AUDITORY BRAINSTEM RESPONSES IN NORMAL AND ABNORMAL PRETERM AND FULLTERM INFANTS

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ABSTRACT

This study describes the assessment of the auditory brainstem responses (ABR) in normal and abnormal preterm and full-term infants. Normal values for wave latencies, interpeak intervals, amplitudes, and amplitude ratios were established in 56 infants (gestational ages: 28-42 weeks) considered neurologically 'optimal' on stringent clinical and imaging criteria. Maturation curves for hearing thresholds were obtained in 42 of these infants. Thresholds were demonstrated at 40 dB between 28 and 34 weeks gestation, at 30 dB between 35 and 38 weeks, and below 20 dB in term infants. These thresholds are lower than previously reported. Curves of latency-intensity function were established in relation to gestational maturity in 54 infants and proved helpful in diagnosing various types of hearing deficit.

Twenty three risk factors were evaluated in relation to their possible effects on the ABR. The presence of periventricular haemorrhage (PVH), abnormal neurological findings, apnoea and gentamicin therapy were associated with concurrent transient

abnormalities. Other risk factors such as hypoxia, hypercapnia and acidosis of more prolonged duration had persistent effects. Various risk factors often had inter-related effects.

Sixty seven infants (gestational ages: 34 weeks or less) admitted consecutively to our neonatal unit were studied during the first week of life. Their ABRs and the findings on ultrasound imaging of the brain were compared, and the ABR abnormalities then categorised as of peripheral, central and mixed type. Ultrasound imaging was normal in 39 infants and showed evidence of PVH in 28. Abnormal ABRs were found in 19 of the 39 infants with normal scans and in all 28 with PVH, including 10 prior to the visualisation of PVH on ultrasound scan. On follow-up studies ABR abnormalities resolved by the age of 6 months in all infants without PVH, while in the PVH group the resolution was slower and 3 remained abnormal.

In a further study of 19 infants (gestation ages: 26-39 weeks) with post-haemorrhagic ventricular dilatation (PHVD) the abnormal ABRs resolved irrespective of persistence or progression of ventricular dilatation. No correlation was found between cerebro-spinal fluid (CSF) pressure and prolonged interpeak intervals but withdrawal of CSF produced increased wave amplitude in some cases.

ABRs have proved useful in the early detection of hearing deficits in neonates and also in showing the influence of prematurity, neurological disorders (such as PVH and PHVD) and various physiological disturbances on the normal ABR.

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Though my work has been both enjoyable and rewarding, it has been a strenuous experience for my family to whom I dedicate this work.

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ABBREVIATIONS

ABR	Auditory brainstem responses
A/D	Analogue/digital
AGA	Appropriate for gestational age
APR	Auro-palpebral reflex
ARC	Auditory response cradle
CCA	Congenital cerebral abnormality
CNS	Central nervous system
CPAP	Continuous positive airway pressure
CS	Caesarian section
CSF	Cerebrospinal fluid
CTG	Cardiotocography
CZ	Vertex
dB	Decibel
EEG	Electroencephalogram
gm	Gram
Hz	Hertz
HL	Hearing level
HD	Hirschsprung disease
IADH	Inappropriate antidiuretic hormone secretion
IPI	Interpeak interval
IPPV	Intermittent positive pressure ventilation
IVH	Intraventricular haemorrhage

KHz	Kilo-Hertz
K Ω	Kilo-Ohms
KPa	Kilo-Pascal
LIF	Latency-intensity function
mmHg	Millimeters of mercury
msec	Milliseconds
MTM	Myotubular myopathy
NCV	Nerve conduction velocity
nHL	Normal hearing level
NICU	Neonatal intensive care unit
nV	Nanovolt
PCA	Postconceptional age
PCO2	Arterial carbon dioxide tension
PDA	Patent ductus arteriosus
PET	Pre-eclamptic toxaemia
peSPL	Peak equivalent sound pressure level
pH	Hydrogen ion concentration
PH	Pulmonary hypertension
PHVD	Posthaemorrhagic ventricular dilatation
Pnx	Pneumothorax
PO2	Arterial oxygen tension
PROM	Premature rupture of membranes
PVH	Periventricular haemorrhage

R/C	Rarefaction/condensation
RDS	Respiratory distress syndrome
SD	Standard deviation
sec	Seconds
SGA	Small for gestational age
SL	Sensational level
TET	Tri-ethyltin
μsec	Microseconds
US	Ultrasound
$\bar{x}$	Mean

INTRODUCTION

Over the last two decades the development of techniques involving evoked potentials (recordings of the brain's electrical responses to stimulation) have proved useful for evaluating the functional integrity of sensory pathways.

The neuronal responses specifically related to sensory stimuli (event-related potentials) are embedded within the EEG. These potentials are usually smaller than those of spontaneous neural activity, and can only be extracted from the EEG by computer averaging. Event-related potentials recorded in response to click stimuli, may be used clinically to evaluate the integrity of the auditory pathway. The main practical applications are to estimate the degree of peripheral hearing deficit, and the diagnosis of lesions affecting the auditory pathways.

A most productive clinical application of auditory brainstem responses (ABR) has been in the newborn infant, where it is now possible to assess the hearing of patients too young to cooperate in standard audiometric testing. Early recognition of hearing deficits can lead to the early and beneficial institution of auditory training and management.

In parallel with these developments there have been tremendous advances in the provision and quality of intensive care for preterm infants. Techniques of respiratory support have led to decreases in both mortality and morbidity in such populations but concern has risen as to the long term neurological prognosis of infants admitted to such units. This has focussed attention on exploring in greater depth the causes of later neurological handicaps.

The present study has arisen out of the on-going neurological interests of the Neonatal Unit at Hammersmith Hospital.

The study of ABR has proved useful in the diagnosis of hearing deficits and in assessing the integrity of brainstem function. In view of this background, the present study sought:

a) To acquire normative data concerning the maturation of both the peripheral and central portions of the auditory pathway in preterm infants and through to the first year of life.

b) To assess hearing in newborn infants, and to determine, where possible, the nature and extent of any hearing deficit present.

c) To demonstrate at an early stage the presence of central (brainstem) lesions in preterm infants, to assess their likely causes, and to determine how they evolved in different clinical contexts.

d) To establish which risk factors seemed particularly related to auditory brainstem deficits (with a view to the more selective use of the ABR in future screening of neonatal populations) and to correlate risk factors with neurological outcome.

e) To investigate the effects on the auditory pathway of periventricular - intraventricular haemorrhage, and post-haemorrhagic ventricular dilatation.

The following chapters discuss the relevant literature, the methods used to investigate the above problems, and the results obtained.

CHAPTER I. AUDITORY BRAINSTEM RESPONSES

I.1. HISTORICAL BACKGROUND

The history of electrophysiology has its roots in the eighteenth century writings of Galvani who suggested that muscular movements were controlled by the production of 'animal electricity'. But the real discovery of the brain's electrical activity was made by R. Caton who reported his findings to the British Medical Association in 1875. Caton recorded electrical changes in the exposed brains of animals. He also observed the phenomenon of continuous fluctuation of surface potentials, when sources of stimulation were eliminated, later to be known as the electrocorticogram. Over fifty years later Hans Berger (1929) recorded the first electrical potentials from the human brain and used the term electroencephalogram (EEG) to describe them. Adrian and Matthews (1934) confirmed Berger's findings. Credit for the first recognition of auditory evoked potentials in the human EEG goes to Davis (1939) who described them as long latency "vertex" potentials.

Further understanding of the nature of the responses was facilitated by the introduction of electronic averaging devices by Dawson(1954). Their use allowed measurement of very small potentials by increasing the signal-to-noise ratio in relation to the

background EEG. It was through the use of electronic averaging methods and the summating of responses (Geisler, Frishkopf and Rosenblith, 1958) that the clinical use of auditory evoked potentials developed.

Investigators began measuring changes in the ongoing electrical activity of the cortex in response to auditory stimuli. The "cortical evoked response" was widely used during the 1960's as a measurement of peripheral auditory function. There was early controversy as to whether the recorded responses were neurogenic or myogenic. The myogenic contribution was emphasised by Bickford et al (1964), and as a result the technique began to lose favour.

The future of evoked response audiometry looked gloomy until new approaches were suggested which applied the averaging technique to aural stimulation, thereby introducing electro-cochleography. This became popular among otologists in Europe and Japan. The electrodes were placed in the ear canal (Yoshie et al 1967), across the tympanic membrane (Aran and Le Bert 1968) or 'far-field' on the scalp* (Sohmer and Feinmesser 1967).

* The engineering term of "far-field" describes the situation where electrodes on the scalp record the activity of distant neural generators.

When brainstem evoked potentials were described by Sohmer and Feinmesser (1967) they recorded four or more negative peaks, occurring within milliseconds of a click stimulus, the electrode pair being placed on the earlobe and the bridge of the nose. Jewett and Williston (1971) gave a clear description of the brainstem evoked potentials. They showed that the far-field potentials of the normal human auditory brainstem responses (ABR) consisted of seven small vertex positive waves designated I to VII (by Roman numerals). These occurred in the first ten milliseconds (ms) following a click stimulus (Fig 1.1). Because these waves had short latencies they could not represent either neural events at the level of the cerebral cortex or myogenic responses mediated through a cerebral reflex arc.

I.2. COMPONENTS OF THE RESPONSE AND THEIR ORIGIN

The submicrovolt potentials occurring during the 10 ms following an acoustic stimulus are best recorded across an electrode pair placed on the vertex and on the mastoid. The potentials consist of a number of waves that differ in their relative amplitudes and have interpeak separations of the order of 1 ms. These responses, which comprise seven vertex positive components, were found to be reproducible even after frequent repetition or the lapse of several days. Figure 1.2 shows a typical recording.

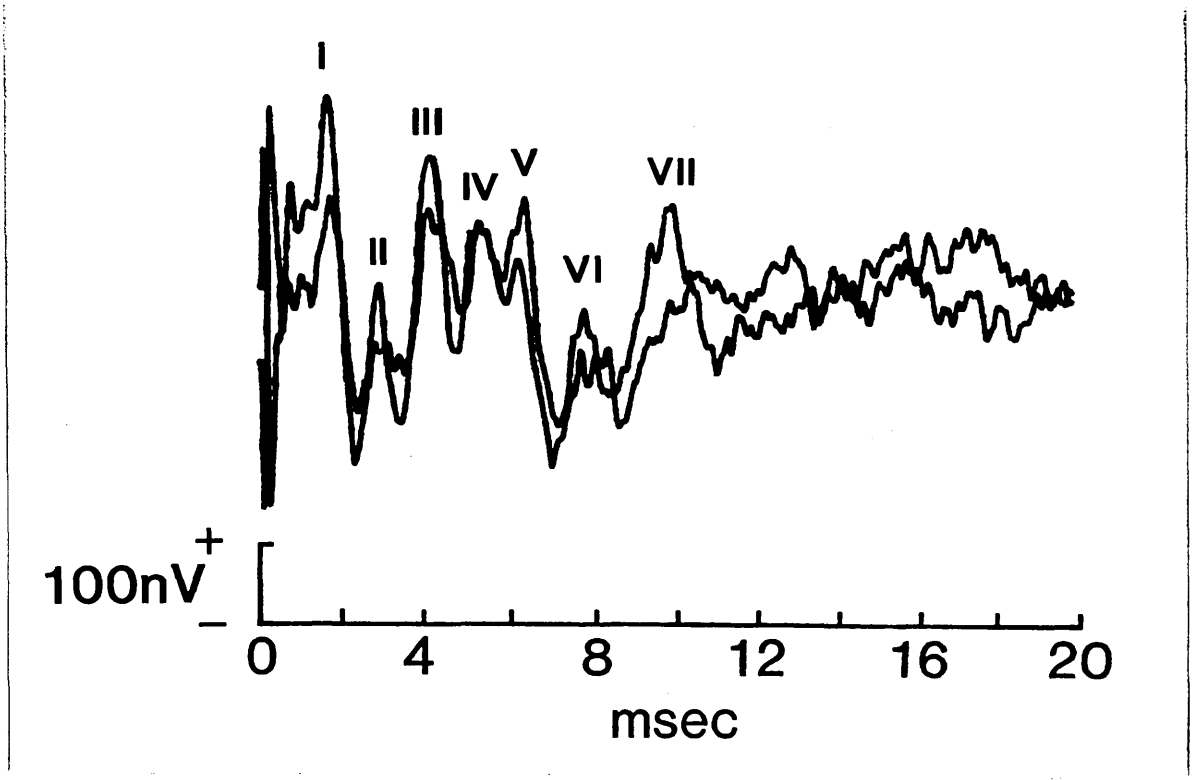


Figure 1.1. Normal ABR. There are seven waves, designated by Roman numerals I-VII. Full term infant. Click stimuli 60 dB, 10/sec.

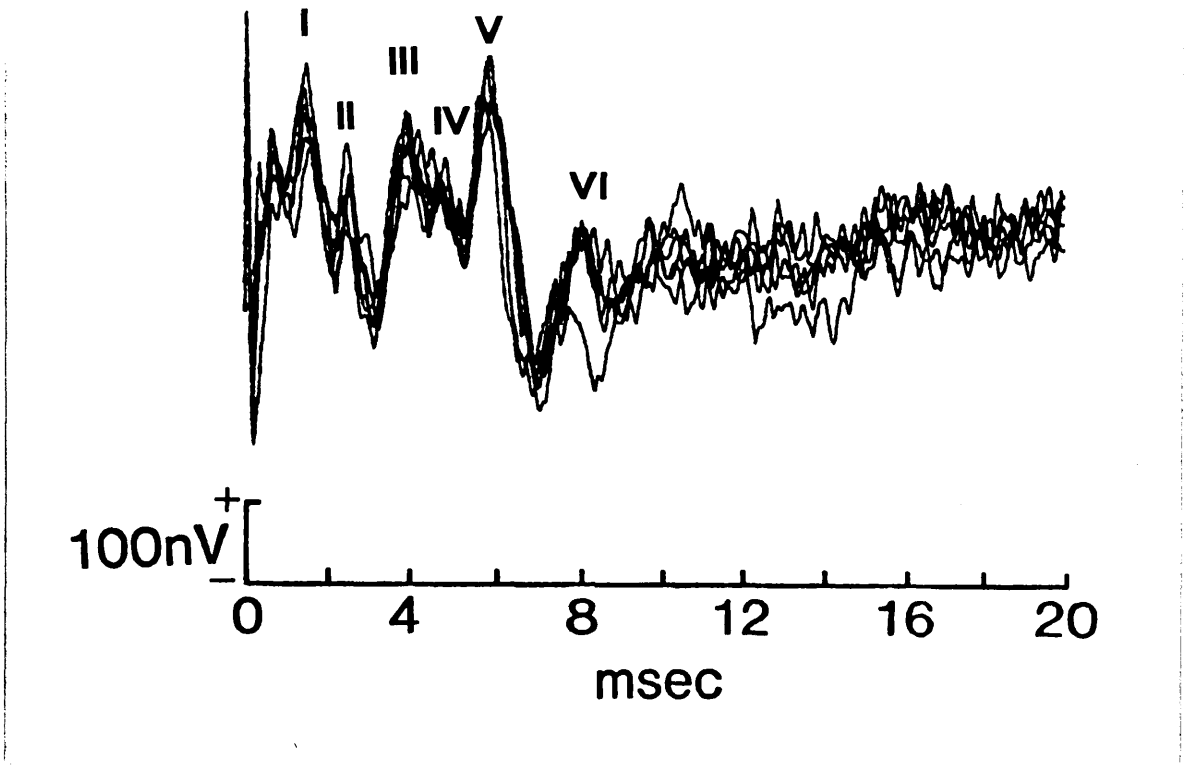


Figure 1.2. Six reproducible, super-imposed ABR responses in a normal full-term infant. Recording was between the vertex and the mastoid ipsilateral to the stimulated ear. Click stimuli 60 dB, 10/sec.

Efforts have been made to ascribe the ABR component waves to neural generators in the brainstem auditory pathway. Investigators have attempted to determine the sources of the waves experimentally in animals (such as the cat) and in man. These efforts have been complicated by controversies over nomenclature.

In 1967 Sohmer and Feinmesser noted that a typical response consisted of four waves, the first two of which were thought to be components of the cochlear action potential, while the two later waves were considered as either repetitive firings of the auditory nerve, or neural discharges from brainstem structures.

In 1970a Jewett showed that the responses recorded from the surface of the head were far-field potentials,resulting from electrical activity in the depths of the brainstem. His initial observations were based on differential recordings from a variety of sites between the hypoglossal and caudate nuclei of the cat, in response to click stimuli. He reasoned that if the tip of his electrodes approached or passed through the source of a potential, an increase in its field strength and a reversal in its polarity should be observed. Based on this concept, he moved his electrodes through the brainstem auditory nuclei and tracts. Correlating depth and surface recordings, he demonstrated that wave I was generated

from the auditory nerve, wave II from near the cochlear nucleus, wave III from near the superior olivary complex and waves IV and V from the region of the inferior colliculus (Figure 1.3). However, he stressed that each wave was "a composite of simultaneous fast and slow activity possibly from a variety of generators".

Further animal studies of the spatio-temporal distribution of the potentials indicated that components I and II in rats and cats (Plantz et al 1974) and components I, II and III in monkeys (Allen and Starr 1978) were asymmetrically disposed over the surface of the scalp, while the later components (IV and V) were symmetrically arranged. More direct techniques were applied using intracranial recordings or by inducing lesions in the auditory pathways in animals while recording from the surface of the head. In assessing these data, it is important to realise that different groups of workers have used different techniques. Achor and Starr (1980a, 1980b) generally used small lesions, while other workers produced much larger ones.

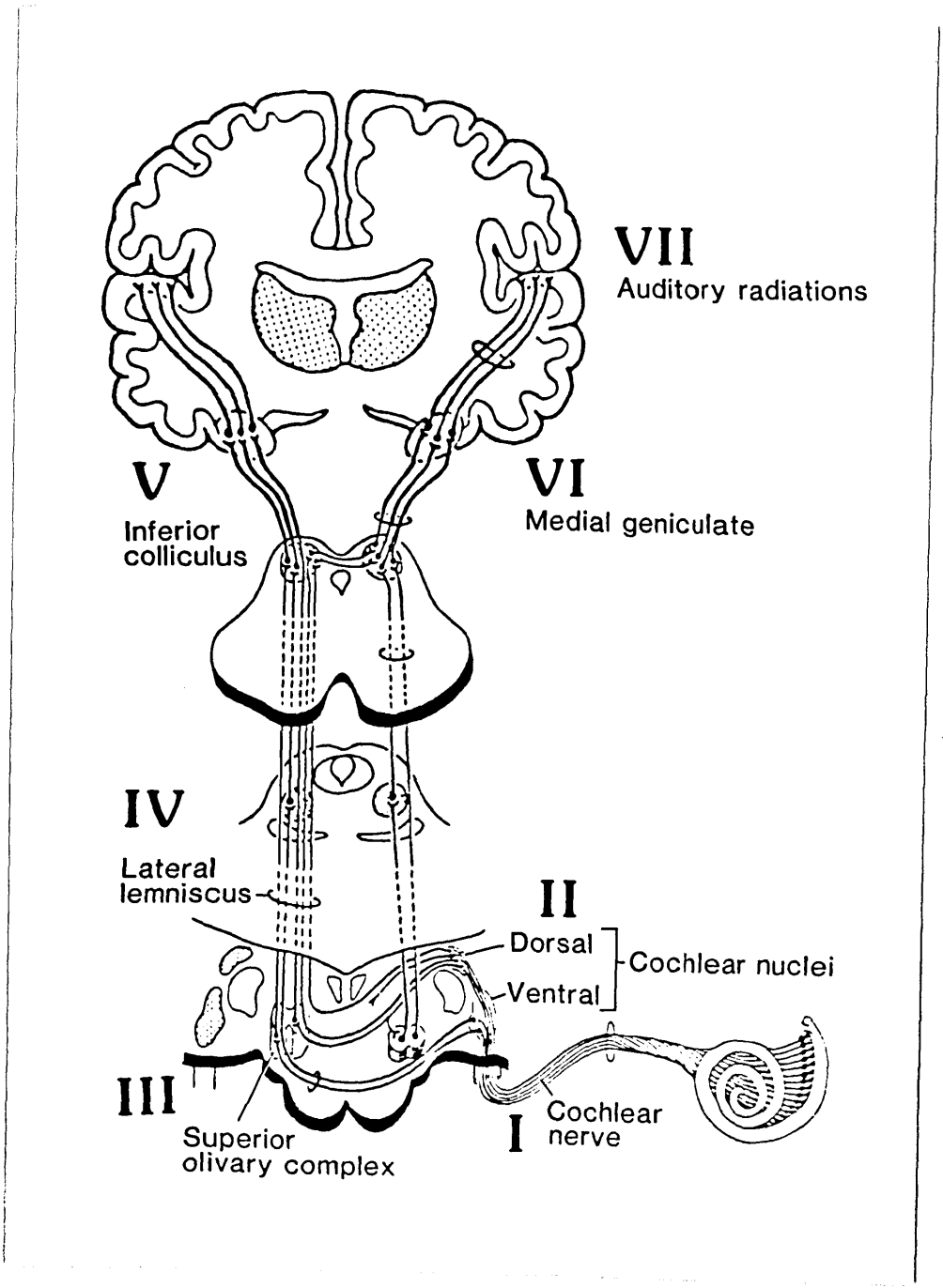


Figure 1.3. Suggested relationship of ABR waves to various structures of the auditory pathway. The input from each nerve ascends both ipsilaterally and contralaterally, and there are crossing fibres at each level as far rostrally as the colliculi. (Adapted from Pansky and Delmas 1980).

Component I: This component is dependent upon the auditory nerve. It occurs simultaneously with the compound action potential of the nerve (N1) recorded at the round window* (Sohmer and Feinmesser 1967, Jewett 1970b, Jewett and Romano 1972). It is of maximal amplitude and reverses its polarity when the recording electrode is adjacent to the nerve (Lev and Sohmer 1972). Isolation of the auditory nerve from the brainstem abolishes all but the first component of the ABR. Destruction of the nerve also abolishes component I (Buchwald and Huang 1975). The cochlear microphonic** may make a small contribution to this component (Achor and Starr 1980a).

Component II: This component depends upon the cochlear nuclei, especially their ventral parts. Its appearance coincides with activity in the nuclei (Jewett 1970b, Lev and Sohmer 1972, Achor and Starr 1980a). It disappears when 8th nerve connections to the brainstem are destroyed ipsilaterally, but not contralaterally

* The round window separates the middle ear cavity containing air, from the perilymphatic space, containing fluid.

** The cochlear microphonics are the evoked potential components derived from the hair cells within the human cochlea.

(Buchwald and Huang 1975). There is a small contribution from wave N2 arising from the auditory nerve and recorded at the round window, Achor and Starr (1980b) have shown that there is also a contribution from the trapezoid body. Moller et al (1981) recorded the VIIIth nerve potential directly in man during surgery. By comparing the obtained latencies with those of surface ABR recordings, they concluded that wave II is generated from the nuclei and intracranial portions of the cochlear nerve.

Component III: This component arises from generators in the region of the superior olivary complex, and is maximal when recorded from this area (Jewett 1970a, Lev and Sohmer 1972). A midline section of the brainstem at the level of the trapezoid body abolishes component III, suggesting a total dependence upon decussating fibres (Buchwald and Huang 1975). Achor and Starr (1980a) have shown that there is activity in both superior olivary nuclei after unilateral stimulation.

The responses occurring after component III show marked variations in morphology and it is important to assess their origin. Earlier experiments suggested a dependence of component IV upon the inferior colliculi, the wave being of maximal amplitude when recorded in these structures. Its polarity was reversed when the

electrode passed through the inferior colliculus (Jewett 1970b). Destruction of the colliculi greatly diminished but did not abolish components IV and V (Lev and Sohmer 1972).

Buchwald and Huang (1975) demonstrated loss of component IV with lesions in the ventral nucleus of the lateral lemniscus. Component IV depends upon both crossed and uncrossed fibres, midline lesions reducing its amplitude but not abolishing it. Jones et al (1976) using a cryogenic technique aiming at slowing conduction in fibres and blocking synaptic transmission, claimed that unilateral cooling of the pons abolished component IV and suggested its bilateral representation.

There is still some controversy about the origin of Component V. Until recently most workers agreed that this component depended upon the inferior colliculus or a structure just anterior to it (Jewett 1970a, Lev and Sohmer 1972, Buchwald and Huang 1975). Destruction of the inferior colliculi or undercutting them abolished component V (Jewett 1970a, Buchwald and Huang 1975). In contrast, Achor and Starr (1980a 1980b) found no evidence that activity of the inferior colliculi had any effect upon the surface recorded ABRs. Component V probably depends on crossed pathways, since midline section at a lower level abolished the response (Buchwald and Huang 1975), while

unilateral cooling delayed, but did not abolish the response to contralateral stimulation (Jones et al 1976).

Components VI and VII: There is little evidence available suggesting that waves VI and VII arise from the thalamus (Stockard and Rossiter 1977). It was speculated that they arose in the medial geniculate body and auditory radiations respectively. Recordings from intrathalamic depth electrodes in humans have so far not been helpful (Hashimoto et al 1981, Chiappa 1982, Velasco et al 1982).

Starr's theory (Starr and Hamilton 1976, Starr and Achor 1979), holds that the activation of different parts of the acoustic pathway produces a summation of the electrical events, and that this gives rise to the different waves observed in surface recordings. Morera et al (1984) performed experimental studies on cats, with surface and intranuclear recordings and reached similar conclusions.

These experiments illustrate the important point that experimental lesions cannot exactly define the precise anatomical locus where a particular component is generated. Further studies with depth electrodes and small lesions at various sites within the brainstem auditory pathways have indicated that neural activity is

widespread at any particular instant after the administration of click stimuli (Achor and Starr 1980b).

I.3 THE HUMAN ABR

The previously mentioned approaches were used in animal work. The location of the source of generators in human beings proved more difficult. Several studies (Sohmer et al 1974, Starr and Achor 1978, Starr and Hamilton 1976, Stockard and Rossiter 1977) examined alterations of the ABR in patients with confirmed eighth nerve and brainstem lesions, and demonstrated that wave I was the only one to remain when lesions involved the ponto-medullary junction, or when the brainstem was extensively damaged.

Alterations in waves II and III were associated with lesions in the medulla and pons, i.e. involving the cochlear nucleus, trapezoid body and superior olive. Lesions in midbrain auditory structures were associated with changes in waves IV and V.

Topographic analysis of the scalp distribution of human ABRs has been investigated by Martin and Coats (1973), Martin and Moore (1977) and Picton et al (1974). They found that wave I was represented ipsilaterally to the stimulated ear and was very similar to the N1 potential recorded with a trans-tympanic needle

electrode. They felt this proved its origin in the auditory nerve. Waves between I and IV reversed their polarity between ipsilateral and contralateral mastoids, which may reflect an origin in the cochlear nucleus and superior olivary complex. Wave V is a far-field projection of lateral lemniscal or inferior collicular components.

Hashimoto et al (1981) attempted to define the origins of various components of the ABR in man at operation. They placed electrodes directly upon the eighth nerve, in the mesencephalic part of the brainstem and in the ventricular system. Their results confirmed the animal data, and provided evidence that activity in the medial geniculate ganglia of the thalamus might be the source of component VI. This is the most direct evidence obtained in man, concerning the origin of the various ABR components.

From these data we can conclude that the generators of the ABR in man are similar to those in animals. All studies have shown the remarkable complexity of the generators producing the response peaks. Controversy persists however as to the precise origin of all the various component waves.

The structures within the auditory brainstem pathway are packed into a relatively small area. The distance between the entry point of the eighth nerve into the brainstem and the inferior colliculus is less than 4.0 cm. The difficulty encountered in differentiating the precise origin of the four waves (II-V) being generated in this region is therefore scarcely surprising.

Controversy continues as to whether the activity arises in nuclear structures or tracts, and as to whether it arises ipsilaterally or contralaterally to the stimulated ear, or even bilaterally. The complex spatial arrangements of the auditory system, the simultaneous activation of generators, and the overlapping of the transient and sustained activity from multiple sites will preclude establishing any specific correlations between a given brainstem site and a particular response peak. In the light of current knowledge the peaks can nevertheless be assigned to certain regions of the brainstem. This is the basis of their usefulness as a clinical tool in neurological diagnosis and of their use in this study.

I.4 TERMINOLOGY

Different authors still use different terms to describe the auditory nerve and brainstem potentials. The terms in current use are listed in table I.1.

Although the responses are termed brainstem potentials, the first wave arises from the auditory nerve. Strictly speaking, they should be referred to as auditory nerve and brainstem potentials, but this is cumbersome.

There is also controversy as to 'which way is up' for the brainstem responses. The notion that an upward deflection reflects a negative response runs contrary to the traditions of physics and engineering in general, in which the correlation of 'upwards' with negativity is derived from the study of the action potentials of nerve impulses. Figure 1.4. shows the same set of ABRs recorded in two different ways depending on whether the positive wave is deflected upwards or downwards. In all ABRs in this study an upward deflection represents a positive response.

I.5 WAVE IDENTIFICATION AND NORMAL FINDINGS

In this thesis the auditory brainstem response waves are labelled I to VII in accordance with the Jewett classification (1971).

TABLE I.1 COMPARISON IN TERMINOLOGY OF AUDITORY BRAINSTEM RESPONSES

	Abbreviation	Authors
Auditory brainstem potentials	ABP	Salamy and McKean (1976)
Auditory brainstem responses	ABR	Starr and Hamilton (1975)
		Galambos and Hecox (1978)
		Sohmer et al (1978)
Auditory evoked responses	AER	Robinson and Rudge (1975)
Brainstem auditory evoked potentials	BAEP	Gibson (1978)
Brainstem auditory evoked responses	BAER	Hecox (1975)
		Stockard et al (1976)
Brainstem evoked responses	BEP	Salamy and McKean (1976)
		Picton (1978)
Brainstem evoked responses	BER	Salamy et al (1975)
		Galambos and Hecox (1978)
		Van Olphen et al (1978)
Brainstem electric response audiometry	BERA	Schulmann-Galambos and Galambos (1979)
Brainstem electic response	BSER	Davis (1976)

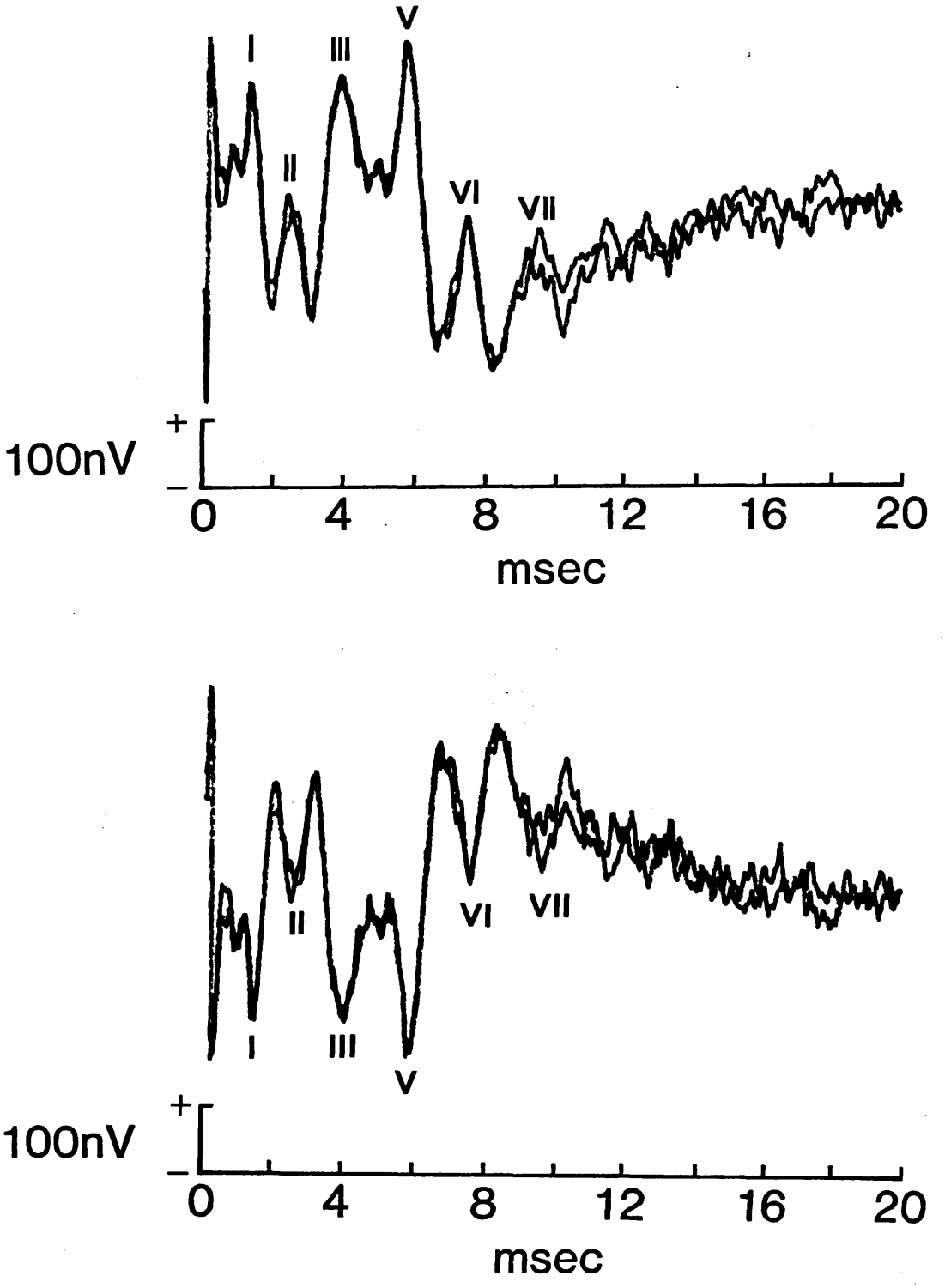


Figure 1.4. The same ABR with vertex positive waves directed a) upwards and b) downwards. 38 week old infant. Click stimuli of 60 dB intensity, at rate of 10/sec.

The time relationship between any response and the stimulus eliciting that response is called the latency. Latency may be further subdivided into absolute latencies and interpeak intervals (Figure 1.5). Beagley and Sheldrake (1978) noticed that the absolute latency of ABR components, in response to high intensity clicks, was approximated by the Roman numerals designating the particular waves. Thus the latency of wave I fell between 1.0 and 2.0 msec, of wave II between 2.0 and 3.0 msec, and so on.

Interpeak intervals (IPI) refer to the interval between two component waves. IPI I-V for instance refers to the interval between the peaks of waves I and V. Both the absolute latency and interpeak intervals are measured in milliseconds. The amplitude of a wave is determined by the difference between the highest peak and the subsequent negative trough (assuming that vertex positive waves are displayed as upward deflections). Amplitudes are measured in nanovolts (nV).

Wave I is identified as the earliest wave. In normal adults it has a latency of over 1.4 msec (Chiappa 1983). The amplitude of wave I is higher when recorded from the external ear canal, than from the ear lobe. Wave III appears between waves I and V, and is approximately equidistant from both unless abnormalities are

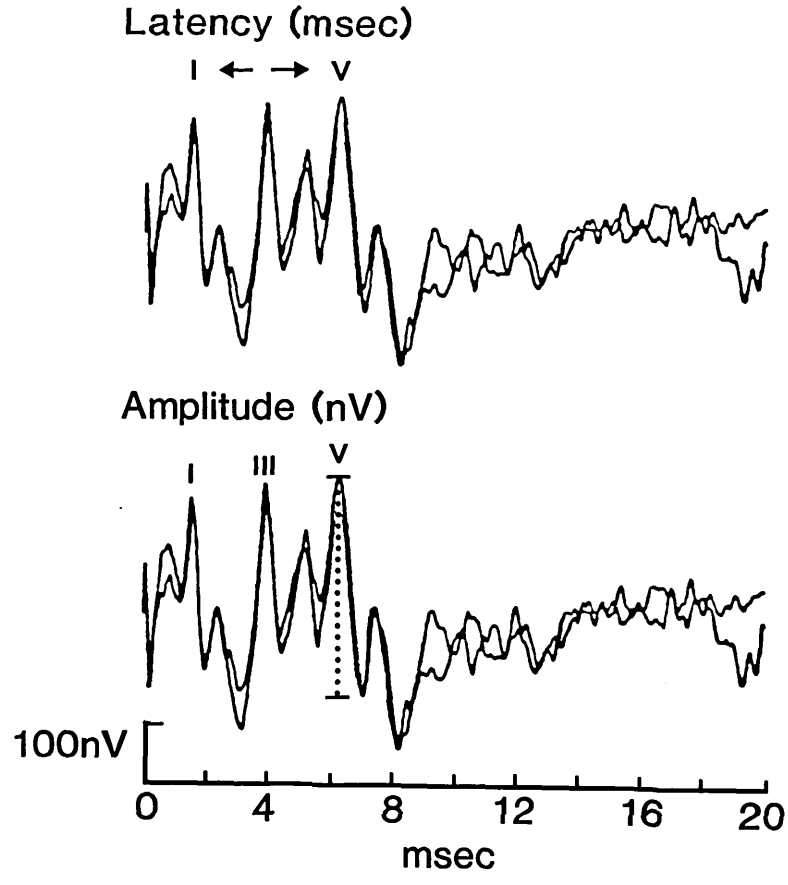


Figure 1.5. The absolute latency is the interval between the onset of the stimulus and the response it evokes. Interpeak interval is the distance between 2 peaks. Amplitudes are measured from the peak of a wave to the following trough.

present. Wave V is usually the most prominent wave with a significantly greater amplitude than that of the other waves. In normal subjects wave V is identifiable near threshold whereas the amplitude of other components tend to diminish at lower level of stimulation. Waves IV and V sometimes interact to produce different patterns. When these waves fuse, the resultant peak is taken as wave V (Chiappa 1983). Waves II, IV and VI are not commonly used in clinical interpretation. By decreasing click intensity these waves tend to diminish markedly. This greatly facilitates the identification of waves I, III, and V.

I.6 CLINICAL APPLICATIONS OF ABR

Two problems immediately arise when the ABR is used for clinical purposes. A distinction must first be made between normal and abnormal results in the context of technical and subject-related factors discussed in the following chapter. Secondly, all results must be interpreted in the context of other relevant information (case history, physical findings, other laboratory and investigative studies).

The two main conditions that may be studied are hearing impairment (audiological disorders) and abnormalities of brainstem function (neurological disorders).

Audiological Disorders

ABRs may be used to predict the degree and type of hearing impairment. When infants with such disorders are screened by ABR an audiological diagnosis can usually be made, provided one takes into account a) the threshold; b) the latency and amplitudes of wave I; c) the latency of wave V, d) the IPI I-V, e) the latency-intensity curve. ABR is the only reliable method for estimating threshold sensitivity in infants (Schulman-Galambos and Galambos 1975, Galambos and Hecox 1978, Lary et al 1985). (The most commonly used criterion for threshold estimation is the minimum intensity required to detect wave V in the response.)

ABR can quantify hearing deficits. The deficits can be classified as mild, moderate or severe. In full term babies, a mild hearing deficit will range from 20 to 40 dB, and a moderate deficit from 40 to 60 dB. Severe deficits will exceed 70 dB.

Diagnostic information in identifying the type of hearing impairment comes from determining the curves of latency-intensity

function (LIF). LIF curve represents the relationship of wave V latency and its changes with intensity. Curves obtained from patients with impaired hearing differ from normal curves, and it is the analysis of these differences that identify the type of hearing deficits. This will be further discussed in chapter V.

Peripheral hearing disorders are not usually associated with changes in wave V latency (Coats and Martin 1977, Stockard and Westmoreland 1981). Interpeak intervals in infants with impaired hearing may be shortened due to the presence of artefact (Stockard and Westmoreland 1981). All this has led to the use of wave I (latency and amplitude) as an index for identifying peripheral lesions.

Neurological Disorders

Certain laboratories use ABR techniques solely for audiological purposes, while others are interested primarily in the neurological information which the ABR can provide. The two approaches should not be separated: the exact hearing status may influence the neurological diagnosis and vice versa.

The application of ABR results to neurological diagnosis is based on certain facts known to reflect the activity of neural structures

in the eighth nerve and brainstem pathways. When these pathways are involved by lesions or disease, certain ABR parameters will be affected. The effect may involve the disappearance of waves, increases in latencies, decreases in amplitude, morphological changes, or any combination of these. Clinical studies are beginning to document important correlations.

The most common changes in ABR seen with lesions of the central nervous system are of three types. The first is a loss or marked attenuation of all the ABR components. The second is a prolongation in latency between various ABR components (mainly an increase in the I to V interval). This measure of 'central conduction time' was developed for neurological evaluation because the absolute latency of all the various waves might be affected by middle ear or cochlear disturbances, whereas the interpeak intervals are relatively independent of both click intensity and hearing loss (Starr et al 1977, Stockard and Rossiter 1977, Rowe 1978). The third type of abnormality is a change in the amplitude ratio of waves V to I (Starr and Achor 1975, Rowe 1978, Chiappa 1983). An amplitude ratio of 0.1 at 60 dB HL is considered normal.

The importance of the ABR is its ability accurately to identify and evaluate auditory and neurological deficits. In any diagnostic

technique which requires a decision process, technical and procedural strategies must be resolved before the establishment of clinical norms. Recognising that the accuracy of ABR assessment is a function of both recording and procedural variables, it was one of the purposes of this study to suggest a series of guidelines which might lead to acceptable standards. It is not good enough without recognising the range of associated variables or technical factors which may limit the validity of the detailed responses.

CHAPTER II FACTORS AFFECTING THE RESPONSE

The ABR is a dependent variable. It has certain measurable properties and is influenced by a host of technical and procedural (instrumental) factors such as the intensity of the stimulus, repetition rate, and acoustic phase. To minimise possible error in specifying a result as abnormal, a certain amount of precision of the input is needed. A number of non-pathological factors such as the nature of the stimulus, recording procedure, and the subject may affect the ABR.

II.1. THE STIMULUS

II.1.1 Intensity

In ABR measurements, stimulus intensities are recorded in one of two ways. They may be recorded as either a certain number of decibels above the threshold for that intensity (decibel sensational level or dB SL), or as the mean threshold of a panel of normal hearing adults (normal hearing level or nHL).

The stimulus intensity influences the frequency of neural firing, and the number of neural elements participating in the discharge. These relations can be represented in the ABR waveform as a function of intensity. Figure 2.1 shows how decreases in the intensity of

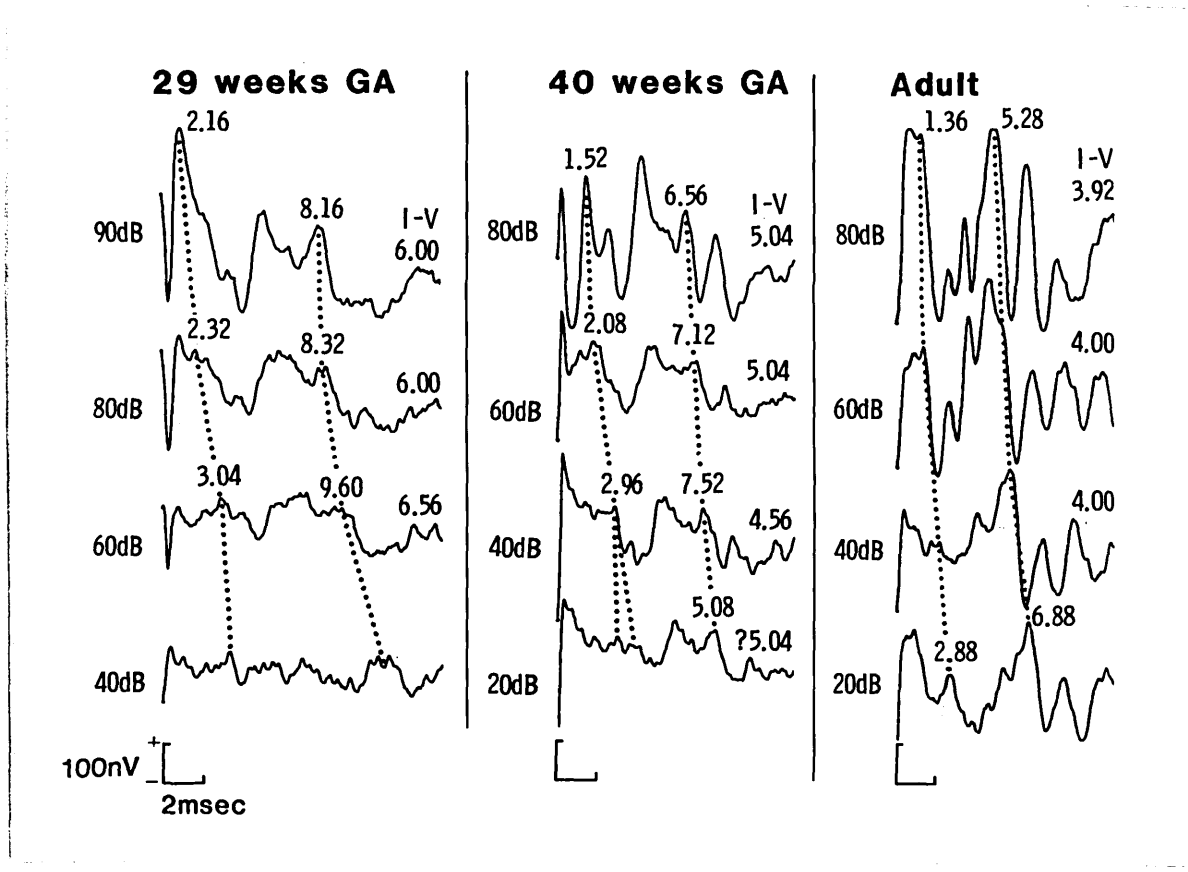


Figure 2.1. Waves I and V as a function of stimulus in 3 subjects (2 infants with gestational ages of 29 and 40 weeks, and one adult). Note the increase in the latencies of waves I and V as the intensity of stimulation decreases.

the stimulus are associated with a corresponding increase in the latency of each wave.

Although ABR waves are usually observed in response to high intensity stimuli, as threshold is approached the likelihood of observing all the component waves is reduced with each intensity decrement. At lower stimulus intensities (about 40 dB) the ABR waves lose much of their peaks or sharpness. Further decreases in stimulus intensity will increase the variability, and make it difficult to identify wave components from variations in background noise. Interestingly, wave V persists long after other waves have receded. It is still present at stimulus intensities that approach threshold (Rowe 1978).

In general, a decrease in stimulus intensity is associated with an increase in component wave latencies (Jewett and Williston 1971, Jewett 1970a, Hecox and Galambos 1974, Picton et al 1977, Starr and Achor 1975, Yamada et al 1975). The reduction in the latency of wave V with increased intensity may be explained by faster synaptic transmission at higher intensities leading to faster overall conduction. A broad band click of moderate intensity activates all regions of the cochlea, but because of the hydrodynamics of the travelling wave on the basilar membrane, the region responding first to high frequency stimulation is the apical region. With a higher

intensity stimulus all regions of the cochlea are activated, the high frequency regions being activated synchronously, and sooner than other regions.

II.1.2 Repetition Rate

Developmental electrophysiologists have found that immature animals are more susceptible to 'fatigue' (Myslivecek 1970). One of the easiest ways in which this is shown is by determining the effects of varying repetition rates on the latency and amplitude of the responses. Jewett and Romano (1972) found that young rats and kittens exhibited diminished responsiveness in terms of both latency and amplitude) at high rates of stimulation. Such a phenomenon may be described as adaptation (Thornton and Coleman 1975, Terkildsen et al 1975), fatigue (Don et al 1977), refractoriness (Pratt and Sohmer 1976) and habituation (Harkins et al 1979). Thornton and Coleman (1975) found that in most subjects the ABR became completely adapted by the third or fourth trial. Decreasing the rate of stimulation produced greater adaptation.

There is some disagreement in the literature regarding the latency-intensity function for wave I. These differences influence IPI measurements. Fria (1980) reported that latency-intensity functions (LIF) for waves I and V were parallel throughout the intensity range, suggesting that the IPI I-V was resistant to

stimulus intensity. Stockard et al (1979) reported that wave I latency increased more than that of waves III and V when stimulus intensity was decreased. Consequently, IPI values involving waves I-III and I-V were shorter at lower intensities.

Reduction in ABR amplitudes with decreasing intensity of stimulation has been recognised. These changes suggest that the ABR represents a series of simple synaptic events which preserve the neural response pattern from one level of the brainstem to the next. The changes in wave I are of particular importance as a function of stimulus-intensity since the subsequent potentials reflect this change without additional modulation. The effects of changes in stimulus-intensity in man are essentially similar to those reported in cats (Jewett 1970a, Picton et al 1974, Starr and Achor 1975). Furthermore, the V:I amplitude ratio increases with decreasing stimulus-intensity, thus the widening range of values reported from normal newborns (Jacobson et al 1982).

The occurrence of 'fatigue' may vary between laboratories and the interpretation of this phenomenon remains controversial. Schulman-Galambos and Galambos (1975) did not find noticeable change in response configuration when over 100,000 stimuli were delivered in 28 consecutive trials to newborn infants. They concluded that the ABR is resistant to fatigue or habituation. Salamy and McKean (1977) arrived at the same conclusion.

In general, increasing the rate of stimulation increases the latency but decreases the amplitude of the response. Don et al 1977, Fujikawa and Weber 1977, Rowe 1978, Chiappa et al 1979, Harkins et al 1979, Van Olphen et al 1979, Yagi and Kaga 1979, Picton et al 1981, Pratt et al 1981, Weber 1982). The effect is most pronounced at repetition rates greater than 10 per second. An exception to this rule is seen when a single component or measure tends to "surface" (or to become more obvious) in each successive experiment (Terkildsen et al 1975, Pratt and Sohmer 1976, Van Olphen et al 1979).

When the stimuli were presented at different rates, differential effects for early and late waves were observed, but there was no consistent pattern (figure 2.2). Some studies have reported that decreasing rates of stimulation prolong the latencies of later waves more than those of earlier waves (Yagi and Kaga 1979). Other studies suggest that such changes of stimulation rate produce no effect on wave I (Pratt and Sohmer 1976), uniformly increase all ABR latencies (Van Olphen et al 1979), affect earlier waves to a greater extent (Hyde et al 1976), cause a decrease in response amplitude (Hyde et al 1976), have no effect (Terkildsen et al 1975), or cause fluctuations of some components but not of others (Scott and Harkins 1978).

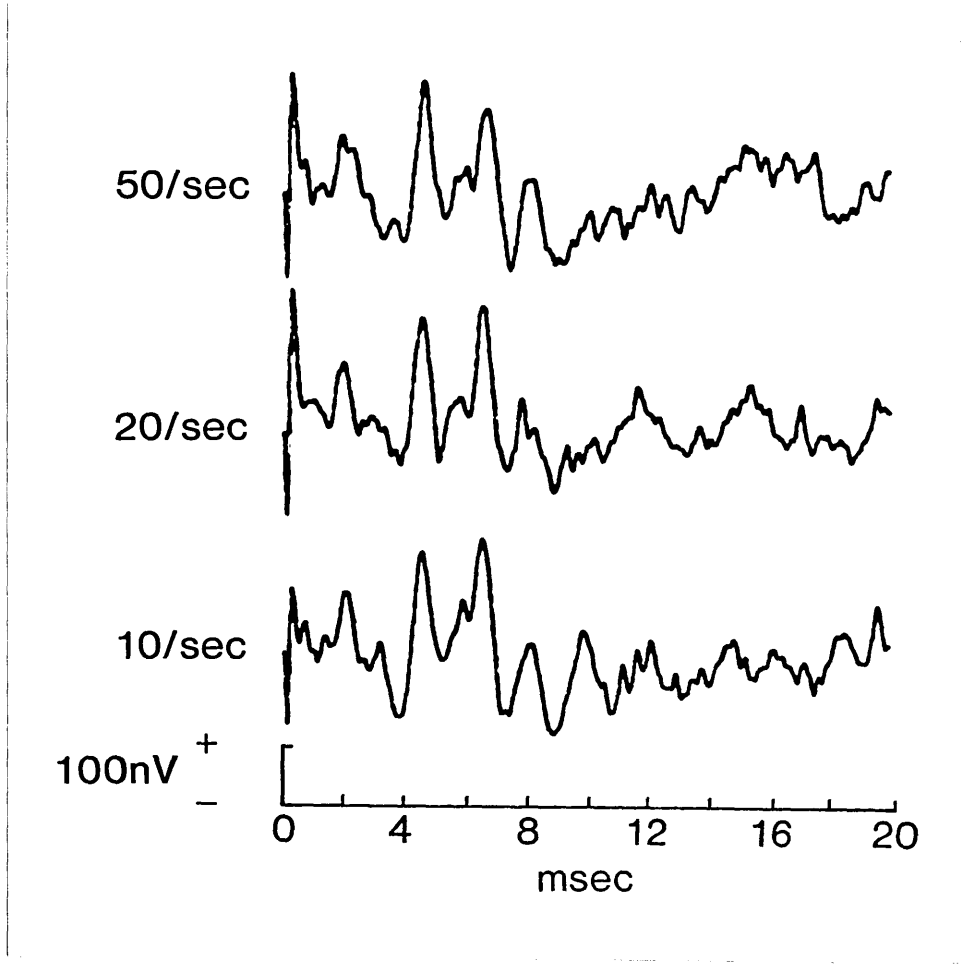


Figure 2.2. ABR at different rates (50, 20 and 10/sec.) but at a constant click stimulus intensity of 60 dB recorded in one infant (GA: 36 weeks). No consistent changes in the ABR pattern was found.

The effects of stimulation rates have been assessed in relation to age. Hecox (1975) compared infants from 3 weeks to 16 months, stimulating them at 10 and 30 clicks/second. He found no age-dependent differences in ABR in relation to the frequency of stimulation. Stockard et al (1979, 1983a) on the other hand reported greater rate-dependent changes in absolute latencies and IPI in newborns.

