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Small-for-gestation birth exerts a minor additional effect on functional impairment of the auditory brainstem in high-risk babies born at late preterm

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HIGHLIGHTS

- Auditory brainstem is impaired in high-risk SGA late preterm babies.
- SGA birth exerts a minor additional effect on the impaired auditory brainstem in late preterm babies.
- Neuroprotective measures should mainly target at associated perinatal problems, although the relative minor SGA effect cannot be ignored.

ABSTRACT

Objective: To address if small-for-gestational-age (SGA) significantly affects the developing auditory brainstem in late preterm babies with perinatal problems (i.e. high-risk), providing valuable information for management of such babies.
Methods: SGA and appropriate-for-gestational age (AGA) babies born at 33–36 weeks of gestation were studied at term using maximum length sequence brainstem auditory evoked response in response to 91–910/s clicks.
Results: Compared with AGA late preterm babies without perinatal problems (i.e. low-risk), the high-risk SGA babies manifested a significant increase in wave V latency and I–V interval at all 91–910/s clicks, and III–V interval at 455 and 910/s. The amplitude was smaller for wave I at 227 and 910/s, wave III at 910/s and wave V at 227 and 910/s. Compared with low-risk SGA babies, the high-risk SGA babies showed similarly abnormalities. Compared with high-risk AGA babies, the high-risk SGA babies manifested slightly different abnormalities.
Conclusions: Brainstem auditory response was abnormal in high-risk SGA late preterm babies. The abnormalities, suggesting brainstem auditory impairment, were slightly different from high-risk AGA late preterm babies.
Significance: SGA birth exerts a minor additional effect on the impaired auditory brainstem in high-risk babies born at late preterm. For these babies, neuroprotective measures should mainly target at associated perinatal problems, although the relatively minor adverse SGA effect cannot be ignored.

1. Introduction

In the last decade, there have been increased reports on neurodevelopmental outcome infants or children who are born at late preterm (usually 33–36 weeks of gestation) (Petrini et al., 2009; Romeo et al., 2010; Talge et al., 2010). However, very limited information is available regarding neurodevelopment for late preterm babies who are born of small-for-gestational age (SGA) due to intrauterine growth restriction (IUGR). SGA is a intrauterine detrimental factor that adversely affect foetus's and baby's brain maturation, which could lead to maturational delay and neurodevelopmental deficits (Arcangeli et al., 2012; Baschat, 2011; Batalle et al., 2012; Løhaugen et al., 2013; Morsing et al., 2011; Østgård et al., 2014; Parra-Saavedra et al., 2014; Réveillon et al., 2013). Whether SGA birth affects functional status and maturation of the auditory brainstem in babies who are born at late is to be studied.

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A number of previous authors have reported their studies of brainstem auditory evoked response (BAER), processed using conventional averaging technique (ie., conventional BAER), in SGA preterm babies or children, and found some abnormalities (Delorme et al., 1987; Henderson-Smart et al., 1991; Jiang, 2015; Jiang et al., 2004; Kesson et al., 1985; Kiefer et al., 2008; Kohelet et al., 2000; Pettigrew et al., 1985; Saintonge et al., 1986; Sarda et al., 1992; Soares et al., 1988; Todorovich et al., 1987). With the maximum length sequence (MLS) BAER – a relatively new technique of recording and processing BAER to increase detectability of abnormalities, we have recently studied brainstem auditory function in SGA late preterm babies who had no major perinatal conditions or problems, i.e. low-risk SGA babies (Jiang and Li, 2015). No major abnormalities were found, except for an increase in wave III and V latencies and I–V interval at certain click rates, suggesting a mild degree of maturational delay in the brainstem auditory pathway. Thus, SGA occurring in late preterm babies has a minor adverse effect on neural maturation of the immature brainstem auditory pathway. So far, there is a lack of BAER reports specifically in SGA late preterm babies who have associated perinatal problems that may affect the auditory brainstem, i.e. high-risk SGA late preterm babies.

Recent studies have shown that BAER and MLS BAER in high-late preterm babies are abnormal, typically an increase in wave V latency, III–V and I–V interpeak intervals, and III–V/I–III interval ratio, suggesting impaired brainstem auditory function (Jiang, 2012b; Jiang et al., 2011,2012). It is unclear whether SGA birth could exert an additional effect on the impaired brainstem auditory function in these babies. To address this issue, on the basis of the subjects and data we previously reported (Jiang et al., 2012), we recruited more subjects, mainly high-risk SGA late preterm babies, and conducted a detailed analysis of the accumulated data. The data of the high-risk SGA late preterm babies were first compared with those of age-matched late preterm babies born with a birthweight appropriate-for-gestational age (AGA) and without major perinatal problems that may affect the auditory brainstem (i.e. low-risk) to detect any abnormalities in the SGA babies. The data were also compared with those of low-risk SGA late preterm babies to examine if associated perinatal problems in high-risk SGA babies exert a major effect on the functional impairment in SGA babies. Finally, the data of the high-risk SGA babies were directly compared with those of high-risk AGA late preterm babies to examine if SGA exerts any additional effect on the functional impairment of the auditory brainstem in high-risk late preterm babies. The knowledge obtained should provide valuable information for whether neuroprotective measures in high-risk SGA late preterm babies should mainly target at SGA or other associated perinatal problems.

