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Brain-stem auditory function in very preterm infants with chronic lung disease: Delayed neural conduction

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Abstract

Objective: To examine brain-stem auditory function at term in very preterm infants who suffered chronic lung disease (CLD).
Methods: Brain-stem auditory evoked response (BAER) was recorded at term with clicks in 25 very preterm infants with CLD and no concomitant other major perinatal problems.
Results: Compared to those in normal term controls, BAER wave V latency and I–V and III–V interpeak intervals in the CLD infants increased significantly (ANOVA $P<0.01$–0.001). III–V/I–III interval ratio also increased significantly ($P<0.01$). The latencies of waves I and III did not differ significantly from the controls. However, no abnormalities were found in BAER wave amplitudes. These BAER findings, obtained at 21/s clicks, were also seen at the rates 51 and 91/s, although the increase in III–V interval tended to be more significant. Click rate-dependent changes in BAER variables in the CLD infants were generally similar to the controls, with slight differences.
Conclusions: BAER components, mainly reflecting central auditory function, increased significantly. The increase in wave V latency and I–V interval is due to the increase in III–V interval.
Significance: Neural conduction in the more central portion of the brain-stem auditory pathway is delayed and thus brain-stem auditory function is impaired in CLD infants.

Keywords: Neonatal chronic lung disease; Central auditory impairment; Neural development; Brain-stem auditory evoked response; Evoked potentials; Preterm infant.

1. Introduction

Newborn infants who suffer serious respiratory problems and need high oxygen concentrations for a prolonged period, typically neonatal chronic lung disease (CLD), may be at risk of neurodevelopmental deficits. Neonatal CLD, defined as the requirement for supplemental oxygen or ventilatory support beyond 36 weeks postconceptional age, is a major lung disease in infants who are born very preterm (Greenough, 1999; Northway et al., 1990). It often continues beyond the full term period. Recently studies have shown that neonatal CLD has a significant adverse influence on growth and development of the immature brain (Katz-Salamon et al., 2000; Murphy et al., 2001; Perlman, 2001; Vohr et al., 2000). An EEG sleep study suggested that neurophysiological organization is adversely affected in neonates with CLD (Scher et al., 1992). Follow-up studies showed that infants with CLD had poorer growth and were more likely to have developmental deficits, including severe visual impairment, cerebral palsy, abnormal muscle tone, mental retardation and learning disabilities (Singer et al., 1997; Skidmore et al., 1990; Vaucher et al., 1988). However, it is not known whether these infants are also at risk of auditory, particularly central, auditory deficits.

Infants who suffer CLD often experience frequent episodes of hypoxaemia or prolonged hypoxaemia. It is well known that severe hypoxemia disturb the metabolism

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of neurons and depress the electrophysiological function of synapses (Johnston et al., 2001). Like other central nervous systems, the central auditory system is also sensitive to hypoxemia. Along with some other studies, our recent studies have shown that hypoxia–ischaemia has a major effect on the neonatal central auditory system (Jiang et al., 2001, 2004, 2005). It is hypothesised that the hypoxaemia associated with neonatal CLD may also affect the central auditory system. So far, such studies are lacking.

The brain-stem auditory evoked response (BAER) is a non-invasive and objective test that reflects functional integrity and development of the brain-stem auditory system (Chiappa, 1990; Henderson-Smart et al., 1991; Jiang et al., 1998; Pratt et al., 1981). The maturational changes in the BAER reflect neurophysiological maturation of the brain-stem auditory system, including peripherally maturation of the cochlea and centrally the increasing synaptic efficiency, dendritic growth and axonal myelination. In both animal models and human infants the BAER has been shown to be a valuable method to study the influence of hypoxia or hypoxia–ischaemia on the developing auditory system, including the neural pathway and the cochlea (Freeman et al., 1991; Hecox et al., 1981; Inagaki et al., 1997; Jiang et al., 2001, 2004, 2005; Kileny et al., 1980; Sohmer et al., 1986a,b). It is likely that the BAER could also be a valuable method to study the influence of prolonged or chronic hypoxaemia on the auditory system in infants who suffer neonatal CLD. We therefore used the BAER to study the influence of neonatal CLD on brain-stem auditory function at term in infants with neonatal CLD to shed light on the influence of neonatal CLD on the central auditory system.