II.1.3 Polarity

Polarity of the phase of the input signal is determined by whether the stimulus is presented in a condensation or in a rarefaction phase. "Rarefaction clicks" are produced by an initial movement of the headphone transducer diaphragm away from the tympanic membrane. "Condensation clicks" result from initial displacement towards the tympanic membrane.

Changing click polarity from rarefaction to condensation has been reported to have an influence on the morphology of the IV-V complex of the ABR. Stockard and Stockard (1981) reported that rarefaction clicks produced larger waves I and V in adults, whereas condensation clicks enhanced wave V in all age groups (Stockard et al 1979). The use of alternating click polarity can affect the morphology of

wave I due to the possible cancellation of out-of-phase components when responses to the separate polarities are summated (Stockard et al 1978b, 1979).

At any age, normal controls show insignificant differences in wave morphology or amplitude, according to the acoustic phase of the stimulus (Stockard and Stockard 1981). Differences have been reported in the literature concerning the effect of phase polarity on latencies. Some authors have claimed that there was essentially no difference between mean latency values for rarefaction versus condensation clicks (Terkildsen et al 1973, Coats and Martin 1977, Rosenhamer et al 1978), whereas others found significant individual variation within each group (Ornitz and Walter 1975, Peters and Worthington 1979, Stockard et al 1978b, 1979). Stockard et al (1978b) reported that rarefaction clicks produced shorter absolute latencies and better resolution of ABRs than condensation clicks. We have confirmed this finding (figure 2.3). The click stimulus influences wave I latency in all age groups (Stockard et al 1979, Ornitz et al 1980). The early firing of auditory nerve fibres coincides with the lateral displacement of the tympanic membrane as initiated by a rarefaction stimulus (Kiang et al 1965). Since the latency of wave V is usually unaffected by acoustic phase, the I-V interval is phase-dependent (Stockard et al 1979). Differences in ABR as a function of phase also suggests that the more apical

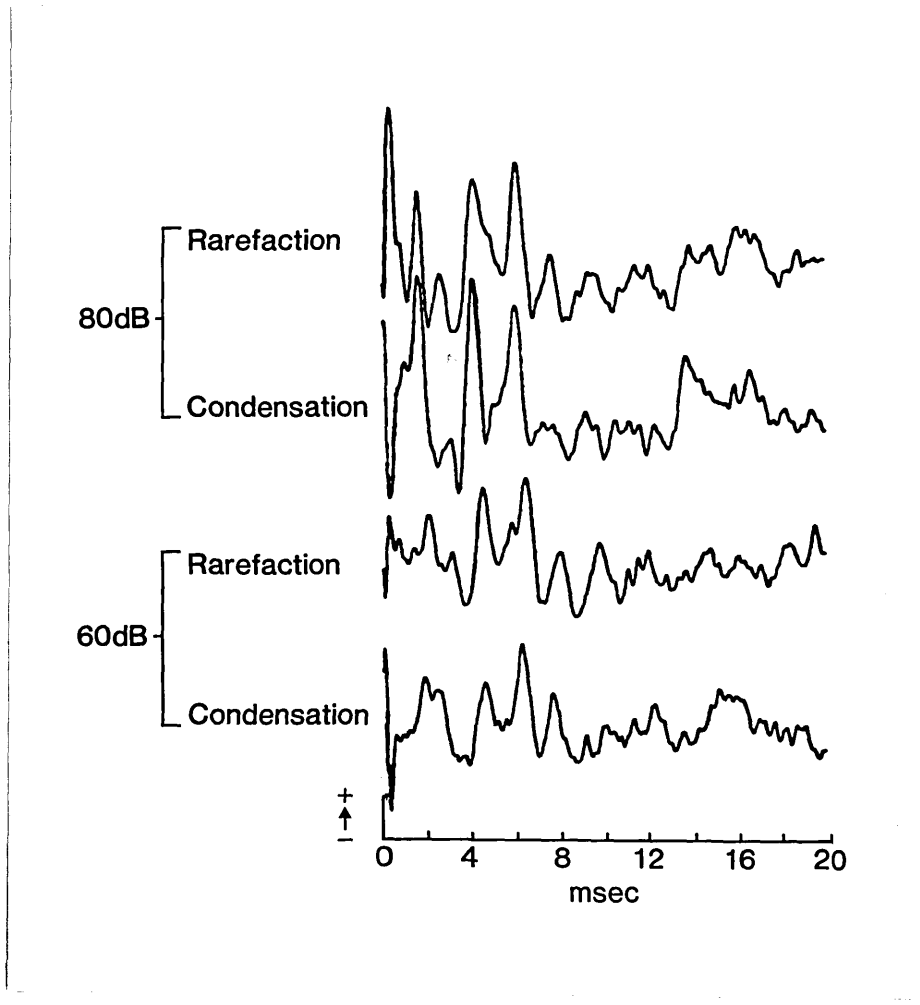


Figure 2.3. The acoustic phases (rarefaction and condensation) are shown at stimulus intensities of 80 and 60 dB. Note that wave I has better resolution with rarefaction phase stimuli than with condensation phase stimuli at 60 dB. The difference is less marked at 80 dB.

sections of the cochlea mature earlier than the basal portions since the former are largely responsible for the difference in ABRs that are so prominent in neonates.

Ornitz and Walter (1975) reported that the latency and shape of the ABR varied according to the initial phase of the acoustic stimulus. According to Stockard et al (1978b) the initial phase of the click (rarefaction or condensation) is an important determinant of ABR latency both in neonates and in patients with high frequency hearing loss.

The use of alternating polarity minimises electrical and mechanical stimulus artefacts. This may be necessary in some cases, for example when high intensity clicks are used to emphasise wave I or to confirm its absence (Stockard et al 1978b). However, the routine use of alternating rarefaction/condensation (R/C) clicks was not advised by Stockard et al (1978b), as it may cause cancellation of R/C out-of-phase components of wave I in the ABRs.

For clinical use, a single phase of stimulation is used, and norms are obtained using that particular phase. Rarefaction clicks were shown to be the most suitable by Stockard et al (1978) although not applicable in every instance. Therefore, it may be necessary to

obtain normative data separately for both 'rarefaction' or 'condensation' stimuli (Stockard and Stockard 1981).

II.1.4 Mode of Presentation: monaural or binaural

The mode of presentation of the stimulus, monaural or binaural, has been shown to influence the ABR. In otoneurologically normal subjects, binaural stimulation usually results in a response of increased amplitude (Jewett and Williston 1971, Blegvad 1975, Starr and Achor 1975, Stockard et al 1978b). Blegvad (1975) found that at all stimulus intensities binaural stimulation produced a higher amplitude of wave V than did monaural stimulation. Stockard et al (1978b) reported that binaural stimulation increased the amplitude of waves III to V, but not that of waves I and II. The observation that binaural interaction occurs in the later components of the ABR (waves IV, V-VI) suggests that the earlier waves are determined exclusively by monaural input (Dobie and Norton 1980). In the infant, these effects closely resemble the adult responses, but with the expected latency delays. Hosford-Dunn et al (1981) and Salamy (1984) concluded that bilateral integration of sound is operative at or near birth.

Binaural stimulation should be avoided in routine clinical testing. This is because monaural abnormalities are common with

brainstem lesions, and may be masked by the response from the normal ear (Stockard et al 1978b). Subjects with unilateral cochlear or central dysfunction might go undetected because stimulation of the normal ear (using binaural signals) might elicit components (Starr 1984). Separate monaural stimulation of each ear also allows comparison of interaural asymmetries in the IPIs, and may thus indicate abnormalities even when the ABRs from each ear are within normal limits when considered individually. Assuming proper identification of components and technically optimal recordings, interaural I-V IPI differences greater than 0.5 msec should be considered abnormal (Stockard et al 1980).

II.2. THE RECORDING PROCEDURE

II.2.1. Electrode placement

One of the most important considerations in obtaining reliable ABRs is electrode placement. Ordinarily, three electrodes are used: one on the vertex (CZ), one on the ipsilateral mastoid (relative to the stimulated ear), and one on the contralateral mastoid processes. The vertex and mastoid electrodes are called the 'active' and 'reference' electrodes respectively. Picton et al (1974) used a variety of differential and referential recordings to establish the distribution of ABRs over the scalp. Wave V was found to be maximal at the vertex but quite broadly distributed across the scalp, being

clearly evident at temporal, parietal and frontal electrodes. Martin and Moore (1977) used a 13 electrode array in an attempt to describe the distributional characteristics of the brainstem potentials. They showed that both latencies and amplitudes of a particular wave maintained their relative magnitude across any electrode site.

Stockard et al (1978b) observed that wave I amplitude increased when the electrode was applied to the ear lobe, instead of to the mastoid process. This increase in wave I amplitude effectively reduced the V:I amplitude ratio. With this electrode configuration, the amplitudes of waves I and III were reduced, wave II became more prominent, waves IV and V were clearly separated and the latency of wave V increased (Thornton 1975b, Fria 1980). Subtle differences in latency, amplitude and definition of certain waves (between simultaneously recorded responses) support the view that separate neural pathways are represented in ipsilateral and contralateral tracings (Hashimoto et al 1979, Prasher and Gibson 1980). The relative absence of wave I in the contralateral response reflects the activation of an exclusively ipsilateral pathway (the acoustic nerve) and constitutes the main difference between ipsilateral and contralateral responses obtained from a normal full-term infant. Waves IV and V are better differentiated in the contralateral response. This fact may be used to emphasize the wave V complex.

II.2.2. Bandpass Filters

To achieve a successful ABR recording, a favourable signal-to-noise ratio is necessary, because the response is imbedded in unwanted myogenic and neurogenic noise. Computer averaging results in considerable noise reduction, but the use of filters prior to averaging can make a further contribution to successful recording. The filters eliminate unwanted low and high frequency information: only those frequencies between the selected low and high frequency cut-off settings being allowed through the 'bandpass '.

The waveform of the ABR is modified according to the bandpass filter used. This is an important factor, which influences the latency, amplitude and morphology of the response. Jewett and Williston (1971) used bandpass filters of 10 Hz and 10,000 Hz, Sohmer and Feinmesser (1970, 1973) used 250 and 5,000 Hz filters, and other investigators (Starr and Achor 1975, Stockard and Rossiter 1977, Stockard et al 1978a) have used 100 Hz and 3,000 Hz filters.

Stockard et al (1978b) found that increasing the high filter setting (-3 db frequency cut off) resulted in progressive decrease in the absolute latencies of all components. Resolution was optimal at a setting of 3 KHz, further increases to 10 KHz not helping to resolve the IV/V complex and only adding high frequency noise.

Increasing the low frequency setting (-3 dB cut-off) from 1.0 to 300 Hz resulted in progressive decrease in the absolute latencies of all components: wave V became smaller relative to wave IV (Stockard et al 1978b).

Stockard et al (1978b) reported that the use of low frequency filters (100 to 300 Hz) had no clinically significant repercussions on waves IV and V, but that it decreased the ratio of the amplitudes of waves V and I. Figure 2.4 compares low filters of 100 and 300 Hz. There is a growing trend to adopt a 100 to 3000 Hz bandpass in clinical testing. Fria (1980) questioned whether bandpass filtering might eliminate information of potential clinical importance as well as unwanted noise. Certain investigators prefer rather broad filter settings (eg 30 Hz to 3000 Hz).

II.3 THE SUBJECTS

II.3.1 Age and Maturation

Maturation has a significant influence on ABR parameters (Hecox and Galambos 1974, Salamy et al 1975, 1978, 1979, Salamy and McKean 1976, Starr et al 1977, Stockard et al 1983a) (figure 2.5). Age affects ABR parameters such as latency and amplitude. Latencies are greatly prolonged in premature infants and neonates, and become progressively shorter in the first two years of life (Mokotoff

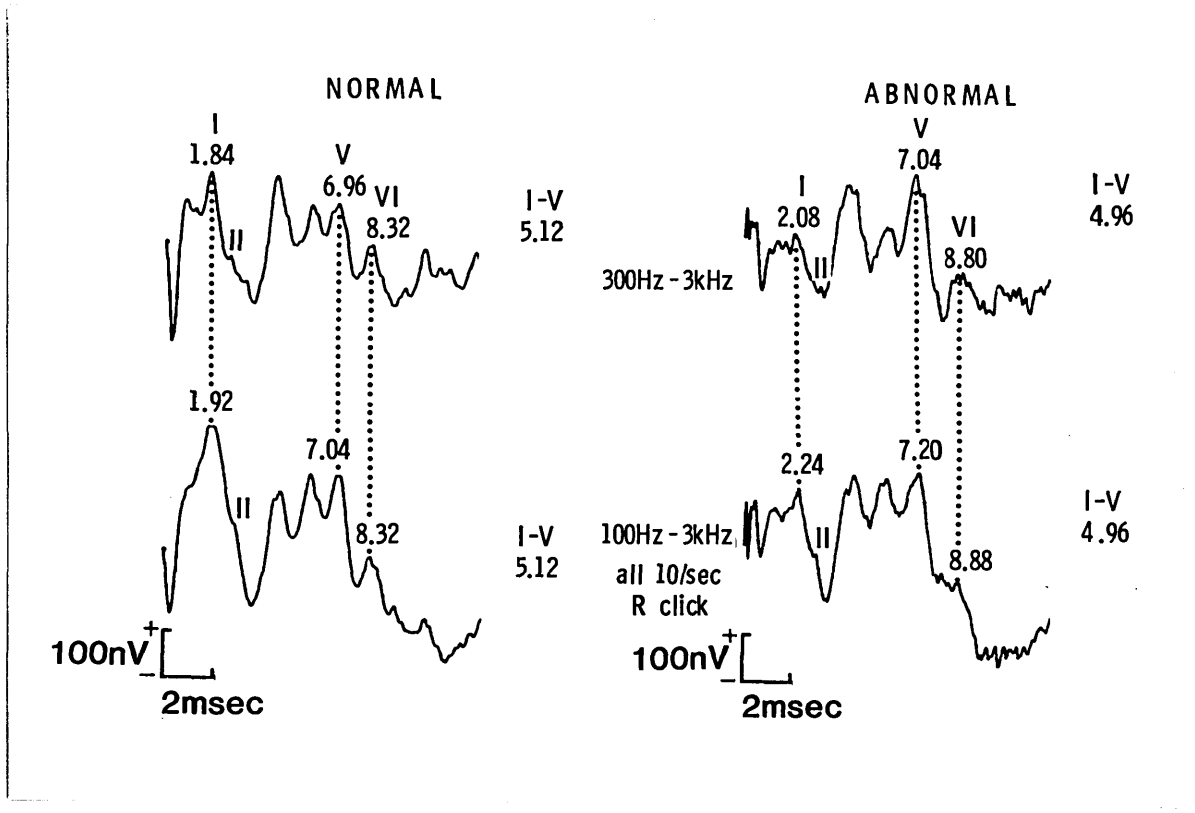


Figure 2.4. ABR recorded in an infant who was clinically and neurologically normal, and from another infant with a diagnosis of periventricular haemorrhage. Two filter settings were applied (300 Hz-3KHz and 100 Hz-3KHz). Wave VI was better defined with the use of the 300 Hz filter. Little change was shown in the latencies of waves I and V.

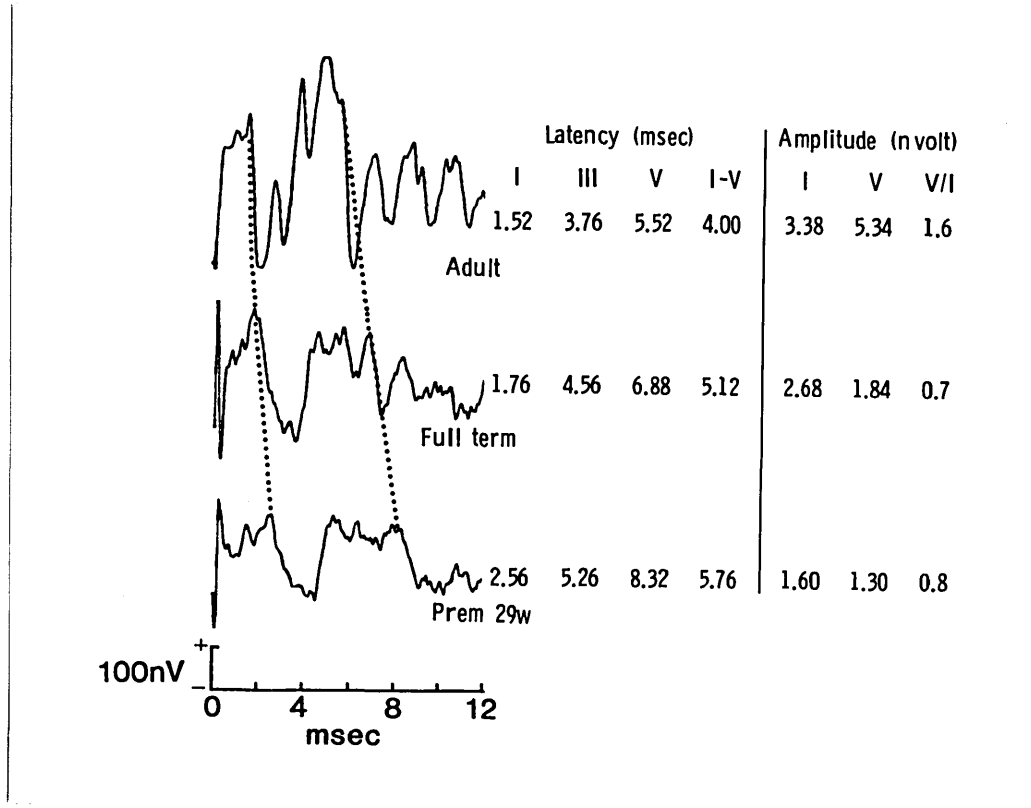


Figure 2.5 Changes in latency (decrease) and amplitude (increase) with maturation in 3 subjects (29 weeks preterm infant, full term infant, and adult).

et al 1977). Figure 2.6 shows the maturation occurring in the course of one week, and figure 2.7 demonstrates maturation as a preterm infant reaches term.

Jewett and Romano (1972) reported that absolute ABR latencies shortened with increasing age, in both the cat and rat. They further noted that the latencies of the earlier waves reached adult values at younger ages than did those of later waves. Leiberman et al (1973b) examined normal adults, infants and neonates and found that there was a progressive shortening in the latency of wave V up to 18 months of age. In these studies only wave V was measured and the authors were not able to distinguish the involvement of peripheral and central mechanisms.

A decrease in absolute latency with increasing age has been observed throughout the second year of life (Hecox and Galambos 1974, Salamy et al 1975, Salamy and McKean 1976). Hecox and Galambos (1974) found that the latency of wave V decreased systematically in infants whose ages ranged from three weeks to 32 months. Salamy and McKean (1976) reported that in infants aged from 20 hours to 12 months the latencies of the first five waves were reduced as the child grew older. The changes in mean latency were

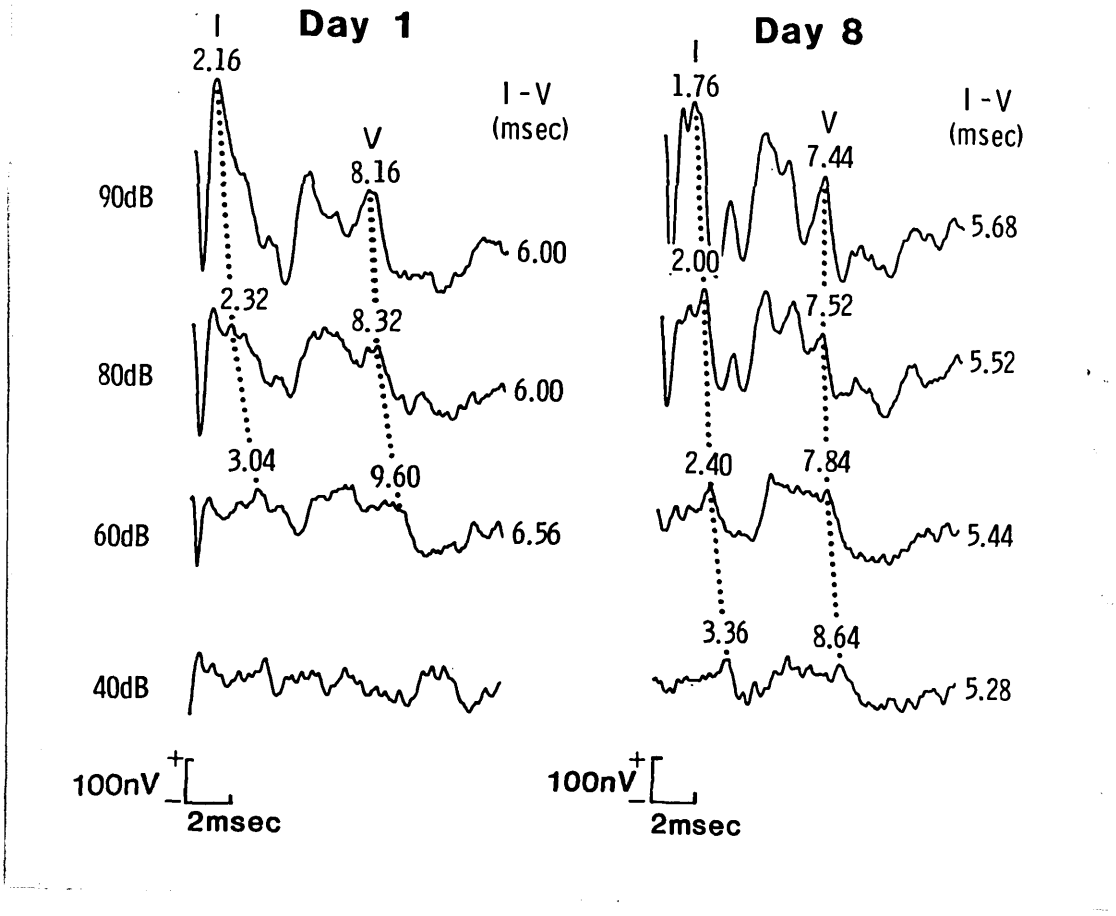


Figure 2.6 Maturational changes over the course of one week, as demonstrated in a preterm infant of gestational age 29 weeks. At 30 weeks there was a decrease in the latencies of waves I,V and of IPI I-V. The ABR was recorded at 4 intensities (90, 80, 60 and 40 dB).

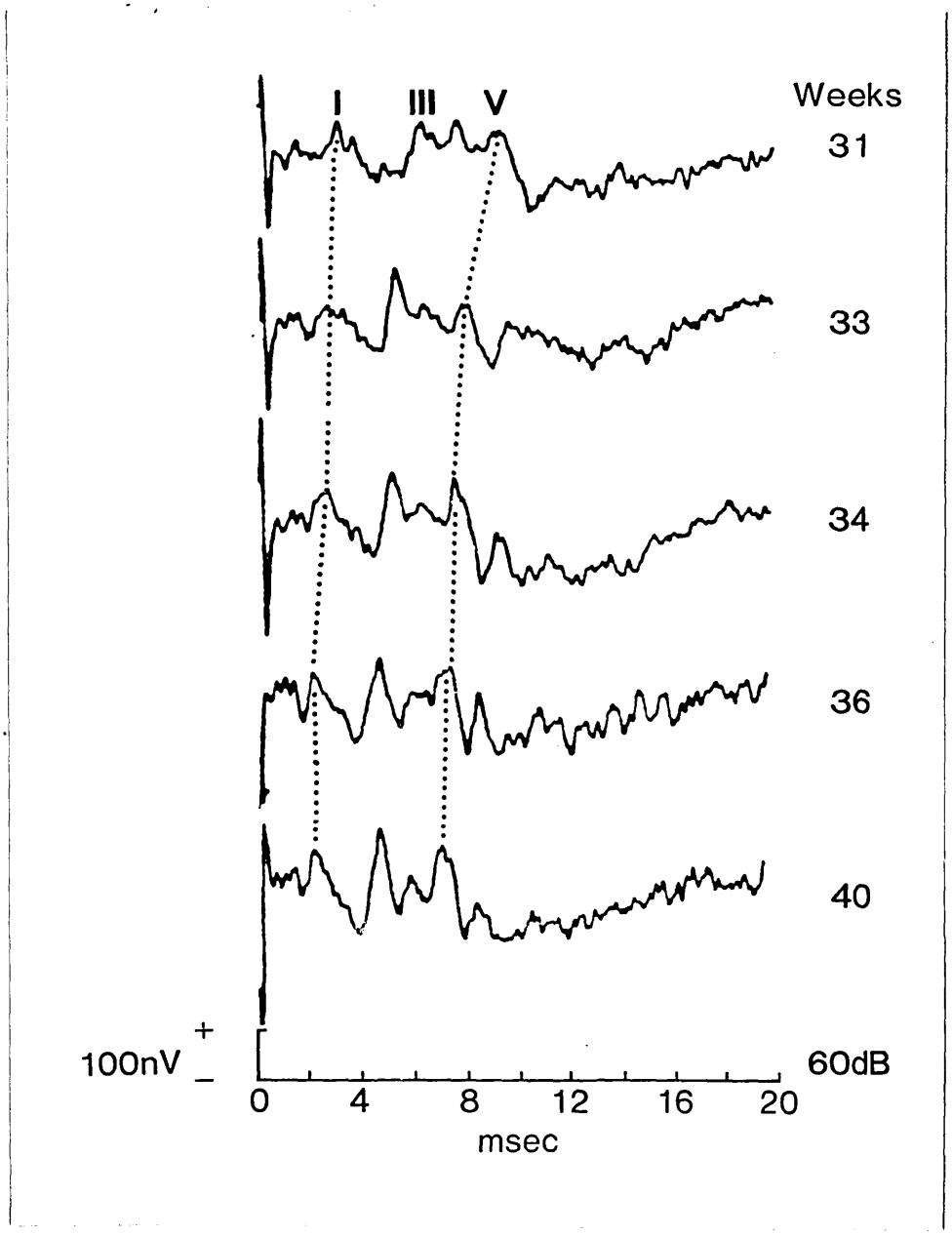


Figure 2.7. Longitudinal changes showing maturational trend (in latencies, amplitudes and waveform), at post-conceptional ages 31, 33, 34, 36 and 40 weeks in one infant. Click stimuli : 60 dB and 10/sec.

greater for wave V (1.12 msec) than for wave I (0.41 msec). In addition, after 6 to 8 weeks of life there was a slight decrease of the latencies throughout the first 12 months of life. The interpeak intervals were also prolonged for infants under two years of age compared to adult values and varied inversely with age. Hecox (1975), Salamy et al (1975) and Salamy and McKean (1976) observed that during the first year of life the I-V IPIs decreased from 5.12 msec (in full term newborns) to 4.2 msec (in 12 month old infants). Salamy and McKean (1976) found an abrupt decrease in I-V interval by six weeks of age,a fairly stable value through the next six months, and then another abrupt decrease between the ages of 6 and 12 months.

There is controversy as to the order in which peripheral and central maturation occur. Peripheral transmission (assessed by wave I) represents activation of the cochlea and conduction through the eighth nerve (Salamy 1984). Central transmission assessed by the IPI between waves I and V represents neural events occurring between the point at which the eighth nerve enters the brain stem and the level of the inferior colliculi. Salamy and McKean (1976) were the first to demonstrate that the peripheral and central components of transmission attain adult latency range by the sixth week, and that by the age of one year central transmission times also reached adult values. Other authors disagreed, claiming that peripheral latencies

continued to decrease up to six months of age and that central transmission times continued to decrease up to 3 or even 5 years of age (Galambos and Hecox 1978, Mochizuki et al 1982).

To interpret decreases of latency with age one must understand the source of latency changes. Changes in neural structure which may account for latency shifts include increases of fibre diameter, progressive myelination and increased dendritic arborisation (Hecox 1975). Myelinated fibres conduct more rapidly than unmyelinated fibres. The age at which the density of central fibres attain adult values, and the relation of fibre diameter to age have not been determined. There are likewise no data relating to innervation density or to the degree of dendritic arborisation with age.

Myelination and the shortening of latency with age have been described (Hecox 1975, Salamy and McKean 1976, Salamy 1984), and there are numerous studies of the myelination of cranial nerves. It has been known for a century that myelination starts in the human foetus at the 30 cm stage (approximately 25 weeks gestation) (Bechterew, 1885). As far as the eighth nerve is concerned myelination is said to be complete at birth. Myelination proceeds caudo-rostrally and the lower brainstem structures are well myelinated before birth (Flechzig 1920, Langworthy 1933, Yakovlev

and Lecours 1967). Rorke and Riggs (1969) have suggested, however, that myelination of the inferior colliculus and medial geniculate bodies is not complete at birth.

Shah et al (1978) studied the correlation between the decrease in ABR latencies during development and the progress of normal myelination. They plotted the concentration of cerebroside (a myelin lipid) in the inferior colliculus of the rat against IPI II-V over a 50 day period, and found a strong inverse relationship between the two measures, which disappeared by the age of 50 days.

Studying tri-ethyltin (TET) intoxication in rats, Amochaev et al (1979) observed increases in absolute latencies and in IPI I to IV readings which they attributed to disturbances in myelination. On stopping the administration of TET the ABR latencies and myelin contents normalised within two weeks. In man, demyelinating diseases affecting auditory pathways in the brainstem produce prolongation of ABR latencies and IPIs (Starr and Achor 1975, Robinson and Rudge 1977, Stockard and Rossiter 1977).

It will be seen that the degree of myelination of the relevant pathways contributes to changes in ABR latencies. This process is thought to be age dependent (Leiberman et al 1973a and Fabiani et al 1979). Some investigators (Dubowitz et al 1968, Moosa and Dubowitz

1972, and Miller et al 1983) found a high correlation between gestational age and nerve conduction velocity (NCV). Increases in NCV depend on myelination brought about by Schwann cells, which are also responsible for the myelination of the auditory nerve. In an extension of these earlier studies Miller et al (1984) compared NCV with latency of wave I and with conduction velocity through the auditory brainstem pathway as reflected by interpeak latency (IPI I-V) in preterm and full term infants. Although they found a linear relationship between wave I latency and NCV, they found a poor correlation between IPI I-V and NCV. This suggests that the factors governing normal maturation of central transmission were not related to myelination of the peripheral nerves. Central transmission is easily affected by many of the risk factors often present in this age group.

There are few studies relating wave amplitudes to maturational change. Leiberman and Sohmer (1973a) observed the highest amplitudes in the responses of infants (compared to neonates or adults). Horiuchi (1975) on the other hand reported that the small amplitudes in infants only reached adult values by the age of two years. Mochizuki et al (1982) observed an increase of amplitude of wave V up to the ages of four years and a decrease thereafter.

Amplitude measurements show substantial variability among normal subjects (Rowe 1978, Chiappa et al 1979, Salamy 1984). This variability has rendered this parameter unacceptable for clinical interpretation (Rowe 1978, 1981, Starr and Amlie 1981, Stockard et al 1983a). The relative amplitudes of the different waves are less variable than their absolute amplitudes. Hecox and Burkard (1982), and Salamy (1984) reported that amplitude ratios follow a pattern similar to the absolute amplitudes of wave V. Gafni et al (1980) reported ratios of less than 1 (0.87) for newborns. This ratio bears no relation to age. This is in contrast to Stockard et al (1983a) and Starr et al (1977). Salamy (1984) states that amplitude ratios shed little light on the developmental processes that determine amplitude.

II.3.2 Sex

Differences between ABR features in male and female subjects have been investigated (Beagley and Sheldrake 1978, Stockard et al 1978a, 1979, McClelland and McCrea 1979). Adult females have shorter latencies than males. Investigators have demonstrated that the absolute latency of wave I was essentially the same in both sexes, but that latencies of waves III and V were significantly shorter in females. The differences have been attributed to shorter anatomical distances in the corresponding segments of the auditory pathway, themselves dependent on the slightly smaller average brain size of

females. The differences in latency are of the order of 0.1 to 0.2 msec and may therefore be accounted for by smaller head/brainstem size. Females also show higher wave amplitudes (Jerger and Hall 1980).

Absolute latencies and IPI in the ABR are not dependent on gender in term newborns (Stockard et al 1980) and separate norms are not needed. Sex differences in absolute latencies and IPIs in preterm infants were only found by Cox et al (1981a), who reported that such differences might be related to the greater vulnerability of males to perinatal injury. The effect disappeared in such infants by the age of four months (Cox et al 1981a). Maturational changes as children of either sex reach adulthood have also been studied. O'Donovan et al (1980) studied a group of 70 children (aged 5 to 11 years) with normal hearing for differences in latency and at different ages. ABR latencies between the ages of 5 and 7 years were the same for both sexes, but latencies in children aged 8 to 11 years differed. A male-female latency difference was shown from age 8 onwards, similar to that seen in adults.

II.3.3 Temperature

Moderate hypothermia prolongs the IPIs. This may lead to errors in interpretation. Stockard et al (1978a) found that a decrease in

brain temperature was associated with increases in interpeak intervals I-III, III-V and I-V. In neurologically and audiometrically normal adults subjected to hypothermia during cardiopulmonary bypass (Stockard et al 1980), the I-V interpeak interval increased beyond the upper limit of normal when the temperature fell below 32° Celsius.

Stockard et al (1978a) had previously shown that prolonged IPIs similar to those seen with central lesions could be produced by temperature decreases alone. Hyperthermia had the opposite effect. Slight decreases in IPI were normally seen in humans and cats subjected to mild hyperthermia (Jones, Stockard and Weidner 1980).

In very small infants, wide temperature fluctuations are common. Temperature was therefore routinely measured in our subjects.

II.3.4 Drugs

The latencies of ABR responses are relatively resistant to pharmacological insults. Of special importance clinically is the fact that IPIs are little affected by most CNS depressants (Stockard et al 1980). Goff et al (1977) recorded the ABRs in patients prior to and during thiopentone anaesthesia and found that response latency was generally unchanged, although amplitudes were reduced by 15%. Stockard et al (1980) showed that with isoflurane anaesthesia

(an agent which diminishes the amplitude of the EEG) ABRs were preserved. IPIs were normal despite the paucity of any spontaneous EEG activity, or even of any clinical evidence of CNS function on reflex testing. High doses of many non-specific CNS depressants, including most general anaesthetics, reduce the amplitudes of the late waves in the ABR.

Drugs affecting specific neurotransmitters involved in the generation and modulation of ABRs, for instance serotonin (Bhargava and McKean 1977) and acetylcholine, alter the relative amplitudes of various ABR waves and will undoubtedly affect IPIs.

The effects of aminoglycoside antibiotics on the ABR have been studied with the idea of developing a means of assessing the ototoxicity of these drugs (Guerit et al 1981). Following rapid intravenous injection in man, amplitude diminished and wave I latency increased, both returning to normal four hours after the injection. With slower intravenous injections, only minor changes in wave I were seen. With oral administration latency changes and disappearance of wave components were seen with subsequent improvement following stopping of medication.

Ototoxic drugs were studied in 15 neonates by Bernard et al (1980). ABR testing was recorded prior to and during treatment with

gentamicin and tobramycin. Changes in ABR were noted in those infants who received the therapy but not in the untreated infants. Cox et al (1982) found a highly significant correlation ($p < 0.001$) between gentamicin administration and hearing loss in the Intensive Care Unit, but the effect was transient.

II.3.5 Alertness

Auditory brainstem potentials are known to be unaffected by whether the subject is alert and attentive, drowsy, asleep, or even unconscious. The ABRs in awake and sleeping human subjects have been investigated in several studies (Amadeo and Shagass 1973, Goff et al 1977, Sohmer et al 1978a, Stockard et al 1978a). Amadeo and Shagass (1973) studied ABRs in six normal adults, both when they were awake and in several stages of natural sleep. Natural sleep had no significant effect on ABR amplitudes or latencies. Sohmer et al (1978a) studied the effects of sedation-induced sleep on the ABRs of six normal children (aged 5 to 10 years). ABRs were recorded while the children were awake, and 15 and 45 minutes after they had fallen asleep. There were no significant latency differences. Picton and Hillyard (1974) studied the effect of attention, and Starr and Achor (1975) studied the effect of alertness on ABR. Both reported that ABRs were unaffected by these factors.

One must finally bear in mind the complexity of the neuro-anatomy of this region of the brain with its ipsilateral and contralateral afferent inputs, internuncial neurons, descending efferent system, and fibres decussating at nearly every level of the brainstem (Hecox 1975). In addition, the ABR in itself reflects algebraic summation of electrical activity, originating from multiple generators, each having a complex cyto-architecture (Jewett and Williston 1971). It is scarcely surprising that ABR patterns in relation to the sites of various anatomical lesions require further exploration and study.

Chapter III. RECORDING APPARATUS AND METHODOLOGY

III.1 EQUIPMENT

An instrument for eliciting ABRs must accomplish four things. It must generate acoustic stimuli, amplify the electrical signals these stimuli produce in the patient, average the elicited waveforms, and display or plot the resultant traces.

The equipment will, therefore, consist of a stimulating unit and a signal processing unit (which will record and display the responses). The processing unit will itself comprise electrodes, amplifiers, filters, averager, display and plotter.

III.1.1. The Stimulator

The stimulus generator used in this study was a Medelec ST10 machine. This produces an electrical wave form which is amplified and then attenuated to a precise intensity level set by the investigator. Intensity can be altered by 5 dB steps, from 0-120 dB hearing level (HL). The signal is then fed to the earphones. The triggering of the stimulus is provided by a computer which immediately stores the data relating to the first 10 msec which follow the triggering pulse. The rate of stimulus presentation is controlled by the computer.

The stimulus transducer is the earphone. It changes the electrical signal to an acoustic waveform with a degree of precision which depends on the quality of the transducer. A discussion of what constitutes an appropriate stimulus and of different methods of stimulation will be found in the section on methodology.

III.1.2. The Recording System

The recording system used during most of this study is shown in figures 3.1.and 3.2. It consists of:

- a headbox (containing preamplifier, filters and a built-in impedance meter).
- a main unit sensor (Medelec ER94 type).
- a computer (Apple II type) for storage and further analysis of the data.

These will be described in turn. A discussion as to their optimum use will be found in the section on methodology.

a) The Headbox

The headbox accepts the signals from the patient and amplifies them to an adequate voltage level, as required by the digital processing section. The responses (evoked potentials) to the acoustic stimuli have to be amplified significantly in order not to be "swamped" by the EEG.

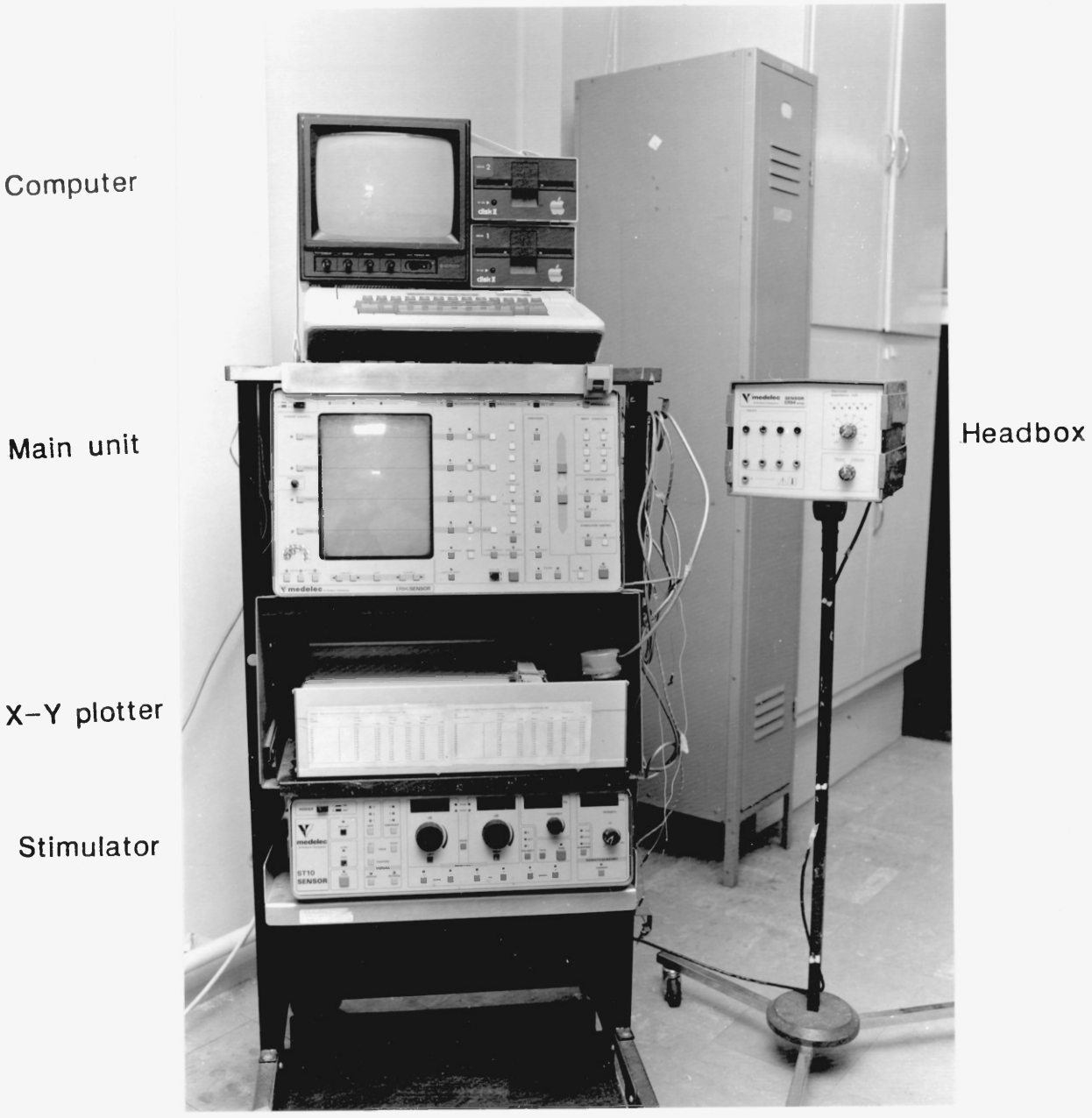


Figure 3.1. The Medelec Sensor used during most of the study. The main unit (ER94), the stimulator (ST10), the X-Y plotter, the Apple Computer with 2 disc drives and the display screen are all mounted on a single trolley.

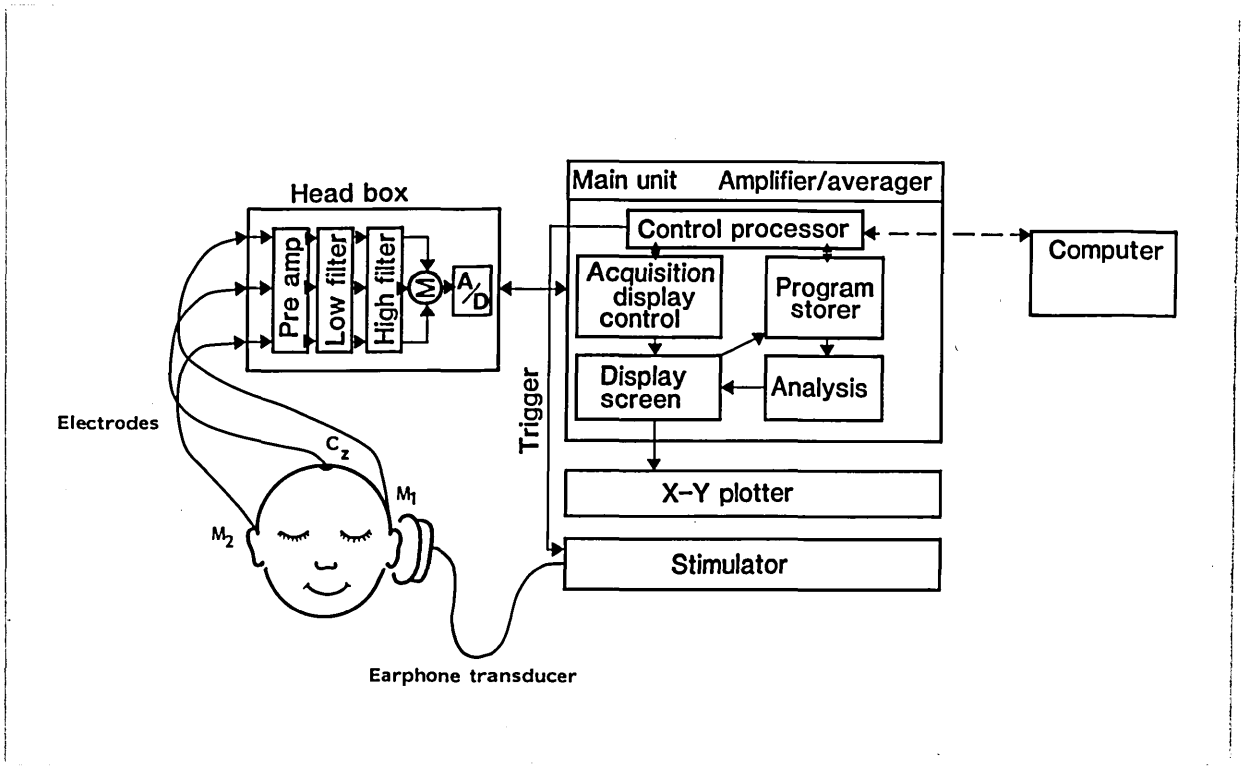


Figure 3.2. Block diagram of the recording and stimulating system. Electrodes Vertex (CZ), M1 and M2 (ipsilateral and contralateral to the stimulated ear respectively are connected to the head box. The head box contains the pre-amplifiers (pre-amp), the filters, multiplexer (M) and analogue-digital converter (A/D). The main unit controls the headbox and stimulator. Acoustic stimuli are transmitted through the transducer (earphone). Traces are either plotted (X-Y plotter) or stored in the computer.

The first amplification is carried out in the preamplifier (there is a further amplifier in the main unit). This headbox then filters the signals, so as to maximally reject interfering signals (noise), while minimally distorting the desired signals.

In the Medelec Sensor Machine, the headbox contains 4 amplifier channels which receive signals from the scalp electrodes. Each amplifier includes high pass and low pass filters. The signals are then passed through a multiplexer (M) which brings the 4 channels of signals into one (figure 3.2). The output of the amplifier is then digitised through an Analogue to Digital (A/D) Converter.

The preamplifier. This connects the scalp electrodes to a differential pair of amplifiers giving very high input impedance with low noise. As with almost all bioelectric recording instruments, the evoked-potential instrument employs a differential input preamplifier. Differential input preamplifiers record only voltage differences between input leads ('differential signals '). Voltages that are the same at the two inputs leads ('common mode signals ') tend to cancel, while voltages that are different at the two inputs 'differential ' signals are passed through and amplified (figure 3.3). In this way, the differential preamplifier

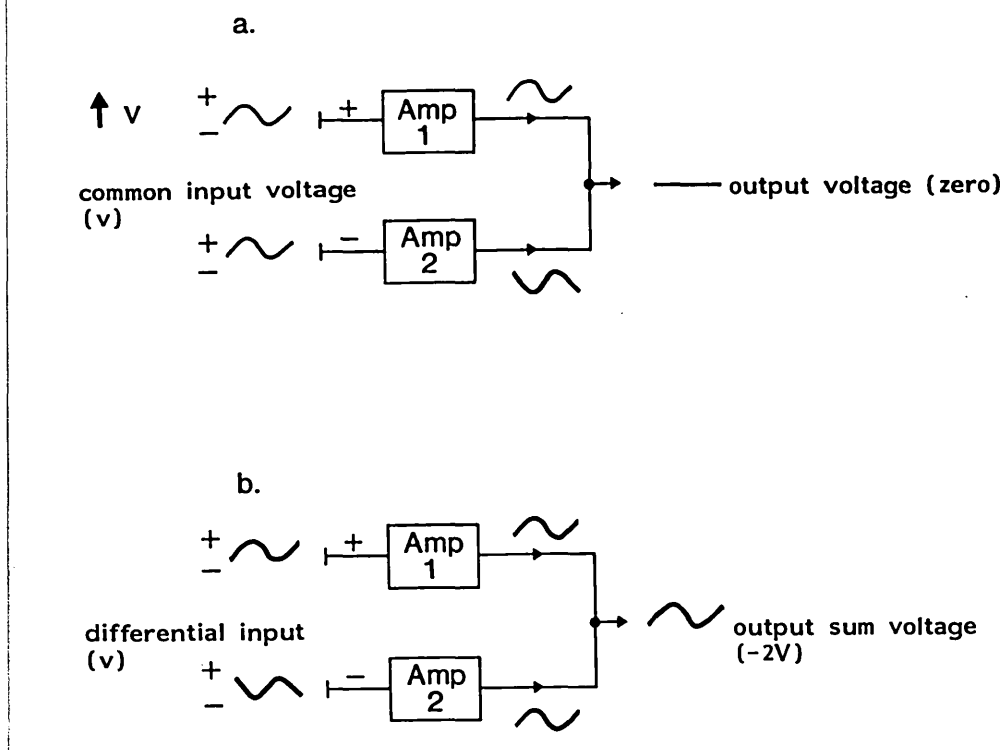


Figure 3.3. Principle of operation of a differential amplifier. The amplifier subtracts voltages applied at its 2 inputs. a) same inputs 'common mode signals' are cancelled. b) different inputs 'differential signals' are passed through and amplified.

selectively attenuates radiated electrical "noise" (for instance from power lines in the building) which tends to be of equal amplitudes at the two preamplifier inputs.

The common mode rejection facility. This is an important part of the amplifier, since it determines the extent to which signals (noise) common to two differential inputs are rejected by the system. The common mode rejection ratio is a measure of the ability of the amplifier selectively to reject the common mode signals. The common mode rejections ratio used was 50,000:1 at 50 Hz (94 dB).

Input impedance. This is the electrical impedance across the preamplifier inputs. The electrodes, after connection, can be checked for good electrical contact by using the built-in impedance meter. This is done by passing a small constant current through the patient and measuring the voltage developed across the patient, calculating the resistance in K Ohms (Ω).

Isolation barrier. This provides isolation of the patient from the power supply of the amplifier and from any equipment used with it. After the signals are digitised, they pass through an opto-coupler to ensure isolation of the patient from electrical hazards. The opto-coupler is a device which takes the electrical signals and

passes them as light across a gap. Photo cells then reconvert the light back to electrical signals. A maximum permissible light intensity is determined, so that no electrical surge can be transmitted through the barrier.

Filters. Each amplifier includes high and low cut-off filters. The bandpass of the recording system is the frequency range between the high and low cut-off points (high and low frequencies). The filters restrict the bandwidth to one suitable for the amplification, thus minimizing extraneous noise signals. The selection of bandpass is important. The response morphology and relative amplitude of the various waves can be altered by changes of bandpass.

, Most modern amplifier systems, (such as the one we used), have the gain, filter settings, and input electrode channel selections controlled from the main unit. This greatly diminishes operator error.

b) The main unit

Ongoing bio-electrical events in the patient (for instance the EEG and ECG) tend to swamp the activity evoked from the specific neurosystem being investigated. In order to observe, record, and

measure "evoked responses", special techniques using computer averaging are used.

Any periodic or repetitive pattern of electrophysiological activity found in the presence of random electrophysiological activity, can be extracted (in terms of its periodicity or repetition pattern) from the random background by means of averaging. Computer averaging of the ABR seeks to extract a relatively small, time-locked electrical response to acoustic stimuli from the larger ongoing electrical activity. In other words, averaging seeks to enhance time-locked responses in relation to non-time locked background "noise".

Averaging seeks to improve the signal to noise ratio. The success of the procedure depends upon the number of samples available. Changes in signal to noise resolution are proportional to the square root of the number of samples investigated.

The gain. Gains are set according to the requirements of 'downstream' sections (the filters, and the main unit) and these differ from instrument to instrument. In the Medelec (Sensor) machine negative feedback from the output amplifiers set the gain of

the input stage to nominally X10 (i.e. the signal is initially amplified tenfold in the preamplifiers).

The artifact auto-rejection facility is of great help. It selectively rejects any epoch that contains points exceeding the A/D convertor limits. Any incoming sample that overloads the system during the sweep time (for instance muscle artefact or the EEG) will be rejected because it is outside the preset sensitivity. Artefact rejection adds greatly to the efficiency of an averager, since irrelevant and unwanted information need not be averaged out by successive runs.

The control processor sets up the parameters required for signal acquisition. These parameters are programmable. They can be stored and retrieved, and can be modified by the user. For the purpose of this study the recording parameters were standardised for all tests, thereby constituting the programme.

Once the ABRs have been averaged, various mathematical calculations can be applied to the results. Time measurement (latencies) and amplitude calculations are carried out using dot

cursors. Facilities were available for summation, subtraction, superimpositions, and inversion of traces.

A permanent record of the traces on the screen may be obtained by an X-Y plotter. The records may also be stored on floppy discs.

c) The computer system

The computer system (Apple II) has a 48K memory, dual floppy disc drives and a display screen unit. It is linked to the sensor via a computer interface (standard RS 232) and has access to all the data stored on floppy disc.

III.2 METHODOLOGY

A Neonatal Intensive Care Unit (NICU) is an electrically and physically hostile environment for the recording of ABRs and a project of this kind involves the capacity to cope with both electrical and human interference (figure 3.4). The standard procedure used will be discussed first. The specific problems encountered in the NICU (and methods for coping with them) will then be listed.