2. Subjects and methods

2.1. Study groups

High-risk SGA late preterm babies (high-risk SGA-LP group): SGA status was defined as birthweight less than 3rd centile for gestation using Babson and Benda growth chart by Fenton (2003). We recruited 45 SGA babies who were born between 33 and 36 weeks (34.5 ± 1.0 weeks) of gestation, determined by the best estimate of last menstrual period, obstetrical record, and clinical examination. Birthweight ranged in 758–1985 g (1423 ± 256 g). These babies had various perinatal conditions or problems that may affect the auditory brainstem, mainly including preterm rupture of membranes, apnea, metabolic acidosis, patent ductus arteriosus, perinatal asphyxia, hypoglycaemia, respiratory distress syndrome, sepsis, pneumonia, hyperbilirubinaemia (Hall, 2007; Jiang, 2015; Wilkinson and Jiang, 2006).

High-risk AGA late preterm babies (high-risk AGA-LP group): AGA status was defined as birthweight greater than 10th centile for gestation using Babson and Benda growth chart by Fenton (2003). There were 47 babies born between 33 and 36 weeks (34.7 ± 1.1 weeks) of gestation, which did not differ significantly from that in the high-risk SGA-LP group using analysis of variance. Birthweight ranged between 1689 and 3210 g (2318 ± 392 g), which was significantly greater than that in the SGA babies ($P < 0.001$). Similar to those in the high-risk SGA-LP group, the AGA-LP babies also had one or more perinatal problems or conditions.

Low-risk SGA late preterm babies (low-risk SGA-LP group): There were 42 SGA babies who were born between 33 and 36 weeks (34.2 ± 0.8 weeks) gestation, without any major perinatal problems or conditions. Birthweight ranged between 783 and 1927 g (1472 ± 243 g), which was less than 3rd centile for gestation using Babson and Benda growth chart by Fenton (2003). Neither the gestation, nor the birthweight differed significantly from that in the high-risk SGA-LP group.

Low-risk AGA late preterm babies (low-risk AGA-LP group): There were 36 babies who had no major perinatal problems or conditions. Gestation also ranged between 33 and 36 weeks (34.2 ± 0.9 weeks), and birthweight between 1680 and 2965 g (2,255 ± 411 g) that was greater than 10th centile for gestation, based on Babson and Benda growth chart by Fenton (2003). The gestation did not differ significantly from that in the high-risk SGA-LP group, but the birthweight was significantly greater than that in the high-risk SGA-LP group ($P < 0.001$).

These subjects were recruited from the neonatal unit of the Children's Hospital, regardless perinatal problems but based on the availability of the study personnel (Cui Wang and 2 other medical postgraduates who were experienced in recording MLS BAER and acknowledged). Informed consent of parents was obtained for each subject before study entry. All subjects were examined at term equivalent age (37–42 weeks postconceptional age – PCA). Significant peripheral hearing is known to affect MLS BAER waveform morphology and make it difficult to accurately and reliably identify BAER wave components, particularly wave I (Jiang, 2012a, 2015). It is therefore important in MLS BAER study to excluding any subjects who have significant peripheral hearing loss. In this study, babies who had a BAER threshold $\geqslant$40 dB normal hearing level (nHL) were excluded from study entry to minimize any significant effect of peripheral hearing problems on the measurements of MLS BAER wave components.

2.2. Recording of MLS BAER

The general study procedures, approved by the Ethics Committee of the Children's Hospital of Fudan University in Shanghai, were the same as we previously reported (Jiang and Li, 2015; Jiang et al., 2012, 2015; Wilkinson et al., 2007). The recording, using Nicolet Spirit 2000 Portable Evoked Potential System (Nicolet Biomedical Inc. Madison, WI, USA), was made while the infant fell asleep naturally, often after a feed. No sedation was used. As in our previous MLS BAER studies, only the left ear was tested for all subjects to keep consistency in recording conditions and reduce recording time. Following site skin preparation, 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 kept <5 kΩ. Recording of MLS BAER commenced immediately after the babies fell asleep. Sweep duration was set as 24 ms for the recording time window. The sampling rate was 16 kHz.

The acoustic stimuli were rarefaction clicks with a duration 100 μs, delivered monaurally through a TDH 39 headphone to the left ear. Initial click intensity was 60 dB nHL for all babies.

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