest to know if perinatal problems or conditions other than hypoxia–ischemia also have such impairment.

We carried out a detailed study of MLS BAER in term babies who were admitted to the NICU due to perinatal problems or conditions other than hypoxia–ischemia. Our primary aims were to detect any abnormality in neural conduction in the auditory brainstem in NICU term babies and determine prevalence of the abnormality. This was mainly achieved by analyzing interpeak intervals, which reflect neural conduction in the auditory brainstem, in MLS BAER. Comparison of the prevalence of abnormal findings in MLS BAER was made with that in conventional BAER to determine if the MLS technique improves early detection of brainstem conduction abnormality in individual babies.

2. Patients and methods

2.1. Subjects

The subjects' data are summarized in Table 1. Since hypoxia–ischemia is a known high risk factor of brainstem auditory impairment in term babies, babies were excluded from the study entry if he or she had hypoxia–ischemia, including clinical signs of HI (hypotonia with reduced or no spontaneous movements, increased threshold for primitive reflexes, lethargy or comatose, absence or very weak suck and requirement of tube feeds, or seizures), umbilical cord blood pH < 7.10, and depressed Apgar score (less than 6 at 5 min), as defined in our previous studies (Jiang et al., 2003, 2010). Excluded were also those who exposed to potentially ototoxic drugs such as aminoglycosides (mainly amikacin), and diuretics (furosemide), Genetic and metabolic disorders associated with hearing loss. Any babies who had a BAER threshold ⩾40 dB normal hearing level (nHL) had been excluded from study entry to avoid any significant effect of peripheral hearing problems on the measurements of MLS BAER wave components so as to analyse MLS BAER variables more reliably and accurately, the same as our previous MLS BAER studies (Jiang, 2012; Jiang and Chen, 2014; Jiang et al., 2003, 2005, 2010; Wilkinson et al., 2007). All our babies passed the neonatal hearing screening. Informed consent of parents was obtained for each baby before study entry. This study was approved by the Central Oxford Research Ethics Committee and the Ethics Committee of the Children's Hospital of Fudan University.

Table 1
Subjects' data in NICU term babies and normal term babies.

	NICU	Normal
Gender (n)		
Male/female	47/59	19/26
Gestational age (weeks)		
Mean ± SD	39.6 ± 1.3*	39.1 ± 1.5
Range	37–42	37–42
Postconceptional age (weeks)		
Mean ± SD	39.7 ± 1.4	39.4 ± 1.3
Range	37–42	37–42
Birthweight (g)		
Mean ± SD	3384 ± 603	3451 ± 471
Range	2485–4640	2565–4539
BAER threshold (dB nHL)		
Mean ± SD	13.1 ± 8.1+	11.0 ± 5.4
Range	5–35	0–20

+NICU babies who had a BAER threshold ⩾40 dB nHL had been excluded from study entry and data analysis to avoid any significant effect of peripheral hearing problems on MLS BAER wave components.

* $P < 0.05$ (t-test) for comparison between NICU and normal term babies.

The study group (NICU babies) consisted of 106 babies born between 37 and 42 weeks (39.6 ± 1.3 weeks) of gestation, determined by the best estimate of last menstrual period, obstetrical record, and clinical examination. Birthweight ranged between 2485 and 4640 g (3284 ± 603 g). Forty-eight babies were recruited from the NICU of Children's Hospital of Fudan University in Shanghai. The remaining 58 babies were recruited from the NICU of the John Radcliffe Hospital of Oxford University in Oxford. Of the 58 babies, 41, who had both conventional BAER recordings and MLS BAER recordings, were from those who were briefly reported before (Jiang et al., 2013). The NICU term infants had various perinatal problems or complications (e.g. hypotension, hypoglycaemia, meconium aspiration syndrome, sepsis, metabolic acidosis, pneumonia, and haemolytic or non-hemolytic hyperbilirubinemia). Some of the subjects had more than one perinatal condition.

The control group (normal term babies) was 45 healthy term babies, 24 from the neonatal unit of Children's Hospital of Fudan University in Shanghai and the remaining 21 from the neonatal unit of the John Radcliffe Hospital of Oxford University in Oxford. The gestational age ranged between 37 and 42 weeks (39.1 ± 1.4 weeks), which was marginally smaller, though statistically significant, than in the study group (Table 1). Their birth weights were between 2565 and 4539 g (3464 ± 473 g), which did not differ significantly from the study group (Table 1). None had any major perinatal conditions. At time of MLS BAER testing, monaural hearing thresholds in the controls were all 20 dB nHL or less.

2.2. Procedures of recording MLS BAER

The procedures and instrumentation of the recording were the same in the two institutes (Children's Hospital of Fudan University and the John Radcliffe Hospital of Oxford University). The Nicolet Spirit 2000 Portable Evoked Potential System (Nicolet Biomedical Inc. Madison, WI, USA) was used to record and analyze MLS BAER and conventional BAER. For all subjects, only the left ear was tested to keep consistency of recording conditions and reduce recording time, the same as in our previous MLS BAER studies (Jiang and Chen 2014; Jiang et al., 2003, 2005, 2010).

All babies were studied between days 2 and 5 after birth. There were no significant differences in the postconceptional ages between the NICU babies (39.7 ± 1.4 weeks) and the normal control babies (39.4 ± 1.3 weeks). Three gold-plated disk electrodes were placed, respectively, at middle forehead (positive), ipsilateral earlobe (negative) and contralateral earlobe (ground). The impedance between any two electrodes was reduced to 5 kΩ or less, which were remained during the whole session of BAER recording. Sweep duration was 24 ms. Recording of the BAER started immediately after the infant fell asleep naturally, often after a feed without using any sedatives. The infant remained asleep throughout the recording session.

Rarefaction clicks with a duration 0.1 ms were delivered monaurally through a TDH 39 headphone to the left ear. We first recorded conventional BAER with 21/s clicks as a basic repetition