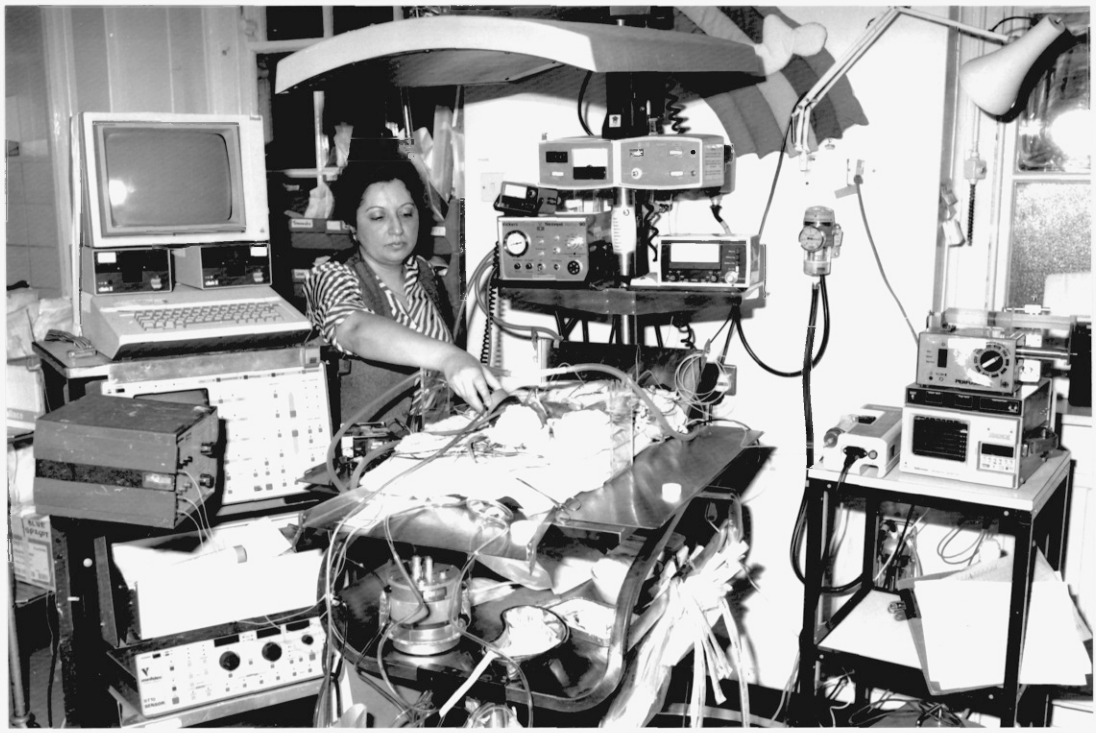


Figure 3.4. ABR testing is carried out on an infant lying in an open incubator in the NICU. The hostile environment for ABR testing involves coping with various interferences including electrical.

III.2.1 Test procedure

In the NICU the infants were tested 'at the bedside'. In practice the infants were lying in open or closed incubators, or cots. To keep muscle artifact to a minimum the subject undergoing ABR testing should, ideally, either be resting quietly or be asleep. In our population it was difficult to achieve a good test position, involving a minimum of myogenic activity from the neck muscles. Babies are best tested during natural sleep, after they have been fed and had their nappies changed.

With infants and children, it may be difficult, time-consuming and often impossible to induce quiet rest or sleep. When there was no medical contra-indication, we used sedatives for older infants or children attending for follow-up. Chloral hydrate (30-50 mg/kg) was administered orally and proved to be satisfactory. It was pointed out in chapter II that sedatives do not significantly affect responses. Every effort was made to test infants without resort to sedation, but whether this was achieved or not was highly dependent on the age and the condition of the infant at the time of testing. Special measures were taken to ensure cooperation without sedation. These include sleep deprivation (of their mid-day nap), and ensuring that the time of ABR testing coincided with feeding carried out at the clinic, prior to testing. In clinical practice, the time

allocated to testing had to be balanced against both the patient's ability to tolerate the testing procedure, and the value of the information generated. This demanded compromises in the number of replications obtained, and in the number of stimulus variables used.

The duration of each test depended on the information required. A full threshold estimation run (with repeat testing for reliability) may take over an hour. In a standard ABR recording both left and right ears were tested separately. The baby usually lay prone with one ear on the mattress. An earphone was held gently over the other ear taking care not to occlude or collapse the external auditory canal. Collapse of the canal will result in appearances simulating a conductive lesion. The earphone used was a TDH 39, especially adapted for paediatric use (figure 3.5). Click stimuli were presented monaurally through the earphone.

Routinely used intensities were initially 80 and 60 dB. These intensities were altered as needed for particular subjects and situations, and according to the responses obtained. If the responses were poor, intensities were increased in 10 dB increments. If the responses were good, with well identified wave components, the stimulus was decreased to 40 dB. Time, infant availability, and the well being of the infant were limiting factors. All recordings

Figure 3.5. The earphone used in the study was a TDH 39 especially adapted for paediatric use in our unit.

were repeated to check for consistency. In certain cases the variability from run to run was an important factor in the analysis and indeed of the diagnosis.

III.2.2. Application of Electrodes:

Three standard electrodes were used: two were connected to the preamplifier inputs and a third was used as a ground electrode (figure 3.6). The active electrode was placed over the vertex, at Cz (midway between nasion and inion) of the international system (Jasper 1958). In babies, the posterior edge of the anterior fontanelle was used as a land mark. The reference electrode was placed over the mastoid process ipsilateral to the ear stimulated (M1). The contralateral mastoid process was used for the ground electrode (M2).

A fourth electrode was sometimes applied to the forehead and used for grounding while M2 was recording the contralateral ear in a second channel. Due to limitations of time and availability of the babies, and to avoid excessive handling, we found it was more convenient to use 3 electrodes most of the time. Occasionally, the ground electrode was placed on the forehead when access to the contralateral mastoid process was prevented when only minimal

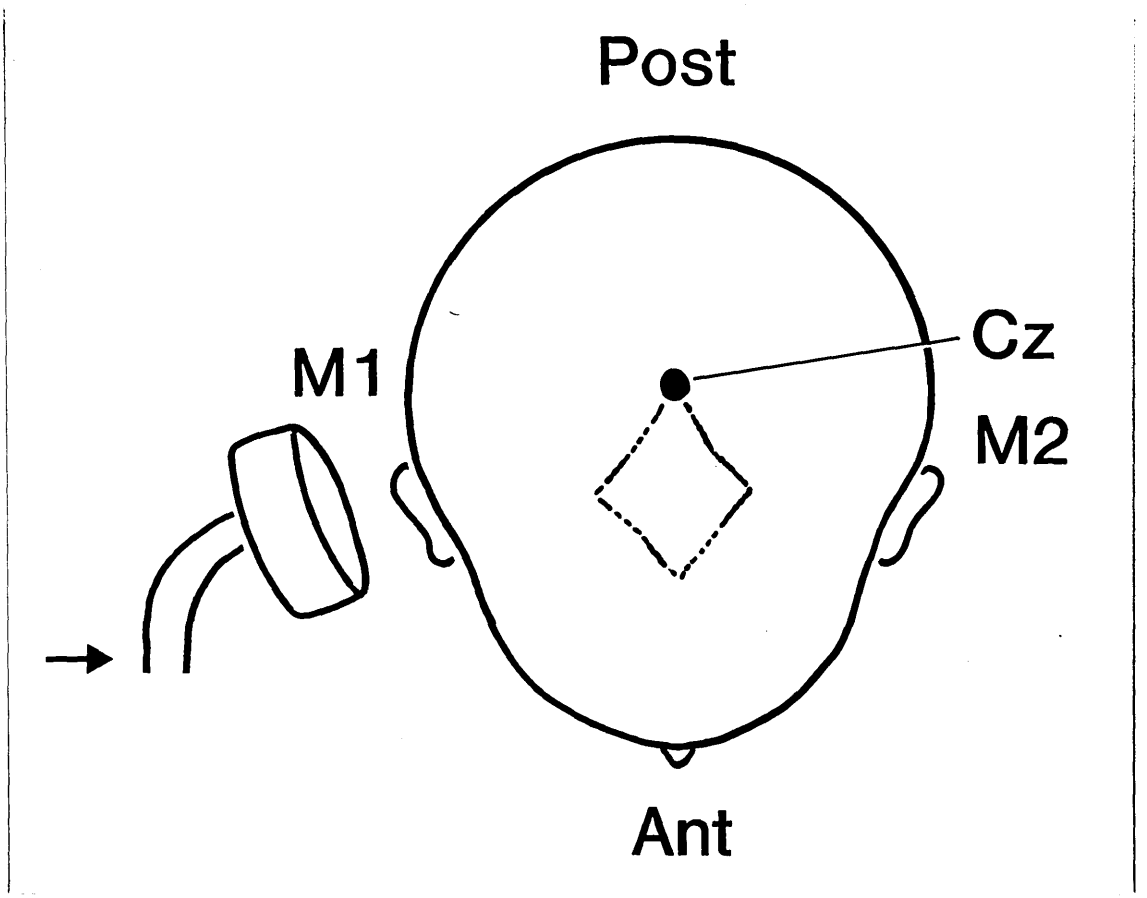


Figure 3.6. Electrode placement for recording. Three electrodes were used, one on the vertex (CZ) as the active electrode, and one over each mastoid. The electrode ipsilateral to the tested ear was called M1 and the contralateral or ground electrode was called M2.

handling was judged permissible or when the position of the head was fixed due to either ventilatory support or to the presence of an intravenous drip.

Standard silver EEG surface electrodes (about 1 cm in diameter, and containing a recess for electrode paste) were used. Electrode sites were first cleaned with surgical swabs. The electrodes were then attached by means of a paste. Initially a thick paste (Bentonite in 5% NaCl solution, with 0.1 ml of glycerine per 5 ml of paste) was used. Evaporation and subsequent hardening of the paste was reduced by placing a piece of cotton gauze over the attached electrode. Cling film was then added (sometimes without the gauze) to secure firm attachment of the electrodes. Later, it was found that Neptic jelly and surgical tape (3M) were adequate. This type of attachment could be applied quickly, was easy to remove, and did not cause discomfort in the babies.

Contact impedances (measured at 1 KHz using the built-in impedance meter) were generally of the order of 1 to 2 KΩ, but on rare occasions impedance was as high as 6 KΩ.

III.2.3 Optimum stimulus in theory and practice

Action potentials are best evoked by a brief stimulus with a rapid onset. An ideal stimulus:

- Should have a sharp onset (for good synchronisation) and be timed accurately (so that response latencies are unequivocal);
- Must be frequency-specific, (so that a chosen section of the cochlea may be selectively stimulated);
- Should be of precisely known intensity, (for threshold assessment).

A click stimulus meets the first requirement but has no frequency-specificity. It nevertheless evokes an excellent "whole nerve" action potential. A frequency-specific stimulus is a pure tone, devoid of any click artefacts. Such a stimulus must have a gradual rise and fall to avoid high frequency transients. This slow rise-time prevents the stimulus from meeting the first requirement. Moreover it does not allow for close synchrony of firing of the individual hair cells within the basal turn of the cochlea.

Three types of stimuli provide a compromise and allow some frequency information to be gained.

Tone pips are induced by passing a single sinusoidal wave, which begins and ends at zero crossing, through high and low pass filters (eg 2 - 0 - 2 msec) (Figure 3.7). Such stimuli only have maximal energy during the period of a single sinusoid.

Tone bursts are periods of tone stimulation which are shaped so that they have a rise time of 1 or more milliseconds, a plateau of maximal energy lasting several milliseconds, and a preset fall time. Figure 3.8 shows a tone burst of 2 - 6 - 2 msec. At lower audiometric frequencies tone bursts do not evoke clear responses.

Clicks provide a precise onset for triggering. They stimulate the whole basal portion of the cochlea almost instantaneously. This results in close synchrony of firing of individual nerve fibres, thereby producing an evoked potential that can be clearly recorded.

Clicks are commonly used in ABR testing as, in general, they tend to produce larger and consequently better defined evoked potentials than other more frequency-specific stimuli such as tone bursts or pips (Picton and Devrieux Smith 1978). Clicks are produced by feeding a short duration monophasic square wave into transducers. The accuracy with which a transducer produces an acoustic output depends on the quality of its construction. The sound output when viewed on an oscilloscope appears rather like dampened oscillation.

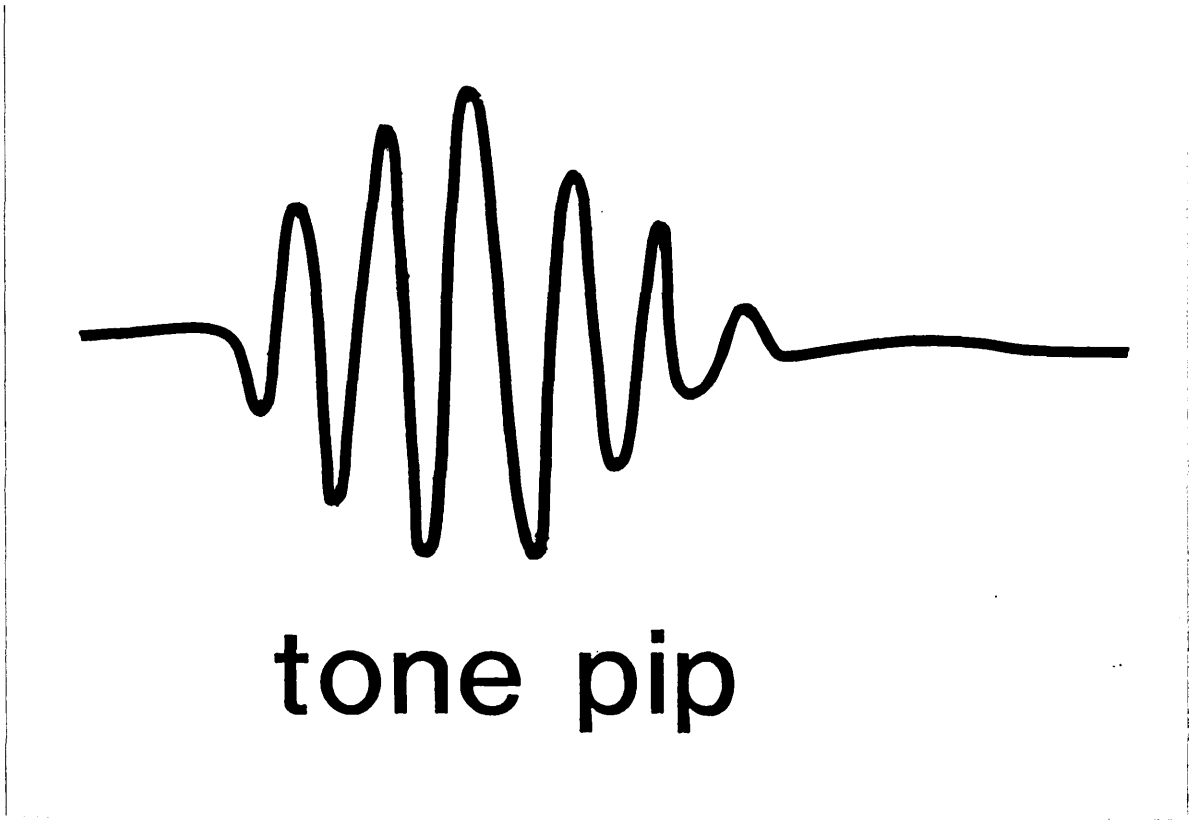


Figure 3.7. A tone pip is a frequency specific stimulus. A useful 'wave envelope' is 2 - 0 - 2 msec.

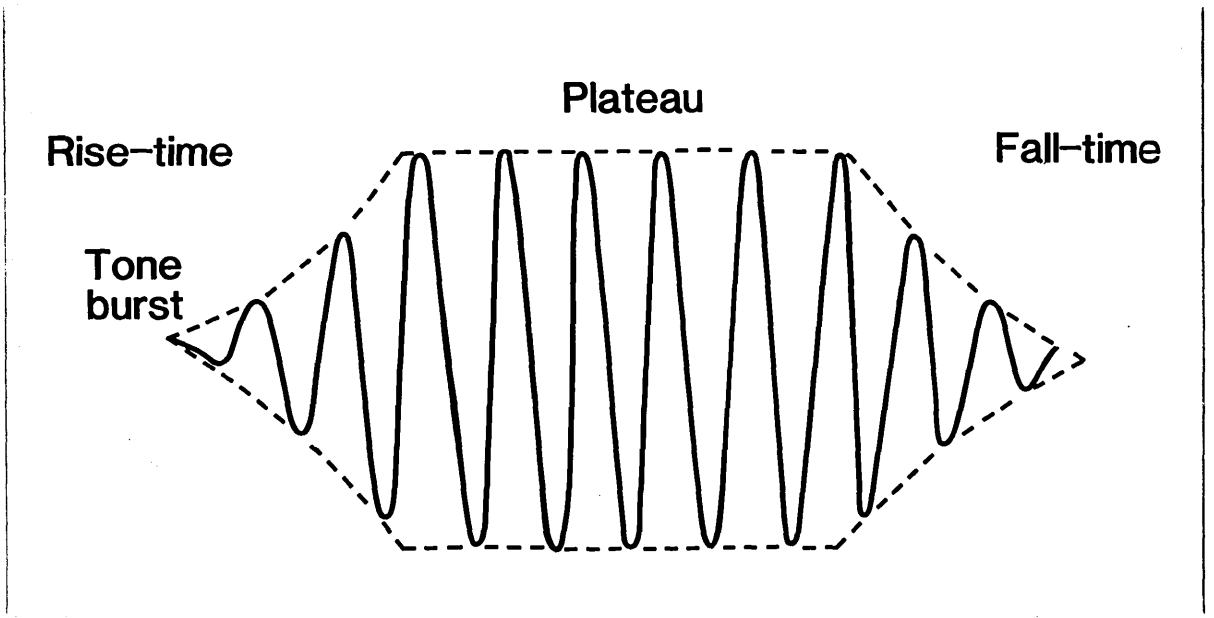


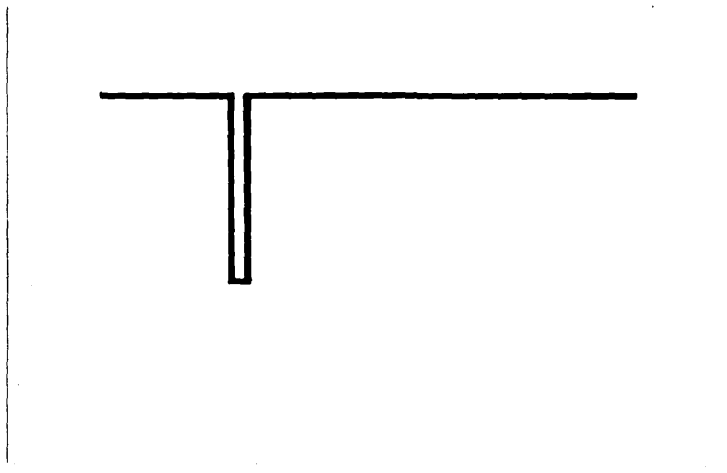
Figure 3.8. A tone burst. The wave envelope has a rise time of 2 msec, a plateau lasting 6 msec and a fall time lasting 2 msec.

Figure 3.9 shows the electrical and acoustical outputs. Analysis of a click stimulus reveals that it contains a wide spectrum of frequencies and that at its onset the higher frequencies predominate (figure 3.10).

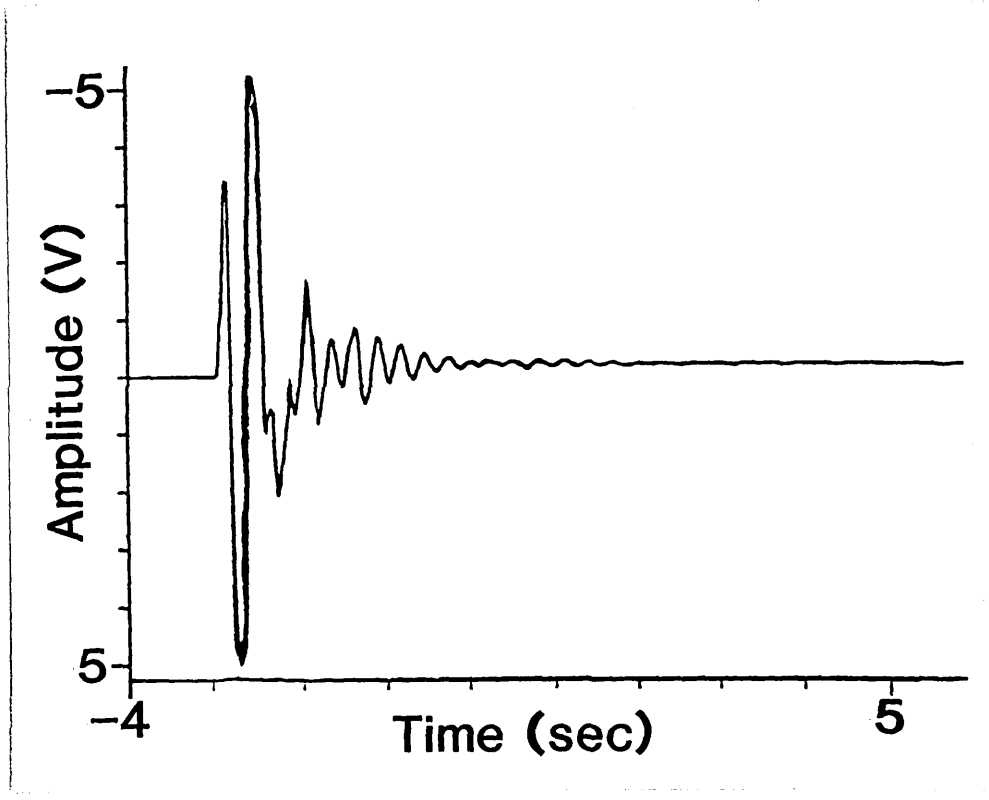
Calibration of the intensity of click stimuli is made difficult by their transient nature. Subjective calibration is the most convenient means of calibrating transient stimuli (Gibson 1978). This is usually done by testing the hearing thresholds of a number of otologically normal adults (with no history of noise exposure) and setting their mean thresholds as the zero (0 dB HL). Another possibility is to compare a given stimulus level with a reference sound pressure level (SPL). In this study Medelec Ltd. used subjective calibration to set the zero level.

III.2.4. Programme (scope of investigation):

The parameters of stimulation were controlled by a separate microprocessor, which allowed up to ten routines, which could be modified and programmed in by the user. Parameters routinely used in the programme are shown in Table III.1. The band-pass low frequency filter was set at 300 Hz (roll-off characteristics 6 dB/octave) and high frequency filters at 3 KHz (-12 dB/octave).



100 μsec click
electrical output



Acoustical output
of the electrical
input to a
TDH 39 earphone

Figure 3.9. Electrical and acoustic outputs from the TDH 39 earphone. The electrical output: 100 μsec click stimulus.

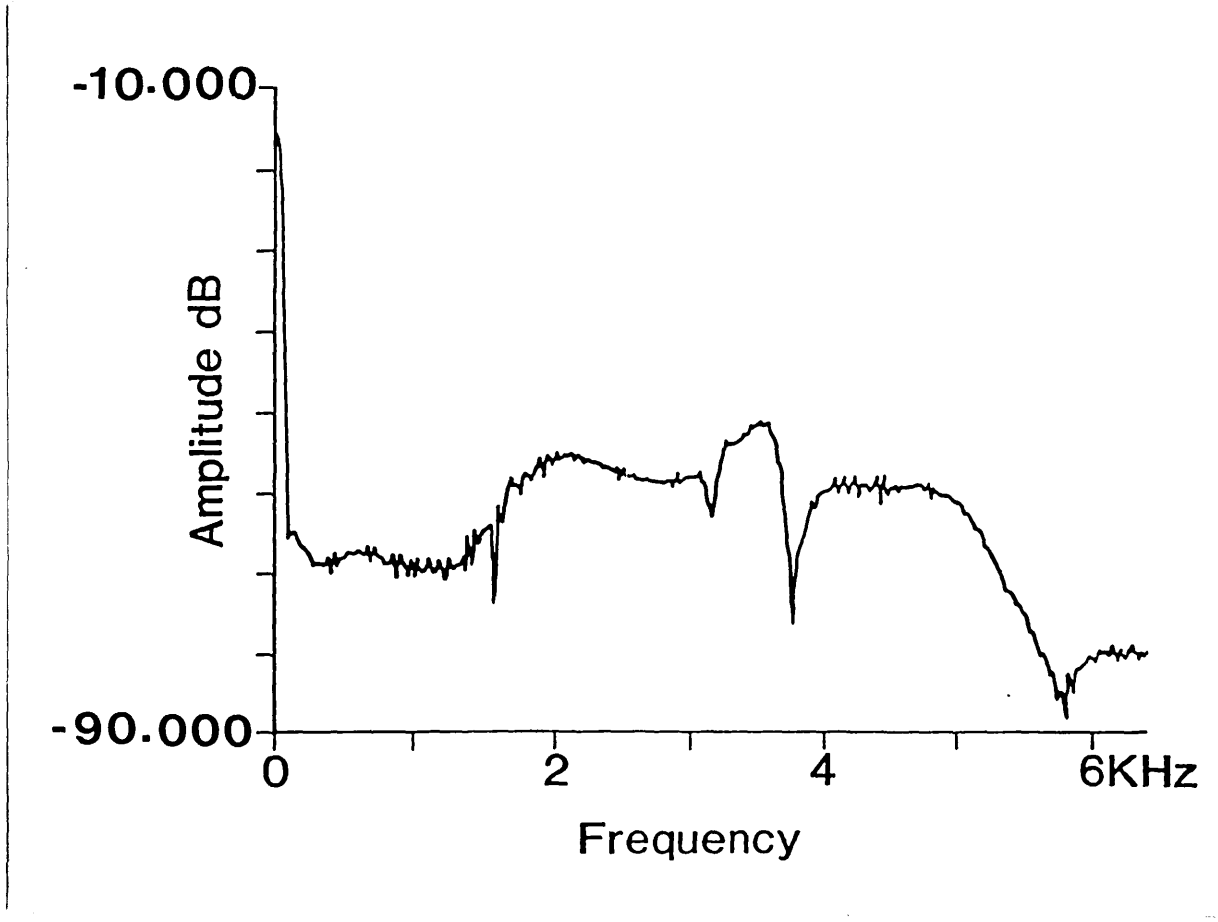


Figure 3.10 The spectral content of a click stimulus with the main energy in the region of 2 to 4 KHz.

We found the use of low frequency filters set at 300 Hz to be most suitable. Many factors affect the feasibility of studying ABRs in the setting of the NICU. Among these are the NICU environment itself, the interference from other equipment, and the time limitation imposed by the handling of sick infants. Clicks were used at a rate of 10/sec. This is generally accepted as the most suitable frequency for neurological diagnosis.

III.2.5 Computer software:

The computer programmes for data acquisition, storage, display and analysis were written by Medelec Ltd. The stored data could be retrieved from the discs by the same programme. The programme initially retrieved an index of patients, whose responses were recorded on the disc being interrogated. Each response could be removed from the disc, displayed on a screen, further analysed, and then either copied on a printer or plotted on an X-Y plotter.

III.2.6. The old Medelec machine

At the onset of this study, a less sophisticated system (Medelec MS6, old version) was used: its components had the following features:

- The amplifier: this was a very low noise biological amplifier which gave a wide range of signal settings and sensitivities.
- The averager had a medium resolution when using a single channel. It did not have an averager expander, to allow the use of more than one channel at the same testing.
- The stimulator had a simple stimulus control system.
- The manual rejection mode involved human error when compared to the automatic rejection mode (where the computer takes over).
- The sweep limits had be to stopped manually when the desired number had been reached.
- Permanent copies of the traces were photographed onto Kodak linagraph direct print paper.

- The parameters of stimulation used were:
  - . Click stimulus: 10/second
  - . Acoustic phase: rarefaction and alternating phases
  - . Analysis time: 20 ms
  - . Gain: 5 μV
  - . Filters: 250 Hz low filter
    1600 Hz high filter

The old Medelec machine (MS6) performed very basic functions compared to the sophisticated functions testable by the Medelec Sensor machine. Table III.1 compares the two machines.

III.2.7 Difficulties in the NICU

The following were some of the difficulties encountered and the means devised for overcoming them:

- Myogenic potentials were overcome by the auto-rejection mode (automatic artifact rejection) in which averaging stops until muscle potentials cease.

- 50-cycle alternating current interference has proved manageable in the Neonatal Intensive Care Unit, as long as scalp electrode impedance was low, and the patients were carefully grounded.

- Specific stimulating difficulties (such as intravenous lines in scalp veins, bad positioning of the patient, difficulties in approach to the other ear, or overactive babies) can be dealt with (to improve the signal to noise ratio), by averaging an

increased number of responses, choosing the correct filter band-pass, and waiting for the patient to have a quiet interval (figures 3.11 and 3.12).

- Interference may be caused by surrounding equipment. Heaters in open incubators were found to cause most interference. In patients with stable temperatures, the heater could be turned off during tests running at one intensity level only. The babies were well wrapped and carefully observed during testing.

- Stimulating and recording equipment and the computer were all mounted on a single trolley. This allowed easy introduction into the limited space on the NICU.

- To cope with time limitation in such babies (and to avoid extensive handling) two trials were run at a single intensity.

TABLE III.1

COMPARISON BETWEEN MS6 AND SENSOR MACHINE

	MS6	SENSOR
-Amplifier and averager	Basic function	Advanced
-Number of channels	Single channel	Up to four channels
-Rejection facility	Manual	Automatic
-Sweep limits	Stopped manually	Preset by computer
-Copy of traces	Photographed onto Kodak linagraph	Plotted by X-Y plotter or stored into computer

TABLE III.2

PROGRAMME

a) Stimulator: (ST10)

Stimulus	click, monaural
Intensity	60 dB
Duration	0.1 ms
Square wave pulse	100 μs

b) Amplifier/Averager (ER94):

High filter	3 KHz
Low filter	300 Hz
Analysis time	20 ms
Sweep limit	1024-2048
Repetition rate	10 Hz
Amplifier gain	2 μV
Display gain	100 nV

a)

b)

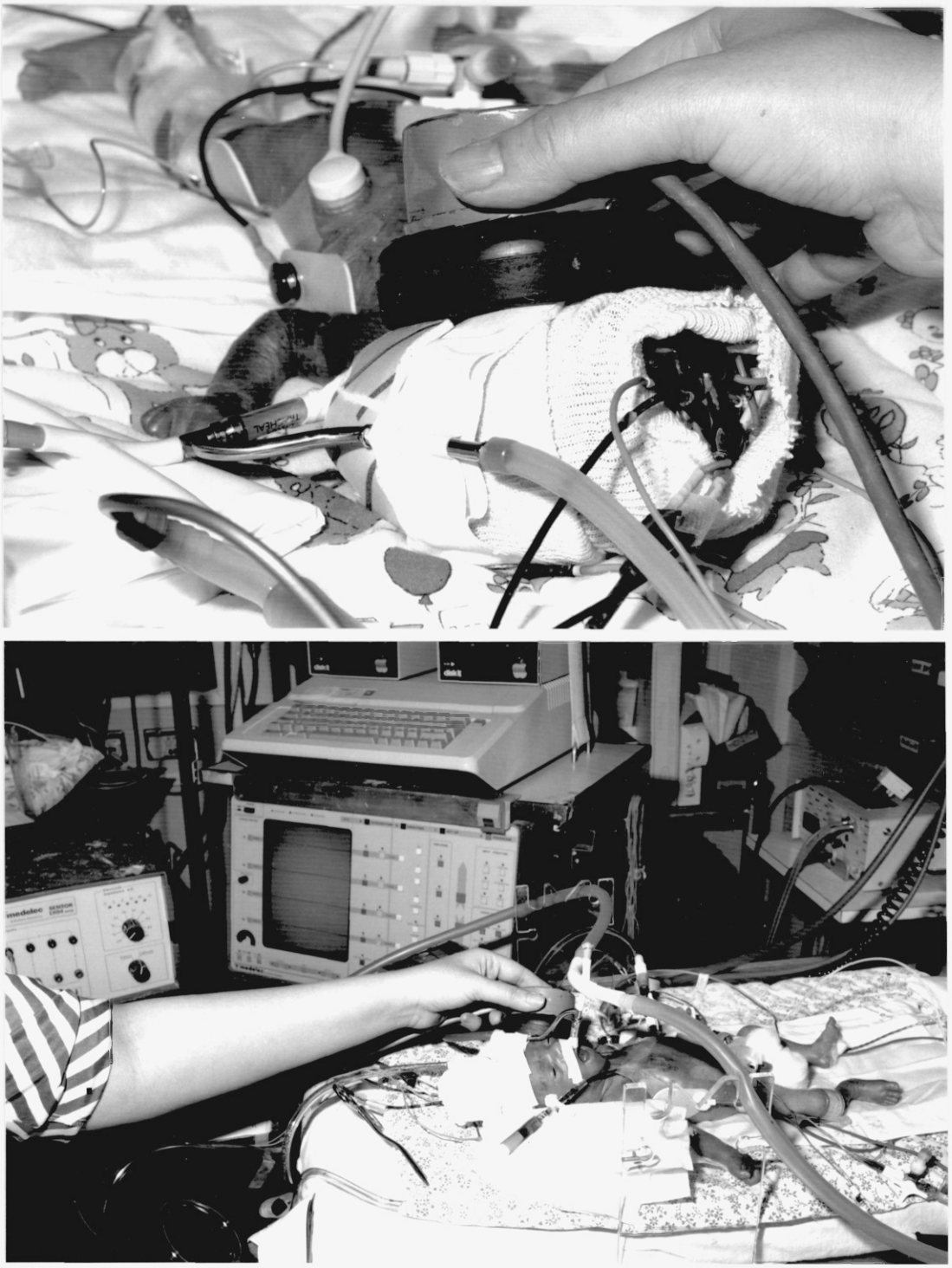


Figure 3.11. Among the difficulties encountered in the Neonatal Intensive Care unit and during ABR testing: a) bad positioning of the baby which makes it difficult to approach the other ear especially when the baby was intubated. b) waiting for an irritable mobile baby to have a quiet interval. ABR testing may exceed 2 hours in such circumstances. .

CHAPTER IV. AUDITORY BRAINSTEM RESPONSES IN NORMAL INFANTS

The clinical usefulness of the ABR involves the recognition of abnormal patterns. This in turn requires that the limits of normality be clearly established. One aim of this study was to establish normative data for clinical use and to draw up maturation curves relating to various parameters of the ABR.

IV.1. Material:

We studied a population of neurologically optimal newborn infants with no apparent neurological deficits (using very stringent clinical criteria) and no abnormalities on cranial ultrasound imaging.

During a period of 15 months (June 1983 to September 1984), ABRs were performed on all neurologically optimal preterm infants, admitted to the Neonatal Unit at Hammersmith Hospital during the first week of their life. The tests were repeated weekly until discharge. Additional full term babies (from the postnatal wards) were also studied. Informed consent from the parents was obtained. Infants were categorised as neurologically optimal if, in addition to fulfilling the following requirements, they were also at low-risk of developing complications:

a) a postnatal complication score of 0 or 1 on a 3-point scale derived from Drillien et al (1980) (See Appendix).

b) repeatedly normal results on sequential neurological examination (according to the protocol of Dubowitz and Dubowitz, 1981). The examinations were considered normal when there were no deviant neurological signs and when alertness, responsiveness, tone, mobility, and primitive reflexes were considered appropriate for the gestational age of the infants.

c) an absence of intracranial pathology, as determined by sequential ultrasound examination.

The gestational age of all infants was determined according to the Dubowitz score (Dubowitz et al 1970). If this differed from maternal dates by more than one week, an estimate derived from motor nerve conduction velocity was taken as an additional index of gestational age (Moosa and Dubowitz, 1972).

Both ears of 56 preterm and full term infants classed as optimal were tested, at times of several occasions. This yielded 190 traces. One hundred and twelve of these traces were obtained during the first four days of life, and will be referred to as the

cross-sectional data. The remaining 78 were obtained in infants followed-up beyond 4 days and provided the longitudinal data.

IV.2. Methods:

The ABRs were recorded in the neonatal unit and in the postnatal ward, on non-sedated infants, who remained throughout in their incubator or cot. A Medelec Sensor machine was used in all cases. Three standard EEG silver disc electrodes were applied to the scalp, the negative electrodes being on the ipsilateral mastoid, the positive on the vertex and the neutral on the contralateral mastoid. Interelectrode impedances were all below 6KΩ, (typical impedances were usually below 2KΩ). Rarefaction acoustic phase signals (clicks) were used as stimuli. These consisted of square waves lasting 100 μsec and were delivered at a rate of 10/sec. The earphones (TDH 39) were held in turn to each of the infants' ears (the other ear lying on the mattress). A total of 1024 to 2048 responses were averaged, through a bandpass filter of 300-3000 Hz. The analysis time was 20 msec. The tests were completed within an hour and both inter and intra-observer error with this technique proved to be negligible. Each test consisted of stimulation of 80 dB, 60 dB and 40 dB. These established the latencies and amplitudes of the different wave components.

The individual waves were labelled I to VII in accordance with the Jewett and Williston (1971) classification. The analysis of the response was performed on reliably reproducible waves. Measurements were carried out by cursors on the oscilloscope. Absolute latency was defined as the time taken between the onset of the stimulus and the response it evoked. Waves I, III and V were known to be the most commonly seen in infant populations.

In our experience wave VI was commonly seen, particularly when more than one intensity was used. It was, therefore, included in this study. Waves II, IV and VII were not included in our analysis, because of their inconsistent pattern.

Difficulties with latency measurements were occasionally encountered. When waves had two peaks a midpoint was taken for latency determination. When peaks were poorly defined, trials were superimposed: this usually allowed a point to be determined. The interpeak interval (IPI) was defined as the interval between two component waves. IPIs I-V and III-VI were determined. Both absolute latencies and interpeak intervals were measured in milliseconds.

The amplitudes of ABR components I and V were assessed in terms of the height of the peak and the depths of the subsequent negative troughs. Amplitudes were measured in nanovolts. The V:I amplitude ratio was also studied.

To demonstrate how ABR measurement changed with age, the latency and interpeak intervals were fitted by linear or quadratic curves as appropriate. The amplitude data were converted to log (x + c) where c is a quantity chosen to make the standard deviation constant, and a straight line relationship was fitted.

IV.3. Results

IV.3.1 Absolute latencies

The results of latency determinations (means and standard deviations) in relation to gestational ages are reported in tables IV.1 to IV.3 and in figures 4.1-4.3 for wave I (using stimulus intensities 80,60,and 40 dB), in tables IV.4 and IV.5 and figures 4.4 - 4.5 for wave III (using stimulus intensities of 80 and 60 dB), in tables IV.6. to IV.8. and in figures 4.6-4.8 for wave V (using stimulus intensities 80, 60, and 40 dB), and in tables IV.9. and IV.10. and in figures 4.9 - 4.10 for wave VI (using stimulus intensities of 80 and 60 dB).

The data were easier to interpret at 60 dB, but at 80 dB the ABRs were more easily obtained. With infants of low gestational age, the individual waves were easier to identify at higher intensities.

At 28 weeks (and at a stimulus intensity of 60 dB), the mean latency and standard deviations of waves I, III, V, and VI were 2.93 ± 0.29 msec, 5.62 ± 0.37 msec, 8.69 ± 0.34 msec, and 9.80 ± 0.485 msec respectively. The data also illustrate how the latency became progressively shorter with increasing maturation, so that at 40 weeks postconceptional age*, the corresponding latencies of waves I, III, V, and VI were 2.03 ± 0.29 msec, 4.63 ± 0.37 msec, 6.95 ± 0.34msec, and 8.42 ± 0.485 msec respectively.

The latency of wave III showed a unique distribution with age (figure 4.4.) in that the limits of the data obtained seemed to draw closer after 35 weeks.

* The postconceptional age is the gestational age plus the chronological age.

IV.3.2 Interpeak intervals (IPI)

Tables IV.11, IV.12 and IV.13 show the means and standard deviations for I-V interpeak intervals at stimulus intensities of 80, 60 and 40 dB respectively. Figures 4.11, 4.12 and 4.13 record the actual data (scatter of the I-V interpeak intervals at stimulus intensities of 80, 60 and 40 dB). Figures 4.14 and 4.15 demonstrate IPI III-VI at 80 and 60 dB.

IV.3.3 Amplitude of waves I and V

The mean amplitudes and standard deviations for waves I and V are shown in tables IV.16 to IV.21 at 80, 60 and 40 dB respectively. The amplitudes of these waves were found to be increased the louder the stimulus. This was best seen when comparing the amplitude of waves I and V at 60 and 80 dB respectively.

The amplitudes of waves I and V increased steadily as the preterm infants approached 40 weeks postconceptional age. At 60 dB stimulus intensity waves I and V reached amplitudes 128.6 and 120.6 nV at 28 weeks. By 40 weeks postconceptional age, waves I and V reached amplitudes of 207.1 and 201.2 nV respectively.

IV.3.4 The V:I amplitude ratio

As intensity increased, the amplitude ratio decreased. The scatter of individual recordings for the amplitude ratio V:I (at 80, 60 and 40 dB) is shown in figures 4.22, 4.23 and 4.24 respectively. It will be seen that the V:I amplitude ratios were influenced by stimulus intensity rather than by maturation. The ratios showed no age-related pattern. The data demonstrate an inverse relationship between click intensity and amplitude ratio.

IV.4. Statistical analysis

All measurements (whether cross-sectional or longitudinal) were plotted separately (see Appendix). As there seemed to be complete overlap between the two groups the data were pooled for the final analysis.

Absolute latencies, interpeak intervals and amplitudes all showed a definite relationship to gestational age at all stimulus intensities. The only parameter that did not show this pattern was the V:I amplitude ratio. Latencies and IPIs decreased steadily with increasing gestation, the decrease being maximal between 29 and 34 weeks. The amplitudes of the various ABR waves increased steadily with increasing age.

The data appeared to show a curvilinear relationship to gestation and were fitted by least squares. The plots were then fitted in regression lines for latencies of waves I, III, V and VI, and interpeak intervals I-V and III-VI (at 80 and 60 dB). The results are shown in figures 4.1, 4.4, 4.6, and 4.9 (for the latencies of waves I, III, V and VI) and in figures 4.11 and 4.14 (for interpeak intervals I-V and III-VI respectively) at a stimulus intensity of 80 dB. Figures 4.2, 4.5, 4.7, and 4.10 are for waves I, III, V and VI respectively, and figures 4.12 and 4.15 for interpeak intervals I-V and III-VI respectively, at stimulus intensity 60 dB. The corresponding data for waves I and V at a stimulus intensity of 40 dB and interpeak intervals I-V are shown in figures 4.3, 4.8 and 4.13 respectively.

A single pooled estimate was used for all determined parameters estimated at particular weeks of gestation. This estimate was calculated from an analysis of variance. This method of estimation allows for the correlations between the two measurements made on each baby.

In the single case of the latency of wave III at 80 dB the variability about the mean curve decreased sharply after 35 weeks of gestation, and separate estimates of standard deviation were used

before and after that age. The decrease in variability was particularly marked in the differences between left and right ears.

Mean wave amplitudes increased with age, and the variation about the mean also increased to some extent. The distributions at fixed age were somewhat skewed to the right. It was found by trial and error that converting the data to log (x+c), where c is a suitable constant, and fitting a straight line to the transformed readings, gave a good description of the data. The quoted lines were found by this method.

In the ratio of amplitude of waves V:I at 80 dB the scatter of points showed no age-dependent effect, ie the amplitude ratio did not vary with age. For the normal range means of the left and right ear were calculated with one and two standard deviation limits to obtain tolerance intervals. To do this ratios were transformed to log 10 (ratio + 0.25). The mean was 0.70 and the SDs were -1SD: 0.48; -2SD: 0.3 and +1SD: 1.0; +2SD: 1.39. At 60 dB the mean and the tolerance interval ratio were transformed to log (ratio). The estimates were: mean = 0.84, +1SD: 1.20, +2SD: 1.72, -1SD: 0.59, -2SD: 0.41. At 40 dB the mean was 1.07, +1SD: 1.39, +2SD: 1.72, -1SD: 0.74, and -2SD: 0.41.

Four of the infants showed wide deviations in relation to the following parameters:

1. Infant A: latency of wave VI at 80 and 60 dB, at 28 weeks PCA (figures 4.9 and 4.10).
2. Infant B: amplitude of wave V at 80 dB at 33 weeks gestation (figure 4.19), and amplitude ratio V:I at 80 and 60 dB at 33 weeks PCA (figures 4.22 and 4.23).
3. Infant C: amplitude ratio V:I at 40 dB (bilaterally) at 32 weeks PCA (figure 4.24).
4. Infant D: amplitude ratio at 40 dB at 33 weeks PCA (figure 4.24).

These infants fulfilled the criteria for inclusion in the study. The significance of the deviations is not immediately apparent. The findings reverted to normal in three of the four infants, when retested at a later date.

IV.5. Discussion:

Our study confirmed Starr's et al (1977) observations that reliable ABR wave components appear at about 28 weeks gestation. Such waves could clearly be elicited using stimulus intensities of

60 dB and even 40 dB, provided the infants were carefully selected as "optimal". Failure to detect ABR waves at this gestational age may be due to clinically inapparent abnormalities such as PVH needing further investigation. That such clinically silent lesions may occur is well documented (Volpe 1977).

Most available ABR data relate to apparently normal preterm infants (Starr et al 1977, Goldstein et al 1979, Despland and Galambos 1980, Cox et al 1982, Stockard et al 1983a). Most of these studies based their normative values on infants with a postconceptional age of 32 weeks or more (Salamy 1984). Such age groups are relatively stable, and at low risk from complications (Cox et al 1981b, Salamy et al 1982, Stockard et al 1983a). Furthermore, many authors have failed to specify the criteria for selection of their "normal" populations. Inconsistencies in the selection of "normal" preterm infants have led to wide variations in the reported normal values for different components of the ABR, at various gestational ages. Our study, and that of Fawer and Dubowitz (1982) carried out in the same department, used the same criteria for subject selection. The difference between the absolute latencies for waves I and V in the two studies may be attributed to technical factors which influence the response, such as the setting of filters, the use of different earphones, and the advent of more

sophisticated equipment. The earphones used in the earlier study were of type TDH39, but in the present study they were made smaller and lighter to avoid compression of the infant's ear canals. Stockard and Westmoreland (1981) and Chiappa (1983) found that latency shifts might occur due to heavy earphones causing obstruction to the external canal and simulating conductive impairment.

Each laboratory clearly has to determine its own normative data, based on the same equipment setting, environment and patient population and to restandardize them with any change in equipment. A change in the setting or equipment will necessitate a re-evaluation of the known norms. Published norms can be used for purposes of comparison but must not be used as exact values against which to test data obtained in quite different settings (Weber 1982, Stockard et al 1983a, Cox 1984).

We have compared the results obtained in the present study with earlier data (Starr et al 1977, Goldstein et al 1979, Despland and Galambos 1979, 1980, Cox et al 1981a, Jacobson et al 1982, Fawer and Dubowitz 1982, Stockard et al 1983a, Salamy 1984). The comparison is summarised in tables IV.22. and IV.23 (p 177-179).

a) Wave I

The latency of wave I, in our study, was in the range reported by Despland and Galambos (1980) and Salamy (1984). Our wave I latencies appeared more prolonged than those of Goldstein et al (1979) and Stockard et al (1983a), but shorter than those of Fawer and Dubowitz (1982) and Cox et al (1981a) figure (4.25). In relation to age, our wave I latencies showed a decrease of 0.08 ms per week, which is similar to that reported by Cox et al (1981a).

b) Wave V

We found the latency of wave V to be similar to that reported by Stockard et al (1983a) and Goldstein et al (1979) in infants aged 32-33 weeks or more. Our data for infants aged 35 weeks or more were similar to those reported by Starr et al (1977) (figure 4.26). The latencies in our study were, however, shorter than those reported by Cox et al (1981a), Fawer and Dubowitz (1982) and Salamy (1984). In analysing the latency change of wave V as a function of age we found this latency to decrease by 0.13 ms per week. This compares with 0.3 to 0.5 ms per week in the study by Schulman-Galambos and Galambos (1975), 0.05-0.4 ms per week in study of Starr et al (1977), 0.1 ms per week in the study by Schulman-Galambos and Galambos (1979a), and 0.04 ms per week in study of Cox et al (1981a).

c) IPI I-V

When we compared IPI I-V in our study with previously reported data we found a close similarity between our data and those reported by Fawer and Dubowitz (1982). By the equivalent of 40 weeks gestation the data reported in studies closely resemble one another (figure 4.27).

d) Amplitude

Amplitude measurements show substantial variability among normal subjects (Rowe 1978, Stockard et al 1978a, Chiappa et al 1979, Salamy 1984). These fluctuations have limited the clinical use of this measurement (Rowe 1978, 1981, Starr and Amlie 1981, Stockard et al 1983a). Despite this variability, maturational changes were demonstrated in our study. There was an increase in amplitude with increasing age.

e) Amplitude ratio V:I

This ratio is less variable than amplitude itself and has proven more useful for clinical purposes. Since wave I is generated outside the CNS, it can be compared with wave V (which is generated at midbrain level) to determine whether the expected relationship between the amplitudes of the responses is present or not (Chiappa

1983). The ratio has been shown to be sensitive to neurological disease in adults and infants (Starr and Achor 1975, Stockard et al 1977, Hecox and Cone 1981b). Hecox and Cone (1981) have suggested that the amplitude ratio is a reliable measure for predicting neurological sequelae.

In our study, amplitude ratios did not vary with age. At 60 dB the general mean was 0.84. These results are in agreement with findings of Gafni et al (1980), who reported a ratio of less than 1 (0.87) for newborns. Our data differed from those of Hecox and Burkard (1982), and Salamy (1984) who found the changes in V:I amplitude ratios to be age related. Salamy pointed out that the difference between the results of Gafni et al (1980) and his own could be attributed to stimulus parameters.

In summary, our data demonstrated that latencies showed a regular and consistent decrease with age, which has not been found in most other studies. Fawer and Dubowitz (1982) showed a similar age-related decrement.

Our results also confirm the observations of previous authors that latencies decrease with increasing age, irrespective of the intensity of stimulation (Jewett and Romano 1972, Leiberman et

al 1973b, Hecox and Galambos 1974, Salamy and McKean 1976, Starr et al 1977, Goldstein et al 1979, Despland and Galambos 1980, Salamy 1984).

The maturation of the auditory system, tested by the ABR technique, appears to be incomplete at birth and to continue maturing throughout the first 4 years of life (Hecox 1975, Salamy and McKean 1976, Starr et al 1977, Salamy 1984).

In this study we report for the first time on interpeak intervals III-VI. We believe that these intervals (not being affected by peripheral lesions) reflect conduction times through the brainstem. By excluding waves I and II, which are influenced by hearing impairment, actual conduction time can be estimated.

Interpeak intervals III-V have been used to exclude peripheral lesions, but the interval is so short that its use is not practical. We were able to measure wave VI in over 90% of our infants. We also found the percentage of cases in which wave VI could be measured increased (up to 96%) in infants nearer to term i.e. 36 weeks onwards. The use of III-VI interpeak interval (which may reflect conduction up to thalamic level) will help assess brainstem function, not being influenced by peripheral factors.

From the present and previous studies reported we can emphasise that one of the major problems in ABR testing is establishing normative data for each laboratory, according to the specific test environments, and the specific equipment, procedures, and protocols used. Establishing norms from infants with low-risk factors at various gestational and post-conceptional ages (from neonatal intensive care unit populations) is a difficult task. Many of these infants are preterm, have a low birth weight and are often sick. A multicentre study would be helpful if it involved standardisation of procedures, protocols, and equipment. The standardisation of procedures would itself involve standardisation of types, intensities and rates of stimulation, presentation phase, sample size, signal amplification, gains, filter settings, electrode placements, and earphone use. Criteria for establishing low-risk status, the ages of the infants tested, and pass/fail criteria would also have to be standardised. Such an approach would generate a large pool of data which would be ideal statistically and would avoid the discrepancies between norms so obvious in hitherto published data.

