Development of visual evoked potentials in neonates
A study using light emitting diode goggles

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SUMMARY We used a signal averager with light emitting diode goggles as the photostimulator to study the development of the visual evoked potentials in 40 normal neonates of between 23 and 42 weeks' gestation. All except two infants of less than 24 weeks' gestation had replicable visual evoked potentials. A negative peak of latency (mean (SD), 308 (21) msec) was present in all infants, but the development of the primary positive peak depended on maturity. Only infants of 37 weeks or more had a consistent positive peak of latency (mean (SD), 220 (22) msec). The practical simplicity and reliability of this technique has distinct advantages over previous conventional recording systems. Neonatal visual evoked potentials are shown to change with maturity.

Visual evoked potentials to light flashes recorded from surface scalp electrodes have been shown to reflect cerebral cortical activity and brain maturation in preterm and term infants. Previous studies have been conducted using either conventional electroencephalographic or averaging recording techniques, with stroboscopic light stimulation. Although this method has gained wide application and has proved a useful diagnostic tool in adult and paediatric neurology, it has not been used much in neonatal units. This could be due to the cumbersome equipment, long recording time (up to five hours), and the variability of neonatal visual evoked potentials shown in earlier studies. Since the development of more compact, technically superior evoked potential recording systems, however, very few replications of these early studies have been undertaken.

The use of light emitting diodes as the light stimulus has further simplified the technique, and it has been shown that reproducible visual evoked potentials can be elicited using these. Only one study, however, has reported this method in newborn infants.

The purpose of the present study was: (a) to assess the feasibility and practicality of using light emitting diode goggles and newer technology to record visual evoked potentials in a neonatal unit; (b) to determine if the visual evoked potentials could be recorded reliably in this population; and (c) to study the development of visual evoked potentials in relation to gestational age.

Patients and methods

The study was conducted in the Neonatal Intensive Care Unit of this hospital and in the postnatal wards at Mount Sinai Hospital, Toronto. This project was approved by the hospitals' ethical committees, and written parental consent was obtained.

Forty neurologically normal neonates of between 23 and 42 weeks' gestation (mean (SD), 34.5 (5.3) weeks) were studied within two weeks of birth. One preterm infant was retested after three weeks. Gestational age was assessed by maternal menstrual history or Dubowitz score. Twenty-three infants were preterm with eight of less than 31 weeks' gestation, and 17 were term. All had Apgar scores of 5 or more at five minutes. All infants with birthweights less than 1500 g had normal cranial ultrasound scans.

The recordings were performed with the infant still in the incubator. Grass gold cup electrodes were placed at the inion (O2), referenced to mid-forehead (Fz). A Nicolet CA 1000 clinical signal averager was used. A bandpass of 1–30 Hz and a gain of 10 or 20 k were used. Both a 0-9 per second and 0-5 per second stimulus rate were used, and the sweep was 1000 msec. The stimulus was a red flash delivered by the NIC-105 light emitting diode goggles. They were
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Two forehead and cheeks, in such a way that little or no extraneous light was admitted during the testing. Two or more averages of 64 trials were recorded to ensure replicability of waveform. Trials with excessive artefact were automatically rejected. Each recording session took no longer than one hour, most requiring less than 30 minutes. Infants were usually tested after a feed, and no infants were sedated. Sleep state was not recorded as others have reported that this does not influence visual evoked potential recordings.2-3

Results

Waveform morphology and maturational changes. (Figure). Replicable waveforms were obtained from all except two infants of less than 24 weeks' gestation. The most consistent finding was a large negative peak (N2) which was present in all infants from 24 weeks' gestation onwards. An early positive peak (P2) could be detected in some infants between 32 and 36 weeks' gestation. A consistent biphasic positive-negative waveform was found, however, in all infants of 37 weeks' gestation or more. In the term infants, two morphologies were commonly seen; nine had a typical prominent P2 followed by N2, as found in older children and adults, eight had a double positive peak, followed by the same late N2.