2. Materials and methods

2.1. Subjects

2.1.1. Very preterm infants with neonatal CLD

We recruited 25 infants who required supplementary oxygen or ventilatory support beyond 36 weeks of postconceptional age to maintain $PaO_2 > 50$ mmHg. All had clinical signs of chronic lung respiratory disease and radiographic evidence of CLD (persistent strands of density in both lungs). At the time of BAER testing, clinical signs of CLD were still present in these infants. There were 12 boys and 13 girls. Their gestational age ranged between 23 and 30 weeks (28.0 ± 1.9 weeks) and birthweight ranged between 559 and 1500 g (1115 ± 254 g).

There are many other major perinatal complications, including congenital malformation and congenital or perinatal infection of the central nervous system, hyperbilirubinaemia, hypoxic-ischaemic encephalopathy, neonatal meningitis and persistent pulmonary hypertension, may affect functional integrity of the auditory pathway. In this study, infants who had any of the above complications were excluded. In order to minimize any confounding effect of major brain lesions to the BAER, infants who had severe (grade III–IV) intraventricular haemorrhage (IVH) and periventricular leucomalacia (PVL) were also excluded.

2.1.2. Normal term controls

Forty healthy newborn infants who had no major perinatal condition or complications served as normal controls. Their gestational age ranged between 37 and 41 weeks (38.8 ± 1.4 weeks). All these infants had a monaural BAER threshold, defined as the minimum intensity of clicks that evoked reproducible wave V at 21/s, of less than 20 dB normal hearing level (nHL) at the time of testing.

2.2. Recording of BAER

The study protocol and procedures were approved by the Central Oxford Research Ethics Committee. Informed consent of parents and the paediatrician in charge was obtained for all subjects. Recording of the BAER was performed at term in all subjects; in the very preterm infants with neonatal CLD the BAER was recorded between 37 and 42 weeks of postconceptional age (39.6 ± 1.8 weeks), and in the term controls it was recorded between day 1 (at least 20 h after birth to allow absorption of any residual amniotic fluid in the middle ear) and day 3 after birth (39.3 ± 1.4 weeks). No statistically significant difference was found between the two groups of infants in the postconceptional ages of BAER testing.

All infants, who lay supine in a cot, were tested in a quiet room. Prior to BAER recording the auditory meatus was inspected and cleaned of any vernix or wax. Recording of the BAER was started shortly after the infant fell asleep naturally, often after a feed. No sedatives were used. A Spirit 2000 Evoked Potential System (Nicolet Biomedical, Inc. Madison, WI, USA) was used to record and analyse the BAER.

The left ear was tested in all infants, although the right ear was also tested in some infants. Three gold-plated disk electrodes were placed at the middle forehead (positive), the ipsilateral earlobe (negative) and the contralateral earlobe (ground), respectively. Inter-electrode impedances were maintained at <10 kΩ, often <5 kΩ. Acoustic stimuli were rarefaction clicks, generated by rectangular pulses 100 μs in duration and delivered monaurally to the TDH 39 earphones.

The intensity of the clicks was 60 dB nHL for all infants. Higher intensities were also used in the very preterm infants with CLD who had a BAER threshold >20 dB nHL and a prolonged wave I latency, suggesting a conductive hearing loss, to obtain reliable BAER waveform with clearly identifiable waves I, III and V ($n=6$). Three repetition rates of clicks were presented in the order of 21, 51 and 91/s in the first run and in reverse order in the second run.

Brain responses evoked by the clicks were amplified, bandpass filtered between 100 and 3000 Hz, and inputted to the averager. If the data exceeded 91% of the sensitivity