TABLE IV.1

Absolute latency of wave I (with 1SD and 2SD): 80 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	2.44	2.68	2.92	2.20	1.96
29	6	2.35	2.59	2.83	2.11	1.87
30	10	2.26	2.50	2.74	2.02	1.78
31	14	2.17	2.41	2.65	1.93	1.69
32	16	2.09	2.33	2.57	1.85	1.61
33	24	2.01	2.25	2.49	1.77	1.53
34	10	1.94	2.18	2.42	1.70	1.46
35	14	1.87	2.11	2.35	1.63	1.39
36	8	1.81	2.05	2.29	1.57	1.33
37	6	1.76	2.00	2.24	1.52	1.28
38	14	1.71	1.95	2.19	1.47	1.23
39	10	1.66	1.90	2.14	1.42	1.18
40	18	1.62	1.86	2.10	1.38	1.14
41	10	1.58	1.82	2.06	1.34	1.10
42	2	1.55	1.79	2.03	1.31	1.07

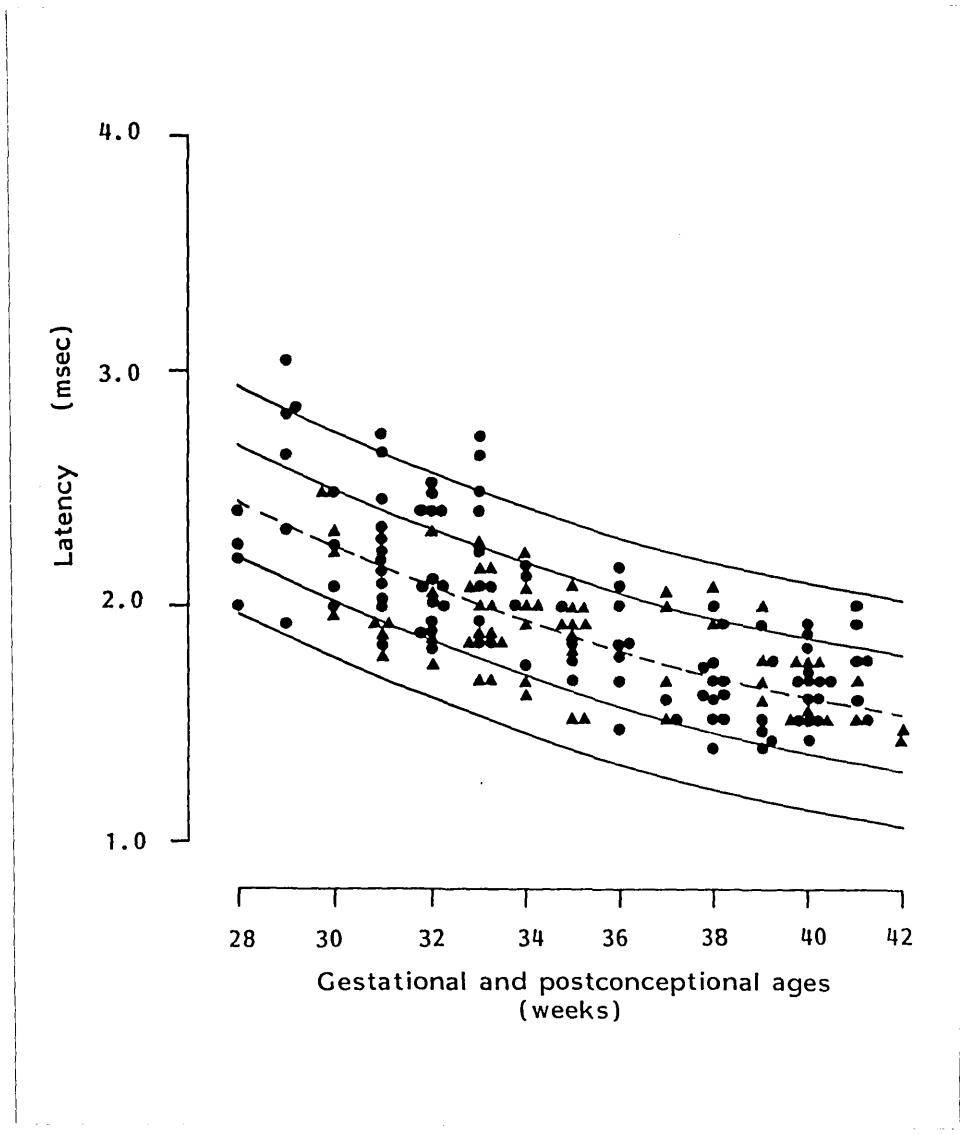


Figure 4.1. Absolute latency of wave I (at 80 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.2.

Absolute latency of wave I (with 1SD and 2SD): 60 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	2.93	3.22	3.51	2.64	2.35
29	4	2.84	3.13	3.42	2.55	2.26
30	10	2.75	3.04	3.33	2.46	2.17
31	16	2.66	2.96	3.25	2.37	2.08
32	20	2.58	2.87	3.16	2.29	2.00
33	26	2.50	2.79	3.08	2.21	1.92
34	10	2.42	2.72	3.01	2.13	1.84
35	18	2.35	2.64	2.93	2.06	1.77
36	8	2.28	2.57	2.86	1.99	1.70
37	8	2.21	2.50	2.80	1.92	1.63
38	14	2.15	2.44	2.73	1.86	1.57
39	14	2.09	2.38	2.67	1.80	1.51
40	20	2.03	2.32	2.61	1.74	1.45
41	10	1.97	2.27	2.56	1.68	1.39
42	2	1.92	2.21	2.51	1.63	1.34

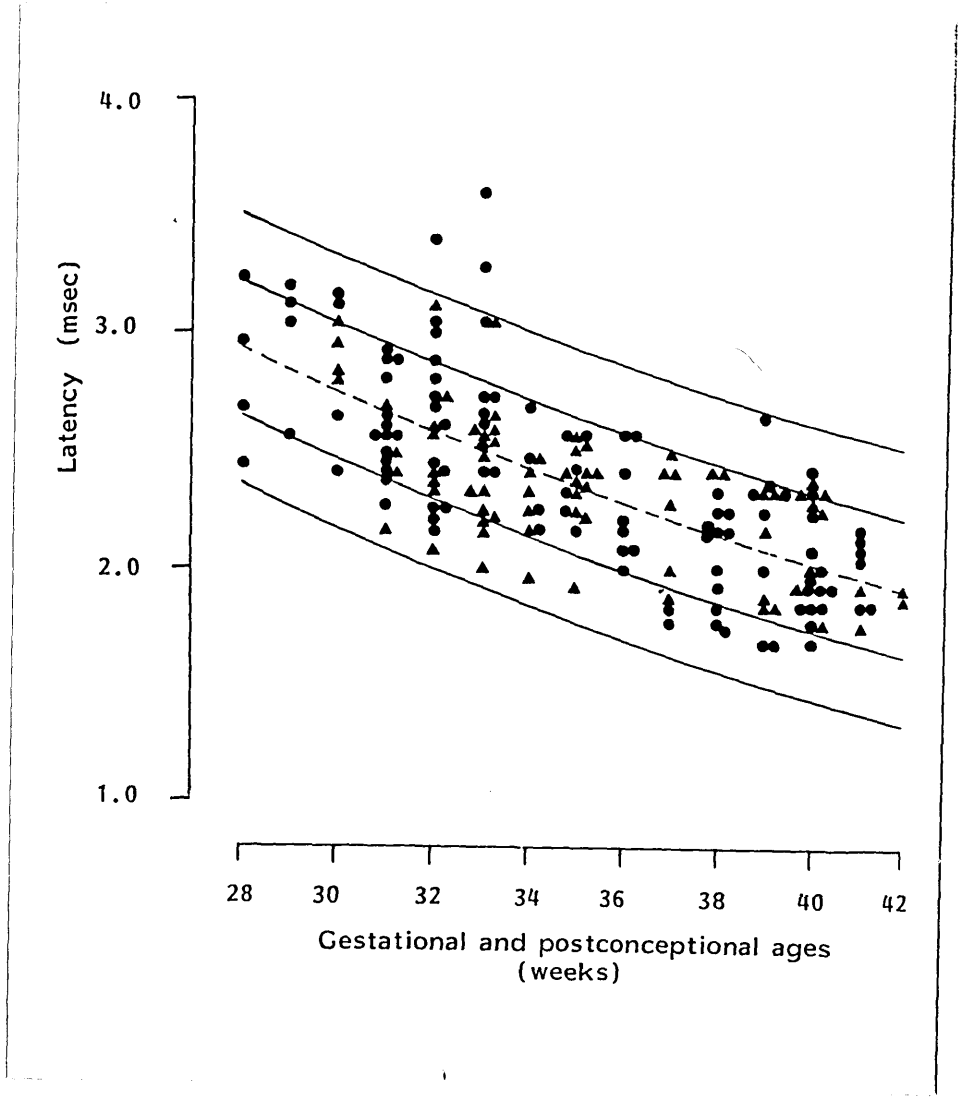


Figure 4.2. Absolute latency of wave I (at 60 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.3.

Absolute latency of wave I (with 1SD and 2SD); 40 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	2	3.65	4.02	4.40	3.27	2.90
29	1	3.56	3.94	4.32	3.19	2.82
30	6	3.48	3.86	4.24	3.12	2.74
31	13	3.40	3.78	4.16	3.03	2.66
32	13	3.32	3.70	4.07	2.96	2.58
33	20	3.24	3.62	4.00	2.87	2.49
34	8	3.17	3.54	2.92	2.79	2.41
35	18	3.08	3.45	2.83	2.70	2.33
36	8	3.00	3.37	2.75	2.62	2.25
37	10	2.92	3.35	2.67	2.54	2.17
38	14	2.84	3.21	2.59	2.46	2.09
39	14	2.76	3.13	2.51	2.38	2.00
40	20	2.68	3.05	3.43	2.30	1.93
41	10	2.60	2.97	3.35	2.21	1.84
42	2	2.52	2.89	3.27	2.13	1.76

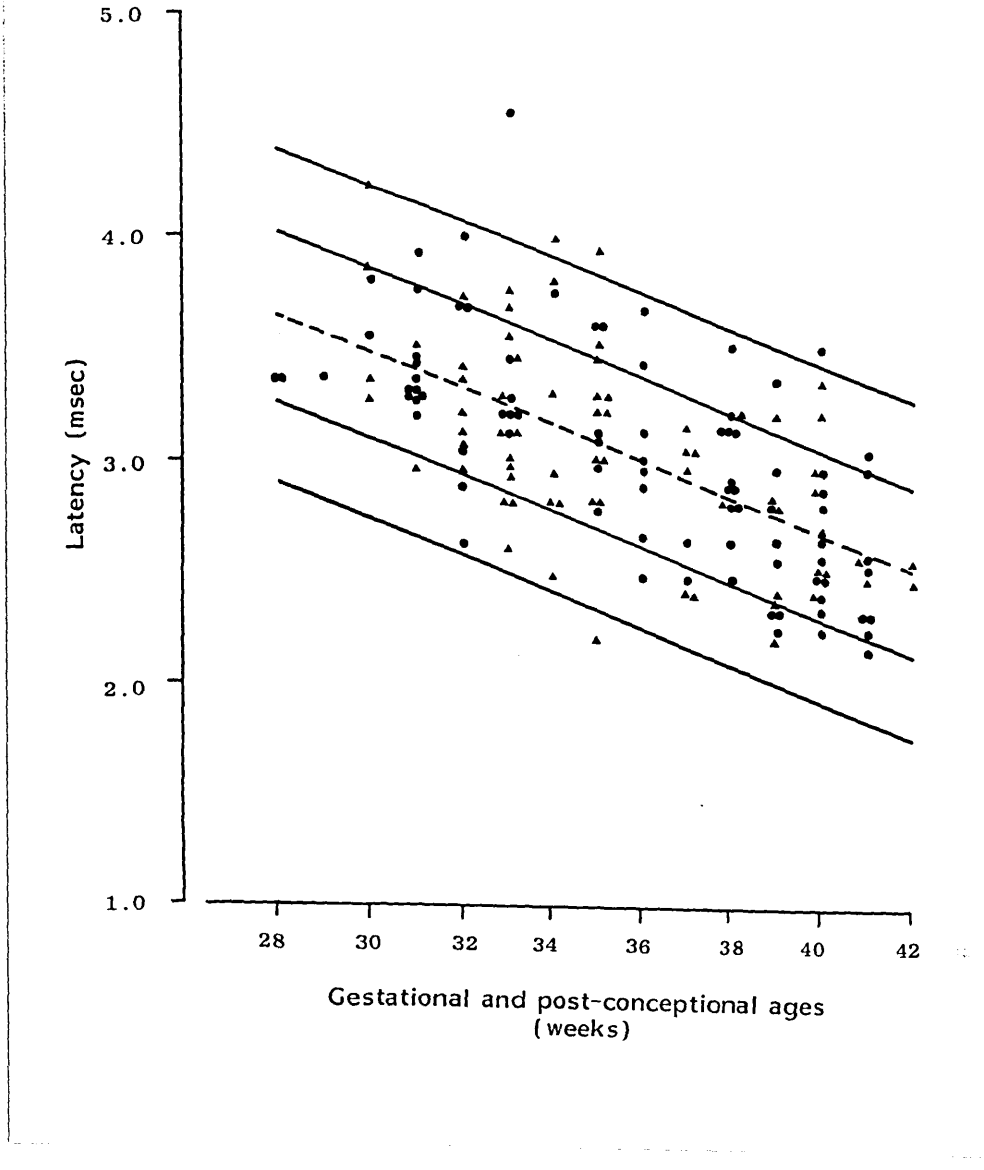


Figure 4.3. Absolute latency of wave I (at 40 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.4.

Absolute latency of wave III with (1SD and 2SD);80 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	5.26	5.75	4.78	6.24	4.29
29	6	5.14	5.64	4.66	6.12	4.18
30	10	5.04	5.53	4.55	6.02	4.06
31	14	4.94	5.40	4.43	5.92	3.96
32	16	4.83	5.32	4.34	5.81	3.85
33	24	4.73	5.22	4.24	5.72	3.75
34	10	4.65	5.14	4.16	5.63	3.67
35	14	4.56	4.90	4.18	5.36	3.85
36	8	4.49	4.76	4.21	5.04	3.93
37	6	4.40	4.68	4.16	4.96	3.86
38	14	4.35	4.62	4.07	4.90	3.79
39	10	4.28	4.56	4.00	4.83	3.72
40	18	4.23	4.50	3.95	4.78	3.67
41	10	4.18	4.44	3.87	4.72	3.62
42	2	4.13	4.40	3.85	4.68	3.57

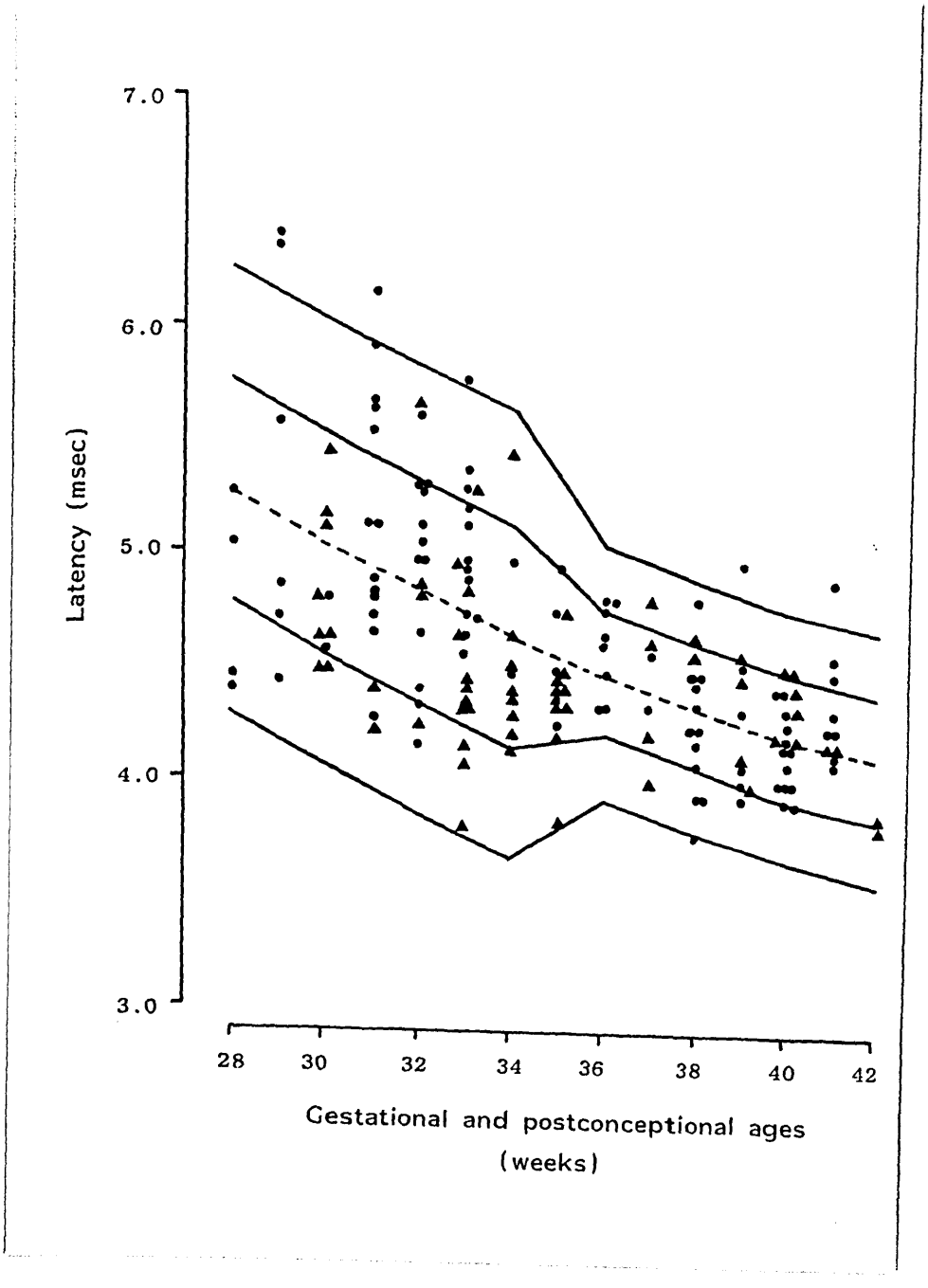


Figure 4.4. Absolute latency of wave III (at 80 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.5.

Absolute latency of wave III with (1SD and 2SD):60 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	5.62	5.99	6.36	5.24	4.87
29	4	5.53	5.92	6.27	5.16	4.78
30	10	5.44	5.83	6.19	5.18	4.20
31	16	5.36	5.75	6.10	5.00	4.62
32	20	5.28	5.68	6.02	4.92	4.54
33	26	5.20	5.60	5.95	4.83	4.46
34	10	5.12	5.50	5.86	4.74	4.38
35	18	5.04	5.42	5.78	4.66	4.30
36	8	4.95	5.34	5.70	4.58	4.22
37	8	4.88	5.26	5.62	4.50	4.14
38	14	4.80	5.18	5.54	4.42	4.05
39	14	4.72	5.10	5.46	4.34	3.98
40	20	4.63	5.01	5.38	4.26	3.89
41	10	4.56	4.92	5.30	4.18	3.82
42	2	4.48	4.86	5.22	4.10	3.73

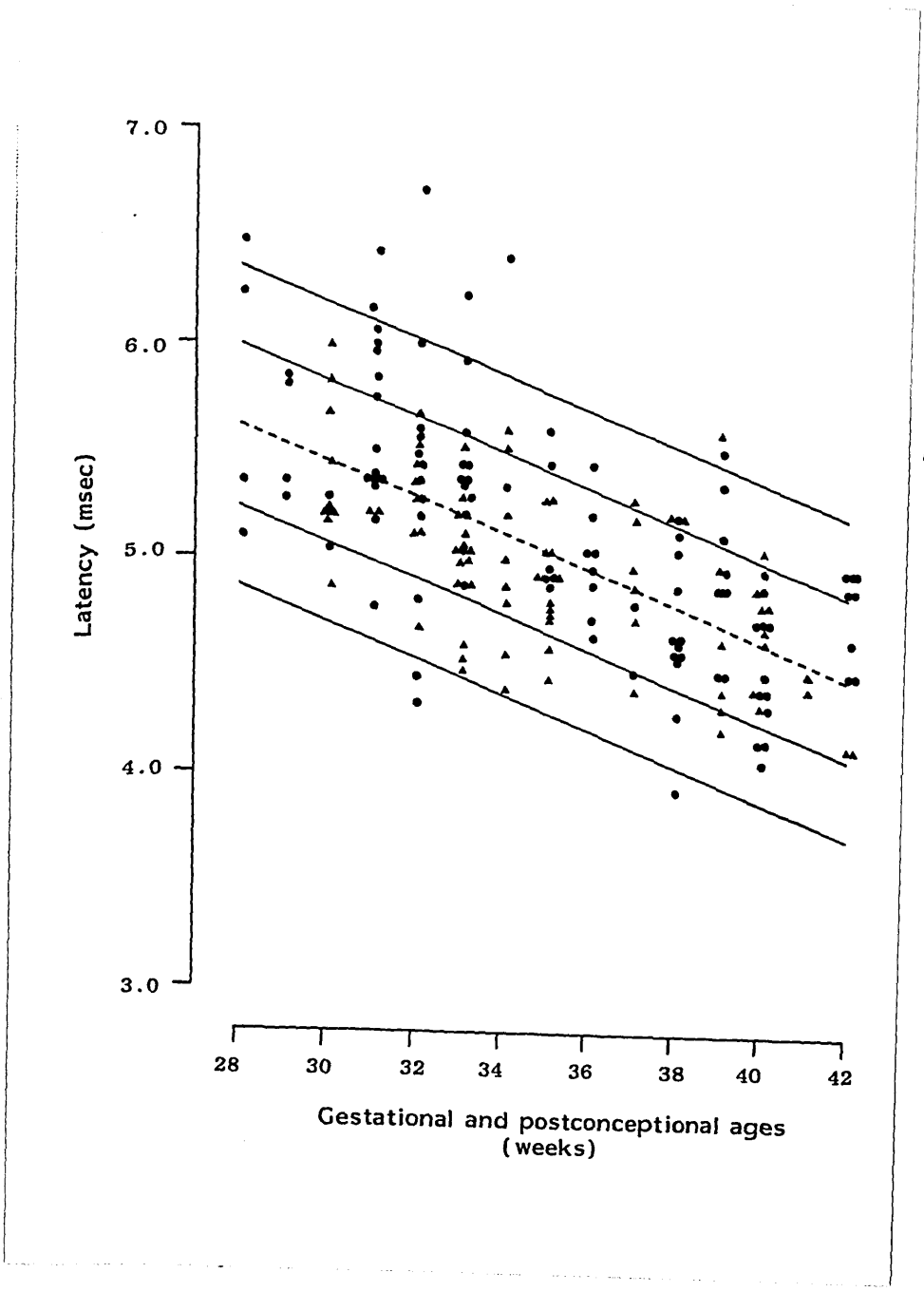


Figure 4.5. Absolute latency of wave III (at 60 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.6.

Absolute latency of wave V with (1SD and 2SD):80 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	8.30	8.60	8.92	7.99	7.68
29	6	8.07	8.38	8.69	7.76	7.45
30	10	7.87	8.18	8.49	7.56	7.25
31	14	7.67	7.98	8.29	7.36	7.05
32	16	7.50	7.81	7.12	7.19	6.88
33	24	7.34	7.65	7.96	7.03	6.72
34	10	7.20	7.51	7.82	6.89	6.58
35	14	7.07	7.38	7.69	6.76	6.45
36	8	6.96	7.27	7.58	6.65	6.34
37	6	6.87	7.18	7.49	6.56	6.25
38	14	6.79	7.10	7.41	6.48	6.19
39	10	6.73	6.04	6.35	6.42	6.15
40	18	6.69	7.00	7.31	7.38	6.07
41	10	6.66	6.97	7.28	7.35	6.04
42	2	6.65	6.96	6.27	6.34	6.03

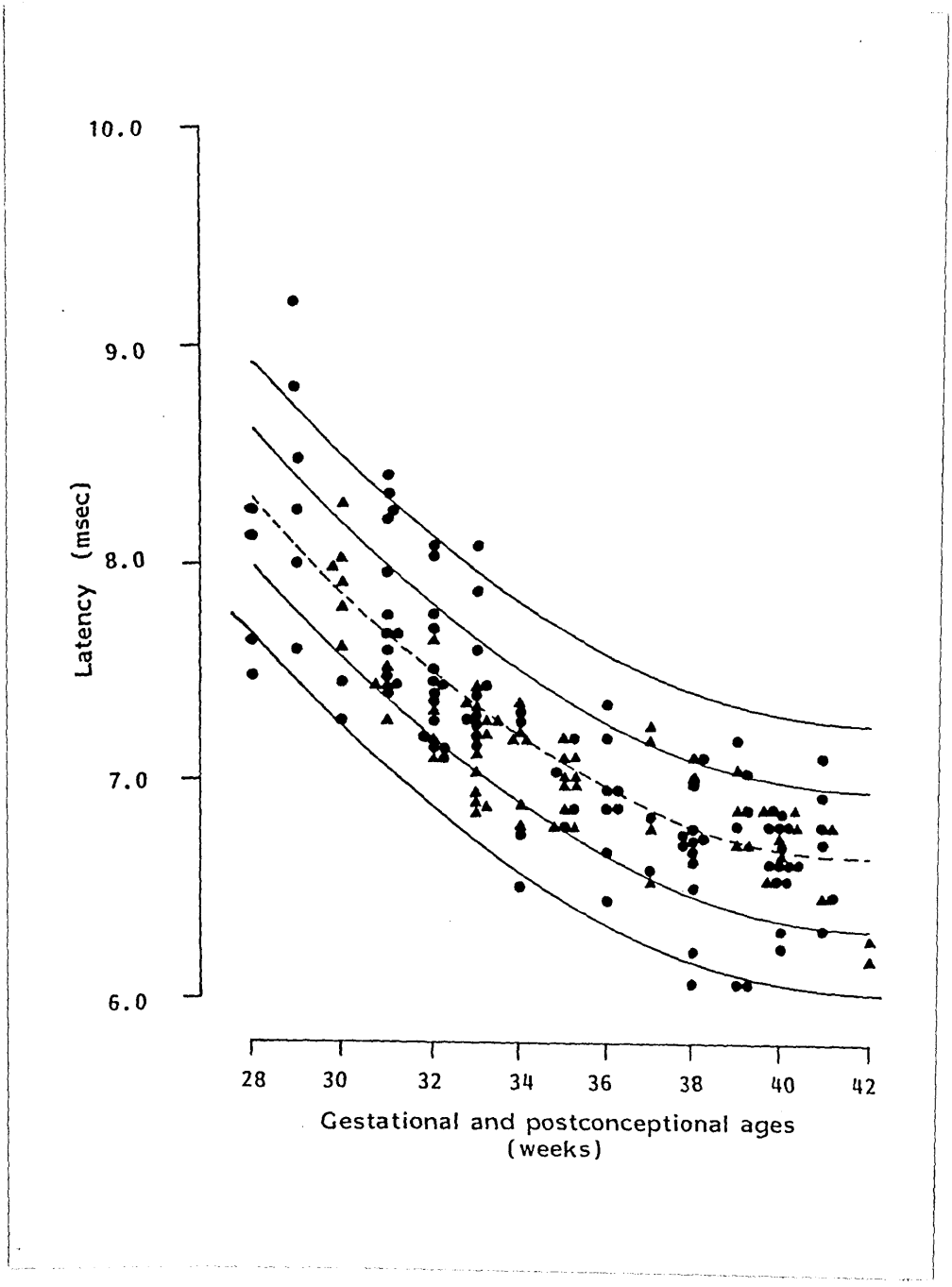


Figure 4.6. Absolute latency of wave V (at 80 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.7.

Absolute latency of wave V with (1SD and 2SD):60 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	8.69	9.03	9.38	8.35	8.01
29	4	8.48	8.82	9.17	8.14	7.79
30	10	8.28	8.62	8.96	7.94	7.60
31	16	8.09	8.44	8.78	7.75	7.41
32	20	7.92	8.26	8.60	7.58	7.23
33	26	7.76	8.10	8.44	7.41	7.07
34	10	7.60	7.95	8.29	7.26	6.92
35	18	7.47	7.81	8.15	7.12	6.78
36	8	7.34	7.68	8.02	6.99	6.65
37	8	7.22	7.57	7.91	6.88	6.54
38	14	7.12	7.46	7.80	6.78	6.43
39	14	7.03	7.37	7.71	6.68	6.34
40	20	6.95	7.29	7.63	6.61	6.26
41	10	6.88	7.22	7.57	6.54	6.19
42	2	6.82	7.17	7.51	6.48	6.14

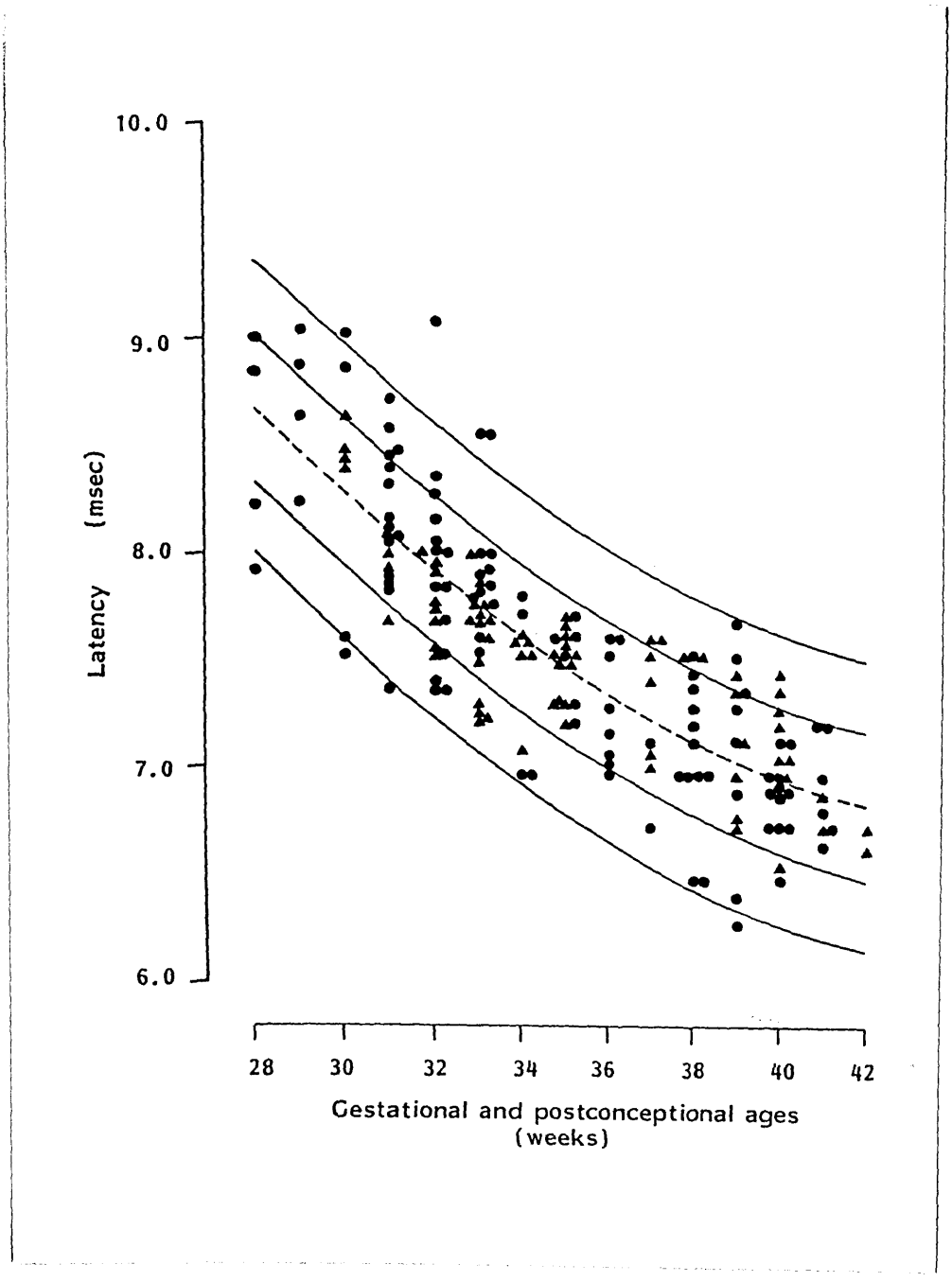


Figure 4.7. Absolute latency of wave V (at 60 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.8.

Absolute latency of wave V with (1SD and 2SD):40 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	9.39	9.88	10.38	8.89	8.39
29	2	9.24	9.72	10.22	8.75	8.24
30	8	9.08	9.57	10.07	8.59	8.09
31	15	8.93	9.42	9.91	8.43	7.93
32	15	8.78	9.25	9.76	8.28	7.78
33	24	8.62	9.12	9.60	8.12	7.64
34	10	8.46	8.96	9.45	7.97	7.47
35	18	8.30	8.80	9.28	7.82	7.32
36	8	8.15	8.64	9.13	7.66	7.16
37	10	8.00	8.50	8.98	8.50	7.00
38	14	7.84	8.34	8.83	7.34	6.85
39	14	7.68	8.18	8.68	7.20	6.69
40	20	7.52	8.02	8.52	7.03	6.53
41	10	7.36	7.88	8.36	6.88	6.39
42	2	7.21	7.72	8.21	6.72	6.24

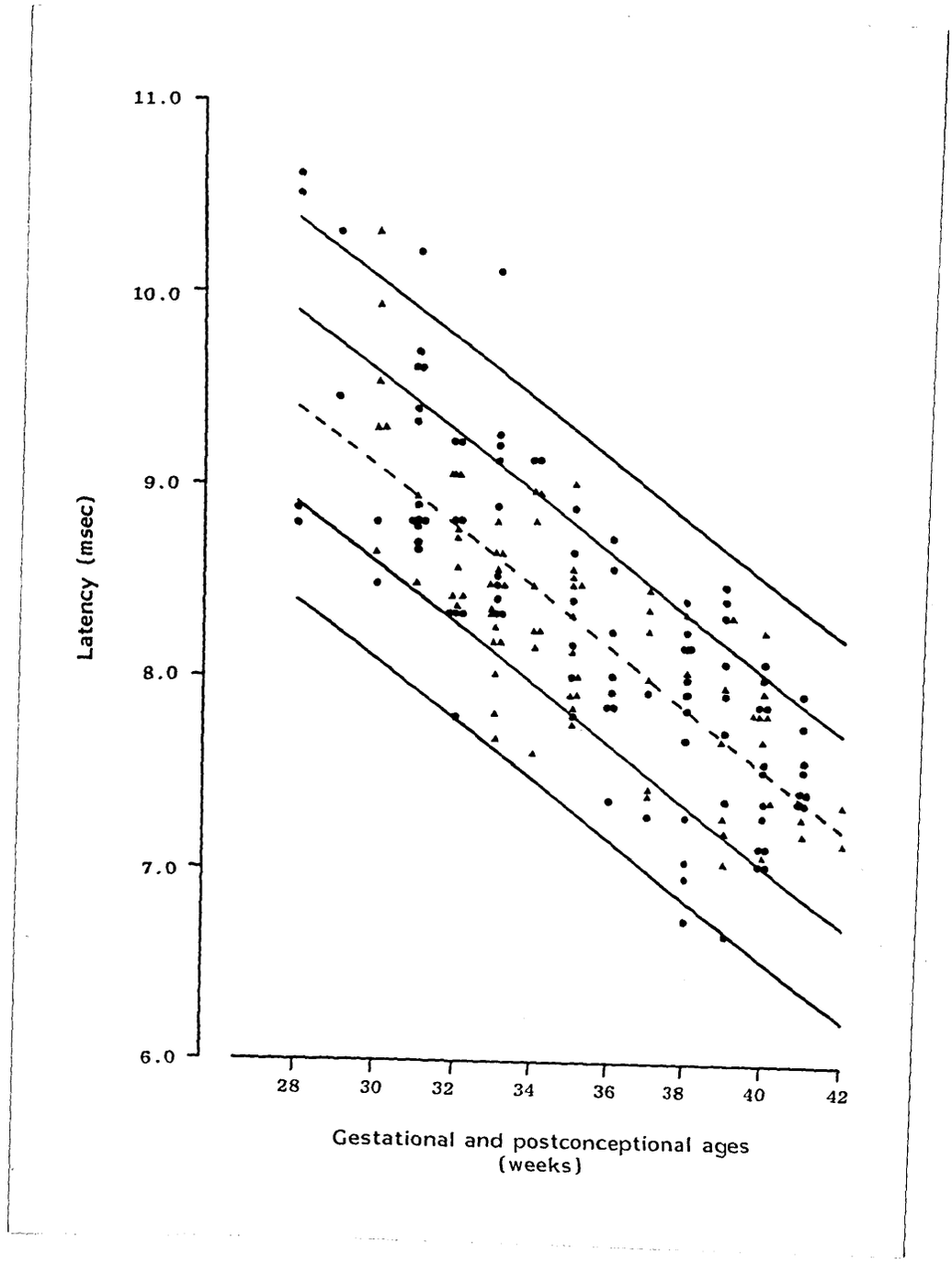


Figure 4.8. Absolute latency of wave V (at 40 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.9.

Absolute latency of wave VI with (1SD and 2SD):80 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	9.83	10.33	10.83	9.33	8.83
29	5	9.63	10.12	10.64	9.14	8.64
30	9	9.44	9.94	10.44	8.94	8.44
31	10	9.26	9.76	10.26	8.76	8.26
32	12	9.10	9.60	10.10	8.60	8.10
33	23	8.94	9.46	9.96	8.44	7.94
34	9	8.80	9.30	9.80	8.30	7.80
35	14	8.65	9.18	9.68	8.16	7.66
36	7	8.55	9.05	9.55	8.05	7.55
37	6	8.44	8.94	9.44	7.93	7.44
38	13	8.34	8.84	9.34	7.84	7.34
39	10	8.14	8.76	8.26	7.75	7.25
40	18	8.18	8.68	9.18	7.68	7.18
41	10	8.12	8.62	9.12	7.61	7.12
42	2	8.05	8.55	9.05	7.55	7.05

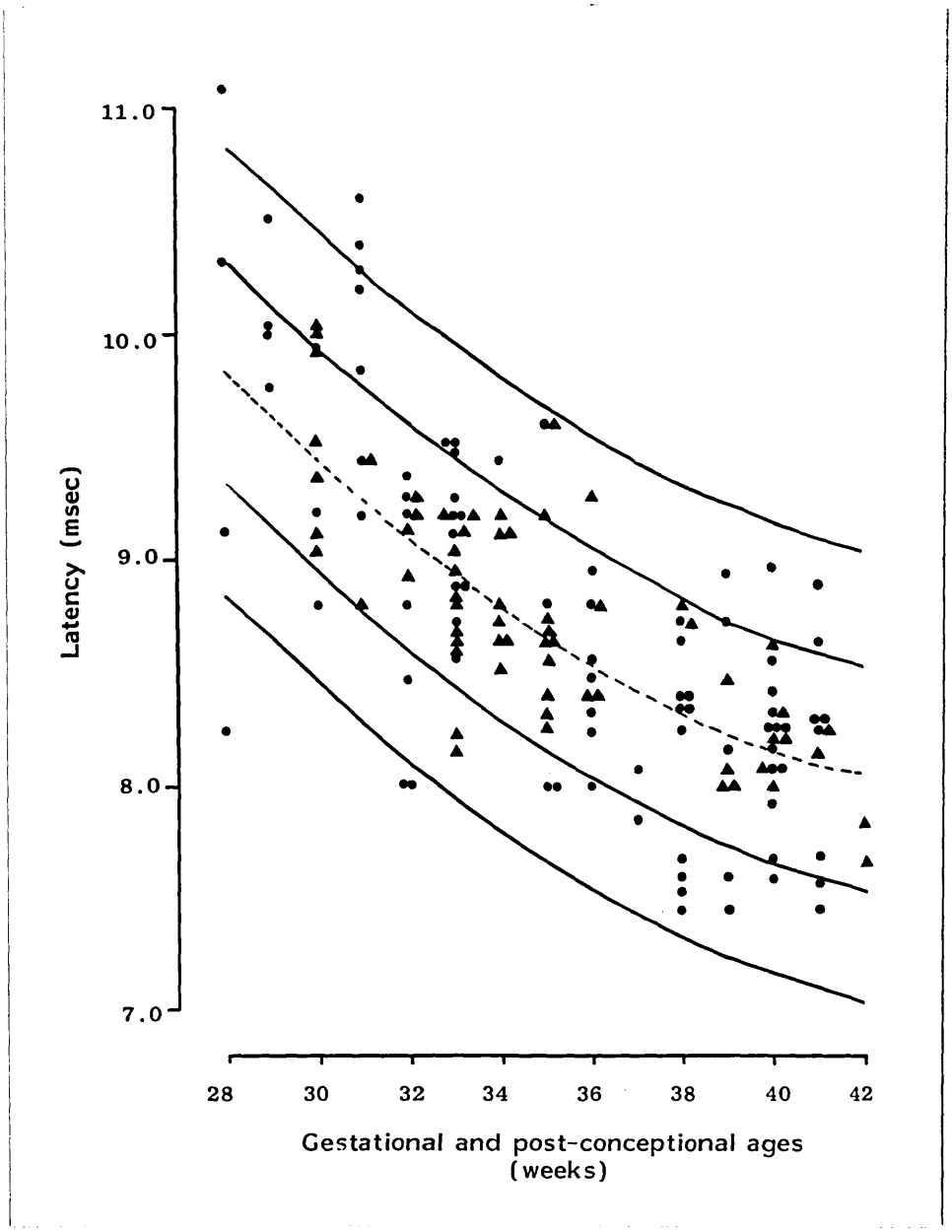


Figure 4.9. Absolute latency of wave VI (at 80 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.10.

Absolute latency of wave VI with (1SD and 2SD):60 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	3	9.80	10.28	10.76	9.31	8.82
29	2	9.68	10.16	10.64	9.20	8.70
30	7	9.59	10.05	10.53	9.08	8.58
31	10	9.45	9.94	10.42	8.96	8.45
32	16	9.34	9.82	10.30	8.84	8.36
33	22	9.24	9.70	10.18	8.73	8.24
34	10	9.11	9.59	10.07	8.62	8.13
35	16	9.00	9.47	9.96	8.50	8.02
36	6	8.87	9.36	9.84	8.39	7.91
37	8	8.76	9.24	9.72	8.27	7.79
38	14	8.65	9.12	9.61	8.16	7.68
39	14	8.54	9.02	9.50	8.06	7.56
40	16	8.42	8.90	9.39	7.93	7.45
41	10	8.30	8.78	9.27	7.82	7.33
42	2	8.19	8.68	9.17	7.70	7.22

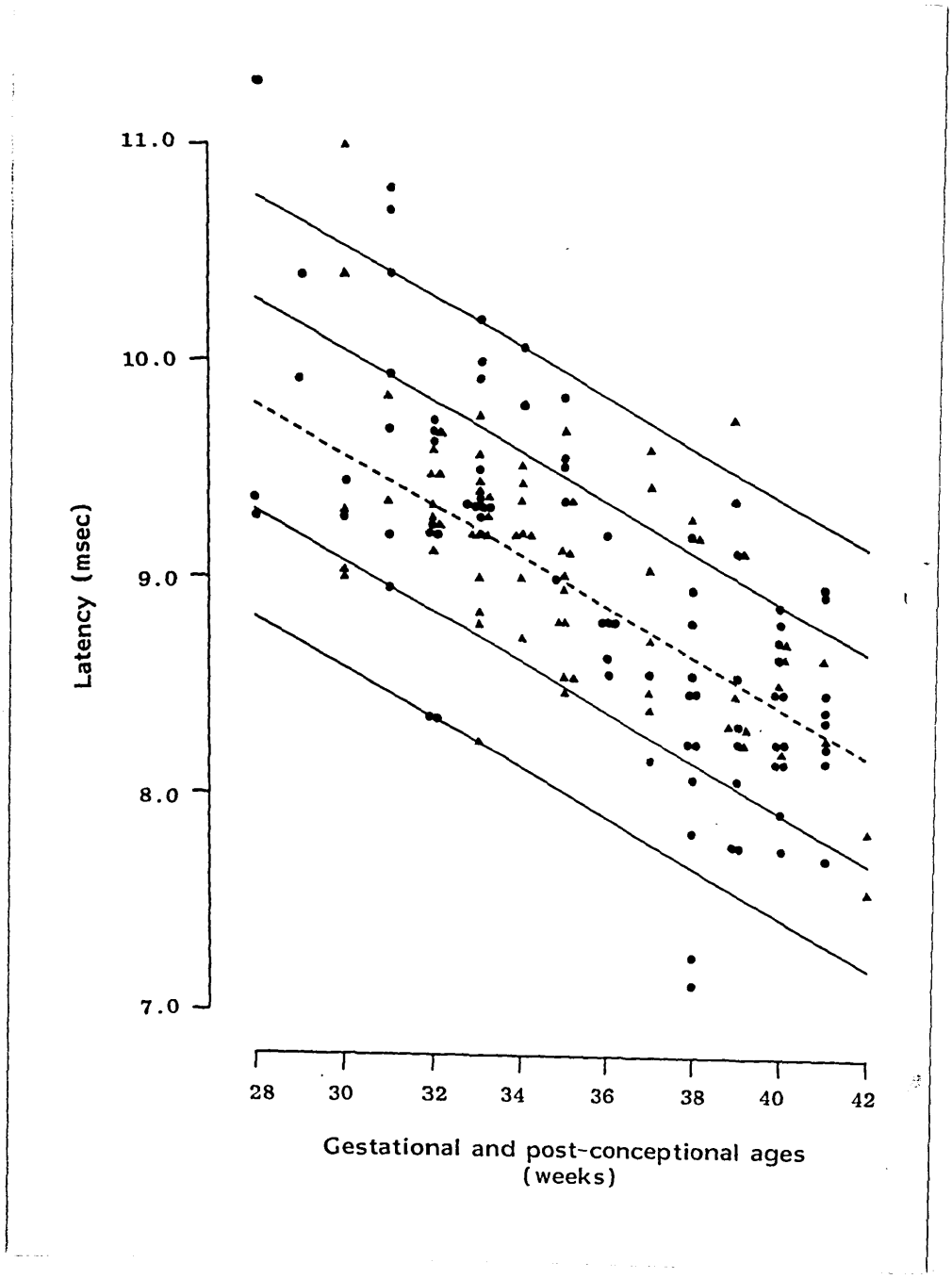


Figure 4.10. Absolute latency of wave VI (at 60 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.11.

Interpeak interval (IPI) I - V : 80 dB

GA	No.	Mean	$\tilde{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	5.86	6.05	6.24	5.67	5.48
29	6	5.73	5.92	6.11	5.54	5.35
30	10	5.61	5.80	5.99	5.42	5.23
31	14	5.51	5.70	5.89	5.32	5.13
32	16	5.41	5.60	5.79	5.22	5.03
33	24	5.33	5.52	5.71	5.14	4.95
34	10	5.26	5.45	5.64	5.07	4.88
35	14	5.20	5.39	5.58	5.01	4.82
36	8	5.15	5.34	5.53	4.96	4.77
37	6	5.12	5.31	5.50	4.93	4.74
38	14	5.09	5.28	5.47	4.90	4.71
39	10	5.08	5.27	5.46	4.89	4.70
40	18	5.07	5.26	5.45	4.88	4.69
41	10	5.08	5.27	5.46	4.89	4.70
42	2	5.10	5.29	5.48	4.91	4.72

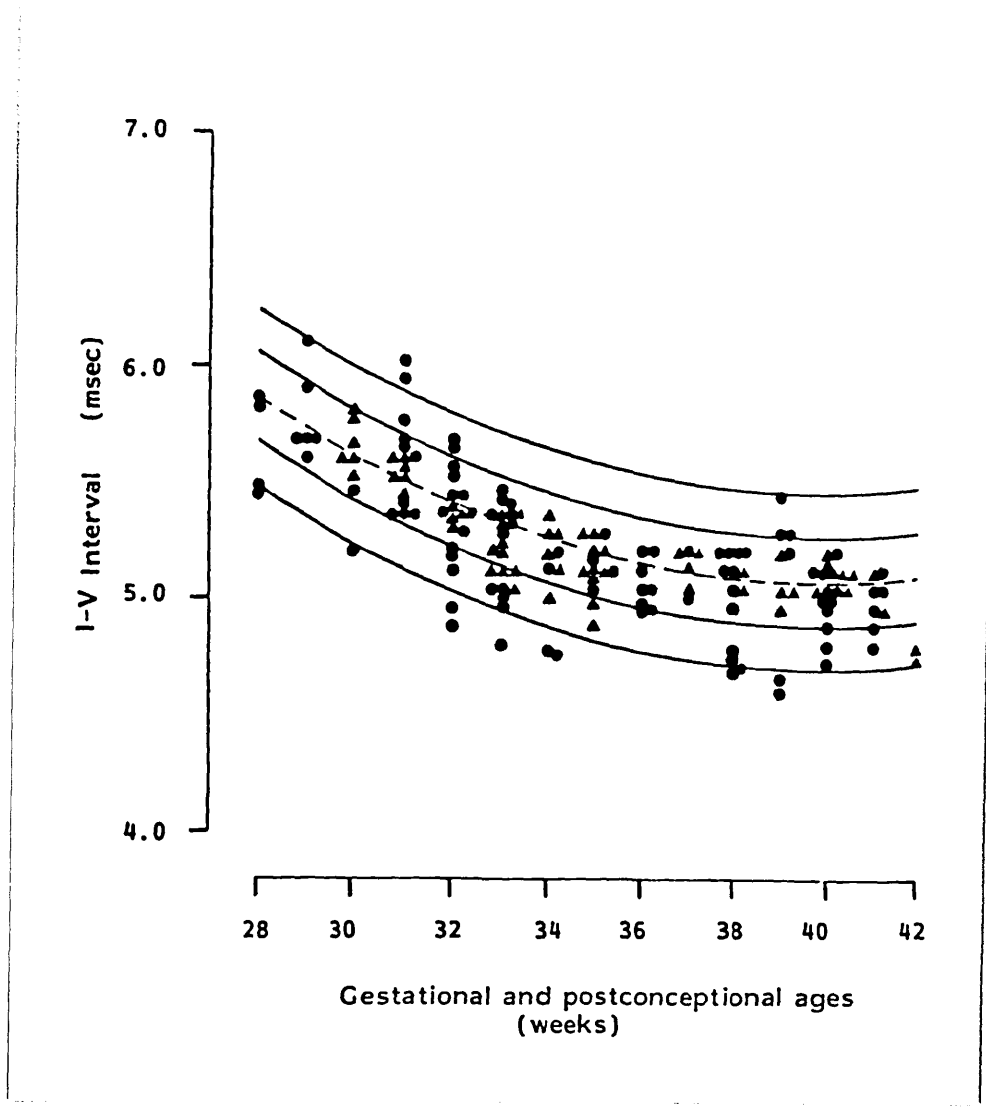


Figure 4.11. Interpeak interval I-V (at 80 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.12.

Interpeak interval (IPI) I - V ; 60 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	5.76	5.96	6.17	5.56	5.35
29	4	5.64	5.84	6.05	5.44	5.24
30	10	5.53	5.73	5.94	5.33	5.13
31	16	5.43	5.63	5.84	5.23	5.02
32	20	5.34	5.54	5.74	5.13	4.93
33	26	5.25	5.46	5.66	5.05	4.85
34	10	5.18	5.38	5.59	5.98	4.77
35	18	5.11	5.32	5.52	4.91	4.71
36	8	5.06	5.26	5.46	4.85	4.65
37	8	5.01	5.21	5.42	4.81	4.60
38	14	4.97	5.17	5.38	4.77	4.56
39	14	4.94	5.14	5.35	4.74	4.53
40	20	4.92	5.12	5.32	4.72	4.51
41	10	4.91	5.11	5.31	4.70	4.50
42	2	4.90	5.11	5.31	4.70	4.50

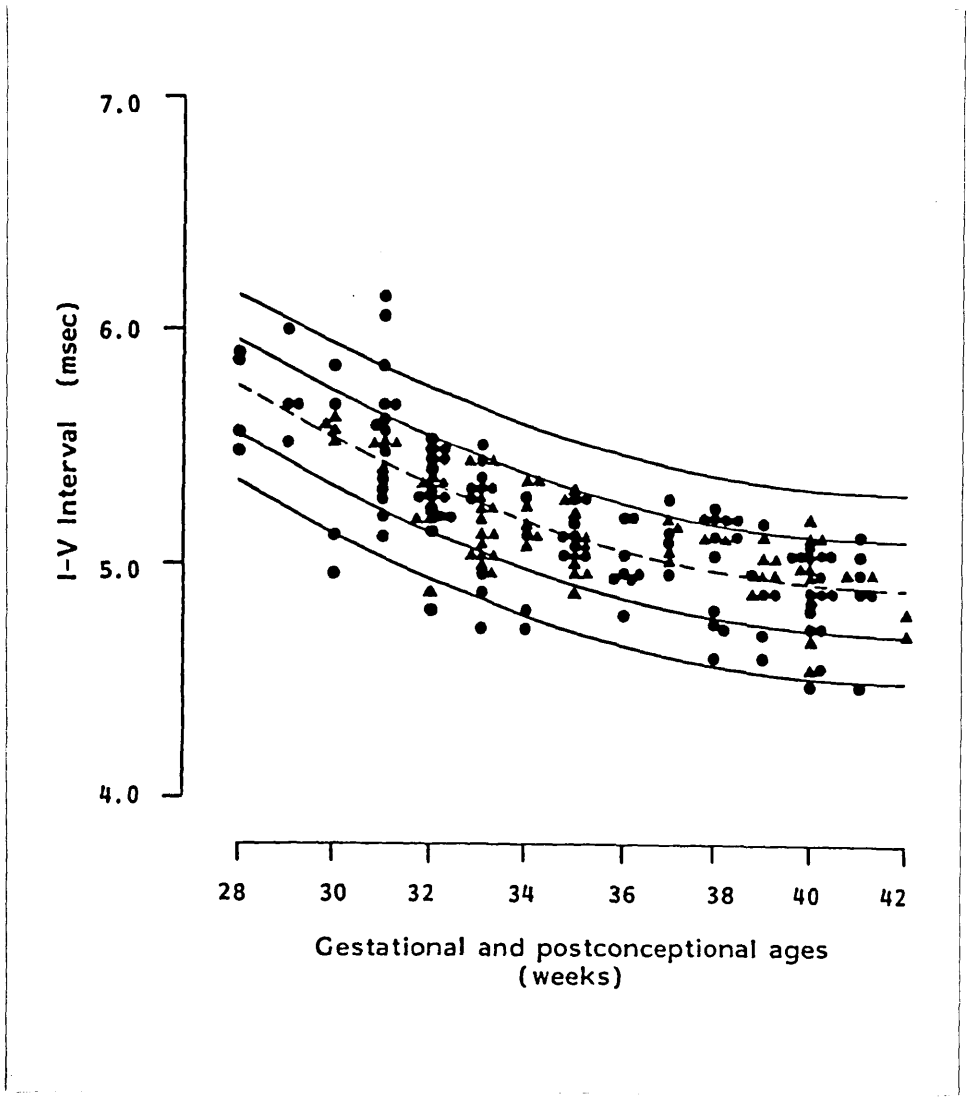


Figure 4.12. Interpeak interval I-V (at 60 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.13.