Peak latency and amplitude. The large N2 seen in all infants over 24 weeks' gestation showed little variation in latency with gestational age, the latency being mean (SD), 308 (21) msec. An easily distinguishable P2 was seen in all term infants and some infants between 32 and 36 weeks' gestation. The latency of this peak was mean (SD), 220 (22) msec. There was no significant difference in the peak latencies when either stimulus rate was used. The amplitude, however, was larger and better defined when a rate of 0.5 per second was used.

Discussion

This study shows that visual evoked potentials elicited by light emitting diode goggles can be reliably recorded in newborn infants as young as 24 weeks' gestation while still in an incubator in a neonatal unit. The equipment used was compact and portable, and the technique simple, causing minimal disturbance to the infants or interference with the duties of the nursing staff.

The morphology of the waveform changed with gestational age. In the two infants tested at 23 weeks' gestation, no clearly identifiable waveforms were present. Between 24 and 31 weeks' gestation, only the late N2 was present. Between 32 and 36 weeks, there was greater variability in waveform morphology; although a N2 was always present, an initial P2 was inconsistently recorded. After 36 weeks, however, all infants showed at least one P2 followed by the N2. These findings are consistent with previous reports that used superimposed, conventional electroencephalographic tracings or averaging techniques with a stroboscopic light source,1 2 4 and with light emitting diode photostimulators.7 Unlike the study by Mushin et al,7 our study included 11 infants of less than 32 weeks' gestation, and hence we were able to define more clearly the development of the visual evoked potentials from 23 weeks onwards. Nevertheless, we are able to confirm their impression that infants below 32 weeks' gestational age have only a single broad N2.

The latency of the first P2 varies from previous studies, probably due to differences in recording techniques, underlying the importance of establishing one's own normative data. Hrbek and

Figure Visual evoked potential waveforms elicited at different gestational ages.
Mares\textsuperscript{1} found a latency of mean (SD), 187 (23) msec in mature infants, and Ellingson noted a mean peak latency of 190 msec—both used superimposed electroencephalographic tracings for wave identification. Our results, which show the latency of \( P_2 \) at mean (SD), 220 (22) msec and \( N_2 \) at mean (SD), 308 (21) msec, are almost identical to those of Mushin \textit{et al.}\textsuperscript{7} who also used light emitting diodes as the photostimulators: their light flashes were delivered 8 cm from the infant’s eyes, however, in contrast with ours which were from light emitted diode goggles held over the eyes.

The relation of the development of visual evoked potentials to the neuronal maturation of the neonatal visual cortex is still unclear. Only one small study (seven infants aged between 25 and 33 weeks’ gestation) has attempted to show such a correlation.\textsuperscript{10} Takashima \textit{et al.} have recently reported detailed morphology of the visual cortices of 39 ‘neurologically normal’ infants from 14 weeks’ gestation to 6 months.\textsuperscript{11} They showed that in preterm infants of less than 32 weeks’ gestation, pyramidal cells consisting of many basilar dendrites are present. By 35 weeks, however, there are vast changes, with the pyramidal cells showing numerous apical and basilar dendritic branches. It is tempting to suggest that the consistency of the \( N_2 \) parallels the development of the basilar dendrites which undergo little further maturation to term; while the emergence of the \( P_2 \) from 32 weeks onwards may be a reflection of the development of the apical dendrites over the last trimester.

Despite well established use of visual evoked potentials in adult and paediatric neurology, this technique has not attracted much attention in neonatal practice. A major hindrance was the complexity and size of older recording equipment. The present study shows that using light emitting diode goggles and currently available signal averagers, replicable visual evoked potentials can be readily recorded in preterm and term infants. This should encourage further studies in high risk newborn infants in intensive care units, and the use of this technique in neonatal follow up studies.\textsuperscript{12}

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