Interpeak interval (IPI) I - V : 40 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	2	5.47	5.78	6.08	5.17	4.87
29	1	5.43	5.73	6.03	5.12	4.82
30	6	5.38	5.68	5.98	5.08	4.77
31	13	5.33	5.63	5.93	5.03	4.72
32	13	5.28	5.58	5.88	4.98	4.67
33	20	5.25	5.53	5.84	4.93	4.62
34	8	5.18	5.49	5.79	4.88	4.57
35	18	5.13	5.43	5.74	4.83	4.52
36	8	5.08	5.39	5.69	4.78	4.48
37	10	5.03	5.32	5.64	4.53	4.42
38	16	4.99	5.28	5.60	4.68	4.38
39	14	4.94	5.24	5.54	4.64	4.33
TO	20	4.89	5.19	5.50	4.59	4.28
41	10	4.84	5.14	5.45	4.54	4.23
42	2	4.78	5.10	5.40	4.52	4.18

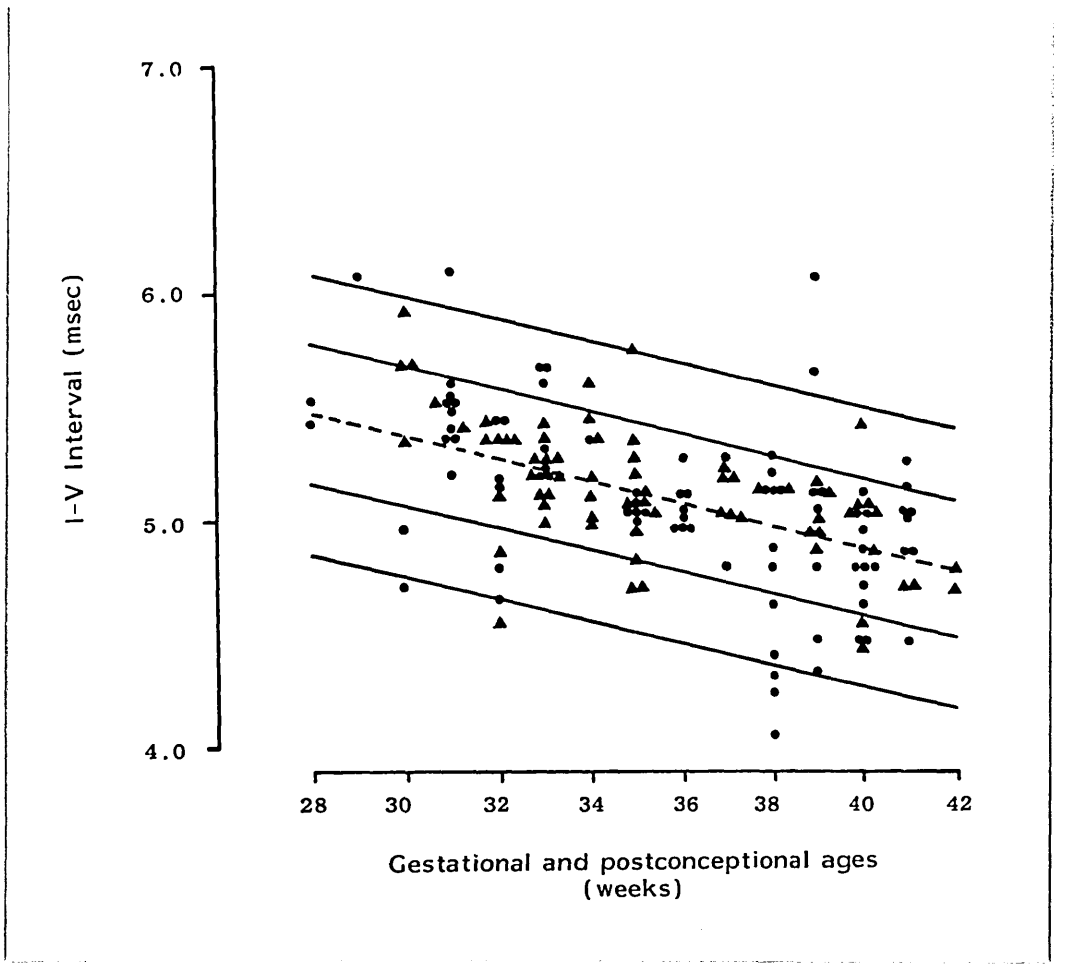


Figure 4.13. Interpeak interval I-V (at 40 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.14.

Interpeak interval (IPI) III-V : 80 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	4.85	5.24	5.62	4.46	4.07
29	5	4.72	5.08	5.48	4.32	3.92
30	9	4.58	4.97	5.36	4.19	3.80
31	10	4.46	4.84	5.24	4.06	3.68
32	12	4.36	4.75	5.14	3.97	3.58
33	23	4.26	4.64	5.04	3.86	3.48
34	9	4.19	4.58	4.97	3.80	3.41
35	14	4.14	4.50	4.90	3.72	3.33
36	7	4.06	4.45	4.84	3.67	3.28
37	6	4.02	4.40	4.80	3.62	3.23
38	13	3.98	4.37	4.76	3.59	3.17
39	9	3.95	4.34	4.74	3.56	3.17
40	18	3.94	4.33	4.72	3.55	3.16
41	10	3.94	4.32	4.72	3.55	3.16
42	2	3.95	4.34	4.73	3.56	3.17

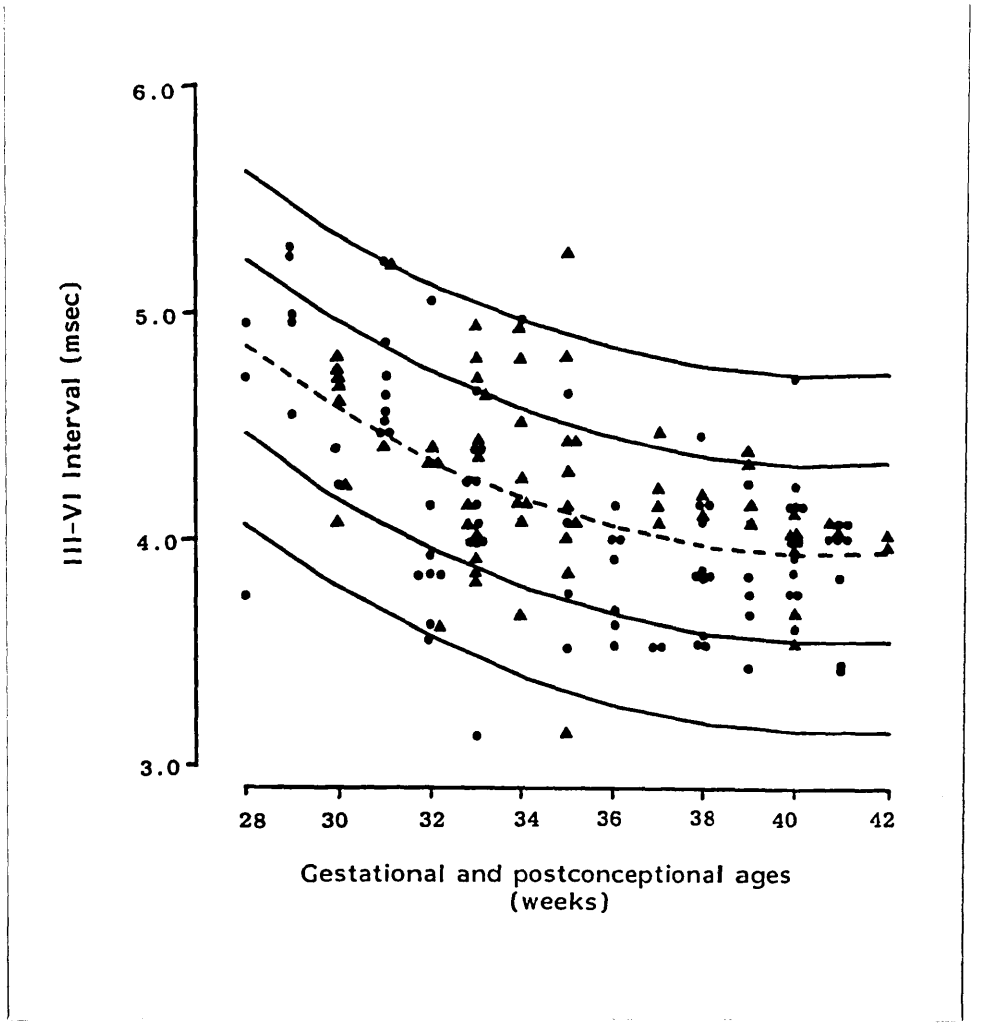


Figure 4.14. Interpeak interval III-VI (at 80 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.15.

Interpeak interval (IPI) III-VI: 60 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	3	4.37	4.71	5.06	4.02	3.68
29	2	4.32	4.66	5.00	3.96	3.62
30	7	4.27	4.60	4.95	3.92	3.58
31	10	4.22	4.55	4.90	3.87	3.52
32	16	4.17	4.50	4.85	3.82	3.47
33	22	4.11	4.45	4.80	3.77	3.42
34	10	4.06	4.40	4.75	3.72	3.37
35	16	4.00	4.35	4.70	3.67	3.32
36	6	3.95	4.30	4.65	3.62	3.27
37	8	3.91	4.24	4.60	3.57	3.21
38	14	3.85	4.20	4.55	3.52	3.16
39	14	3.80	4.15	4.50	3.46	3.11
40	16	3.75	4.10	4.45	3.42	3.06
41	10	3.69	4.05	4.40	3.37	3.01
42	2	3.64	4.00	4.35	3.32	2.96

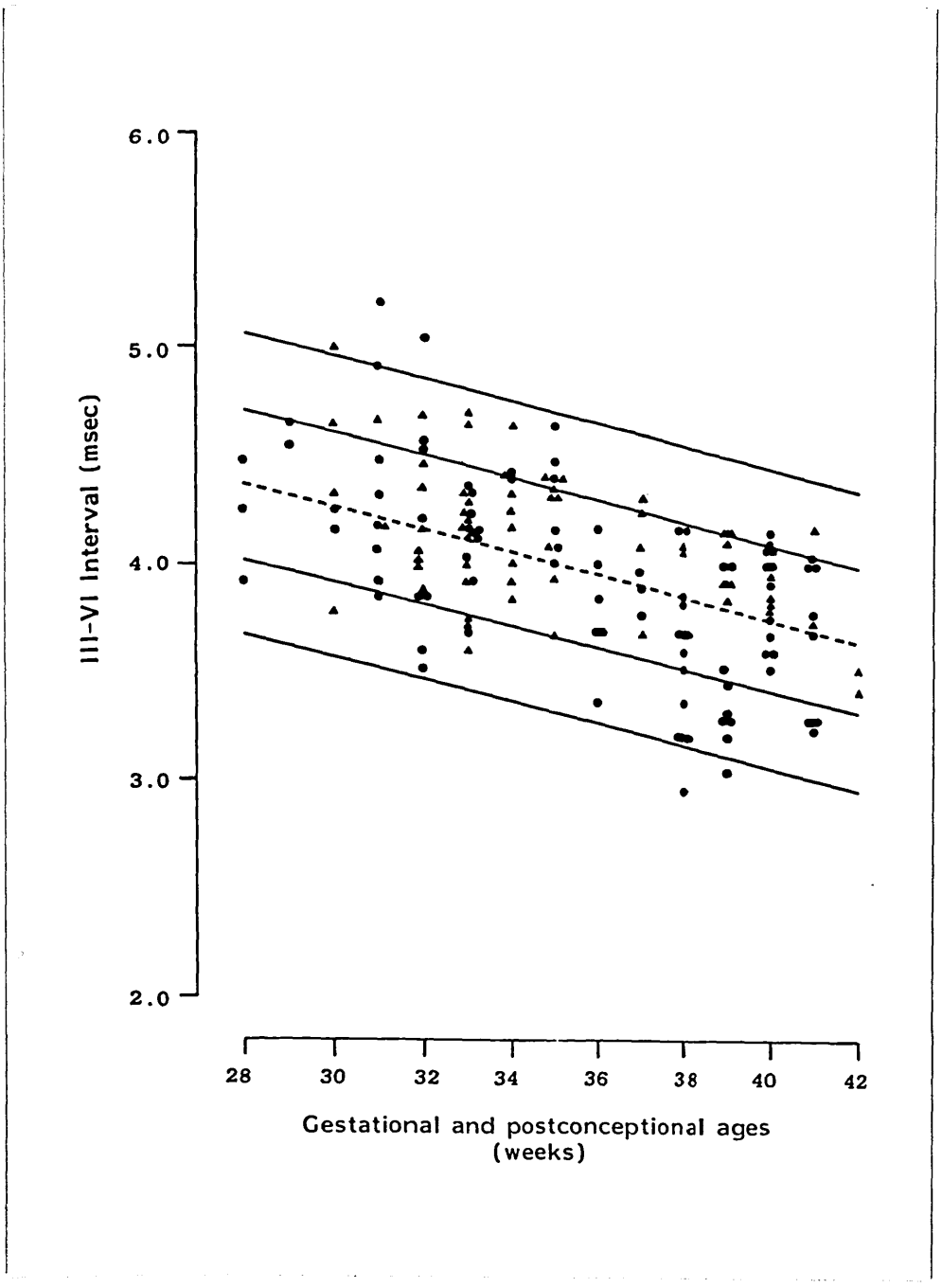


Figure 4.15. Interpeak interval III-VI (at 60 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.16.

Amplitude of Wave I ; 80 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	185	276.2	366.3	117.9	62.2
29	6	195.7	279.7	381.5	126.4	69.2
30	10	206.3	292.5	397.4	135.1	76.4
31	14	217.1	305.7	413.0	144.1	83.8
32	16	228.3	319.2	429.4	153.3	91.4
33	24	239.7	333.1	446.2	162.7	99.2
34	10	251.5	347.3	463.5	172.4	107.2
35	14	263.6	362.0	481.2	182.4	115.4
36	8	276.0	377.0	499.5	192.6	123.9
37	6	288.7	392.4	518.2	203.1	132.5
38	14	301.7	408.2	537.4	213.9	141.4
39	10	315.2	424.5	557.1	225.0	150.5
40	18	328.9	441.2	577.3	236.3	159.9
41	10	343.1	458.4	598.1	248.0	169.5
42	2	357.6	476.0	619.4	260.0	179.4

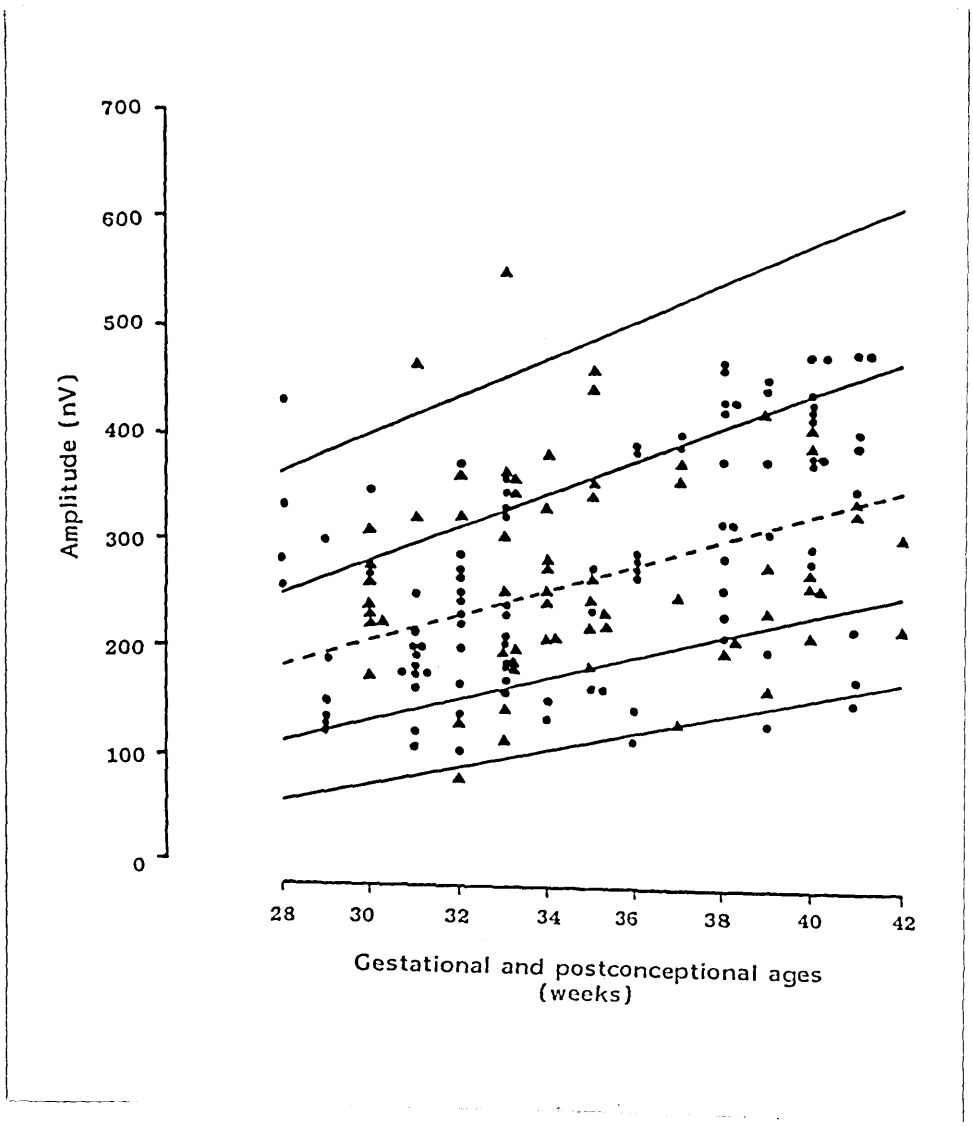


Figure 4.16. Amplitude of wave I (at 80 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.17.

Amplitude of Wave I ; 60 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	128.6	181.7	245.0	83.82	46.4
29	4	134.4	188.6	253.2	88.8	50.6
30	10	140.3	195.7	261.7	93.8	54.8
31	16	146.4	202.9	270.3	98.9	59.03
32	20	152.6	210.3	279.1	104.1	63.4
33	26	158.9	217.9	288.0	109.4	67.9
34	10	165.4	225.6	297.2	114.9	72.4
35	18	172.0	233.4	306.6	120.4	77.1
36	8	178.7	241.4	316.1	126.1	81.8
37	8	185.6	249.6	325.8	131.8	86.7
38	14	192.6	258.0	335.8	137.7	91.6
39	14	199.8	266.5	346.0	143.7	96.7
40	20	207.1	275.2	356.3	149.9	101.8
41	10	214.6	284.1	366.9	156.2	107.1
42	2	222.2	293.2	377.7	162.6	112.5

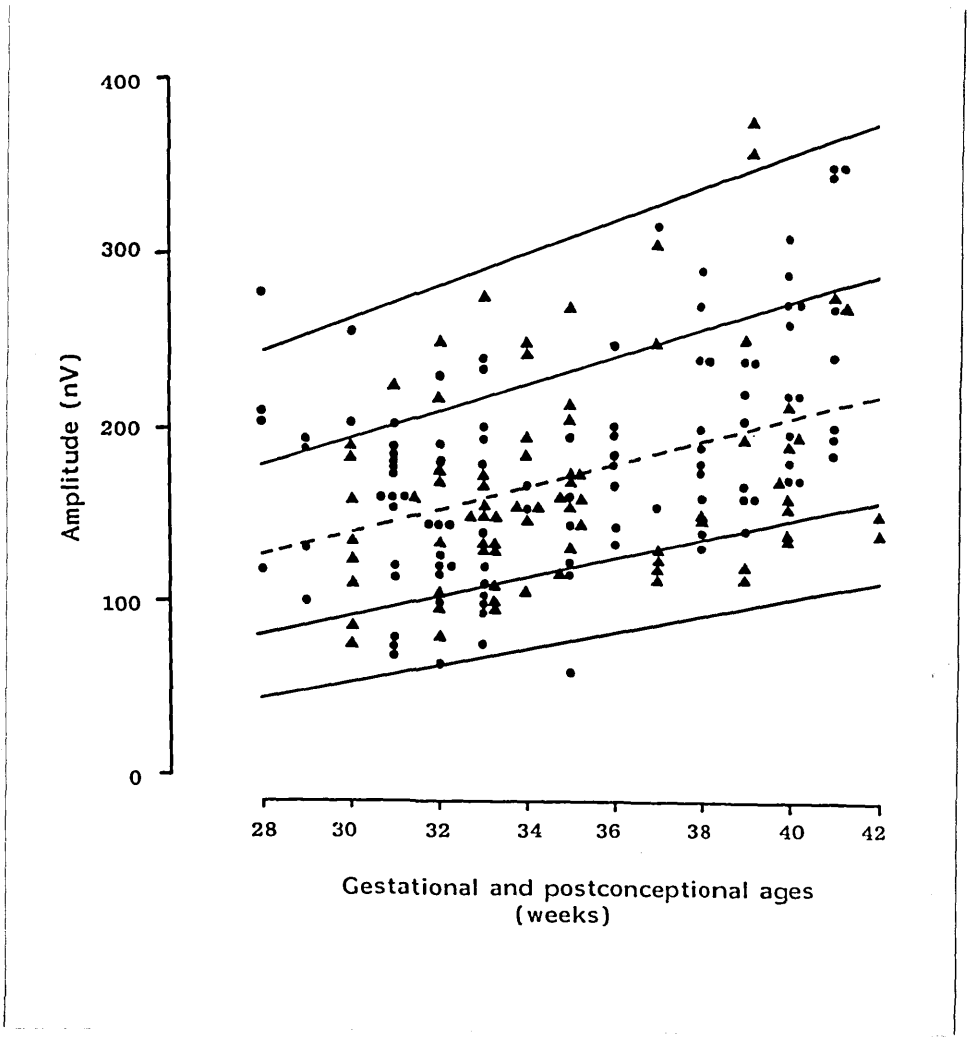


Figure 4.17. Amplitude of wave I (at 60 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.18.

Amplitude of Wave I ; 40 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	2	104	144	194	73	48
29	1	107	148	200	75	50
30	5	112	153	205	79	53
31	12	115	158	211	82	55
32	12	119	163	217	85	57
33	15	123	168	225	88	60
34	8	127	173	229	91	62
35	12	132	178	237	95	65
36	8	135	183	242	98	68
37	6	140	190	251	101	70
38	14	144	194	256	105	73
39	14	150	200	265	110	75
40	18	153	205	270	112	79
41	10	158	210	278	116	82
42	2	163	217	285	119	85

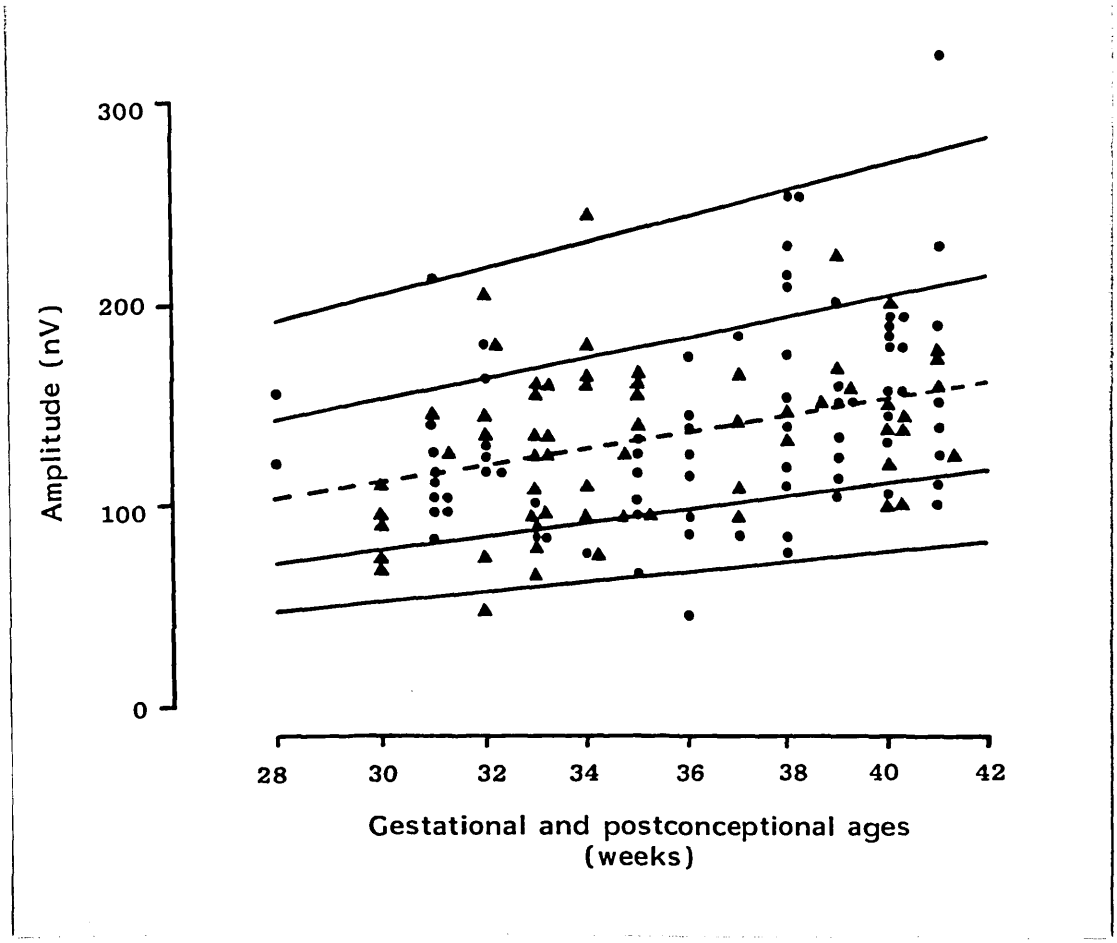


Figure 4.18. Amplitude of wave I (at 40 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.19.

Amplitude of Wave V ; 80 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1S0	$\bar{x}$-2SD
28	4	144.6	203.3	273.8	95.6	54.74
29	6	150.0	209.8	281.6	100.1	58.5
30	10	155.5	216.4	289.5	104.7	62.3
31	14	161.1	223.2	297.6	109.	66.2
32	16	168.8	230.0	305.8	114.1	70.19
33	24	172.6	237.0	314.2	119.0	74.2
34	10	178.5	244.1	322.7	123.9	78.2
35	14	184.6	251.3	331.4	128.9	82.5
36	8	190.7	258.7	340.2	134.1	86.8
37	6	197.0	266.2	349.2	139.3	91.1
38	14	203.3	273.8	358.4	144.6	95.6
39	10	209.8	281.6	367.7	150.0	100.1
40	18	216.	289.5	377.2	155.5	104.7
41	10	223.1	297.6	386.9	161.1	109.34
42	2	230.0	305.8	396.8	166.8	114.1

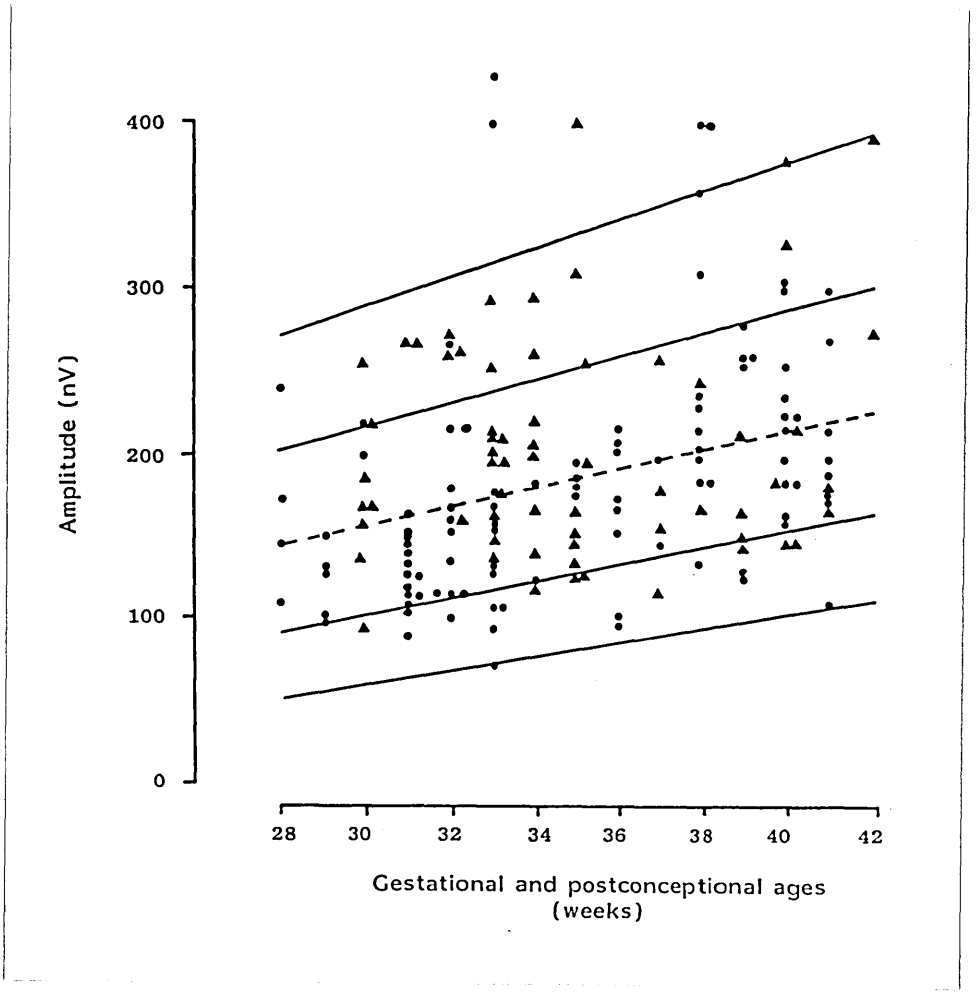


Figure 4.19. Amplitude of wave V (at 80 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.20.

Amplitude of Wave V : 60 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	120.6	170.8	235.7	81.8	51.9
29	4	126.2	178.0	245.1	86.1	55.2
30	10	132.0	185.5	254.8	90.6	58.6
31	16	137.9	193.2	264.8	95.2	62.2
32	20	144.1	201.2	275.1	100.0	65.9
33	26	150.4	209.4	285.7	104.9	69.7
34	10	157.0	217.9	296.7	110.0	73.6
35	18	163.8	226.7	308.1	115.2	77.6
36	8	170.8	235.8	319.8	120.6	81.8
37	8	178.0	245.1	221.9	126.2	86.1
38	14	185.5	254.8	344.5	131.97	90.6
39	14	193.2	267.8	357.4	137.9	95.2
40	20	201.2	275.1	370.7	144.1	100.0
41	10	209.4	285.7	384.5	150.4	104.9
42	2	217.6	296.7	398.7	157.0	110.0

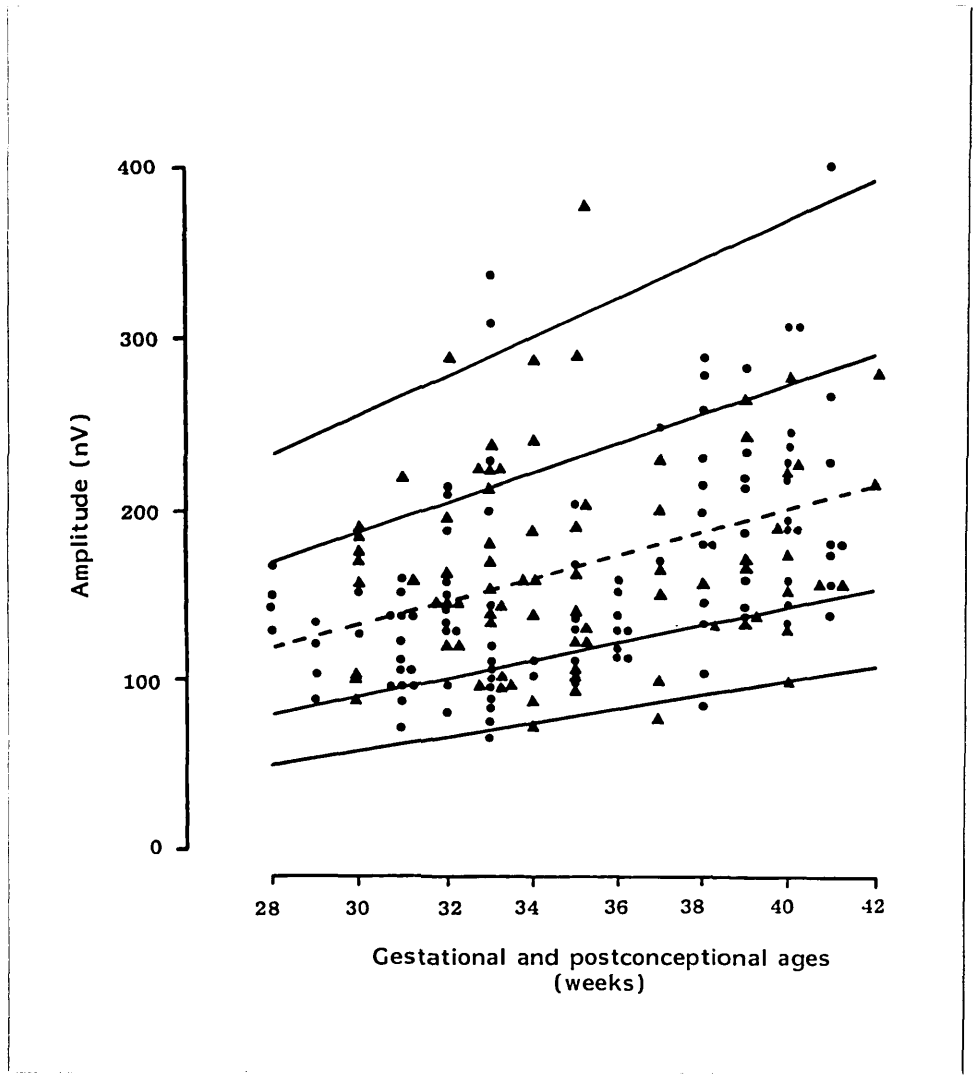


Figure 4.20. Amplitude of wave V (at 60 dB) plotted as a function of age. This figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

TABLE IV.21.

Amplitude of Wave V : 40 dB

GA	No.	Mean	$\bar{x}$+1SD	$\bar{x}$+2SD	$\bar{x}$-1SD	$\bar{x}$-2SD
28	4	105	145	194	74	48
29	1	108	150	199	75	51
30	6	113	155	207	80	54
31	13	118	160	214	83	56
32	12	122	166	221	87	59
33	16	127	172	230	90	62
34	10	131	177	235	94	65
35	12	136	182	245	98	68
36	8	140	189	250	102	71
37	6	145	194	258	106	74
38	14	150	201	265	109	77
39	14	155	208	274	114	81
40	18	161	214	282	118	84
41	10	166	220	290	123	87
42	2	172	228	299	127	91

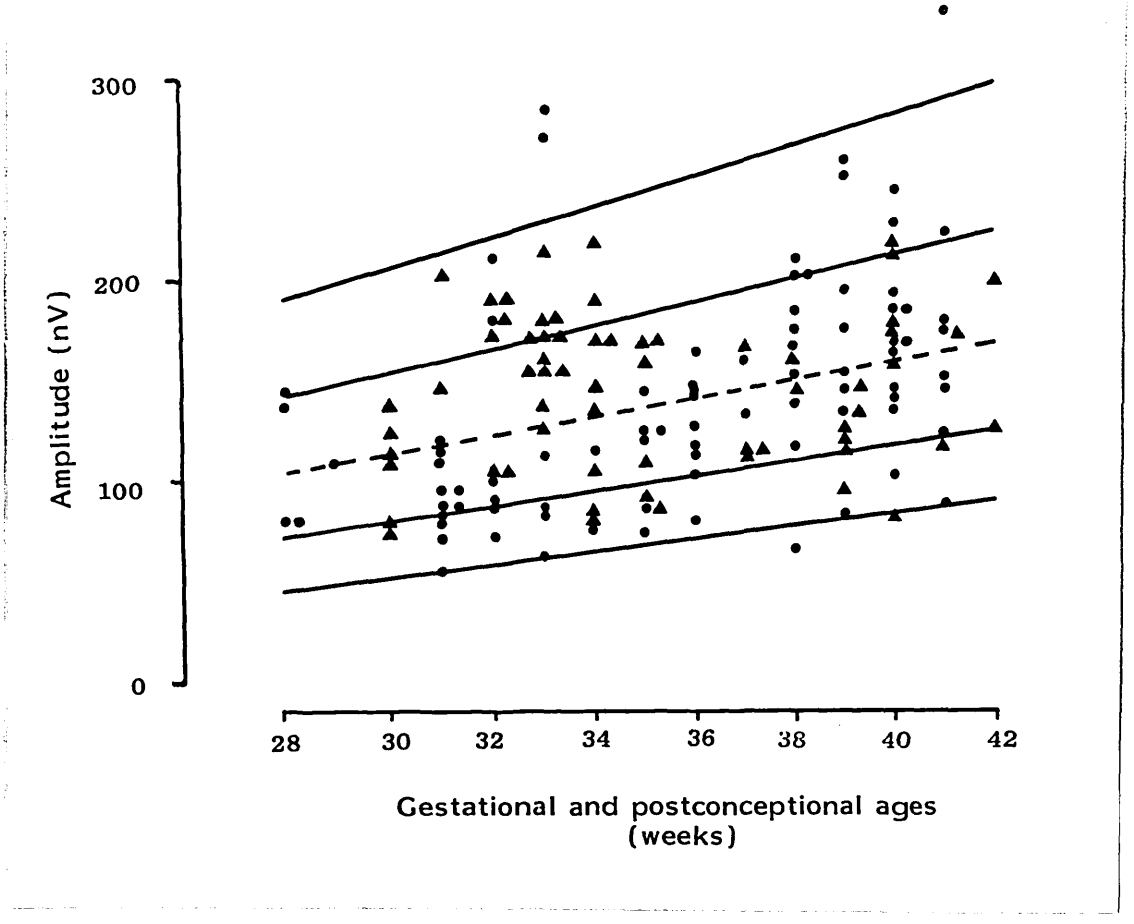


Figure 4.21. Amplitude of wave V (at 40 dB) plotted as a function of age. The figure shows the mean (dotted line) with 1 and 2 standard deviations. Individual measurements are plotted as cross-sectional (circles) and longitudinal (triangles) data.

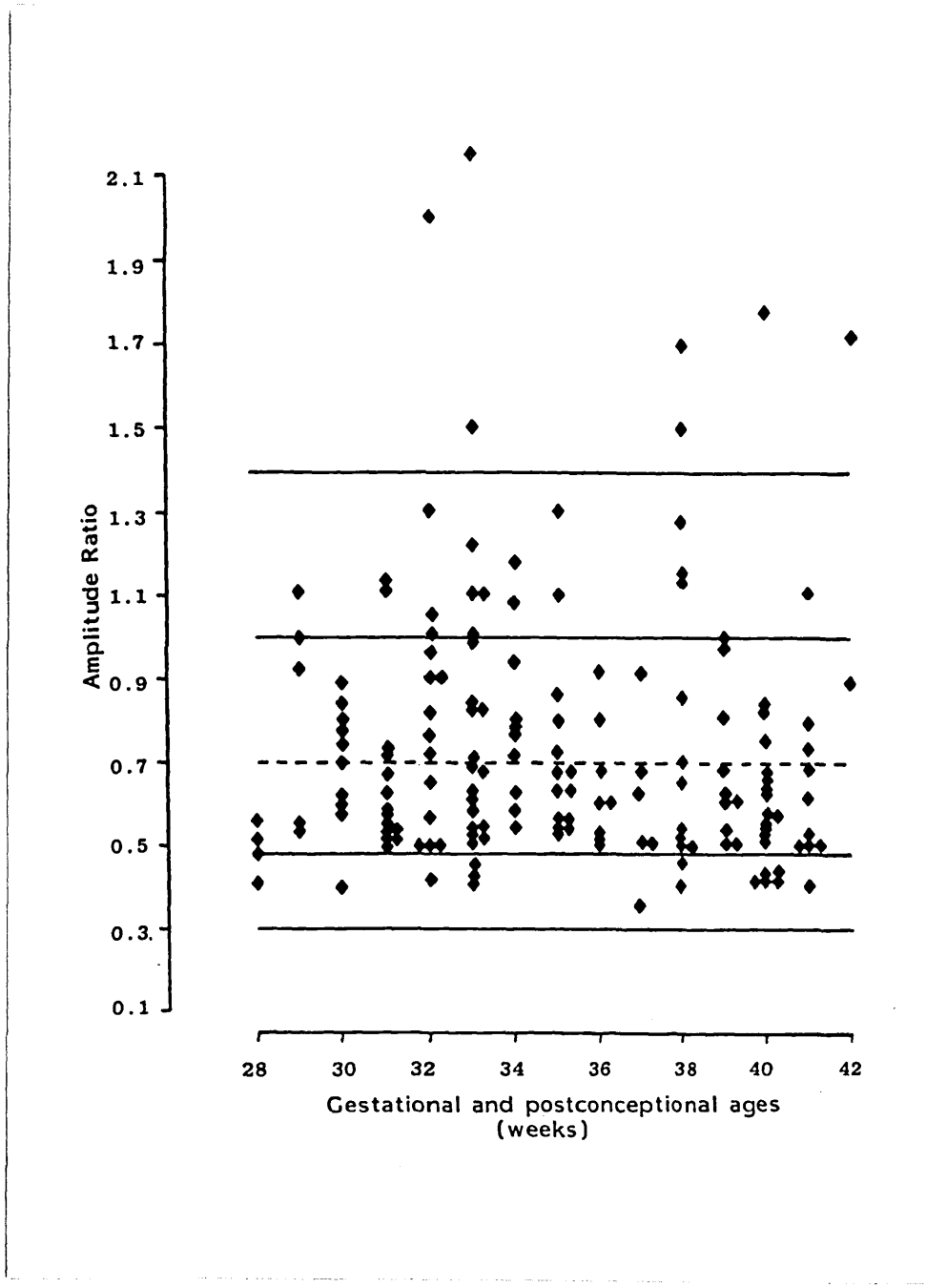


Figure 4.22. Amplitude ratio V:1 (at 80 dB) plotted as a function of age. The figure shows the mean (dotted line) with 1 and 2 standard deviations.

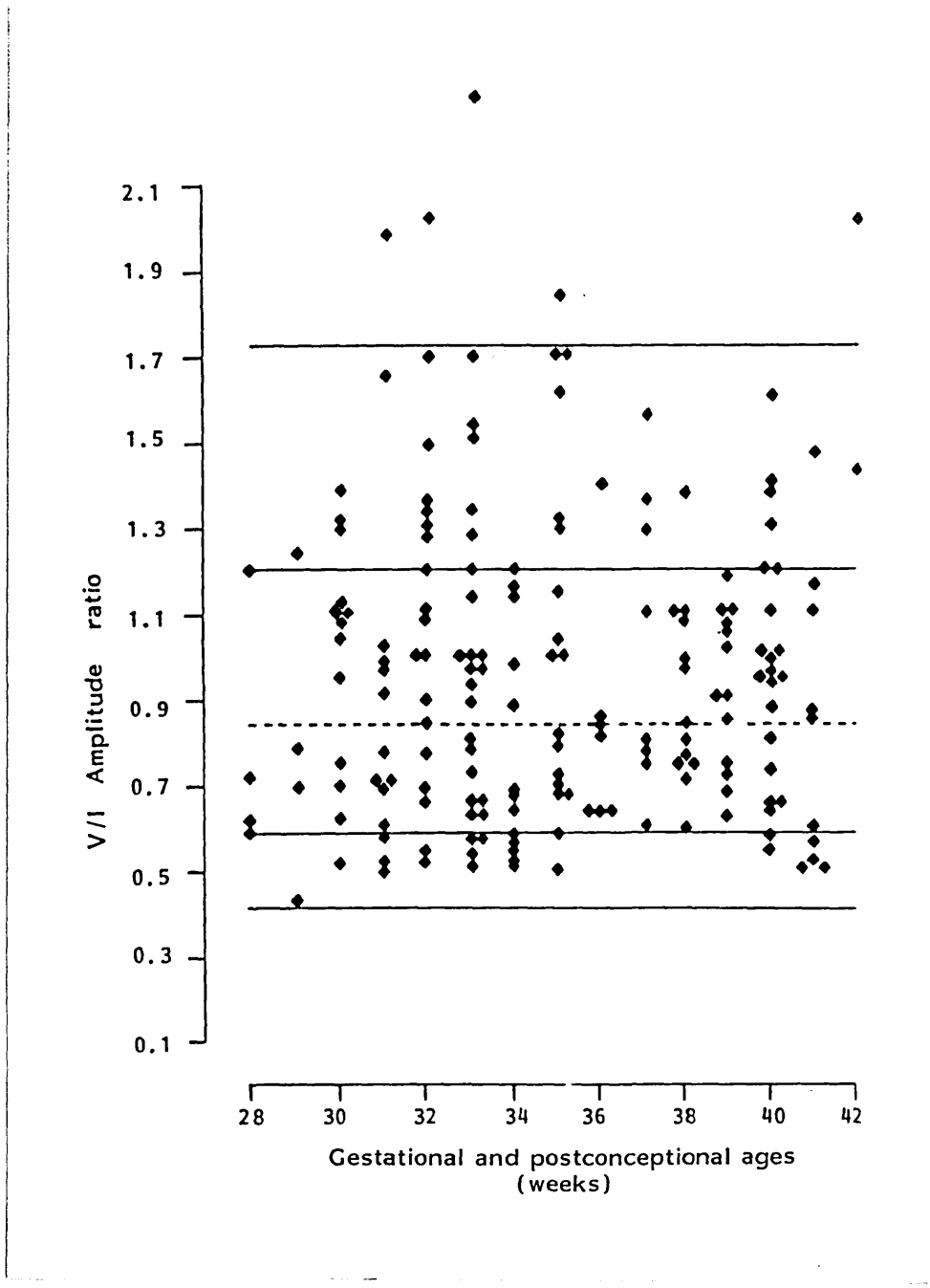


Figure 4.23. Amplitude ratio V:1 (at 60 dB) plotted as a function of age. The figure shows the mean (dotted line) with 1 and 2 standard deviations.

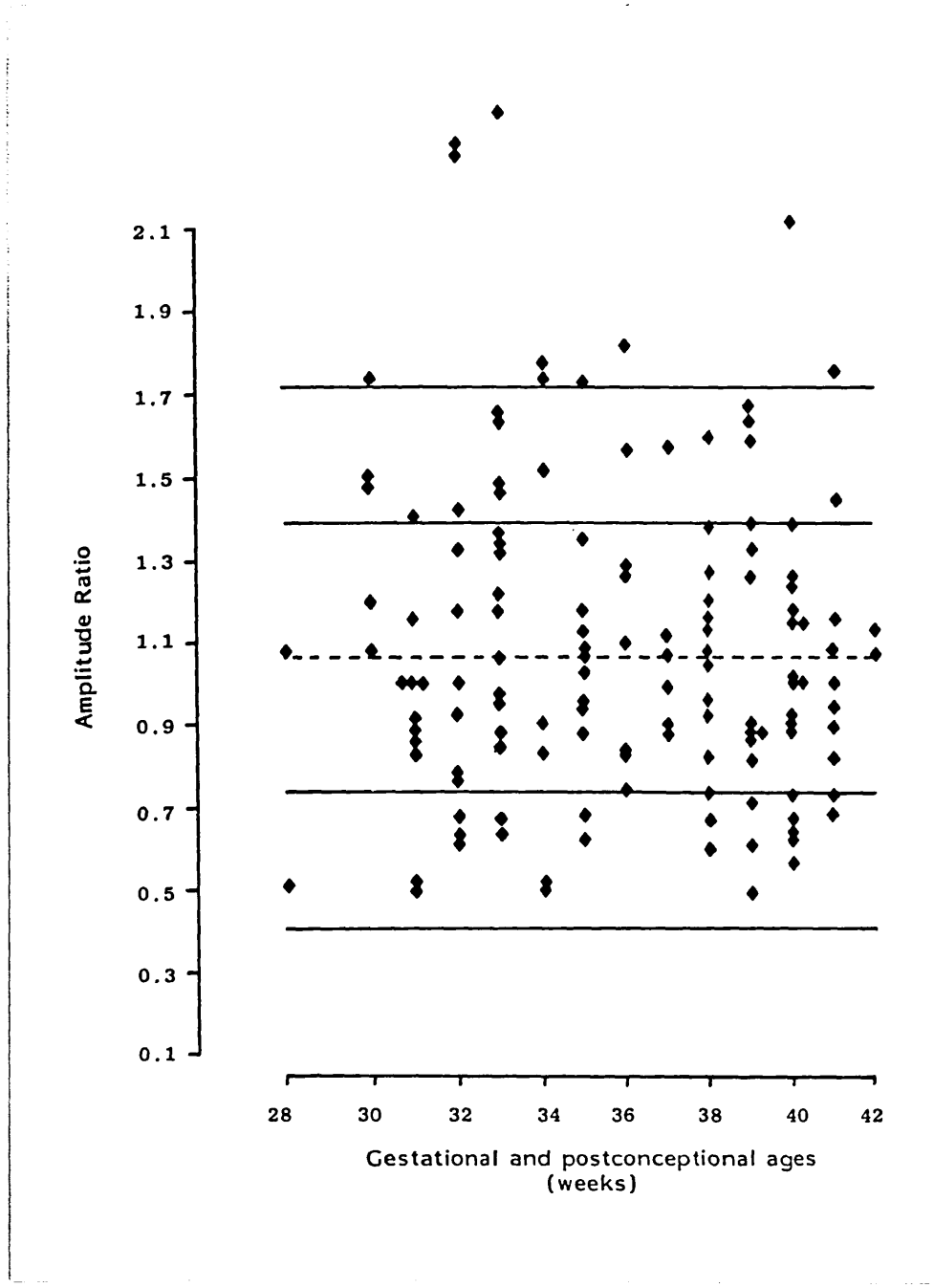


Figure 4.24. Amplitude ratio V:1 (at 40 dB) plotted as a function of age. The figure shows the mean (dotted line) with 1 and 2 standard deviations.

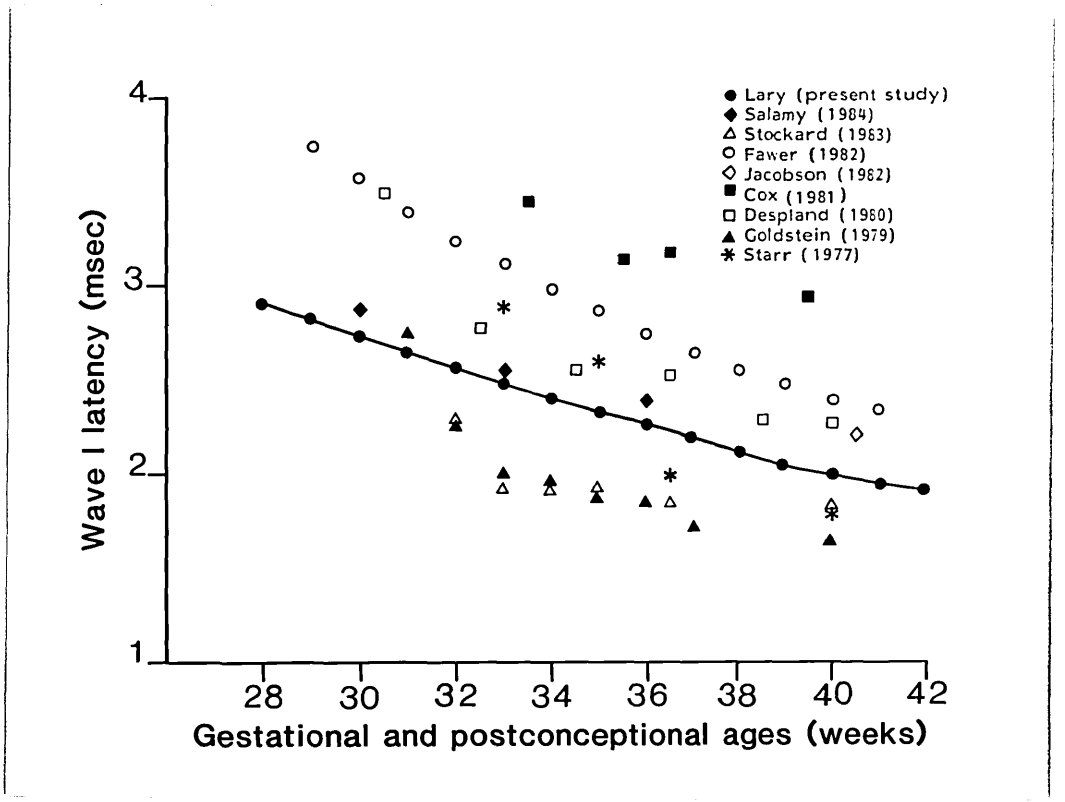


Figure 4.25. Wave I latency as a function of age as reported in nine studies.

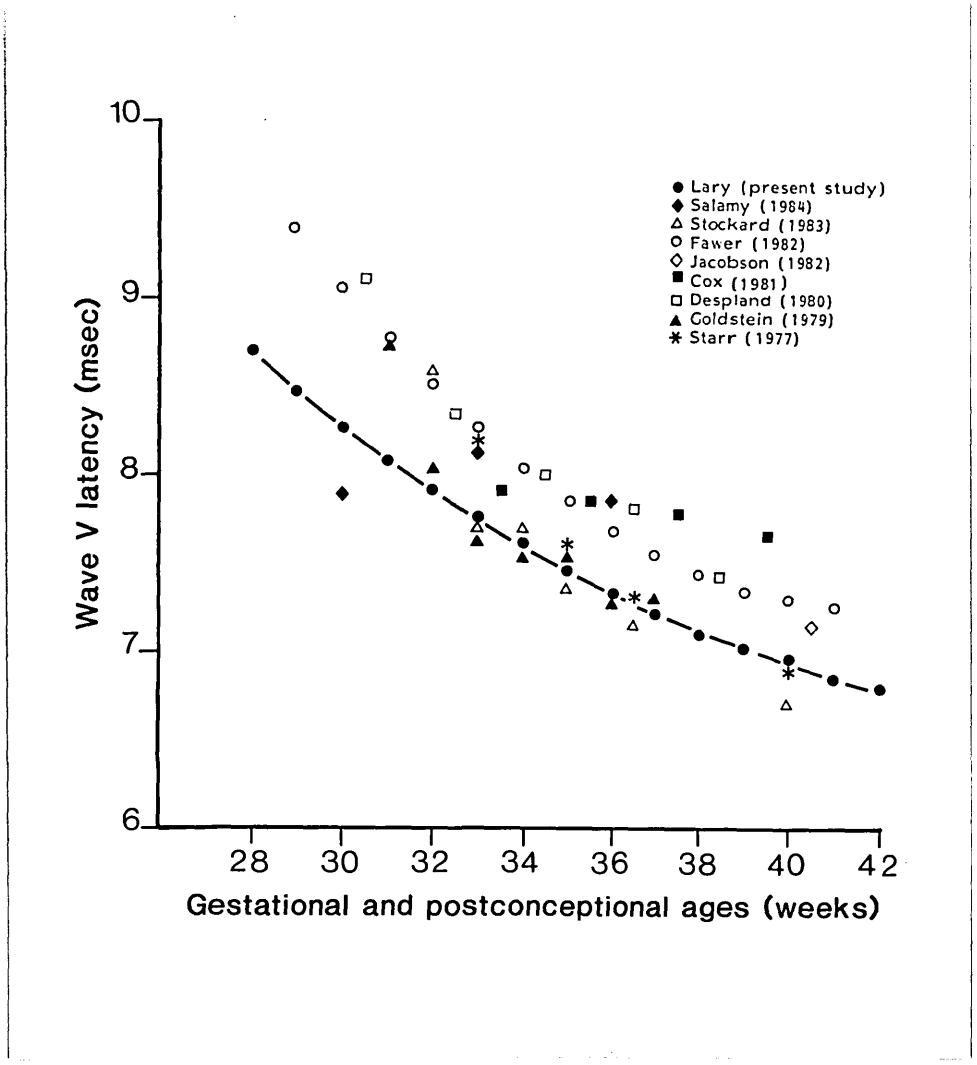


Figure 4.26. Absolute latency of wave V plotted as a function of age as reported in nine studies.

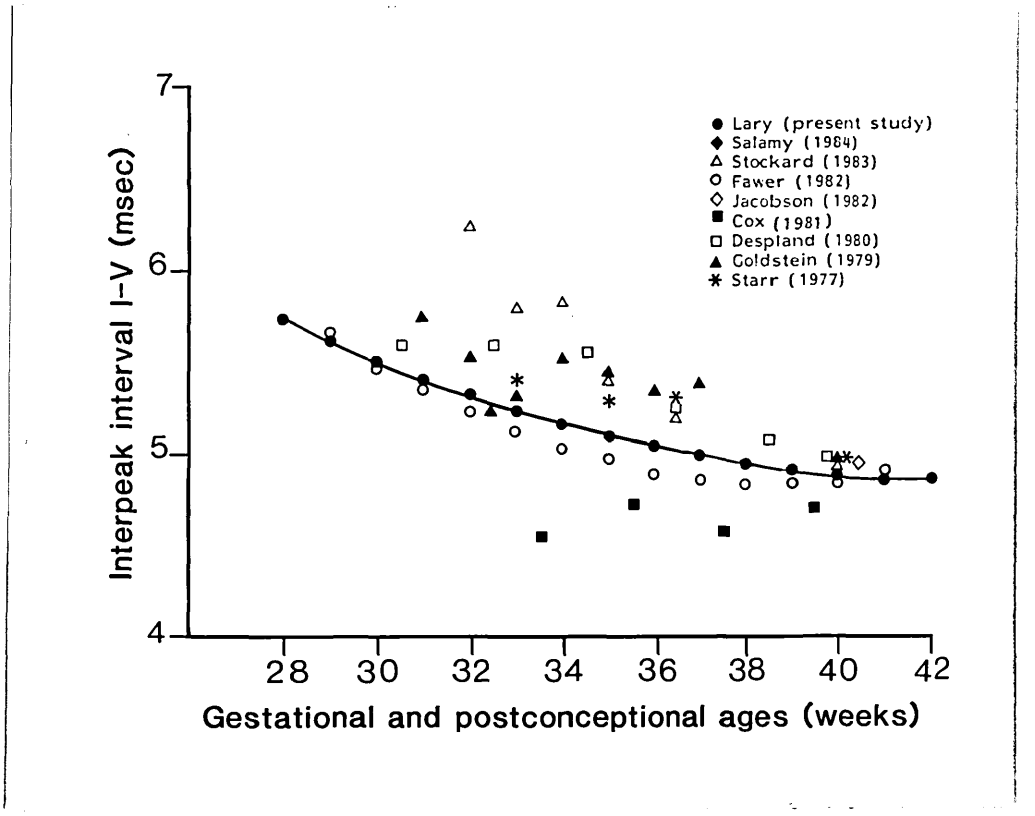


Figure 4.27. Interpeak interval I-V as reported in nine studies. Mos studies report similar data to the time the infant has reached the age 40 weeks.

TABLE IV.22

INTERLABORATORY COMPARISON OF WAVE LATENCIES (I AND V) AND INTERPEAK INTERVAL (I-V)

GA	REF*	WAVE I Absolute latency $\bar{x}$	SD	n	WAVE V Absolute latency $\bar{x}$	SD	n	I-V IPI Interpeak interval $\bar{x}$	SD	n
28	1	2.93	0.29	4	8.69	0.34	4	5.76	0.20	4
29	1	2.84	0.29	4	8.48	0.34	4	5.64	0.20	4
"	2	3.75	0.33	4	9.40	0.38	3	5.65	0.28	3
30	1	2.75	0.29	10	8.28	0.34	10	5.53	0.20	10
"	2	3.58	0.32	2	9.06	0.36	2	5.49	0.27	2
"	3	2.90	0.70		7.91	1.22				
30-31	4	3.50	0.53	74	9.10	0.32	74	5.60	0.55	74
31	1	2.66	0.29	16	8.09	0.34	16	5.43	0.20	16
"	2	3.42	0.31	5	8.77	0.36	5	5.34	0.26	3
"	5	2.75	0.68	4	8.77	0.38	2	5.76	0.78	3
32	1	2.58	0.29	20	7.92	0.34	20	5.34	0.20	20
"	2	3.27	0.31	10	8.50	0.37	10	5.23	0.27	10
"	5	2.28	0.43	10	8.04	0.69	7	5.53	0.63	10
"	6	2.31	0.32	8	8.58	0.58	8	6.26	0.39	8
32-33	4	2.78	0.22	74	8.36	0.54	74	5.62	0.30	74
33	1	2.50	0.29	26	7.76	0.34	26	5.25	0.20	26
"	2	3.13	0.31	9	8.25	0.36	9	5.12	0.26	9
"	3	2.55	0.47		8.22	0.54				
"	5	2.02	0.39	8	7.62	0.47	7	5.34	0.53	7
"	6	1.93	0.22	14	7.71	0.24	14	5.78	0.21	14
"	7	2.90			8.20			5.40		

33-34	1	3.45	0.40	20	7.90	0.40	24	4.55	0.47	20
34	1	2.42	0.29	10	7.60	0.34	10	5.18	0.20	10
"	2	2.99	0.30	5	8.03	0.36	5	5.03	0.26	5
"	5	1.98	0.29	13	7.51	0.28	8	5.53	0.41	13
"	6	1.93	0.34	24	7.71	0.36	24	5.81	0.29	24
34-35	4	2.56	0.25	74	8.00	0.28	74	5.54	0.29	74
35	1	2.35	0.29	18	7.47	0.34	18	5.11	0.20	18
"	2	2.88	0.32	5	7.84	0.36	5	4.96	0.26	5
"	5	1.87	0.23	17	7.52	0.42	6	5.42	0.54	17
"	6	1.95	0.20	30	7.34	0.31	30	5.39	0.28	30
"	7	2.60			7.60			5.30		
35-36	8	3.14	0.40	20	7.85	0.51	22	4.71	0.38	20
36	1	2.28	0.29	8	7.34	0.34	8	5.06	0.20	8
"	2	2.77	0.32	8	7.67	0.36	8	4.90	0.26	8
"	3	2.43	0.40		7.84	0.49				
"	5	1.87	0.27	14	7.28	0.45	11	5.36	0.47	14
36-37	4	2.53	0.19	74	7.80	0.45	74	5.27	0.38	74
"	6	1.83	0.20	35	7.17	0.27	35	5.26	0.31	35
"	7	2.00			7.30			5.30		
37	1	2.21	0.29	8	7.22	0.34	8	5.01	0.20	8
"	2	2.66	0.31	10	7.54	0.37	10	4.87	0.26	10
"	5	1.71	0.18	8	7.53	0.48	6	5.41	0.59	8
37-38	8	3.17	0.59	17	7.79	0.59	20	4.57	0.42	17
38	1	2.15	0.29	14	7.12	0.34	14	4.97	0.20	14
"	2	2.57	0.31	6	7.43	0.37	6	4.85	0.26	6

38-39	4	2.30	0.19	74	7.42	0.19	74	5.09	0.16	74
39	1	2.09	0.29	14	7.03	0.34	14	4.94	0.20	14
"	2	2.49	0.31	5	7.34	0.36	5	4.85	0.26	5
39-40	8	2.95	0.20	14	7.65	0.19	14	4.7	0.29	14
40	1	2.03	0.29	20	6.95	0.34	20	4.92	0.20	20
"	2	2.42	0.32	9	7.29	0.37	9	4.87	0.27	9
"	3	2.07	0.36		7.11	0.28		4.99	0.31	
"	4	2.28	0.27	74	7.35	0.46	74	5.07	0,41	74
"	5	1.64	0.18	30	6.74	0.22	23	5.10	0.26	30
"	6	1.81	0.22	62	6.72	0.32	62	4.90	0.28	62
"	7	1.80			6.90			5.00		
40-41	9	2.23	0.28	38	7.16	0.44	38	4.94	0.39	38
41	1	1.97	0.29	10	6.88	0.34	10	4.91	0.20	10
"	2	2.35	0.32	4	7.26	0.37	4	4.90	0.27	4
42	1	1.92	0.29	2	6.82	0.34	2	4.90	0.20	2
42-43	4	2.28	0.20	74	7.17	0.10	74	4.83	0.20	74
	9	2.24	0.36	94	7.11	0.26	94			

*: The references relate to the inter-laboratory comparison study (Table V.23).

TABLE IV.23

KEY TO REFERENCES IN TABLE IV.22 AND DESCRIPTION OF PARAMETERS USED

NO	REFERENCE	RATE (/SEC)	PHASE R/C	INTENSITY (dB)	FILTER (HZ)
1.	Lary (present study)	10	R	60 nHL	300-3000
2.	Fawer and Dubowitz (1982)	10	?	60	250-1600
3.	Salamy (1984)	?	?	60 nHL	?
4.	Despland and Galambos (1979, 1980)	10	?	60	150-1500
5.	Goldstein et al (1979)	8-12	?	65 SL	100-3000
6.	Stockard et al (1983a)	10	R	110 peSPL	100-3000
7.	Starr et al (1977)	10	R+C	65 SL	100-3000
8.	Cox et al (1981a)	33	?	60 nHL	150-1500
9.	Jacobson et al (1982)	10.4	R+C	60 nHL	150-3000

peSPL: peak equivalent sound pressure level
nHL: normal hearing level
SL: sensational level
R: rarefaction phase
C: condensation phase

CHAPTER V. NORMATIVE DATA FOR AUDIOLOGICAL DIAGNOSIS

V.1. THE AUDIOLOGICAL BACKGROUND:

The prevalence of hearing deficits among the graduates of NICUs has been estimated to be as high as 2-4% (Starr et al 1977, Cox et al 1981, Roberts et al 1982, Stein et al 1983). In infants of very low birthweight (less than 1500 gms) the figures ranged from 2.1% to 17.5% (Campanelli et al 1958, Drillien 1964, Stewart and Reynolds 1974, Davies and Tizard 1975, Schulman-Galambos and Galambos 1975, Schulte and Stennert, 1978). Early identification of infants with hearing loss is important, since normal language development,early learning and the acquisition of social skills depend upon hearing.

Until a decade ago, reliable objective assessment of neonatal auditory function had not generally proved feasible and accurate information was not usually obtained until the child was two to five years old. Although testing procedures and screening techniques steadily improved over this period it was the development of ABR techniques that was to revolutionize the whole subject.

The tests previously used fell into two groups, according to the type of stimulus used. In one group, gross uncalibrated sounds were used (such as bells and rattles) from which a rough estimate of frequency spectrum and intensity could be derived. In the other group calibrated sound generators were used.

During the neonatal period auditory assessment was limited to the use of loud stimuli. The types of response elicited were the auro-palpebral reflex (APR), the startle (Moro) reflex, and arousal responses taking the form of generalised body movement. The APR consisted of contraction of the orbicularis oculi muscles, seen as quick eye closure, or screwing up of the eyes if they were already closed. Generally speaking, the assessment of hearing during this period was qualitative and not quantitative. There was, moreover, the difficulty in differentiating unresponsiveness due to deafness from other forms of unresponsiveness.

The early detection of hearing loss in infants necessitated the mass screening of neonates. Commercially available portable sound generators were used. Most of these delivered a band of noise of high frequency (3600 Hz). The intensities of the outputs ranged from 70 to 100 dB sound pressure levels (SPLs). The instruments were usually held at a standard distance from the infants' ears. Infants who failed to respond received audiological follow-up.

Downs (1972) screened 20,000 infants and found 12 to be deaf. There was an estimated false positive rate of 3%. Feinmesser and Bauberger-Tell (1972) reported five deaf infants out of 17,708 neonates screened. On follow-up four additional deaf infants were found. This led the authors to question the validity of the whole screening procedure.

Changes in heart rate following auditory stimulation have also been investigated. Bartoshuk (1962) repeatedly elicited cardiac acceleration in response to intense auditory signals. Beadle and Crowell (1962) reported changes in pulse rate in a single normal neonate following auditory stimulation: there was no consistent acceleration or deceleration in relation to either frequency or intensity change. Bartoshuk (1964), however, obtained larger increases in heart rate for signals of successively greater intensity. Steinschneider, Lipton and Richmond (1966) reported increases in heart rate and decreases in latency of response as the intensity of the stimulus increased. In general, these studies used relatively intense sounds. Some used broad band noise.

Changes in respiration rate during auditory stimulation have been investigated. Heron and Jacobs (1969) reported various respiration changes in infants with normal hearing following stimulation by

frequency modulated tones. Bradford and Rousey (1972) reviewed this whole approach and concluded that these were diagnostically useful procedures.

Galvanic skin responses to auditory stimulation have not proved generally practical. Hardy and Bordley (1951) reported problems in the conditioning of unco-operative and neurologically impaired children. Unfortunately these are the very children for whom the procedure is needed.

Simmons and Russ (1974) and Simmons (1976) described an automated procedure (the "crib-o-gram") for neonatal auditory screening. The test sought to establish when the baby moved in response to speech. A motion-sensitive transducer on the cot detected the infant's movements, and recorded them on a strip. Twenty recordings, each lasting 16 seconds, were made during each 24 hour period. Half way through each sample a signal was emitted from a loudspeaker. Auditory responses were determined by comparing the infants' movements recorded before and after the signal. The authors reported 777 failures among the 7,655 neonates screened, but only five of these 777 infants turned out to have documented hearing loss.

The auditory response cradle (ARC) developed by Bennett (1975, 1979) evaluated behavioural responses to sound by using a microprocessor-based device. This consisted of a trolley-mounted unit, comprising a pressure-sensitive mattress and a head rest. These incorporated non-contacting sensors which respond to head turns, startles or head jerks, body activity and respiration. A 2600 Hz high pass noise of 85 dB SPL was transmitted through probes inserted into the baby's ears. The responses were analysed by the automatic microprocessor. The test was completed in 2-10 minutes.

Recent users of this technique (Bhattacharya et al 1984) found that when the ARC was used as a mass screening test, 439 out of 5,553 neonates failed the first screening test. Eighty-eight (1.6%) failed a second screening test, in which 61 were shown to have normal hearing. This gave a false positive rate of 1.1%. The remaining infants showed hearing deficits (detectable by other means) on follow-up. The ARC may be a promising screening test. The test is binaural, and problems will remain for infants with unilateral hearing loss, as well as for infants with hearing loss of less than 85 dB. The test cannot be used for sick infants in NICUs.

The development of auditory evoked potentials has expanded the possibilities of objective testing of hearing function. Early

research centred on cortical responses. These were found to have poor reliability due to the effects of state variability and interference from other cerebral electrical activity and muscle potentials (Davis 1976).

On the other hand, the auditory brainstem responses (ABR), as first recorded by Jewett and Williston (1971), appear to have great promise. Of the factors which helped the ABR rapidly to become a popular procedure for hearing tests (particularly in the newborn) were: reproductivity and consistency of responses from patient to patient; and the fact that it was not affected by the level of alertness, muscle artefact or ongoing cerebral electrical activity (Stockard and Rossiter 1977).

The ABR has proved its reliability for the audiometer assessment of adult and paediatric populations (Jerger et al 1980). Recently, investigators have advocated its use for screening the high risk newborn (Schulman-Galambos and Galambos 1979a, Galambos and Despland 1980, Marshall et al 1980, Galambos et al 1982).

From the above review we can conclude that there is widespread agreement on the desirability of a clinical programme for early detection and measurement of hearing in infants. Mass screening of

all live births is impractical, therefore registers of high risk factors* have been used. These infants will include those with the following risk factors which may raise the suspicion of predisposing the child to hearing impairment: (a) family history of hearing loss (b) congenital perinatal infection (c) congenital malformation: defects of the ears, nose, throat, palate or lips (d) birthweights below 1500 gms (e) hyperbilirubinaemia and (f) asphyxia.

* Childhood Deafness in the European Community published by the Commission of the European Community 1979 NO. EOR 6473, Luxembourg

V.2. DETERMINING HEARING THRESHOLDS IN PRETERM AND TERM INFANTS

V.2.1. Introduction

The use of ABR is particularly useful in newborn infants, in whom traditional methods of behavioural audiometric assessment, (such as the crib-o-gram and the cradle) are only of diagnostic value in infants with high levels of hearing loss, and will only pick up severe bilateral deafness.

Several investigators have compared electrical response audiometry (particularly the ABR) with behaviourally determined thresholds. Mokotoff et al (1977) compared ABR results with impedance thresholds in 81 infants and children and established the ABR as a highly reliable test. Pratt and Sohmer (1978) found that ABR thresholds differed by +6 dB from behavioural thresholds in adults. Jerger et al (1980) reported a threshold agreement between electrical and behavioural tests in 94% of the 141 children tested. Ruth et al (1983) compared behavioural observation, audiometry and the ABR in 63 infants with normal hearing whose ages ranged from 1 to 12 months. They concluded that the ABR provided the most consistent threshold for all subjects tested, regardless of age. Comparisons between laboratories were difficult because of the

different ways the ABRs were performed and because of the different methods used for behavioural testing.

The world wide prevalence of severe hearing loss in newborns is said to be in excess of 2:1000 live births and the prevalence of any degree of hearing impairment may be as high as 5:1000. Although ABRs have been used in many centres to screen populations at risk, very limited data are available on the hearing capacity of normal preterm infants. Moreover, inconsistencies in selection of "normal" preterm infants have led to wide variations in the reported normal values for different components of the ABR at various gestational ages. In addition there has, to date, been no systematic study of the hearing threshold in these preterm infants. This gap in the literature has created major difficulties in estimating hearing deficits and elevated thresholds in high-risk neonates before discharge from the neonatal unit.

One of our aims was to draw up maturation curves for the hearing threshold as determined by ABR in a population of neurologically optimal newborn infants, who had no apparent neurologic deficit on very stringent clinical grounds or on cranial ultrasound imaging.

V.2.2. Material and Methods

Between September 1983 and September 1984 ABRs were performed on 42 neurologically optimal preterm infants admitted to the Neonatal Unit at Hammersmith Hospital. Additional term babies from the postnatal wards were also included. Their gestational ages ranged from 27-42 weeks (mean 34.5 weeks) and their birthweights from 950 to 3,700 g (mean 1,962 g).

The hearing threshold was defined as the minimum intensity needed to elicit wave V of the ABR. To determine this threshold, a stimulus of 40 dB was first applied. Depending on the presence or absence of a response, the intensity of the stimulus was increased or decreased. Each trial was repeated two or three times to ensure reproducibility.

Calibration is important in defining the loudness of the stimulus. In this study a stimulus of 40 dB (nHL) corresponded to a 73 peak equivalent sound pressure level (pe SPL) as measured by Bruel Kjaer Sound Pressure Level (SPL) Meter (type 2209), artificial ear (type 4125) and condenser microphone (type 4144).

The acoustic milieu in the neonatal and postnatal wards (or inside the incubators) was measured using a Bruel and Kjaer Sound

Pressure Level Meter (type 2203). The sound level weighting scale was set at dB A, which is an arbitarily chosen standard covering the spectrum of frequencies involved in normal hearing. Noise levels in air were in the range of 58-62 dB SPL (mean 60 $\pm$ 2). In the incubators (Vickers model 142) noise levels were 49-55 SPL (mean 52 $\pm$ 3).

V.2.3 Results

Ambient noise levels seemed to have no effect on hearing thresholds measured in the same infants, in the different environments in which the recordings were performed (cots and open or closed incubators in the Neonatal Intensive Care Unit, or postnatal wards). Similar thresholds were obtained in infants irrespective of where minimum hearing thresholds were analysed with respect to gestation and postconceptional age. Both ears of 42 infants were tested, the 84 traces were classified as cross-sectional data. Some cases were followed up, providing 60 additional traces which were classified as longitudinal data. The 144 ABR traces constitute data for the threshold determination. The determination of hearing threshold is illustrated in figure 5.1.

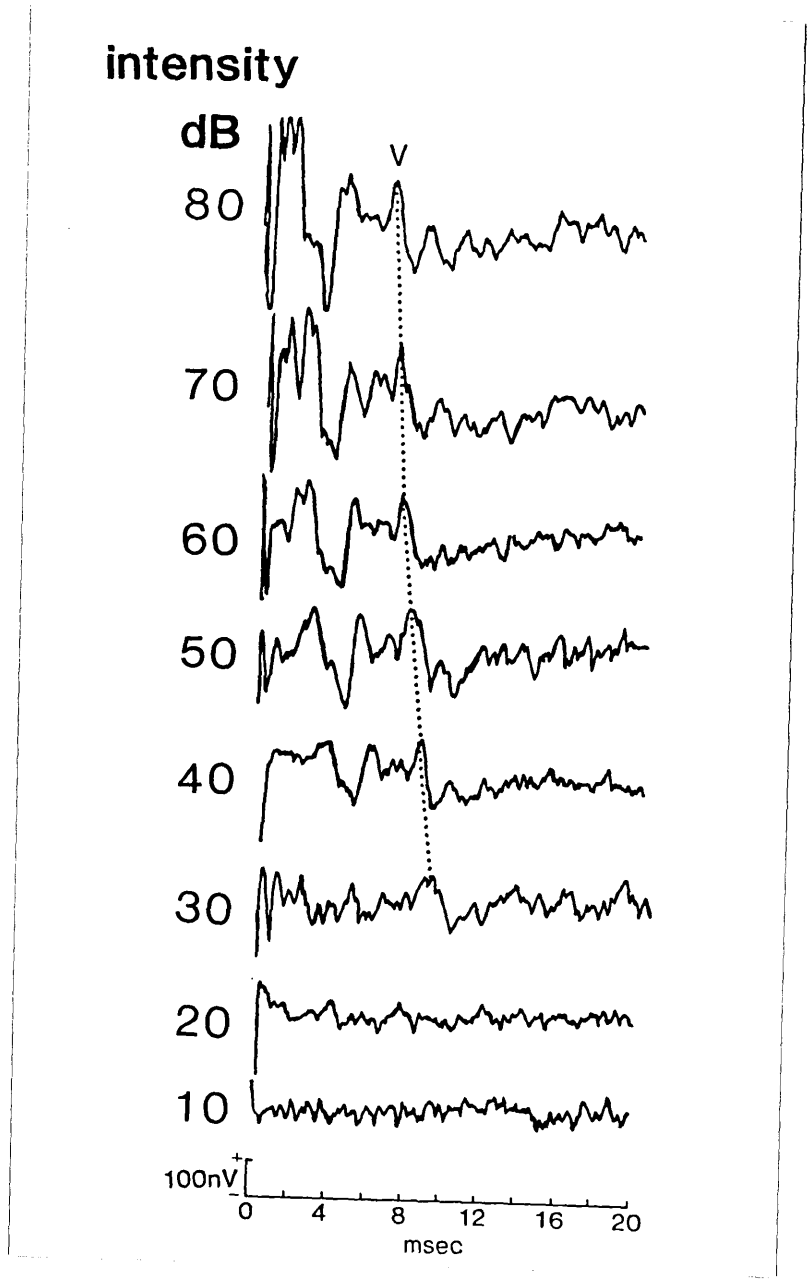


Figure 5.1. ABR (normal infant, GA: 33 weeks) as a function of stimulus intensity (10 - 80 dB HL). There is a progressive delay of wave V as intensity is reduced. The identification of wave V at the minimum intensity (30 dB) determines the hearing threshold. The stimuli were clicks (repetition rate: 10/sec).

Thresholds for infants of appropriate gestational age (AGA) and for infants small for gestational age (SGA) were plotted separately, as were longitudinal and cross-sectional data. Eleven infants were studied longitudinally and the progressive reduction in their thresholds in shown in figure 5.2. The ABR complexes initially had poorly defined waveforms, and thresholds were high. As the infants approached a postconceptional age of 40 weeks, well defined waveforms and lower thresholds developed. Figure 5.3 illustrates the longitudinal changes in threshold reduction for a given subject. Data derived from the longitudinal follow-up on these infants paralleled the cross-sectional data (figure 5.4).

V.2.4. Statistics

All data were pooled for statistical analysis. The hearing threshold decreased steadily with increasing gestational age. As the thresholds appeared to have a linear relationship to gestational age, straight lines were fitted by least square.

Because of the imprecision of the standard deviation estimated at particular single weeks of gestation, a single pooled estimate was used.

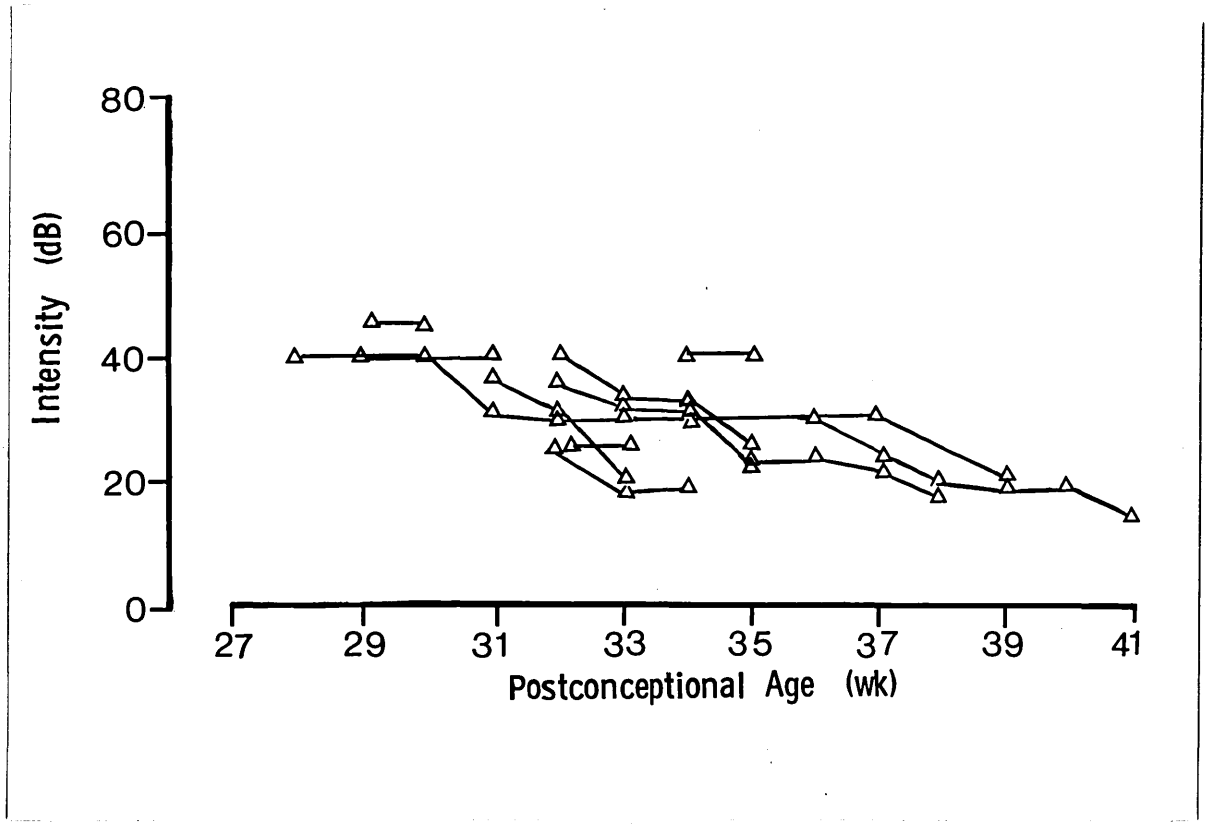


Figure 5.2. Longitudinal study of 11 infants, showing that thresholds decreased as the infants matured. The lower the gestational age, the higher the threshold.

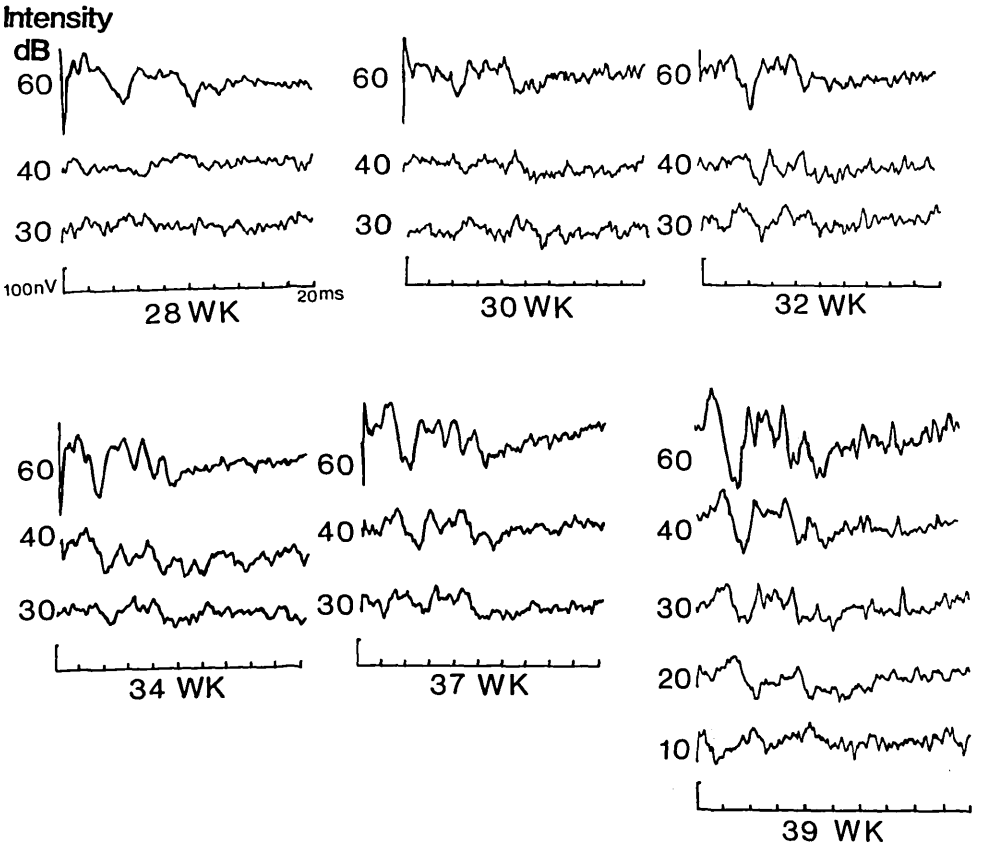


Figure 5.3. Preterm newborn infant born at 28 weeks gestation studied sequentially until 39 weeks postconceptional age. Longitudinal changes in ABR waveforms and thresholds. A hearing threshold of 30 dB is present at 30 weeks and there are later changes in latencies, amplitude, and waveforms.

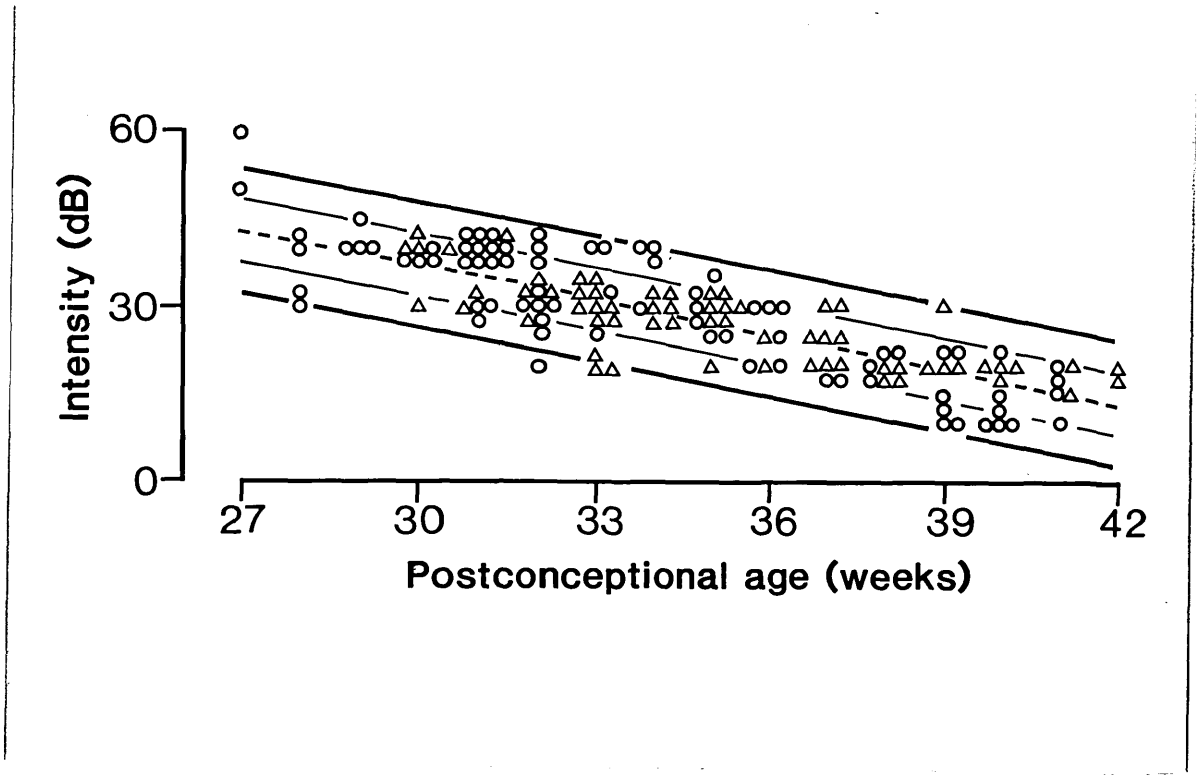


Figure 5.4 Regression lines and confidence limits for hearing thresholds in preterm and term infants. Circles represent cross-sectional data (84 ears) and triangles longitudinal data (60 ears), as described in text.

We assumed that threshold reading for one ear at a particular age could be written as the sum of two parts, $y = y1 + y2$ (when y1 is the same for both ears of a given baby and has variance σ_1^2 while y2 differs between the two ears and has variance σ_2^2). This model allows for the observed correlation between the two threshold measurements made on each baby. If a one-way analysis of variance (Armitage 1971.) provides mean squares of A and B between and within groups of babies respectively, σ_1^2 and σ_2^2 can be estimated by (A-B) /2 and B, and the variance appropriate to a measurement on a single ear is then $\sigma_1^2 + \sigma_2^2$. The mean threshold and values for 1 and 2 standard deviations above and below the mean are plotted against gestational age in figure 5.4. The raw data are given numerically in table V.I.

From these curves we would expect neurologically optimal preterm infants with gestational ages ranging from 28-34 weeks to have hearing threshold at 40 dB, and infants with gestational ages of 35-39 weeks thresholds of 30 dB or less. Figures 5.5 demonstrates threshold levels at different gestational ages (29-39 weeks).

TABLE V.I.

ABR HEARING THRESHOLD IN RELATION TO GESTATIONAL AGE (GA) OR POSTCONCEPTIONAL AGE (PCA)

GA & PCA		Hearing Threshold				
(weeks)	n	mean	+1SD	-1SD	+2SD	-2SD
27	2	43.4	48.8	38.0	54.1	32.6
28	4	41.4	46.8	36.0	52.1	30.6
29	4	39.4	44.8	34.0	50.2	28.6
30	8	37.4	42.8	32.0	48.2	26.6
31	18	35.4	40.8	30.0	46.2	24.7
32	14	33.4	38.8	28.0	44.2	22.7
33	16	31.4	36.8	26.1	42.2	20.7
34	10	29.4	34.8	24.1	40.2	18.7
35	14	27.5	32.8	22.1	38.2	16.7
36	8	25.5	30.8	20.1	36.2	14.7
37	10	23.5	28.9	18.1	34.2	12.7
38	8	21.5	26.9	16.1	32.2	10.7
39	10	19.5	24.9	14.1	30.3	8.7
40	10	17.5	22.9	12.1	28.3	6.7
41	6	15.5	20.9	10.1	26.3	4.8
42	2	13.5	18.9	8.1	24.3	2.8

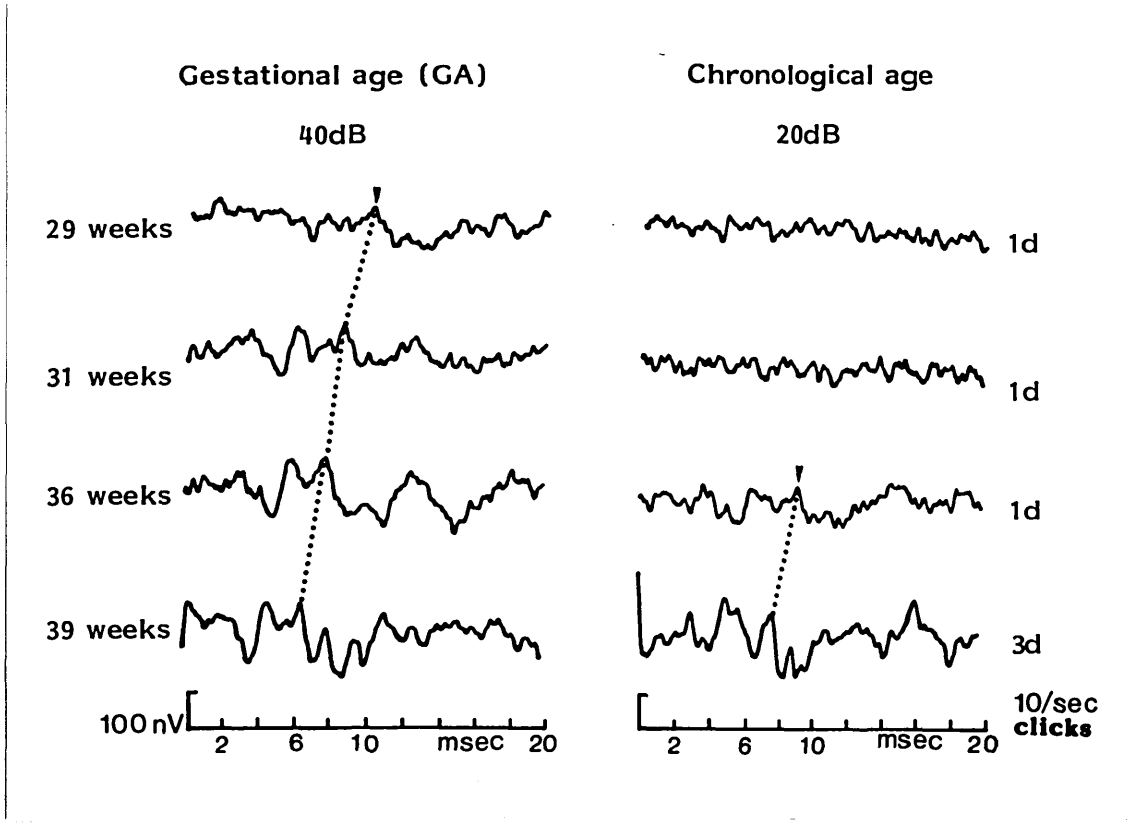


Figure 5.5. Auditory brainstem responses recorded from 4 infants (3 preterms on day 1, and 1 full-term on day 3) at stimulus intensities: 40 and 20 dB. Note the appearance of wave V at 20 dB and at 36 weeks gestational age, and the presence of a hearing threshold at 40 dB at all gestational ages even at 29 weeks.

V.2.5 Discussion

Our studies suggest that neurologically optimal preterm newborns have a much lower hearing threshold than previously reported. Having selected an optimal population, we were able accurately to define hearing thresholds lower than any previously recorded in all tested infants, even in those with gestational ages as low as 28 weeks.

The ABR hearing threshold in full term newborn infants has been thought to be within the range found in normal adults. Schulman-Galambos and Galambos (1975, 1979a) estimated that the difference was 20 dB, and Mokotoff et al (1977) thought the difference to be no greater than 20 dB. Kaga and Tanaka (1980) reported that, by the age of 5 months, practically all normal *infants showed auditory brainstem responses* at 20 dB, but that it was only at the age of 3-4 years that the threshold fell to the adult level of 10 dB.

There is still controversy concerning thresholds in preterm infants. Gestational age is the main factor determining the presence or absence of responses. Although Starr et al (1977) reported the presence of responses in preterm infants of 28 weeks gestational age, Stockard and Stockard (1981) found that responses were often

absent in preterm infants of 30 weeks gestation. With gestational ages of over 32 weeks the thresholds appeared at 85 or 75 dB SPL (Stockard et al 1983a). Recently Salamy (1984) found that in infants under 30 weeks post-conceptional age, 50% displayed recognisable waves at 60 dB HL.

Galambos and Hecox (1978) considered that the ABR first appeared between 26 and 28 weeks of gestation. They used a strong stimulus of 70 dB above adult threshold. Their findings were confirmed by Hecox and Burkhard (1982).

In our neurologically optimal population we found no case in which a threshold could not be determined. This suggests that difficulties experienced by earlier authors in obtaining hearing thresholds may have been due to abnormalities (audiological, neurological or both) in the patients, to environmental causes (ambient noise levels), or to inadequate sensitivity of the equipment.

Using our criteria we were unable to identify any neurologically 'optimal' infants with a gestational age below 27 weeks. At such very young ages there are always substantial risk factors. In our

experience of neurologically sub-optimal infants aged less than 28 weeks the ABRs have been consistently absent.

Fawer and Dubowitz (1982) failed to elicit ABRs at 40 dB in 50% of the infants tested in neonatal unit. Roberts et al (1982) failed similarly with preterm infants at 40 weeks postconceptional age. This was attributed to immaturity and ambient noise. In the present study ambient noise did not seem to interfere with threshold, and technical improvement in our equipment (compared with that used earlier in the same unit by Fawer and Dubowitz (1982) resulted in higher sensitivity.

Mjoen et al (1982) reported that 85% of their high risk neonates (GA: 27-44 weeks) had threshold level of 0-30 dB HL. As the individual ages were not specified, it was not possible to correlate particular ages with particular thresholds. Difficulties in obtaining a hearing threshold may be associated with neurological problems. Such problems were encountered in some infants with high risk factors such as severe asphyxia, hyperbilirubinaemia, or periventricular haemorrhage (PVH). Some of the babies with PVH showed elevated hearing thresholds and delayed evolution towards the lower thresholds appropriate to their ages (figure 5.6). Follow-up studies for hearing and speech in these babies at the ages of

2 and 3 years showed delay in language development. Although this suggests that the hearing threshold may predict later problems with language development, further study is needed to support this view as the number of the infants is not sufficient to draw conclusions.

The determination of hearing thresholds may prove to be useful in neonatal screening. For clinical purposes, a threshold of 20 dB above that expected for the infant's age should raise suspicion of hearing loss.

By using stringent criteria of selection and appropriate statistical analysis, this study provides normal thresholds in relation to gestational age. The data can be used for the screening of hearing in a population of high risk preterm infants.

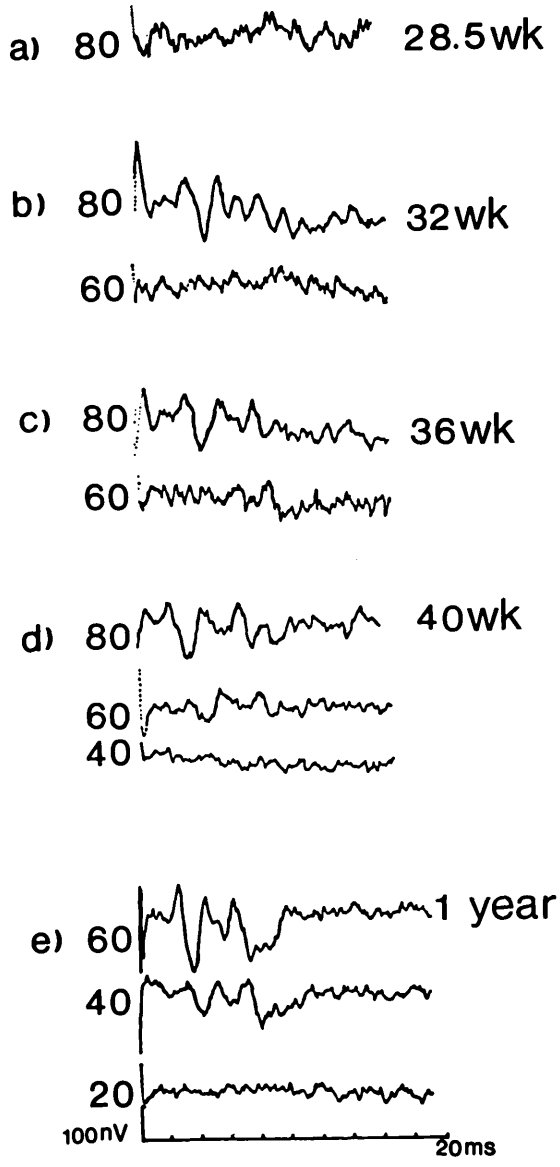


Figure 5.6. Longitudinal study of a premature infant (GA: 27 weeks) with periventricular haemorrhage. First ABR (a) recorded at postconceptional age of 28.5 weeks. This failed to show threshold at 80 dB. Later ABRs showed elevated thresholds and delayed threshold reduction compared to other infants of the same age. At 32 weeks (b) there is a good response at 80 dB but no response to a stimulus of 60 dB. At 36 weeks (c) a threshold has appeared at 60 dB. By term (d) responses were present at 80 and 60 dB but there was still no response at 40 dB. At the age of one year (e) the threshold had decreased to 40 dB, but still showed no response at 20 dB. This baby was followed up at a Hearing and Speech Centre. Normal hearing was confirmed audiologically at 2.7 years, but there was delay in expressive language and in articulation.

V.3. LATENCY-INTENSITY FUNCTIONS

V.3.1 Introduction

Diagnostic information can be obtained by determining how the latency of wave V changes with the intensity of the stimulus. The responses are plotted as latency-intensity function curves. Curves showing this relationship have been published worldwide, and resemble one another closely (Hecox and Galambos 1974, Starr and Achor 1975, Yamada et al 1975, Salamy et al 1975, Stockard and Rossiter 1977). The wave V latency becomes shorter as the stimulus intensity increases. The changes tend to be slightly larger at lower intensities and slightly smaller for strong signals (Galambos and Hecox 1978). Several investigators have suggested that the distinction between conductive and sensorineural impairment can be made on the basis of latency-intensity functions (Yamada et al 1975, Picton et al 1977, Galambos and Hecox 1977, 1978, Picton 1978). Most of these studies were done on adults or full term newborn infants, and few on preterm infants (Despland and Galambos 1980, Stockard et al 1983a).

Our aim was to draw latency-intensity functions curves for preterm and full term infants at low-risk, who fulfilled the clinical criteria discussed earlier in Chapter IV. Such infants presumably have normal hearing. Their gestational ages ranged from

28-42 weeks. We believe such curves can provide a basis for assessing various types of hearing impairment.

V.3.2. Materials and Methods

ABRs were tested on 54 infants with gestational ages ranging from 28-42 weeks. The 84 traces of both ears of the 54 infants were classified as cross-sectional data. Some cases were followed up, providing 40 additional traces which were classified as longitudinal data and a total of 94 traces.

The infants were classified into 3 groups according to their gestational and postconceptional ages. In the first group, the ages ranged from 28-32 weeks, in the second group from 33-37 weeks and in the third group from 38-42 weeks. The latencies of wave V at various stimulus intensities were studied. The intensities used were 20,30,40,60 and 80 dB.

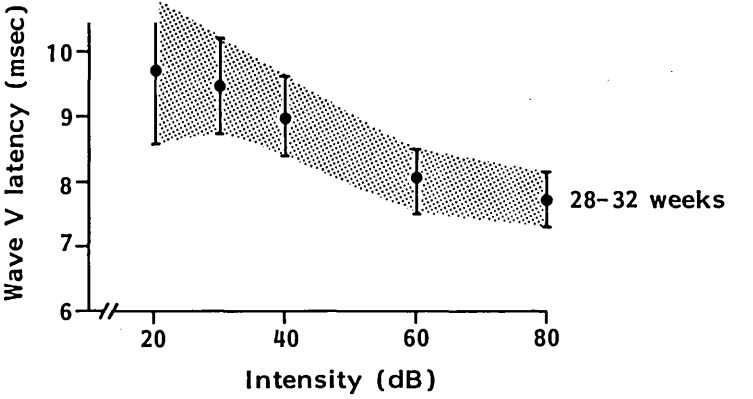
V.3.3. Results

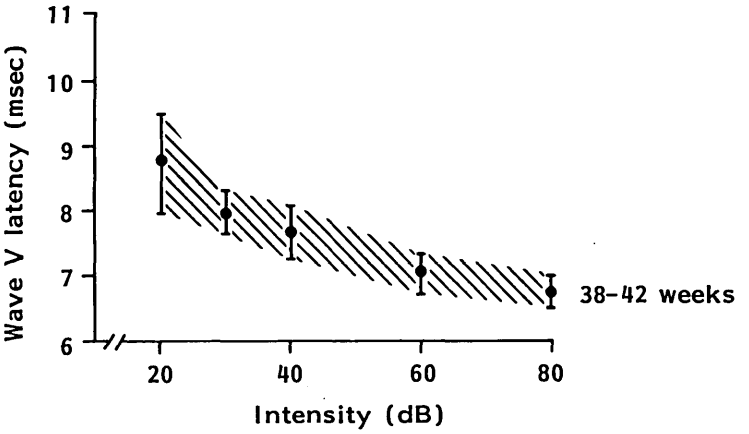
The latencies of wave V at various intensities of stimulation are shown in table V.2. Figure 5.7 records data (a) in the first age group (28-32 weeks), (b) in the second age group (33-37 weeks) and (c) in the third age group (38-42 weeks).

TABLE V.2

Latency intensity function of wave V in relation to gestational age (GA) and post-conceptional age (PCA). The neonates are divided into three age groups: 28-32 weeks, 33-37 weeks, and 38-42 weeks.

INT	GESTATIONAL AND POSTCONCEPTIONAL AGES											
	28 - 32 WKS				33 - 37 WKS				38 - 42 WKS			
dB	n	mean	1SD	2SD	n	mean	1SD	2SD	n	mean	1SD	2SD
20	3	9.74	1.18	2.4	18	9.5	0.78	1.5	28	8.76	0.8	1.6
30	20	9.48	0.75	1.5	24	9.03	0.5	1.0	4	7.93	0.35	0.7
40	44	9.0	0.64	1.2	68	8.34	0.5	1.0	60	7.63	0.46	0.93
60	54	8.1	0.48	0.96	70	7.5	0.32	0.64	58	7.0	0.34	0.68
80	50	7.75	0.45	0.9	62	7.1	0.3	0.6	54	6.7	0.28	0.56





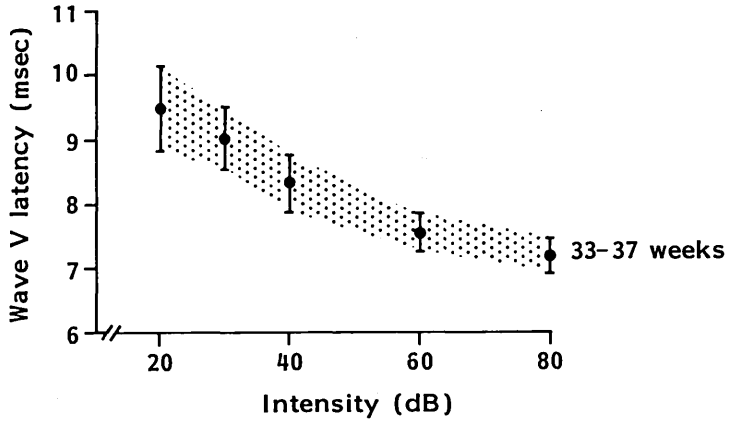


Figure 5.7. Latency intensity curve for wave V (with circles and bars representing mean + 1 SD) in 3 age groups: a) 28-32 weeks; b) 33-37 weeks; c) 38-42 weeks.

Figure 5.8 summarises the mean values and standard deviations of wave V latencies at different intensities of stimulation for each age group.

V.3.4. Clinical application of L.I.F. curves

In conductive deafness, the effective stimulus reaching the cochlea is reduced. When a patient with a conductive deficit of 40 dB is tested with a 60 dB click, only 20 dB reach the cochlea. The response will correspond to a stimulus of 20 dB only. When the latency-intensity function for wave V is plotted, the slope is normal but the latency is abnormally prolonged. The pathological curve is parallel to the normal curve but is displayed upwards (figure 5.9 a).

In sensorineural hearing impairment, latency-intensity curves show a rapid decrease in wave V latency from an elevated threshold at low intensities of stimulation to near normal latencies at higher intensities. This was shown by Yamada et al (1975) and Galambos and Hecox (1977, 1978) who found that patients with sensorineural impairment (confirmed audiometrically) had prolonged wave V latencies at low intensities of stimulation. As the stimulus intensity increased wave V latency decreased to approximately normal values (figures 5.9 b).

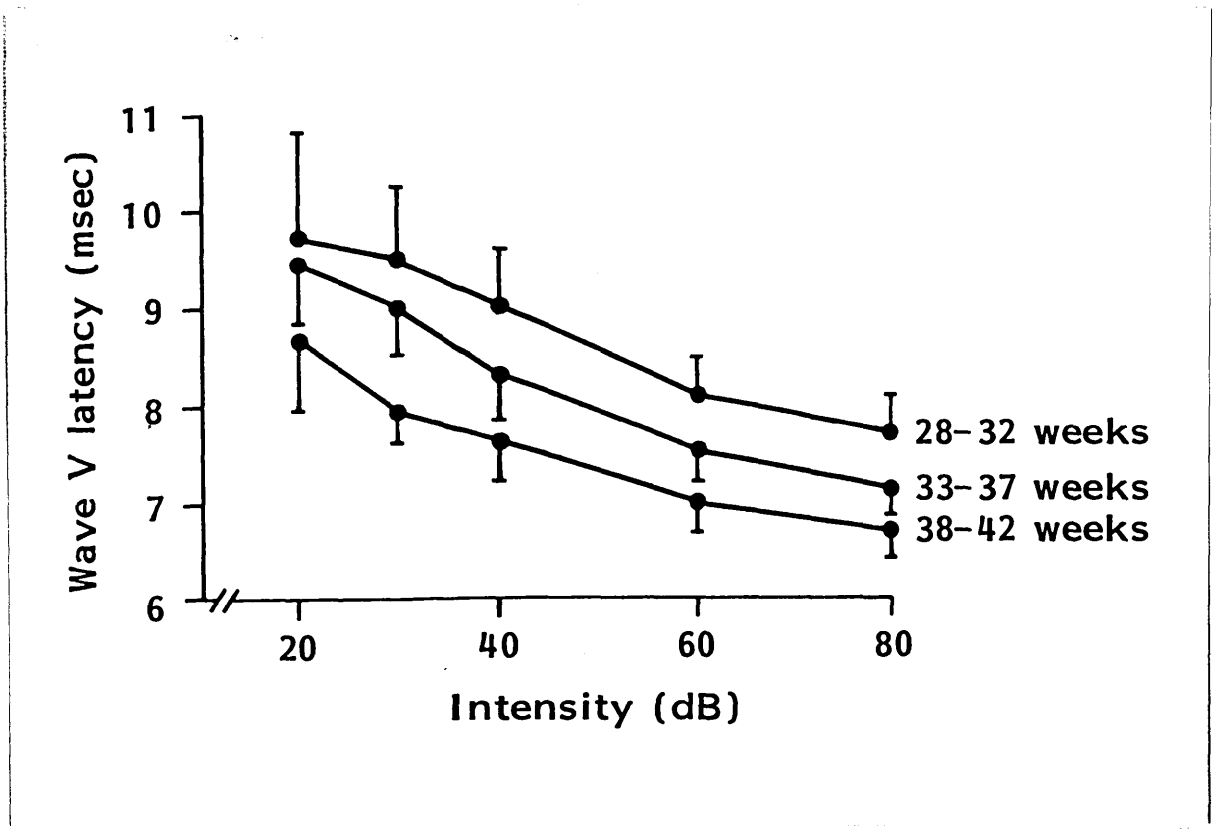


Figure 5.8. Normal latency intensity curves for preterm and term infants between 28 and 42 weeks. The circles and bars represent the mean values (+ 1 SD) at different intensities (dB). The curves are drawn separately for each gestational age group. Note the decrease in latency with age, at all intensities of stimulation.

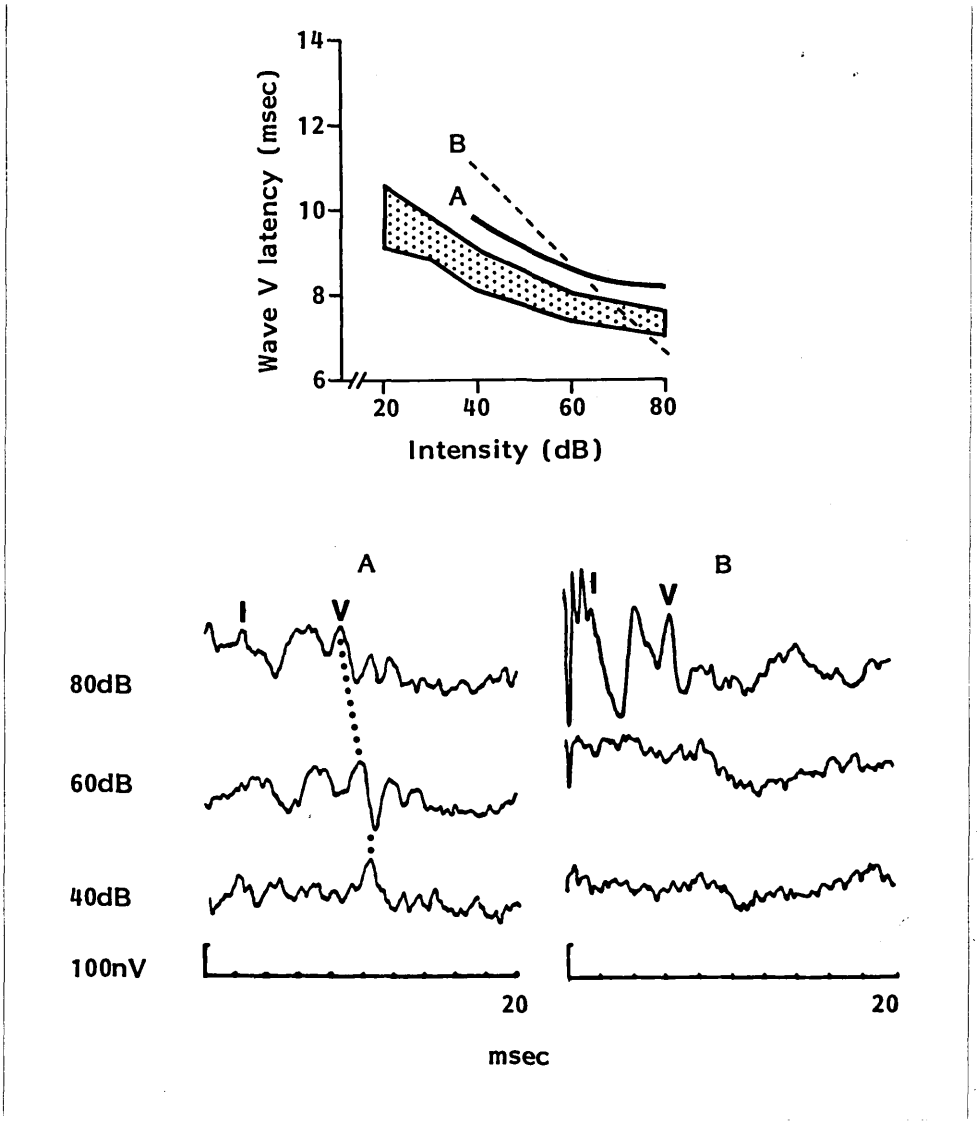


Figure 5.9. Latency-intensity curves (straight and dotted lines A and B) in two infants with hearing deficits plotted against background of normal data (hatched area) for age group 33-37 weeks. Curves A and B relate to figures A and B. Curve A suggests conductive deafness in an infant aged 33 weeks: the curve parallels that displayed by normal infants and the latency of wave V is prolonged beyond 2 SD. Curve B suggests hearing deficit of sensorineural type in an infant aged 34 weeks. At high intensities there is an elevated threshold with rapid decline of wave V latency. Curve B intersects the range of normal data and the waves have normal morphology. Both ABR traces: rarefaction phase stimuli at 10/sec.

V.3.5. Discussion

The latency of wave V was plotted over a 20-80 dB range of intensity for determining latency-intensity curves. The age-related changes were compared in 3 groups of infants of different ages. We found that a 20 dB reduction in the intensity of the stimulus (from 60 to 40 dB) was associated with 0.9 msec increase in wave V latency in the first age group (28-32 weeks), with a 0.84 msec increase in the second age group (33-37 weeks), and with a 0.63 msec increase in the third group (38-42 weeks).

The latency-intensity function of wave V is not only affected by the intensity of the stimulus but also by maturation. Stockard et al (1983a) found that the slope of the L.I.F. curve of wave V was often steeper in early prematurity (<32 weeks) than in the full term newborn. Stockard et al (1983a) also reported that the wide scatter of values among preterm individuals obscured the developmental trend. This may have been due to the fact that the criteria for selection of the 'normal' controls may have resulted in the inclusion of patients with disorders not suspected clinically.

Our latency intensity data could not be compared with previously published material because they covered a wider span of gestational ages (from 28 to 42 weeks). Most previous work has been done on full term neonates.

CHAPTER VI. RISK FACTORS AND THE ABR IN PRETERM INFANTS

VI.1. Introduction

The interaction of multiple disordered events or "risk factors" occur fairly often in preterm infants needing admission to intensive care units. These antenatal, perinatal, and postnatal factors may influence both immediate and long term neurological outcome. Hearing impairment is a frequent complication of prematurity, in 'at risk' infants. The prevalence of such impairment is said to be at least 20 times greater in 'at risk' preterm infants than in their full term healthy counterparts (Stennert et al 1978; Simmons 1980, Salamy et al 1980).

ABRs may be used both to detect auditory and neurological disturbances in the NICU, and to document physiological maturity. Researchers have shown a relationship between abnormal ABR and such neonatal risk factors as low birth weight (Benitez et al 1979, Barden and Peltzman 1980, Galambos and Despland 1980), asphyxia (Goldstein et al 1979, Barden and Peltzman 1980, Kileny et al 1980), acidosis (Galambos and Despland 1980), hyperbilirubinaemia (Chisin et al 1979, Benitez et al 1979, Kotagal et al 1981), intracranial

haemorrhage (Hazel et al 1980, Galambos and Despland 1980, Marshall et al 1980), respiratory disorders (Benitez et al 1979), apnoea (Abramovich et al 1979), and aminoglycoside therapy (Bernard et al 1980 and Cox et al 1982, 1984)

The main problem in determining such relationships has been that in previous studies ABRs have not usually been elicited early enough, i.e. during the period when the risk factors were at their height. Moreover no systematic attempt has been made to determine whether early and later disturbances carry differences in later prognosis, according to whether the ABR abnormalities were transient or more persistent.

The aims of this study were:

1. To evaluate neonatal risk factors in relation to their possible effects on the ABR and to determine the most significant of such risk factors.
2. To investigate how various risk factors were related to both concurrent and later (long-term) ABR findings. For this purpose the ABR results were analysed during the first week of life, at the time of discharge from hospital, and at follow-up visits.

VI.2. Materials and Methods:

We investigated 67 infants with gestational ages of 34 weeks or less admitted consecutively to our neonatal unit over a period of 20 months. Their gestational ages ranged from 27-34 weeks (mean: 30.7 weeks) and their birth weight from 760-2600 grams (mean: 1403 grams).

Information concerning risk factors present during the first week of life was obtained from the medical case notes and was recorded on protocol forms. Later events (occurring after the first week) were recorded separately. The clinical and/or biochemical abnormalities observed during the first week were then correlated with the ABR findings during this period using the criteria of abnormality described below.

VI.3. Definition of abnormalities

The ABR abnormalities were classified into four categories:

a) Severe impairment: In this category the ABR traces showed a complete absence of waves, or identifiable waves were of severely reduced amplitude when recorded at high intensities of stimulation (80 and 90 dB) (figure 6.1).

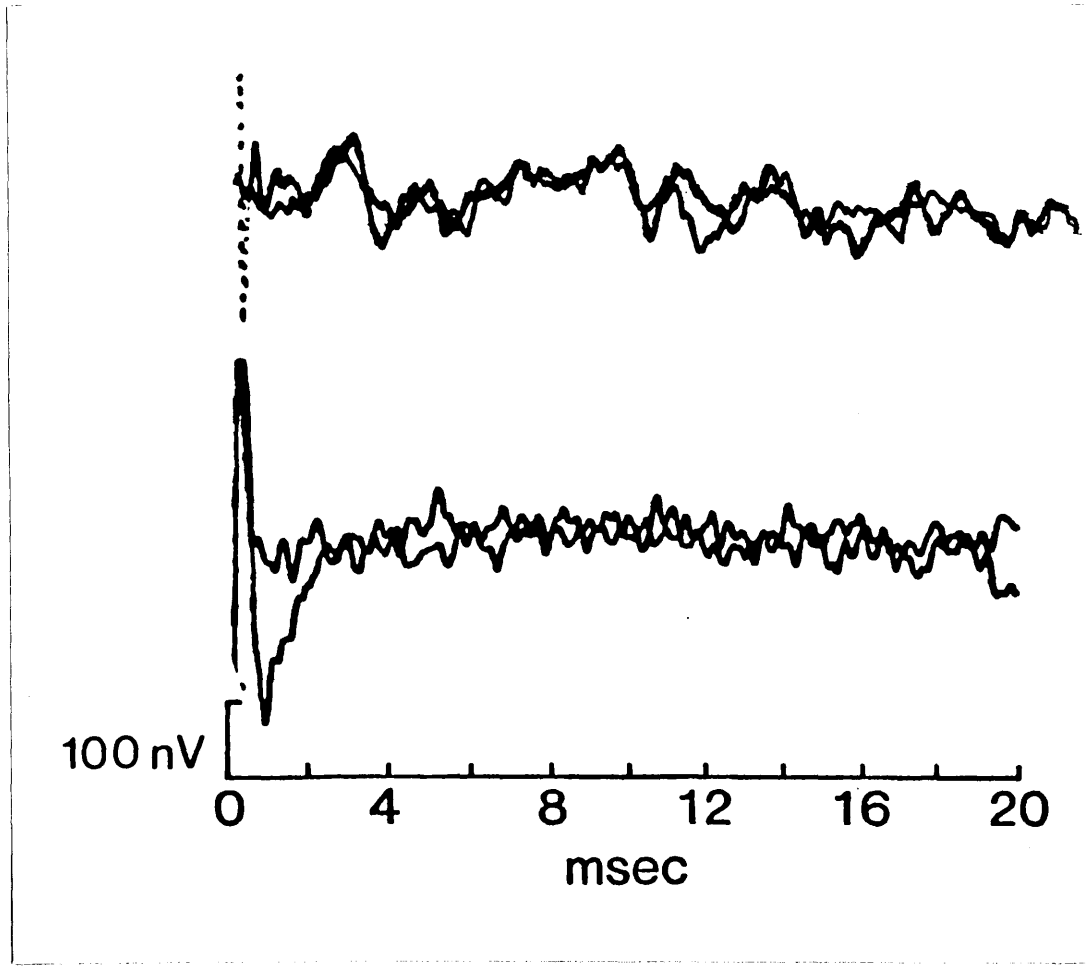


Figure 6.1. Severe impairment. The top trace shows a severely reduced response. The lower trace shows absence of the normal ABR waves. Click stimuli at 80 dB were used in both traces.

b) Mild peripheral (cochlear and/or auditory nerve) impairment. This was characterised by either absence of wave I, or by an increase of its latency beyond 2 SD from the mean (figure 6.2).

c) Central (brainstem) impairment. This was characterised by:

1) an abnormal interpeak interval (IPI) between waves I-V. IPIs exceeding the mean by more than 2 SD were considered abnormal (figure 6.3a).

2) abnormalities of wave V. These were considered to be present if the latency exceeded the mean by more than 2 SD and if there was marked distortion of wave morphology and diminution of the amplitude of wave V (by 70% or more) when compared to the amplitudes of waves I and III (figure 6.3b).

3) the presence of fusion between waves V and VI (often leading to spurious prolongation of IPI) (figure 6.3c).

4) an abnormal amplitude ratio between waves V and I. The ratio was considered abnormal if it was less than 0.4 at 60 db, and less than 0.3 at 80 dB.

d) Mixed deficits. These consisted of combinations of 'mild peripheral' and 'central' impairments.

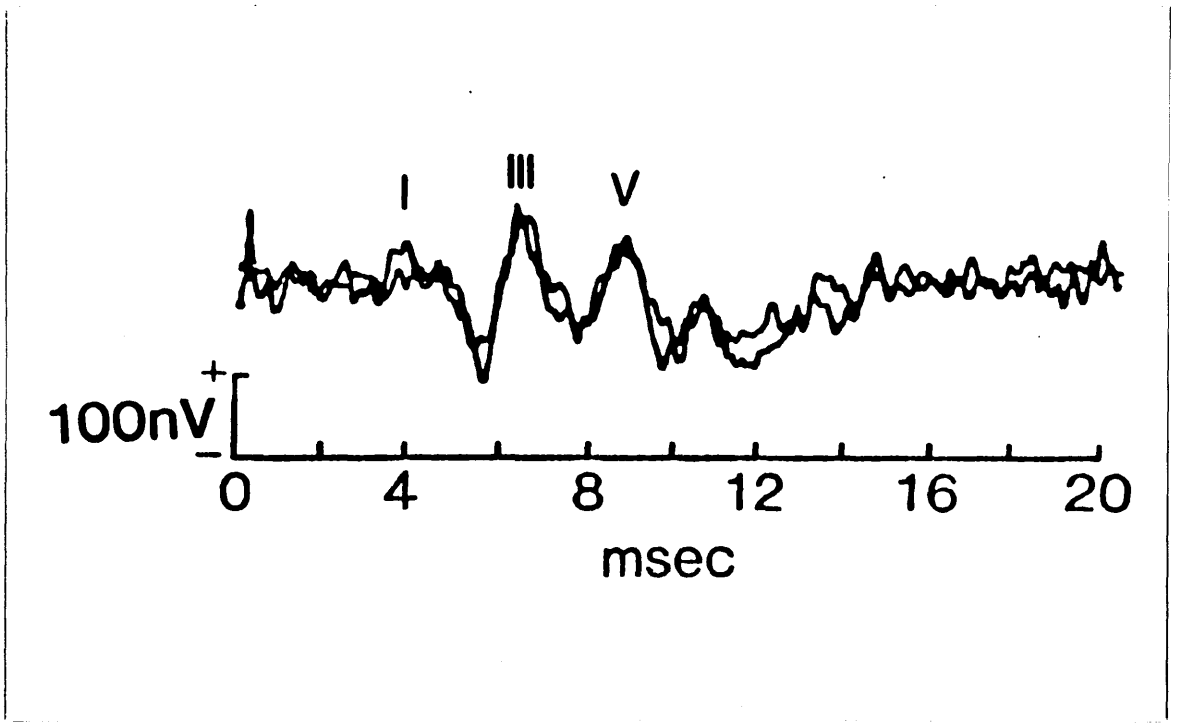


Figure 6.2. Mild peripheral deficit in an infant (GA: 33 weeks). Latency of wave I = 4.0 msec. (i.e. exceeds the mean by more than 2 SD).

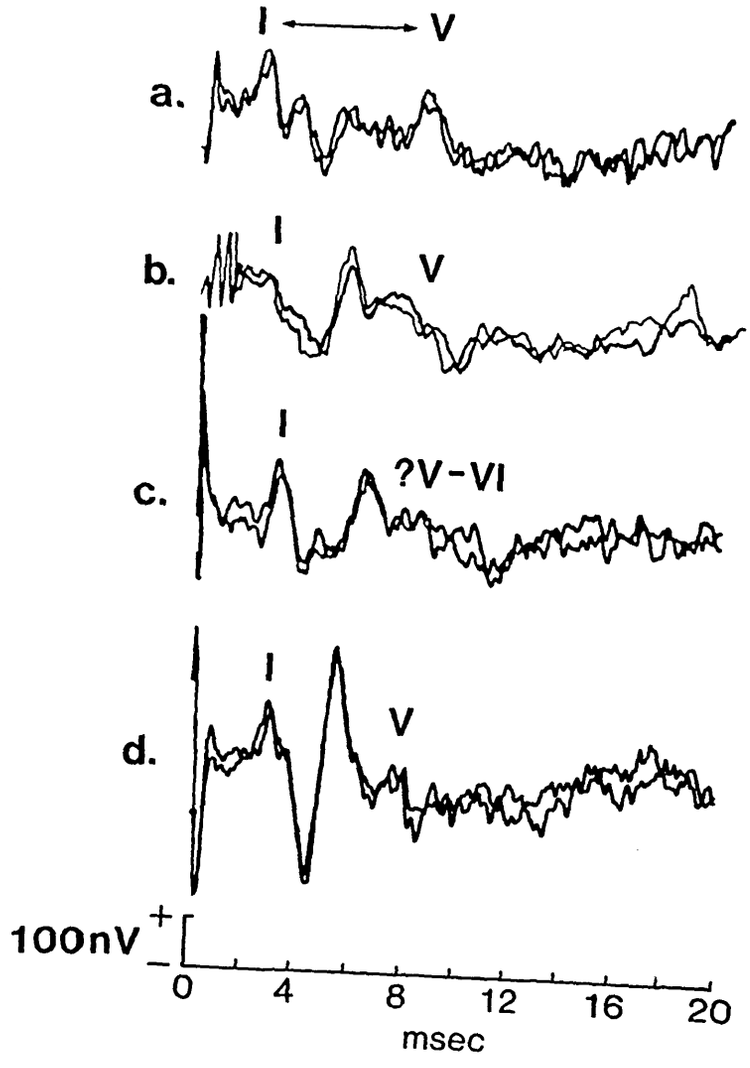


Figure 6.3. Central brainstem deficits.
a) prolonged I - V interval
b) abnormal wave V morphology
c) fusion between waves V and VI
d) abnormal V:I ratio.

The specific risk factors evaluated are listed in Table VI.1. A copy of the protocol is included in the Appendix.

The information and diagnosis on these infants were based on the medical case notes. Some definitions and comments concerning the risk factors assessed may be appropriate.

The pregnancy was considered abnormal if it had been complicated by:

* Pre-eclamptic toxaemia (PET): this was defined as hypertension with either proteinuria or oedema occurring at 24 weeks or later in the pregnancy.
* Hypertension: this was defined as a blood pressure exceeding 140 mmHg systolic and/or 90 mmHg diastolic.
* Antepartum haemorrhage, whether caused by placental abruption or placenta praevia.

Type of delivery: these were listed as vaginal vertex, vaginal breech, or caesarian section. Forceps deliveries were recorded separately.

Drugs (maternal): this refers to drugs given in labour. A wide variety of drugs had been used. For statistical purposes only dexamethasone and betamimetic tocolytics were considered.

TABLE VI.1.

RISK FACTORS ASSESSED, IN RELATION TO THEIR POSSIBLE EFFECTS ON THE ABR

OBSTETRIC
Pregnancy:
- Pre-eclamptic toxaemia
- Hypertension
- Antepartum haemorrhage

Mode of delivery:
- Vaginal vertex
- Breech
- Caesarian section

Fetal distress
- Cardiotocography
- Meconium

Drugs (steroids and β-mimetics)

NEONATAL
Gender
Gestational age (weeks)
Birth weight (grams)
Apgar score
- 1 minute
- 5 minutes

Asphyxia
Assisted ventilation
pH (< 7.2)
- Number of episodes during first week
- Episodes lasting more than one week

Hypoxia (P02 < 5 KPa)
- Number of episodes during first week
- Episodes lasting more than one week

Hypercapnea (PC02 < 8 KPa)
- Number of episodes during first week
- Episodes lasting more than one week

Apnoea:
- Associated with bradycardia

Jaundice:
- Peak bilirubin (umol/l)
- Duration
- Phototherapy
- Exchange transfusion

Respiratory distress syndrome
Cardiovascular system
- Patent ductus arteriosus

Blood disorders:
- Polycythaemia
- Anaemia

Infections
Drugs
- Aminoglycoside
- Others

Periventricular haemorrhage
Convulsions
Abnormal neurological signs
- During first week
- At discharge

Fetal distress: this was considered present when cardiotocography (CTG) had demonstrated late fetal heart deceleration, or persistent fetal tachycardia or bradycardia. Another index of fetal distress was the passage of meconium in infants presenting by the vertex.

Asphyxia: this was considered to have occurred when the Agpar score was less than 4 at 1 minute, or 5 or less at 5 minutes. Asphyxia was also considered to have been present when intubation lasting more than 4 minutes had to be resorted to.

Ventilatory support: this referred to the need for continuous positive airway pressure (CPAP) or intermittent positive pressure ventilation (IPPV). The duration of the ventilatory support was noted.

Acidosis: this referred to an arterial pH of less than 7.2. The number of such episodes during the first week of life was assessed and taken to indicate severity. Persistent acidosis (lasting more than 1 week) was recorded separately.

Hypoxia: this was considered present if the P02 fell to less than 5 KPa. The number of estimations during the first week was recorded separately from similar episodes occurring after the first week.

Hypercapnia: this was considered present if the PCO2 exceeded 8 KPa. The number of estimations during the first week was recorded separately from hypercapnic episodes ocurring after the first week.

Apnoea: this was defined as cessation of respiration for 20 seconds with cyanosis. Episodes considered relevant were those requiring stimulation. Any associated bradycardia (defined as a heart rate of less than 100 beats/min) was also recorded separately.

Jaundice: infants were devided into 3 groups, according to whether the bilirubin levels were less than 200 μmol/l, 200-240 μmol/l, or higher. The duration of jaundice was also recorded. Phototherapy or exchange transfusion were recorded separately.

Respiratory distress: was defined by the presence of a raised respiratory rate, grunting respiration, rib retraction, with or without characteristic X-ray findings.

Infection: this was only considered present if blood or cerebrospinal fluid cultures were positive.

Drugs (neonatal): all drugs administered to the infants were considered. For statistical analysis infants receiving aminoglycosides were analysed separately.

Neurological examination was carried out during the first week of life, at the time of discharge from hospital, and again at follow up visits at 40 weeks PCA, and 6 monthly therafter up to 2 years of age. Infants were classified as neurologically abnormal on the basis of abnormalities of tone, movement or alertness. Infants not suitable for testing were classified separately.

Initially 23 risk factors were investigated in relation to the presence or absence of ABR abnormalities irrespective of type. Possible relationships were then further investigated according to whether the ABR abnormalities had been encountered during the first week of life, at the time of discharge, or later during follow up visits.

The data from the infants were analysed using the Minitab and BMDP statistical packages. Two different methods of statistical analysis were employed:

a) a series of 2x2 chi-square analyses, to determine the significance of the association of each risk factor separately with the ABR.

b) stepwise logistic regression, to determine whether those risk factors found to be of significance in the chi-square analyses were independently associated with the ABR abnormalities.

VI.3 RESULTS

A) During the first week of life

Of the 67 infants analysed for risk factors, 47 (70%) had abnormal ABRs. The remaining 20 infants showed normal ABRs. Table VI.2 shows the statistically significant risk factors encountered in association with ABR abnormalities detected during the first week of life. Of the neonatal risk factors, PVH and the presence of abnormal neurological findings were highly correlated with ABR abnormalities ($p < 0.001$ for each). The presence of apnoea (with bradycardia) and gentamicin therapy were also highly correlated ($p < 0.005$), as - to a lesser extent - was acidosis ($p < 0.025$).

Stepwise logistic regression analysis showed that the factors most highly correlated independently with the presence of ABR abnormalities during the first week of life were the presence of PVH ($P<0.001$), abnormal findings on neurological examination and apnoea (+ bradycardia) ($p < 0.01$ for each).

TABLE VI.2.

RISK FACTORS THAT REACHED STATISTICAL SIGNIFICANCE (BY CHI-SQUARE ANALYSIS) IN RELATION TO ABNORMAL ABR DURING THE FIRST WEEK OF LIFE

RISK FACTOR	P
PVH	0.001
Early abnormal neurological signs	0.001
Apnoea (+ bradycardia)	0.005
Gentamicin therapy	0.005
Acidosis during first week	0.025

B) At time of discharge from hospital

Of the 67 infants, 51 (76%) had normal ABRs and 15 (22%) had abnormal ABRs at the time of discharge from hospital. One infant died during the hospital stay. Risk factors correlated with ABR abnormalities still present at discharge are listed in table VI.3. Six risk factors were highly correlated, the most significant being acidosis during the first week, the presence of PVH, and abnormal neurological findings at discharge ($p < 0.001$ for each). The need for ventilatory support, hypercapnia and blood disorders (anaemia) all reached p value of <0.005. Abnormal Apgar scores at 1 minute, gentamicin therapy and hypoxia (present during the first week of life) were also significantly correlated, reaching or exceeding the 1% significance level.

Stepwise logistic regression analysis showed PVH and abnormal neurological findings to be the most significant risk factors ($P < 0.001$ and < 0.01 respectively) independently associated with persisting ABR abnormality at discharge.

C) At follow up:

During follow-up outpatient visits, we were able to perform 57 ABR examinations on 30 infants, including those who had abnormal ABRs at discharge (n=15). In some infants repeated ABR recordings were needed. The ages of the infants followed-up in this way ranged from 2-24 months.

TABLE VI.3

RISK FACTORS THAT REACHED STATISTICAL SIGNIFICANCE (BY CHI-SQUARE ANALYSIS) IN RELATION TO ABR ABNORMALITIES STILL PRESENT AT DISCHARGE

RISK FACTOR	P
Acidosis during first week	0.001
PVH	0.001
Neurological signs:-at discharge	0.001
-during first week	0.005
Ventilatory support	0.005
Hypercapnia exceeding 1 week	0.005
Blood disorders (anaemia)	0.005
Hypoxia during first week	0.010
Abnormal Apgar at 1 minute	0.010
Gentamicin therapy	0.010

In 3 of the infants with abnormal ABRs at the time of discharge, the ABR remained abnormal at follow up. These infants were referred to hearing specialists by the age of 6 months. Three further infants died after discharge. The risk factors of greatest relevance in terms of persistent ABR abnormalities (Table VI.4) were hypoxia or hypercapnia persisting beyond the first week and an ABR that was already abnormal at discharge. Repeated episodes of acidosis exceeding 1 week reached the 2.5% significance level.

The factors most predictive of persistent ABR abnormality (by stepwise logistic regression) were ABR abnormalities still present at discharge and hypercapnia exceeding the first week of life ($P < 0.01$ and 0.02 respectively).

VI.5. Discussion:

From this study we can identify some factors which have transient and others which exhibit persistent effects on the ABR. Risk factors with transient effects were PVH, early abnormal neurological findings, apnea and gentamicin therapy. Persistent ABR abnormalities were found in association with factors (such as hypoxia, hypercapnia, and acidosis of more prolonged duration) which might have impaired the oxygenation of tissues or caused alteration to the vaso-regulatory system. In support of this hypothesis, it

TABLE VI.4.

RISK FACTORS THAT REACHED STATISTICAL SIGNIFICANCE (BY CHI-SQUARE ANALYSIS) IN RELATION TO ABR ABNORMALITIES AT FOLLOW-UP

RISK FACTOR	P
Hypoxia exceeding 1 week	0.005
Hypercapnia exceeding 1 week	0.005
ABR results at discharge	0.005
Acidosis exceeding 1 week	0.025

should be recalled that the centres governing cerebral autoregulation (for instances the response to CO2) are thought to be located in the brainstem (Langfitt and Kassel 1968, Meyer et al 1969). Hypercapnia is a well known cause of general cerebral vasodilatation, including the brainstem (Nakagawa 1982) and persistent hypercapnia may have an effect on brainstem function. Although PVH was significantly related to ABR abnormalities present both initially and at discharge, it ceased to be a significant factor in relation to abnormalities still present at follow-up.

One of the objectives of ABR testing before discharge is to identify an 'at risk' group for which follow-up assessment is strongly indicated. A substantial hearing impairment at the time of discharge tends to be sustained at follow-up, though there may be resolution of some milder losses. This underlines the fact that the follow-up test is the proper basis for referral to the audiologist.

Various studies have examined the effects of isolated risk factors on the ABR, and the relation of various risk factors to hearing impairment (Goldstein et al 1979, Marshall et al 1980, Barden and Peltzman 1980, Galambos and Despland 1980, Kileny et al 1980, Hecox et al 1981, Roberts et al 1982, Cox et al 1984, Bradford et al 1985). Although investigators have agreed that abnormal ABR results are often observed in NICU infants, there is disagreement

about which factors are significant in abnormal ABR results. Risk factors such as low birth weight(Barden and Peltzman 1980, Benitez et al 1979, Galambos and Despland 1980), and low gestational ages of 26-30 weeks (Galambos and Despland 1980) were associated with abnormal ABR results. On the other hand, Marshall et al (1980) found no correlation between ABR abnormalities and gestational age or birthweight, but found that intraventricular haemorrhage was the most significant risk factor. Roberts et al (1982) reported that the apparent relation between abnormal ABRs and IVH was an indirect one, related to low gestational age. He found no other high-risk factor affecting the ABR. Kileny et al (1980) reported that asphyxia might influence the ABR and Barden and Peltzman (1980) found that asphyxia plus low birth weight were influencing factors. Despland and Galambos (1980) reported that the association of acidosis with hypoxia correlated significantly with abnormal ABRs. Hyperbilirubinaemia associated with abnormal ABR results has been supported by Benitez et al (1979), Chisin et al (1979), Kotagal et al (1981), and Mjoen et al (1982), while Perlman et al (1983) and Nakamura et al (1985) found that hyperbilirubinaemia causes only transient and reversible damage. Marshall et al (1980), however found no significant relationship with hyperbilirubinaemia. Bernard et al (1980) associated abnormal ABR results with aminoglycoside therapy. Later Cox et al (1982, 1984) found its effect is only transient which disappear on follow up studies. In contrast,

Galambos and Despland (1980) and Marshall et al (1980) reported that aminoglycoside does not affect the ABR. Recently Ito (1984) found that in infants who had received phototherapy or aminoglycoside therapy there was a statistically significant prevalence of abnormal ABRs. Hecox and Cone (1981) found that ABR abnormalities associated with anoxia carried predictive value in relation to neurological outcome while Stockard et al (1983c) disagreed.

These studies confirm the association of risk factors with abnormal ABR findings, but disagreement about the significant factors has led to questioning the validity of ABR testing in the NICU (Downs 1982). Several elements may contribute to the discrepancies in the fore-mentioned studies including statistical sampling error, variations in risk assessment, and lack of standarisation of ABR testing methods and criteria. But these are not sufficient to account for the differences. The present study may help explain the basis of the discrepancies. Firstly, due to high inter-correlations of various risk factors, different samples of babies may yield different significant risk factors. Secondly, the time at which the ABR testing is carried out is highly relevant, and has seldom been taken into account. The ABR is time-dependent in relation to the postnatal age. We have shown that factors significantly related to ABR abnormalities during the first week of life were no longer significantly related at the time of discharge

from the hospital. This suggests that certain risk factors exert transient influences on the ABR, which at the time of testing may or may not show these effects. The present study confirms the studies of Stockard and Stockard (1981), and Cox et al (1981b) that in premature infants there is a high prevalence of early abnormal ABRs which revert to normal by the time of discharge.

Our studies also showed that ABR abnormalities correlated significantly with abnormal findings on neurological examination carried out during the first week of life, and at the time of discharge. This confirms Cox's assumption (1984) that transient ABR abnormalities should be considered as similar to other transient neurological disorders (for instance alterations of muscle tone or of the reflexes) which frequently occur in preterm infants and which resolve during infancy (Drillien 1964).

Although many studies have shown the association of jaundice and abnormal ABRs (Benitez et al 1979, Chisin et al 1979, Mjoen et al 1982, Wennberg et al 1982), and some have reported its transient effect on the ABR (Perlman et al 1983, Nakamura et al 1985) our study and that of Streletz et al (1986) found no statistically significant correlation with jaundice. The author believes that additional risk factors are necessary to alter the background which

increases the affinity of brain structures for bilirubin or which enhances the vulnerability of neurons thus precipitating damage.

From the present study and others (Cox et al 1984 and Duara et al 1986) it is apparent that there is no single predisposing cause for ABR abnormalities. Multiple factors play a role, depending on the maturity of the brain and on the degree of inter-correlation between various risk factors. The presence of a given risk factor may potentiate or precipitate the effect of another. Any attempt to analyse factors which predispose to ABR abnormalities must take into account both anatomical and physiological factors affecting the distribution and the regulation of the cerebral blood flow, and in particular the effects of such changes upon the auditory brainstem pathway. It is against this background of decreased blood supply, acidosis and anoxia, and their neurophysiological repercussions that the preterm ABR has to be investigated.

In conclusion, there are multiple risk factors that may be encountered in association with abnormal ABRs. These are not necessarily causative. To establish causal factors one ought to study infants longitudinally, with repeated analysis from birth. This is technically difficult. Moreover repeated ABRs in sick infants in an intensive care environment could be deemed invasive

using present methods. In future it may prove feasible, using newer techniques depending on high resolution magnetic current detection. The association of early hypercapnia with persistently abnormal ABRs may represent a hitherto unreported effect of the physiological changes, induced by altered blood flow.

CHAPTER VII. THE ABR AND PERIVENTRICULAR HAEMORRHAGE

VII.1. Introduction:

Periventricular and intraventricular haemorrhages (PVH-IVH) have been shown to be common in the preterm infant (Papile et al 1978, Ahmann et al 1980, Levene et al 1981). Computerised tomography and later real-time ultrasound have provided the basis for such diagnoses. The infants developing lesions of this kind usually exhibit clear neurological evidence that they have been severely damaged around the time of the haemorrhage (Krishnamoorthy et al 1977, Papile et al 1978, Volpe 1981). Those less severely affected usually show more subtle or even no abnormal neurological findings and have so-called 'silent haemorrhages' (Krishnamoorthy et al 1977, Volpe 1977, Lazzara et al 1980, Dubowitz et al 1981).

The ABR findings may offer information on the hearing status and on the extent of brainstem involvement, and hence may suggest neurological deterioration. The association of hearing deficits (as determined by ABR studies) with PVH-IVH has been investigated

(Marshall et al 1980, Barnet et al 1980, Galambos and Despland 1980, Ito 1984). Pathological studies by Spector and co-workers (1978) revealed haemorrhage in the inner ear in 23 out of 24 cases with major intracranial haemorrhage. Structures involved included the primary nerve cell bodies of the cochlea and the eighth nerve itself.

The spread of the haemorrhage into the brainstem has been analysed in clinical and pathological studies (Larroche 1977, Volpe 1977, Volpe 1978, Tarby and Volpe 1982, Pasternak and Volpe 1979, Wigglesworth 1984) but has received less consideration in ABR studies (Starr et al 1977, Despland and Galambos 1980, Fawer et al 1983). Larroche (1977) described how effused blood in severe haemorrhage spread through the ventricular system into the subarachnoid space, extending over the brainstem. Pasternak and Volpe (1979) described a clinical syndrome indicative of total brainstem failure following intraventricular haemorrhage. The neurological changes included apnea, dilated and non-reactive pupils, and the absence of spontaneous and reflex eye movements, absent corneal and gag reflexes, absent responses to sound, and absent limb movement. Infants with PVH-IVH should be considered at high risk for brainstem injury and should be closely followed up with appropriate studies.

The main objectives of this study were: a) to elicit ABRs on preterm infants (admitted to the Neonatal Intensive Care Unit) during the first week of life as a means of detecting peripheral (hearing) and central (brainstem) abnormalities, and b) to compare the ABR results with brain ultrasound findings in infants with and without PVH studied during the first week of life and followed-up thereafter.

VII.2. Subjects and Methods

The infants studied had all been admitted to the Regional Neonatal Intensive Care Unit at Hammersmith Hospital between November 1981 and July 1983. Infants who were well enough to be tested during the first week of life were included in the study provided that their gestational ages were 34 weeks or less. The study of severely ill and clinically unstable infants was postponed until they had improved, as was the study of infants who could not be handled and of infants with convulsions. Sixty-seven preterm infants were entered into the combined ABR and brain ultrasound study.

The first examination was performed during the first week of life, as soon as the clinical condition allowed. The age at which

PVH was first diagnosed was recorded and the severity of the haemorrhage was graded on the I to III point scale of Levene (1981). The ABR was tested at fairly loud intensities (60 dB normal hearing level, as established in young adults with normal hearing). Higher intensities (80 dB, and even 90 dB) were used in very premature infants, when testing time was limited. Subsequent ABR testing was done whenever clinical and technical conditions allowed, 40 dB stimuli being used as the lowest intensity capable of detecting minimal hearing deficits.

The methods used have been described in Chapter III. During the course of the study two machines were used. The first was a Medelec MS6 model, using a bandpass filter of 250-1600 Hz, the second a Medelec Sensor machine using a filter of 300-3000 Hz. Control data for each machine and setting were derived from our neonatal unit population. The first controls used were those descibed by Fawer and Dubowitz (1982). Our normative data using the Medelec Sensor were outlined in Chapter IV.

After the initial ABR test, serial recordings were carried out at intervals of 1-2 weeks whenever possible, until discharge. Infants with abnormal ABRs had follow-up studies carried out as outpatients.

Clinically normal infants with initially normal ABRs were not followed-up. The number of recordings from each infant ranged from 1 to 14 (total: 317 recordings).

The ABR abnormalities encountered were categorised as 'severe impairment', 'mild peripheral (cochlear and/or auditory nerve) impairment', 'central (brainstem) impairment', and impairment of 'mixed type'. The terms have been previously defined in Chapter VI (p 216-220).

VII.3. Results

VII.3.1. Tests performed during the first week of life:

67 preterm infants entered the comparative study between ABR and ultrasound findings (US). Twenty of these 67 infants had normal ABR responses. Of the 47 infants with abnormal ABRs 12 showed severe impairment, 1 mild peripheral impairment, 22 central impairment, and 12 impairment of mixed type.

39 of the 67 preterm infants had normal ultrasound scans throughout their hospital stay. PVH-IVH was diagnosed in the remaining 28 infants. The relation between US findings and the presence or absence of ABR abnormalities is shown in table VII.1.

TABLE VII.1.

ABR FINDINGS IN INFANTS WITH AND WITHOUT PVH DURING THE FIRST WEEK OF LIFE (n=67)

		ABR		TOTAL
		NORMAL	ABNORMAL	
ULTRASOUND	NORMAL	20	19	39
	ABNORMAL (PVH)	0	28	28
	TOTAL	20	47	67

In the 67 preterm infants included in this study, the ABR results were normal in 20 and abnormal in 47 infants. On US scan 28 of these 47 infants had PVH and 19 did not. We have devided our findings into 2 groups in an attempt to compare ABRs in those with PVH (n=28) and those without (n=39).

1) ABR results in infants with PVH:

All 28 infants with PVH had abnormal ABRs. The abnormalities found were severe impairment in 11, central (brainstem) impairment in 12, and mixed impairment in 5. In infants with severe impairment, 6 had complete absence of waves and 5 had severely reduced responses. None of the infants with PVH showed a separate mild peripheral lesion.

2) ABR results in infants without PVH:

Of the 39 infants in this group, 19 showed abnormalities. These consisted of 1 infant with severe impairment, 1 with a mild peripheral deficit, 10 with central deficits, and 7 with mixed abnormalities. The remaining 20 infants with normal ABRs also had normal US scans.

The prevalence of various types of ABR abnormality in infants with and without PVH is shown in figure 7.1.

Although both groups of infants showed similar types of ABR abnormality, findings indicative of brainstem dysfunction (central abnormalities, including the mixed category) were particularly frequent in the PVH group. The pattern of central (brainstem) impairment included fusion of waves V and VI in association with poor wave V morphology, prolonged interpeak intervals (IPI) and abnormal amplitude ratios. The comparative frequency of central abnormalities in the two groups is shown in figure 7.2.

Of the 28 infants who developed PVH, 14 had grade I, 8 grade II, and 6 grade III haemorrhage. The types of ABR abnormality encountered in infants with haemorrhages of varying severity are shown in figure 7.3. In infants in whom US scans showed unilateral haemorrhage, there was no consistent difference in the laterality of the abnormal central (brainstem) responses: the side of the haemorrhage was not constantly ipsilateral or contralateral to the side of the central abnormality. The absent ABR responses were more often seen on the same side as the haemorrhage. The numbers were small however, and it was difficult to draw conclusions.

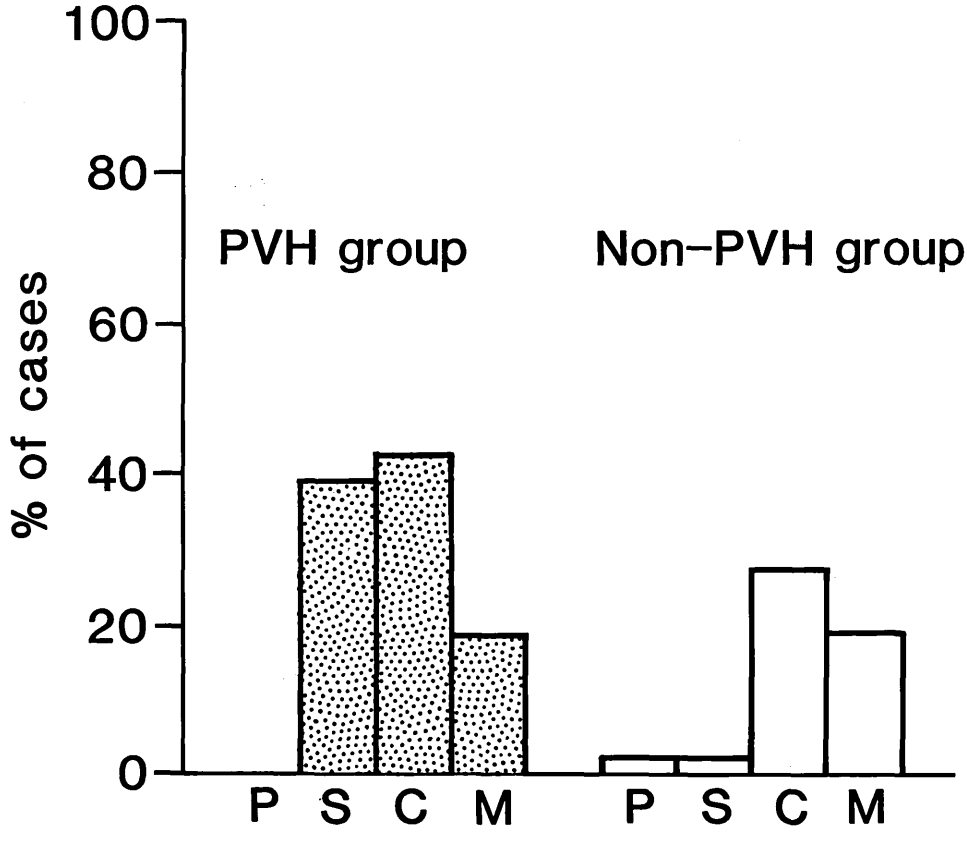


Figure 7.1. Prevalence of the 4 types of ABR abnormality in PVH (shaded) and non-PVH (non-shaded) group of infants. P = mild peripheral abnormality; C = central (brainstem) abnormality; M = abnormality of mixed types; S = severe abnormality. An isolated peripheral abnormality was only encountered once in a baby in the non-PVH group.

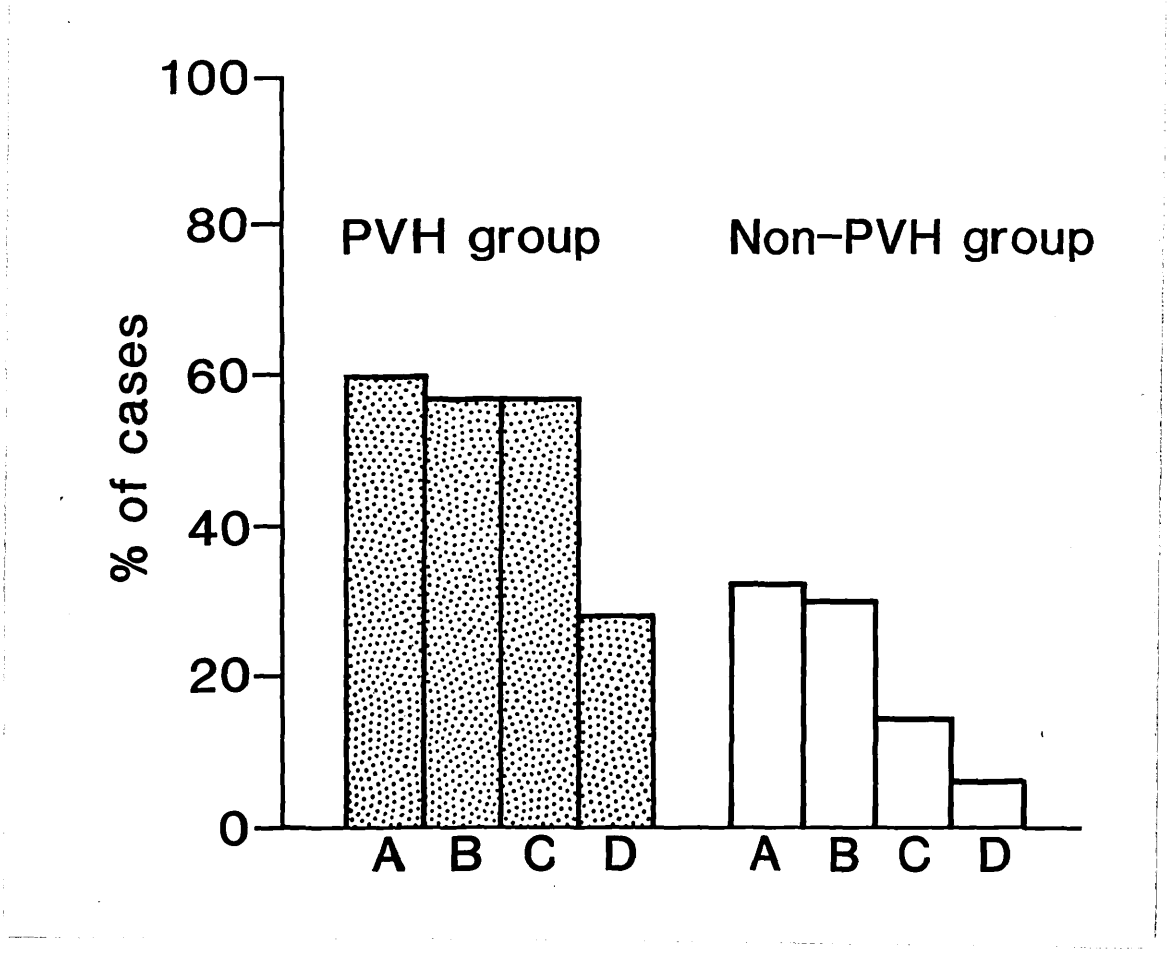


Figure 7.2. Prevalence of central abnormalities (indicative of brainstem dysfunction) in infants with and without PVH.
A = prolonged interpeak interval I-V
B = poor morphology of wave V
C = fusion of waves V and VI
D = abnormal V:I ratio

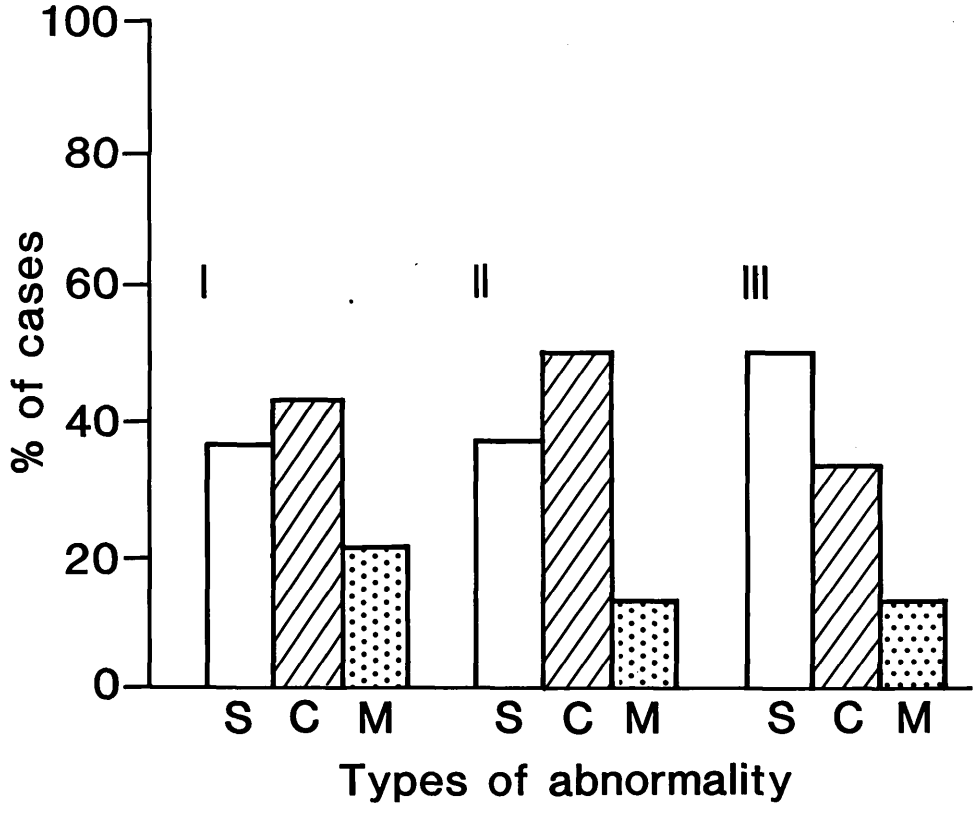


Figure 7.3. Severity of haemorrhage (grades I, II, III) and types of ABR abnormality. S, C, and M indicate 'severe', 'central', and 'mixed' abnormalities respectively.

Ten infants who had ABRs recorded during the first 3 days of life (before they had developed evidence of PVH on ultrasound scan) had abnormal responses (figure 7.4). 3 showed ABR abnormalities of central type and 7 had absent responses, or responses of severely reduced amplitude. In all but one case the abnormalities were bilateral.

The PVH and non-PVH groups were compared with respect to the presence or absence of other risk factors present during the first week of life and that may influence the ABR. These factors have already been discussed on the same 67 infants in Chapter VI. The results are present in table A3, in the Appendix.

VII.3.2. Follow-up studies

a) ABNORMAL ABRs ASSOCIATED WITH PVH (n=28)

Of the 28 infants with PVH and initially abnormal ABRs, 10 showed normalization of the ABR within the first month of life, and 12 within 2-4 months. In other words, a total of 22 infants (78%) had normal ABRs by the age of 4 months, i.e. at a time near the expected date of delivery (40 weeks postconceptional age). In a further 2 infants the responses were initially abnormal and were still

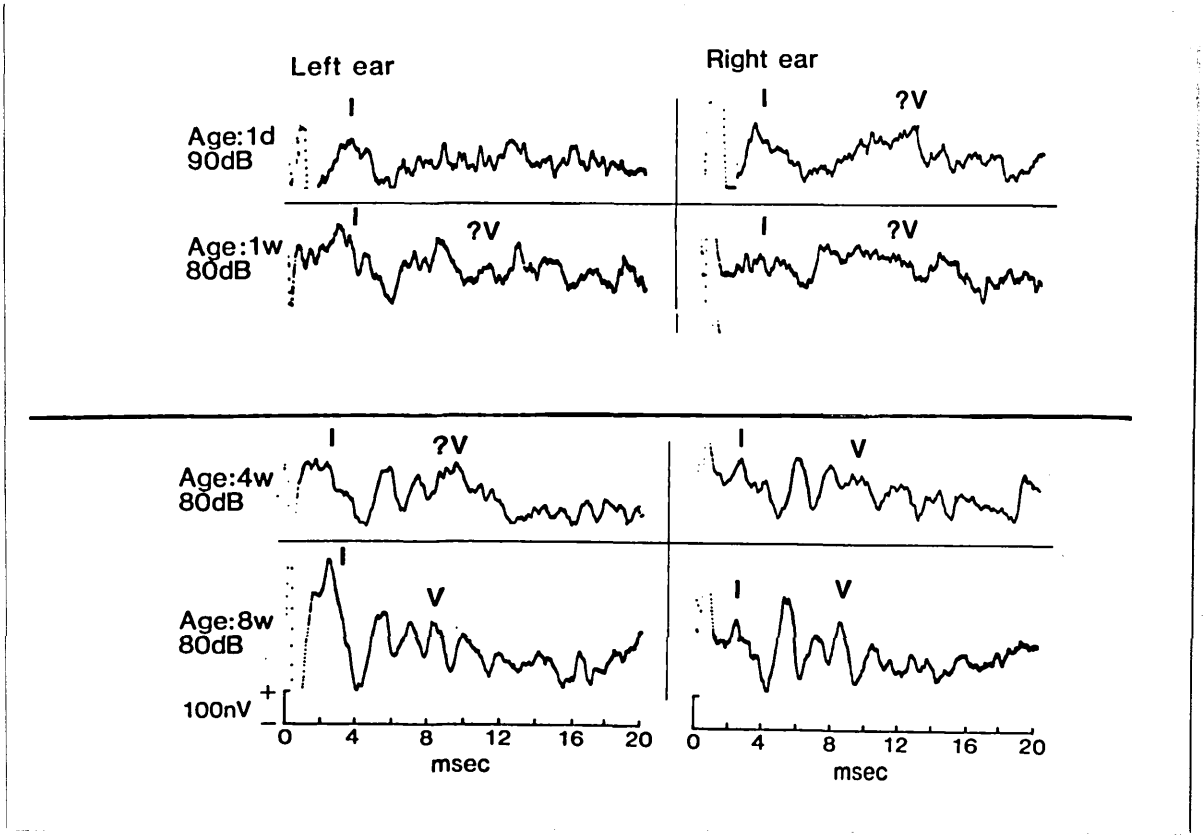


Figure 7.4. Several ABR traces of an infant (GA: 29 weeks) first performed on day 1. Responses from both ears were abnormal, at a time when the US showed no evidence of haemorrhage. On day 3, PVH was confirmed by US. Subsequent traces illustrate the evolution of the ABR changes over a period of 8 weeks. The latencies, I-V intervals and amplitude ratios were all within the normal range,and wave forms were easily identifiable. (stimulus: 10 clicks/sec, rarefaction phase).

impaired at around 40 weeks PCA but were found to be normal at 5 months when the infants were next tested. Only 3 infants still had abnormal ABRs at later follow-up (at 6 months in 2 infants, and at 8 months in one). These infants were referred for audiological assessment and management. The remaining infant died during hospitalisation at the age of 2.5 weeks and had been too ill to be retested (figure 7.5).

The records of these infants were further analysed to see whether the resolution of ABR abnormalities was related to the type of impairment. In 11 infants with severe impairment, 7 showed normal ABR at 2-14 weeks, and 1 reverted to normal by the age of 5 months. The remaining 3 infants continued to have severe deficits. Of the 12 infants with central abnormalities, the ABRs in 10 reverted to normal between 2 and 10 weeks of age, and one infant reverted to normal at 5 months. The remaining infant died. In 5 infants with mixed deficits the ABRs reverted to normal between 3 and 10 weeks of age. In summary, the initial ABR abnormality resolved by the age of 5 months in 24 infants irrespective of the type of abnormality. No particular pattern of improvement was noted for particular types of ABR abnormality.

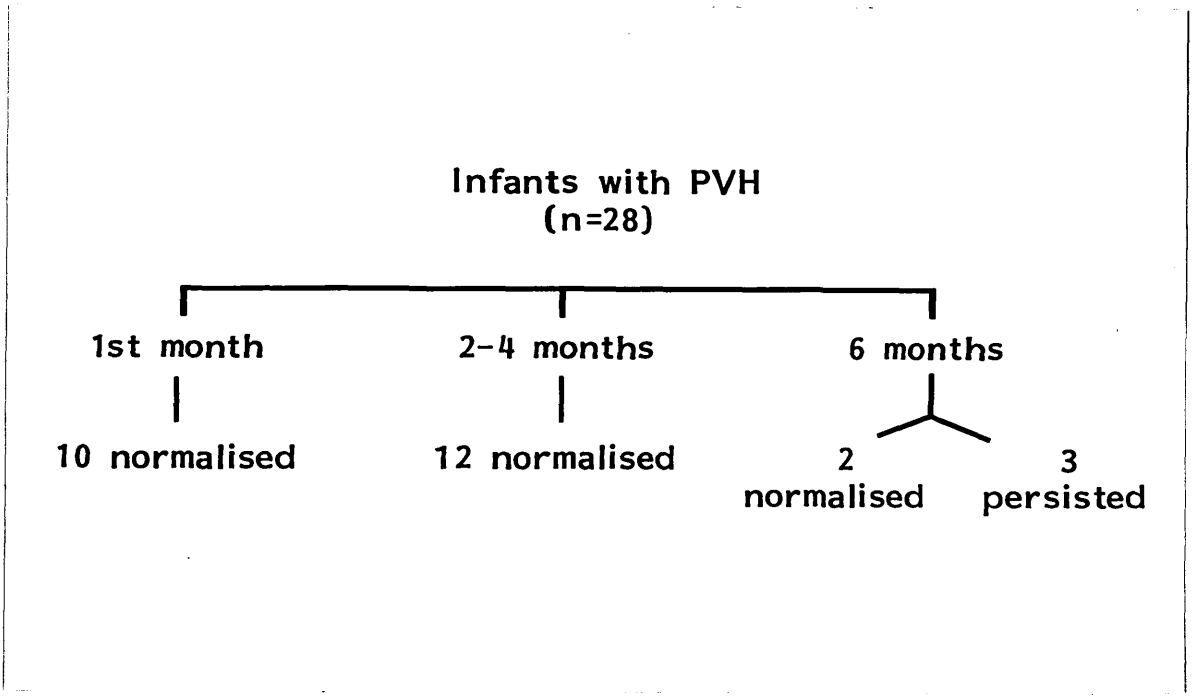


Figure 7.5. Time taken for ABRs to normalize in infants with PVH. The infants were classified according to their chronological age (1 month, 2-4 months, 6 months). By a postconceptional age of 40 weeks (equivalent to term) 78 infants had normalised their ABRs.

b) ABNORMAL ABRs WITHOUT PVH (n=19):

Of the 19 infants in this category, 16 showed normalisation of their ABRs by the first month of life, and 2 by the age 2-4 months. Thus 18 of 19 infants (95%) had normal ABRs by the age of 4 months, i.e. by the expected date of delivery (40 weeks PCA). In the remaining infants the reversion occurred by 6 months (figure 7.6).

The 19 infants with abnormal ABRs but no PVH were further assessed in relation to how different types of ABR abnormality evolved. The single infant with severe impairment showed a normal response by 4 weeks of age, and the infant with a mild peripheral deficit had a normal ABR by 2 weeks. Of 10 infants with central abnormalities 8 had normal ABRs at 2-6 weeks, 1 by 11 weeks, and 1 by 6 months. All 7 infants with initial abnormalities of mixed type showed normal responses by the age of 6 weeks.

Again it will be noted that within 2-11 weeks the ABRs reverted to normal, no specific pattern of improvement being associated with particular types of ABR abnormality.

Table VII.2 compares the follow-up studies in the 2 groups of infants (those with and those without PVH). The rate of resolution (expressed as the time taken for abnormal ABRs to normalize) was

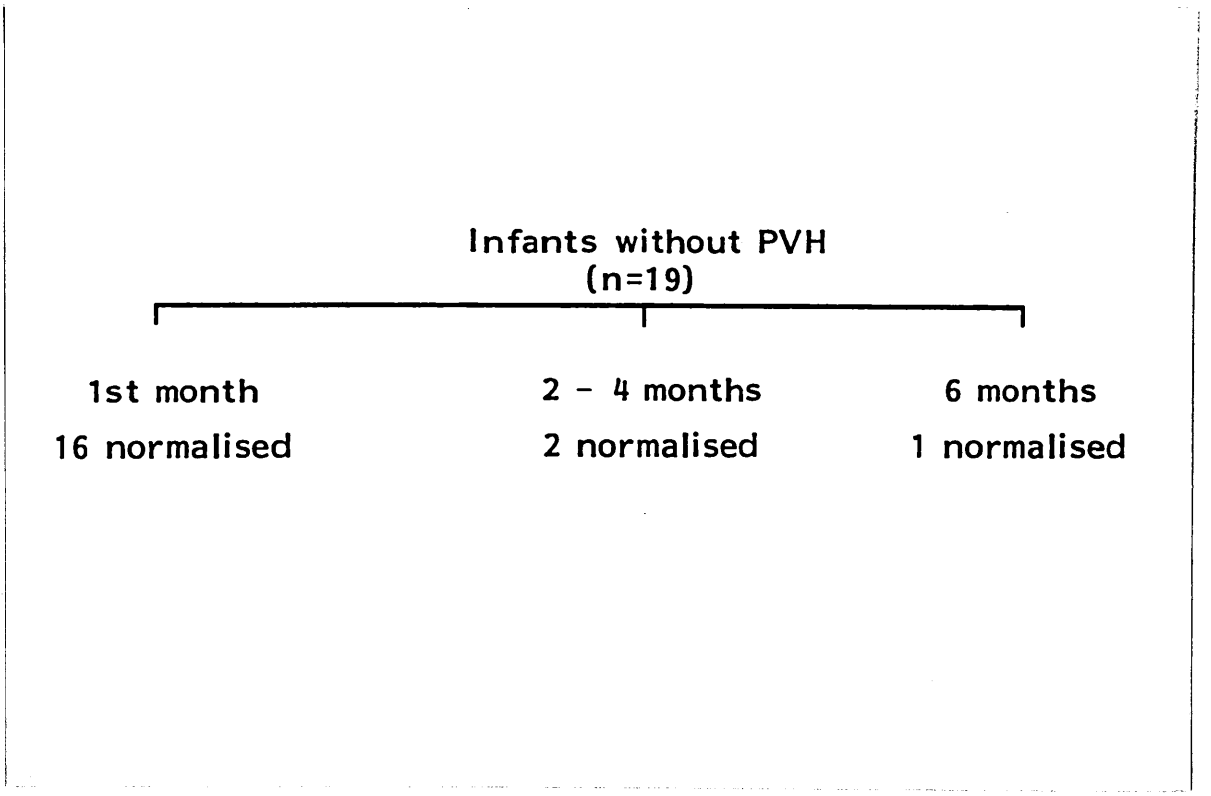


Figure 7.6. Time taken for ABRs to normalise in infants without PVH. Infants were classified by chronological age. By 40 weeks postconceptional age (equivalent to term) 95% of infants had normal ABRs.

TABLE VII.2

COMPARATIVE STUDY OF THE TYPES OF ABR ABNORMALITY ON FOLLOW-UP IN INFANTS WITH AND WITHOUT PVH

TYPES OF IMPAIRMENT	SEVERE	MILD PERIPHERAL	CENTRAL	MIXED
PVH GROUP (n = 28)				
Initial ABR	11	0	12	5
Death	-	-	1	-
Follow-up (with time taken to normalise in weeks)	8 7 (2-14 W) — 1 (22 W)	-	11 10 (2-10 W) — 1 (22 W)	5 (3-10 W)
Persistent abnormal ABR	3	-	-	-
NON PVH GROUP (n = 19)				
Initial ABR	1	1	10	7
Follow-up (with time taken to normalise in weeks)	1 (4 W)	1 (2 W)	10 9 (2-11 W) — 1 (26 W)	7 (2-6 W)

compared in the 2 groups with initially abnormal ABRs. In the PVH group it was only by the 6th week that 50% had normalized. In the non-PVH group the rate of resolution was more rapid: 50% had normalized by the second week (Figure 7.7).

VI.5. Discussion

This study revealed abnormalities of the ABR during the first weeks of life in all 28 infants with evidence of PVH on US scan. Moreover, in 10 infants tested soon after birth ABR abnormalities were present before PVH was evident. In the non-PVH group only half had abnormal ABRs.

The ABR abnormalities demonstrated during the first week of life resolved at different rates, according to whether PVH was present or not. Those in the non-PVH group normalised more rapidly than those with PVH. At or near the infants' expected date of delivery (40 weeks PCA) all ABRs in the non-PVH group became normal except in 1 infant whose ABR only normalised at 6 months. In the PVH group, on the other hand, abnormal responses were still demonstrated in 5 infants (17%) at 5 months. Three of these infants were subsequently found to have persistent hearing impairment. The other 2 showed normal ABR patterns by 6 months.

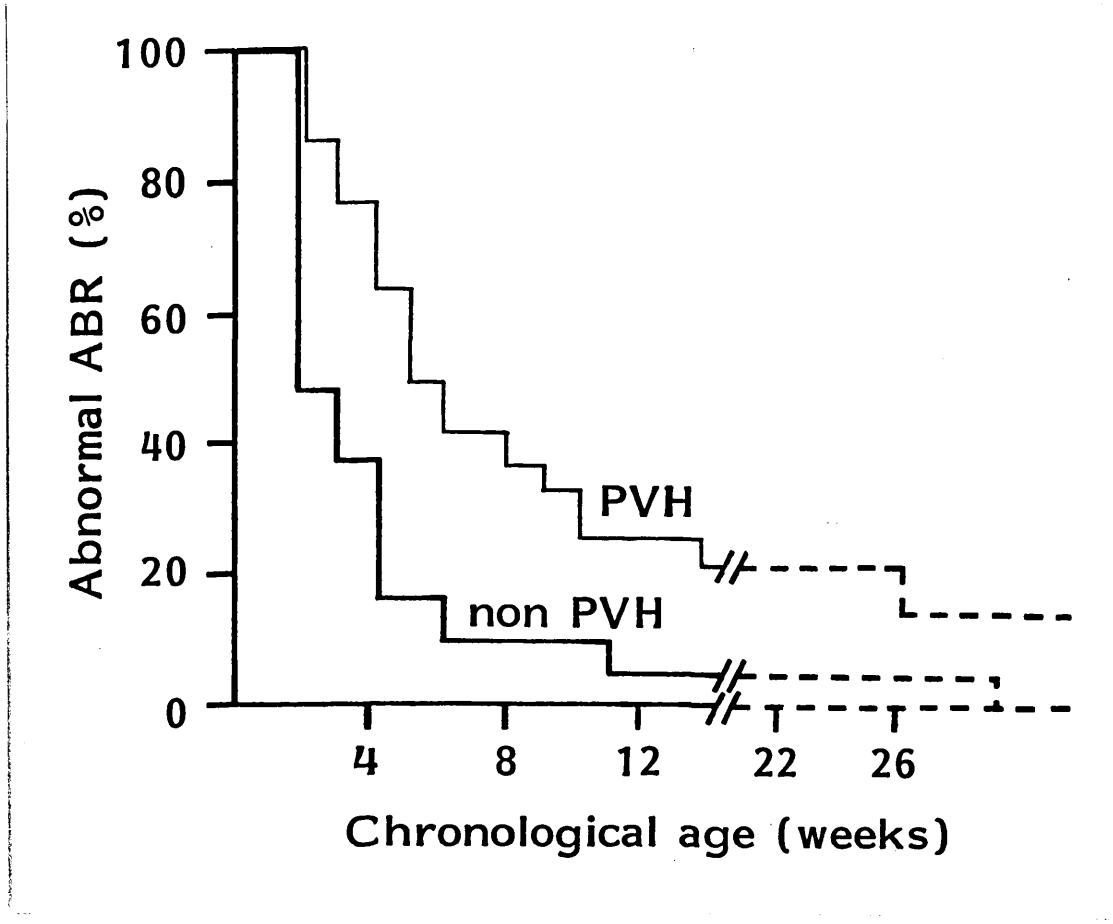


Figure 7.7. Rate of resolution of ABR abnormalities in PVH and non-PVH groups. By the second week 50% of the non-PVH infants had normalised compared with only 12% of the PVH group. In the PVH group 50% of abnormal ABRs had normalised by six weeks.

Although we defined several types of ABR abnormality we were careful not to allocate specific patterns of ABR to specific neurological disorders. We found a consistent abnormality of the ABR in infants with PVH, namely the presence of fusion between waves V and VI. This was usually associated with an abnormal morphology of wave V. These changes, together with the ones described above (prolonged IPI, abnormal V:I ratio) can be considered as evidence of a compromised brainstem.

Intraventricular haemorrhage has been considered a major risk factor in causing hearing loss (Marshall et al 1980, Galambos and Despland, 1980, Barnet et al 1980, Ito 1984). Describing 6 infants with unobtainable ABRs, Marshall et al (1980) attributed the failure in 5 to intracranial haemorrhage. The criterion for passing the ABR test was the presence of a wave V at a stimulus intensity of 60 dB. But this criterion only indicates the presence of a hearing threshold. It does not take into account the latency of wave V, the latencies of other waves, or interpeak intervals. Moreover, the intracranial haemorrhages had been diagnosed clinically (by unspecified criteria) and confirmed by CT scan or autopsy, which meant that "silent haemorrhages" (unsuspected clinically) had not been included. Furthermore, the time between clinical diagnosis and the CT scan was not mentioned. Roberts et al (1982) reported 10

patients with intraventricular haemorrhage among 75 preterm infants: 3 of the 10 infants failed to exhibit ABR components at 40 dB and 7 failed even at 70 dB. 9 infants improved in predischarge testing but 1 patient with meningitis and asphyxia had a persistently abnormal ABR. Although Roberts used 2 intensity levels (70 and 40 dB) there were no comments on ABR latencies, and the diagnosis of haemorrhage was only verified by CT or ultrasound scan when suspected clinically. Clinically 'silent' haemorrhages were again clearly missed in this particular study, and again the clinical criteria for suspecting haemorrhage were not specified.

Other authors (Despland and Galambos 1980, Galambos and Despland 1980, Schulmann-Galambos and Galambos 1975, Mjoen et al 1982) have described central types of ABR abnormality (prolonged brainstem conduction time) in a few case reports of PVH-IVH. Fawer et al (1983) in this unit looked at a larger group of infants with intraventricular haemorrhage. In 21 infants with a definite diagnosis of intraventricular haemorrhage, there was a high prevalence (95%) of ABR abnormalities including absent responses and prolonged interpeak intervals.

The information obtained in the present study (as to the exact time of appearance and rates of normalisation of ABR abnormalities)

allows better interpretation of various disorders. In previous studies, the ABR findings had not been related to the time at which the diagnosis of IVH had been made. Nor were they related to the evolution of the haemorrhage.

We could not show any consistent correlation between ABR abnormalities and the site (ipsilateral or contralateral) of the haemorrhage. Brainstem nuclei can act as generators, contributing to both the ipsilateral and contralateral ABR responses (Thornton 1978).

Throughout this thesis we have discussed the use of ABR as an index of brain stem integrity. Views differ as to the severity of the various abnormalities that the ABR can detect, and about their relation to the primary haemorrhage. PVH-IVH is an ongoing process and appears when certain mechanisms controlling haemodynamic and biochemical function are disturbed (for instance by hypoxia or hypercapnia).

Why do ABR abnormalities occur in the presence of PVH? The effects of increased intracranial pressure on the brainstem have been incriminated but such an explanation seems unlikely in our preterm population. Some abnormal responses in infants with PVH

might be explained by haemorrhagic dissection of the brainstem (Stockard and Stockard 1981). Such a process might extend to the auditory canal (Spector et al 1978), thus explaining the initial severe impairment in some infants. The critical pressure associated with blood vessel rupture or other factors is unknown. Volpe (1981) described a neurological syndrome consisting of deep coma or stupor, respiratory abnormalities, seizures, fixed pupils and flaccid quadriplegia. Tarby and Volpe (1982) discussed how this syndrome appeared to be related to the movement of blood through the ventricular system affecting, sequentially, the diencephalon, midbrain, pons and medulla.

Recent studies have suggested mechanisms relating ABR abnormalities to cerebral ischaemia and other haemodynamic disturbances. Sohmer et al (1984) showed absent brainstem responses in such cases. In studies on cats and humans, Goietin et al (1983) stressed the close relationship between adequate cerebral perfusion pressure and the ABR waves. It is generally accepted that the compromised neonatal brain loses its ability to maintain a properly regulated blood flow. This is thought to be the initial factor in the pathogenesis of germinal layer haemorrhage and of subsequent intraventricular haemorrhage (Levene 1981). The concept of cerebral autoregulation is clearly crucial to this argument.

In the present study we have shown that all infants with PVH had abnormal ABRs. Moreover infants with PVH had more severe ABR abnormalities than those without PVH, and their abnormalities persisted longer. The very occurrence of the ABR abnormalities in infants who later develop PVH suggests that the ABR may be reflecting a more fundamental abnormality than the haemorrhage itself. The factors which predispose to periventricular haemorrhage (see table A3, in Appendix) may be identical with - or related to - those causing the electro-physiological abnormalities reflected in the abnormal ABR.

CHAPTER VIII. THE AUDITORY BRAINSTEM RESPONSE IN INFANTS WITH POST-HAEMORRHAGIC VENTRICULAR DILATATION

VIII.1. Introduction

Progressive ventricular dilatation is a frequent sequel of intraventricular haemorrhage. Extravasated blood tends to collect in the posterior fossa, producing an obliterative arachnoiditis (Volpe 1981). The most common site of obstruction to CSF flow is at the posterior end of the 4th ventricle (Larroche 1972), less common sites being the aqueduct (Larroche 1972) and the tentorial opening. The meninges around the brainstem are thickened and may show a persistent rusty-brown discolouration owing to infiltration with hemosiderin-laden macrophages. The foramina of Luschka and Magendie are often occluded and the entire ventricular system may be dilated.

Disturbances in auditory brainstem responses have been reported in disorders associated with ventricular dilatation in both infants and children. (Starr and Amlie 1981, De Vlieger et al 1981, Kraus et al 1984). The use of the ABR to assess the possible repercussions of ventricular dilatation (PHVD) upon the brainstem has been described in a few case reports (Starr and Amlie 1981, Stockard and Stockard 1981).

One aim of this study was to evaluate the ABR abnormalities seen in infants with PHVD and to determine whether such abnormalities could be altered by drainage of cerebrospinal fluid (CSF).

VIII.2. Material and Methods:

Of the 855 infants admitted to the Hammersmith Hospital Neonatal Intensive Care Unit between October 1981 and April 1984, 145 were found to have periventricular haemorrhage (PVH) on ultrasound scanning during the first week of life. Eighteen of these 145 cases (12.1%) developed PHVD. Two further infants, transferred to the unit with established PHVD (at the ages of 2 and 8 weeks respectively) were included in the study. Of these 20 infants with PHVD, 19 were fit for testing. The remaining infant was critically ill and considered unsuitable for ABR assessment. He subsequently died.

The diagnosis of PHVD was made in infants with PVH when two or more ultrasound measurements of ventricular width exceeded by at least 4 mm the 97th percentile of the measurements appropriate for the gestational age (as determined by Levene ,1981).

Of the 19 infants with PHVD, 16 were preterm (gestational ages 26-34 weeks) and 3 full term (38-39 weeks). Gestational ages were determined from gestational assessment (Dubowitz et al 1970) and maternal dates. These agreed within one week in all cases.

Kaiser and Whitelaw (1985) studied the CSF pressure in 9 of these 19 infants. This was done within a couple of hours of their ABRs having been carried out in 6 infants. The pressures were recorded by direct measurement during lumbar or ventricular taps, using a Gaeltic pressure transducer attached to the needle in the ventricular or subarachnoid space. The upper limit of normal CSF pressure was taken as 6 mmHg (78 cm water).

The ABR procedures used were similar to those outlined in Chapter III.

Four aspects were studied:

a) Assessment of the ABRs at the time of maximum ventricular dilatation (n=19).

b) The evolution of the ABR abnormalities in relation to the occurrence of PVH-IVH and to the development and resolution of the ventricular dilatation (n=12).

c) The general relationship between ABR abnormalities and CSF pressure (n=9).

d) The ABR changes in response to withdrawal of cerebrospinal fluid (CSF) by either shunting or periodic drainage (lumbar puncture or ventricular tapping)(n=7).

VIII.3. Results:

A) EFFECTS OF PHVD (AT TIME OF MAXIMUM VENTRICULAR DILATATION) ON THE ABR:

ABRs were assessed in 19 infants during the phase of maximum dilatation of the ventricles. Five records were normal and 14 abnormal. The abnormal tracings revealed a variety of patterns:

a) Two infants had 'severe' impairment (absent response in one, and markedly reduced response in the other).

b) Two infants had 'peripheral' abnormalities.

c) Five infants had 'central' abnormalities. Three showed prolonged I-V interpeak intervals (>2 SD from the mean), one with an absent wave V, and one with an abnormal V:I amplitude ratio.

d) Two infants had short I-V IPI but normal wave configuration.

e) Three infants had abnormal and non-reproduceable traces on repeated testing. These were classified separately

The clinical details of these 19 infants are summarised in table VIII.1.

TABLE VIII.1
CLINICAL DETAILS OF INFANTS WITH PHVD (N=19)

CASE No	SEX	GA	B.WT gms	CLINICAL DETAILS	OUTCOME OF PHVD
1	M	26	880	asphyxia IPPV RDS PDA	P (died)
2	F	26	940	RDS IPPV Pnx	P (shunt)
3*	M	26	580	RDS IPPV PDA fits CCA	P
4	F	28	730	asphyxia IPPV Pnx PDA NEC	(died)
5	F	28	1100	IPPV RDS PDA jaundice	S
6	M	28	1420	RDS IPPV PDA Pnx	T
7	F	28	830	RDS IPPV PDA infection	T
8	M	28	1450	RDS IPPV PH'	S
9	F	28	1190	RDS IPPV PDA PH'	T
10	F	29	1380	asphyxia RDS jaundice	P (shunt)
11	F	29	920	asphyxia IPPV jaundice HD	S
12	M	30	2000	RDS IPPV PDA jaundice	T
13	M	32	2240	RDS IPPV PH' fits	T
14	M	32	1410	RDS IPPV IADH	P (shunt)
15*	M	32	1640	MTM IPPV PH' jaundice	P (died)
16	M	34	2600	cardiac dysrhythmia jaundice	T
17	F	38	2600	factor V deficiency	P (shunt)
18*	M	38	2870	MTM IPPV PH'	S
19	M	39	2740	polycythaemia, fits	P (shunt)

CCA: congenital cerebral abnormality, HD: Hirschsprung disease, IADH: inappropriate ADH secretion, IPPV: intermittent positive pressure ventilation, MTM: myotubular myopathy, PH: pulmonary hypertension, PDA: patent ductus arteriosus, Pnx: pneumothorax, RDS: respiratory distress syndrome. P: progressive PHVD, S: static PHVD, T: transient PHVD.

* infants 3, 15, 18 had non-reproducible traces. Infant 3 had severely reduced responses.

B) EFFECTS OF THE EVOLUTION OF THE PHVD ON THE ABR: (n=12)

Eleven preterm infants were involved in this part of the study. During the first week of life brain ultrasound scans had shown PVH-IVH of variable severity. During the same time ABRs were recorded and showed abnormalities in all 11 preterm infants. A single full-term infant with PHVD who was also studied showed an initially normal ABR. Sequential ABRs were performed and showed improvement at a time when the ventricular dilatation was still present on the scans, and in fact progressing. In 5 of the 11 preterm infants the ABRs returned to normal although there was still marked dilatation of the ventricles (figure 8.1). In 3 of the preterm infants, the ABRs remained abnormal at the ages of 10, 14 and 20 weeks respectively. During this period the ventricles diminished in size, but remained moderately dilated. In one infant the ABR remained abnormal and the child was referred to hearing specialists. Two infants died at ages 2 and 4 weeks respectively.

The initial ABR in the single fullterm infant in this group was normal. Slowly progressive ventricular dilatation occurred over the next 10 weeks. A repeat ABR early during the this period remained normal. Subsequent ABRs (done at 3 months) showed deterioration.

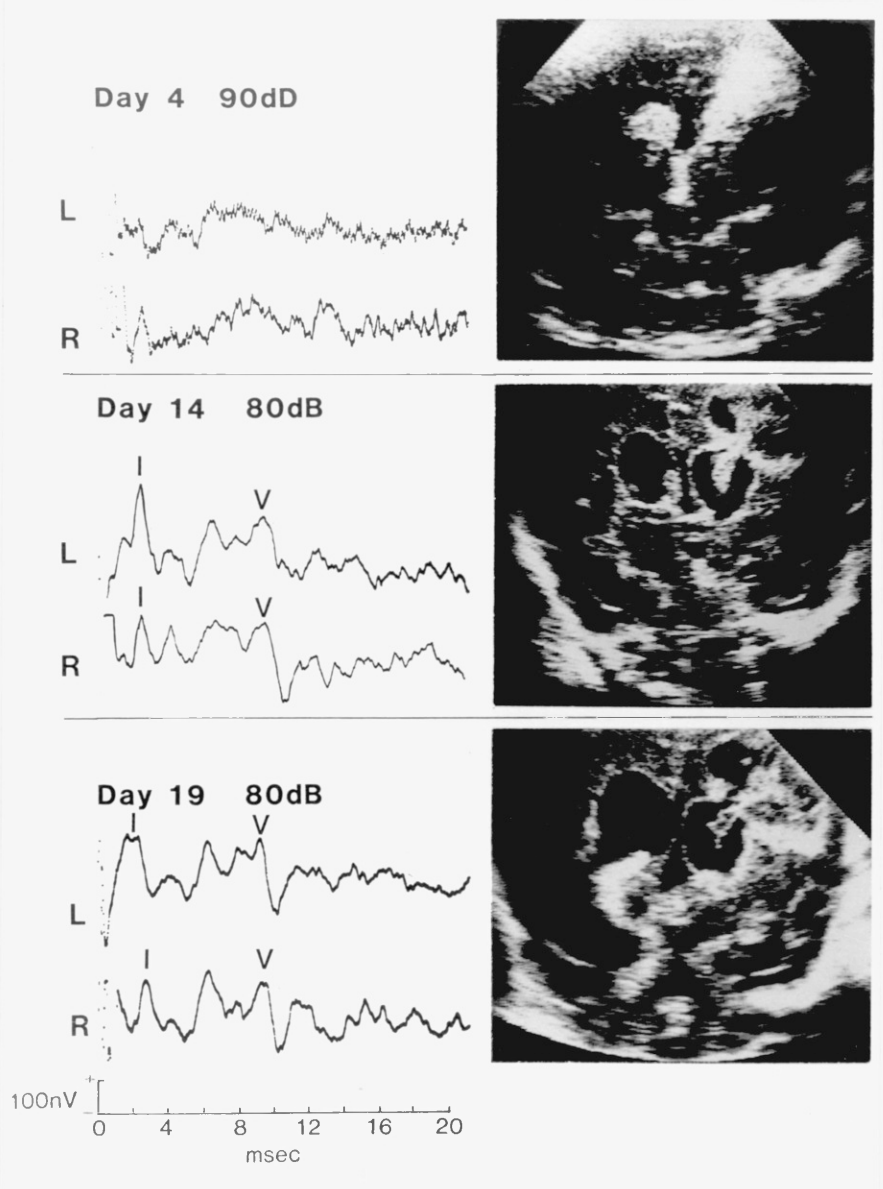


Figure 8.1. An infant born at 32 weeks gestation developed bilateral intra and periventricular haemorrhages (on day 3). ABRs on day 4 were abnormal (latencies,intervals, and waveforms) at 90 dB on each side. By the second week, the ABR showed marked improvement of waveforms but the I-V interval remained prolonged. Ventricular dilatation and cyst formation were now present on US scan. By day 19, the ABR had reverted to normal, but there had been further dilatation on the US. All stimuli: clicks at 10/sec (rarefaction phase).

C) EFFECTS OF CSF PRESSURE ON THE ABR

Serial CSF pressures were recorded on 9 infants, also being studied by serial ABR. In 6 infants (5 preterm and 1 fullterm) 21 direct CSF pressure measurements were recorded on the same day as the ABR had been performed. There was no correlation between the level of CSF pressure and the presence of ABR abnormalities as assessed by the I-V IPI. (Figure 8.2).

D) EFFECTS OF CSF DRAINAGE ON THE ABR

In 7 infants with PHVD the ABRs were studied before and after drainage of CSF. Four infants were treated by repeated ventricular tap or lumbar puncture. The ABRs were abnormal before CSF drainage was carried out. Two to 6 hours after CSF removal, repeat ABR showed little change but ABRs carried out 24 hours after CSF drainage showed an increase in amplitude in two cases (figure 8.3). This particular study could not be carried out on the other 2 patients because of their clinical condition (one was too ill, and the other was too irritable for ABR testing).

Four infants had shunts inserted. Pre-shunt ABRs were normal in one, unequivocally abnormal in another, and showed a pattern of uncertain significance in the remaining 2 (i.e. normal wave morphology and hearing thresholds, but interpeak intervals shorter

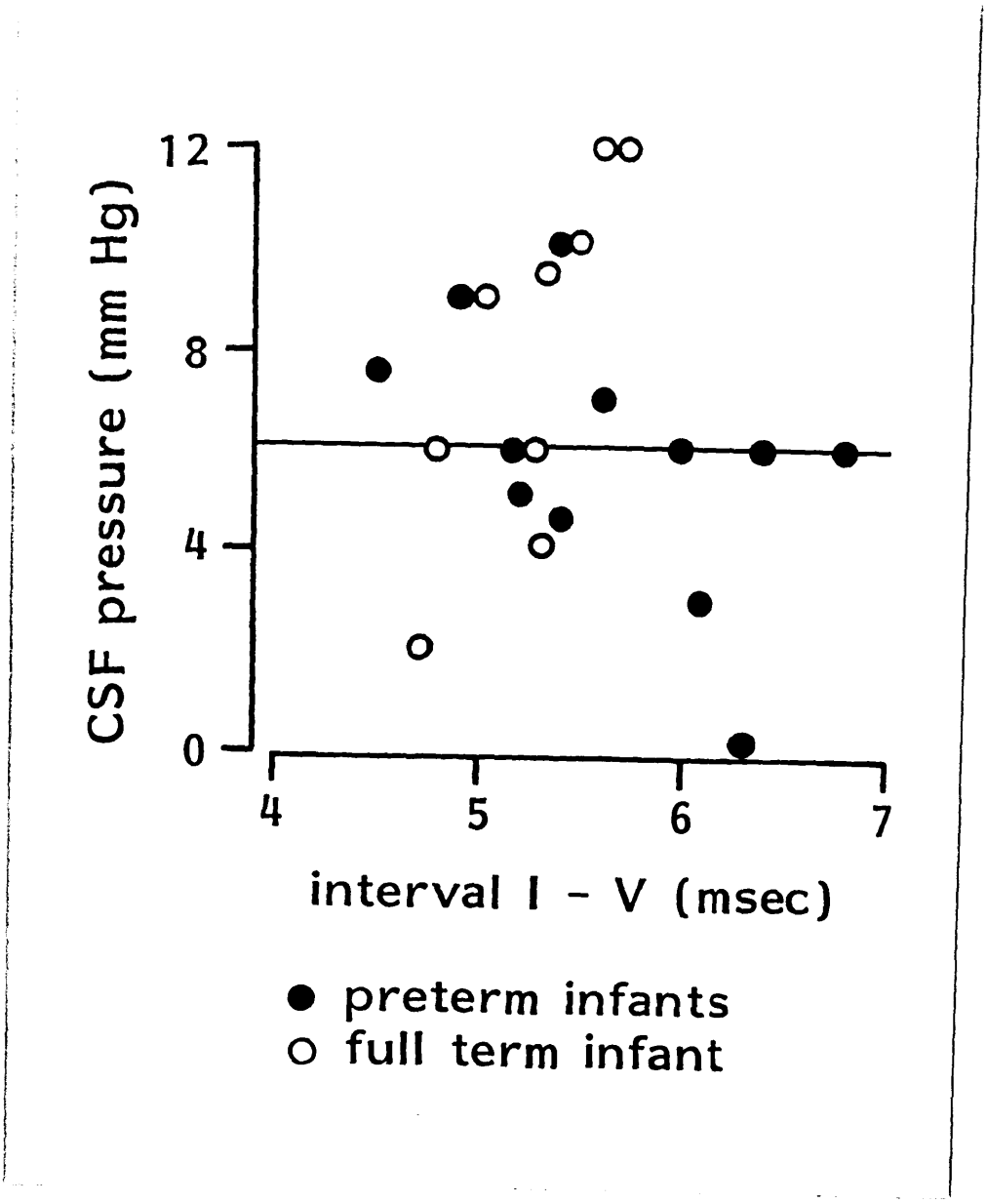


Figure 8.2. Simultaneous CSF pressures and interpeak interval I-V recorded on 12 occasions in 5 preterm infants (black circles), and on 9 occasions in 1 full-term infant (white circles). The upper limit of normal CSF pressure is shown by the horizontal line.

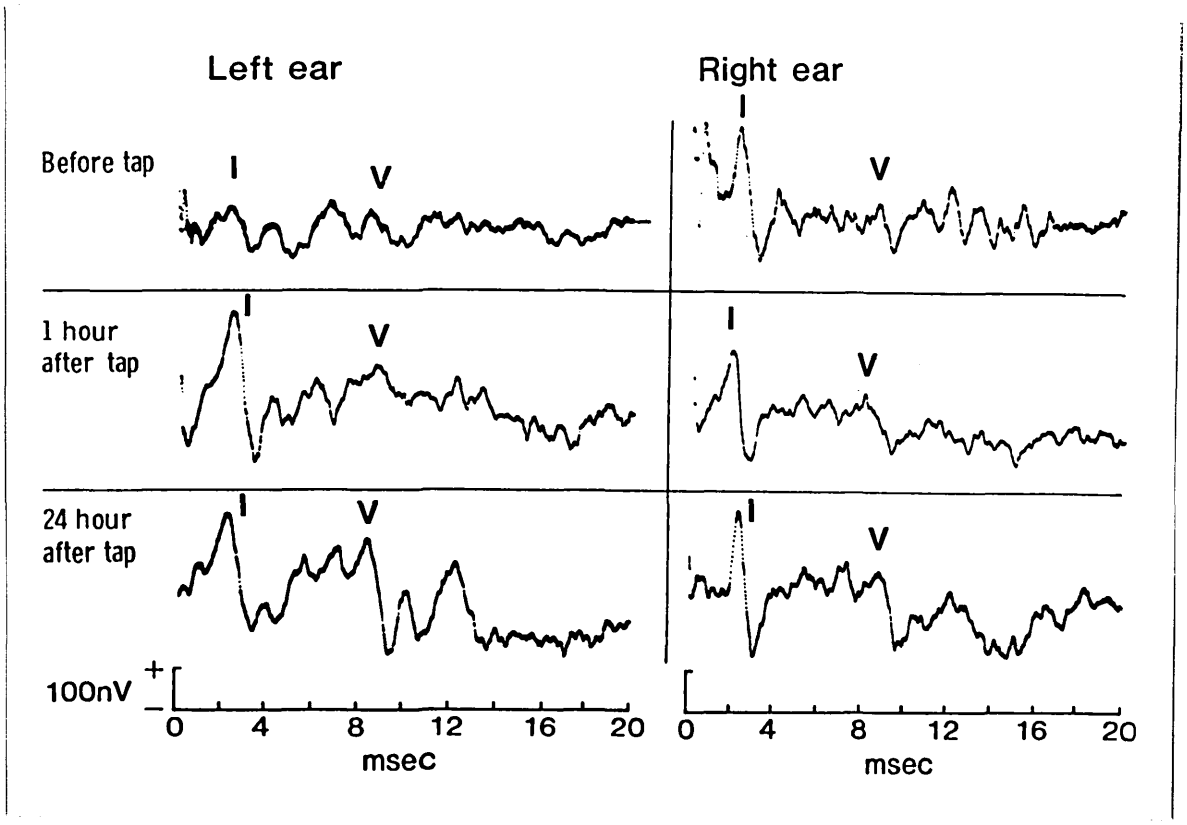


Figure 8.3. Effect of ventricular tap on the ABR. Female infant (GA 29 weeks) with right-sided PVH-IVH on US scan. Before drainage the ABRs (from both left and right) showed abnormal waveforms and latencies. One hour after CSF tap there was little change in the ABR (a unilateral increase in the amplitude of wave I on the left). The responses remained abnormal. When ABRs were repeated 24 hours later, there was marked improvement, particularly on the left, where both latencies and I-V interval were now within normal limits. The right side remained abnormal (prolonged I-V interval and abnormal waveforms). All stimuli at 80 dB and 10 clicks/sec.

than appropriate for their ages). The shunting procedure had no effect on the ABR in one patient in whom the ABR was normal before shunting or in 2 patients who had abnormalities in the ABR of uncertain significance. The abnormal pre-shunting ABR recording in one infant showed a dramatic post-shunting response, the ABR reverting to normal within a week (figure 8.4).

VII.4. Discussion:

We have shown that in preterm infants ABR abnormalities may not develop synchronously with, or evolve in parallel with the development of PHVD. Initially abnormal ABRs all reverted to normal despite variable persistence of the ventricular dilatation. The ABR deteriorated in a single full term infant during worsening of PHVD. Intermittent drainage of CSF in two infants was followed by an increase of amplitude of the ABR waves after 24 hours but not earlier. Persistent CSF shunting in one infant was followed within a week by improvement of definitely abnormal ABRs. There was no correlation between CSF pressure and I-V interpeak intervals.

To my knowledge this is the first time that ABRs have been studied during the development of neonatal PHVD, or that the effects of intermittent drainage of CSF have been investigated. Previously reported ABR abnormalities in children with hydrocephalus were in

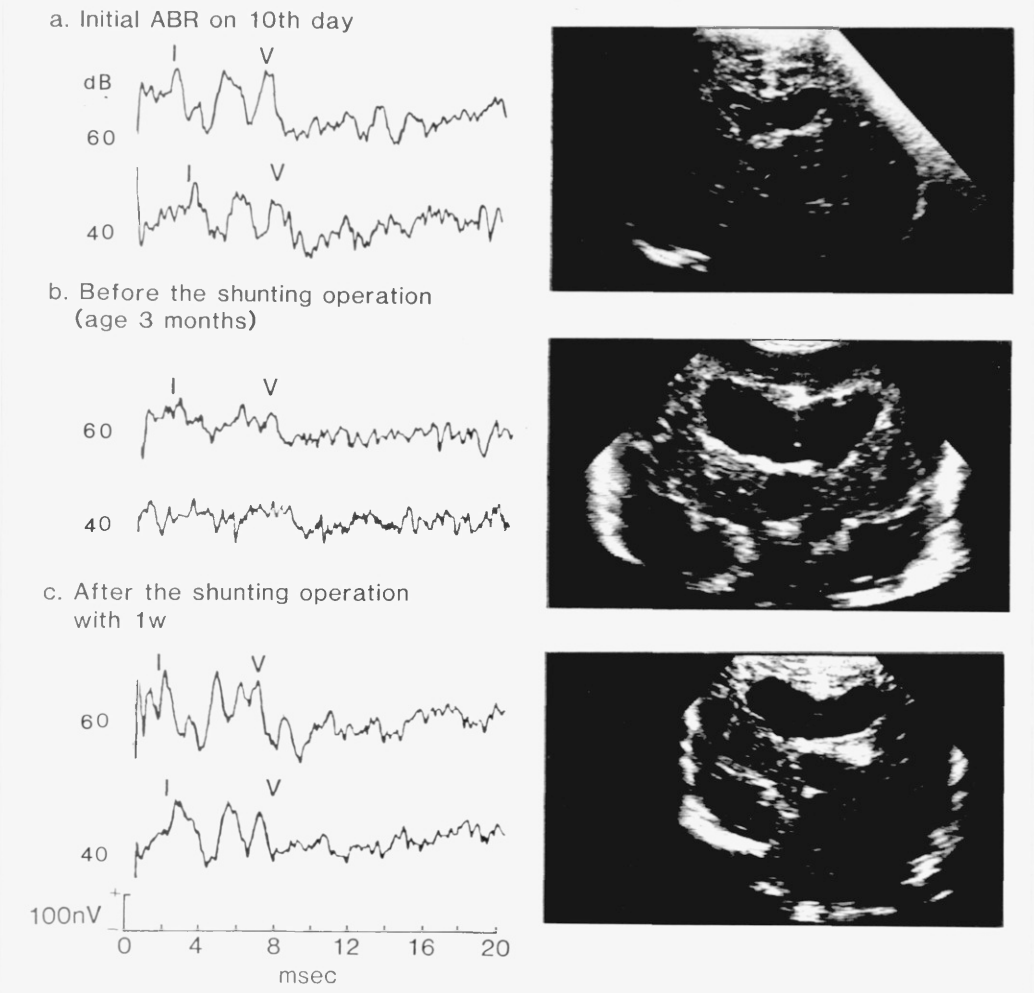


Figure 8.4. Effect of shunting on the ABR in a full-term infant with PHVD a) Initial ABRs show normal latency and wave configuration at 60 and 40 dB. US shows some ventricular dilatation. b) Effects of progressive ventricular dilatation lasting over 3 months (marked deterioration of wave configuration, and disappearance of responses at 40 dB). Both lateral ventricles show marked dilatation on US performed on the same date as the ABR. c) ABR performed one week after shunting, showing reversion to normal. The US scan showed that the ventricles, while still dilated, had diminished in size. All stimuli:10 clicks/sec.

much older subjects (Stein et al 1983, Kraus et al 1984) or in children of unspecified age (Starr and Amlie 1981). Previous investigators (De Vleiger et al 1981, Starr and Amlie 1981) showed that in the presence of ventricular dilatation there were increased I-V interpeak intervals which they attributed to increased intracranial pressure. In the present study, we found there was no correlation, either positive or negative, between the I-V interpeak interval and intracranial pressure. Our findings relate primarily to preterm infants.

The mechanisms whereby the brain of preterm infants can adapt to increased intracranial pressure are open to speculation. One may be the balance between increased ventricular volume and the resorbtion of extracerebral CSF. When the limits of compensation are reached, a sustained rise in the intracranial pressure will ensue, giving rise to the classical signs of increased intracranial pressure (i.e. increasing head circumference, tense anterior fontanelle, and suture diastasis) (Volpe 1977). Pathological studies have also shown that in preterm infants with PHVD considerable degrees of ventricular dilatation can occur before there is any rise in intracranial pressure (Larroche 1977, Wigglesworth 1984). Periventricular oedema, produced by CSF extravasating through ruptures in the ependyma, may compress periventricular capillaries causing ischaemic injury (Wozniak et al 1975). Hill and Volpe (1981) have finally

stressed that the immature state of the periventricular tissue and the additional fact that it has been compromised by a variety of hypoxic-ischaemic insults may influence its adaptation to increased intracranial pressure.

Another factor influencing this adaptation is the relatively large subarachnoid space within the cranium of the premature infant (Larroche 1977, Pape and Wigglesworth 1979). Among preterm infants there is a wide variation in the size of the brain and of the extracerebral space, depending upon the pressures to which the head has been subjected in utero and upon variation in foetal maturity and nutrition (Wigglesworth 1984). These facts are probably relevant to our findings concerning the relation between intracranial pressure and I-V interpeak intervals. The data should probably not be extrapolated to full term infants, or to older children. In our single full term infant with prolonged ventricular dilatation (lasting over 3 months) the ABR showed marked deterioration in the presence of increased intracranial pressure, reverting to normal following shunting. Nagao et al (1979) have demonstrated disruption of neural activity in the auditory brainstem pathway following experimentally induced intracranial hypertension in cats (the intracranial pressure was raised by expansion of a supratentorial balloon). They reported associated reductions in the amplitudes of waves IV and V, and prolonged latencies of waves III,

IV and V. Although increased intracranial pressure and ABR abnormalities have been described in animals and humans (Nagao et al 1979,1983, Benna et al 1982), Kraus et al (1984) found ABR abnormalities in post-shunted patients, showing no signs of increased intracranial pressure. Much less is known about the specific interrelationships between intracranial pressure and brainstem function. Goodman and Becker (1973) studied the vascular pathology of the brainstem induced by intracranial hypertension in cats. They reported that as intracranial pressure rose there was a parallel progression of vascular disturbances, first in the microcirculation and finally in the macrocirculation. Such reversible ischaemic changes in the brainstem due to alterations in blood flow may account for the changes in ABR on intermittent withdrawal of CSF witnessed in some of our patients. In an experiment on cats Nagao et al (1980) observed gradual changes in the ABR (progressive reduction in the amplitude of waves IV and V) with gradual increase in ICP (produced by ballon inflation) followed by progressive recovery during a 3 hour period after the balloon had been deflated. They suggested that these changes were due to direct mechanical pressure. The changes were clearly not irreversible. Another explanation for our data could be cell recovery from interstitial oedema (or effused CSF) a recovery reflected in an increase in wave amplitude.

The findings in the present study show that in preterm infants the changes in ABR cannot be used to monitor the management of PHVD. On the other hand, the ABR documents the presence of brainstem dysfunction associated with PVH.

SUMMARY AND CONCLUSIONS

The general purpose of this thesis was to determine 'normal' auditory brainstem responses (ABR) in preterm and full term neonates, so that abnormal or atypical findings could be identified and assessed. The infants studied were categorised as 'neurologically optimal' if they were at low risk of developing neurological complications. In 56 infants judged to be optimal, ABRs were investigated at 3 stimulus intensities (80, 60 and 40 dB). The absolute latencies of waves I, III, V and VI and the interpeak intervals (IPIs) of waves I-V, and III-VI were studied. The amplitudes of waves I and V and the amplitude ratio of these waves (V:I ratio) were determined. At all stimulus intensities the various parameters examined (except the V:I ratio) showed a definite relationship to gestational age. Using stringent criteria for selection and appropriate statistical analysis, normative data were established for infants from 28 to 42 weeks of gestational or postconceptional age. Latencies and IPIs decreased steadily with age, while amplitudes increased consistently as the infant grew older. In our experience of infants aged 28 weeks or more, identifiable ABRs were found in all instances, however immature the infant provided associated risk-factors were absent or only minimal.

Hearing thresholds were defined as the minimum stimulus intensities needed to elicit wave V of the ABR. The maturation curves for thresholds were determined by ABR on neurologically optimal infants, using the same criteria for selection. From these curves it was established that infants with gestational and postconceptional ages ranging from 28-34 weeks had hearing thresholds at 40 dB, while infants from 35-39 weeks had thresholds of 30 dB or less. Older infants had still lower thresholds.

The features of various types of deafness could be identified by determining latency-intensity function curves. We established such curves from the latency-intensity function of wave V in three different age groups (28 to 32 weeks, 33 to 37 weeks, and 38 to 42 weeks). By analysis between the differences from normal curves and those obtained from patients with impaired hearing, one can draw conclusions as to the type of impairment present (whether conductive or sensorineural).

Another aim was to assess the effects of neonatal risk factors and to investigate whether individual or combined risk factors were more frequently associated with persisitently abnomal ABRs. Twenty three clinical factors (obstetrical and neonatal) were analysed from birth till the end of the first week of life. Possible correlations were sought between these early risk factors and the persistence of

ABR abnormalities at different points in time: during the first week of life, at discharge from hospital, and during follow up visits.

Using multiple Chi-sqaure tests it was shown that periventricular haemorrhage, and abnormal neurological signs achieved statistical significance ($P < 0.001$) in their association with ABR abnormalities detected during the first week of life. The following early risk factors were found to be significantly related with ABR abnormalities still present at discharge: acidosis, periventricular haemorrhage, and abnormal neurological findings ($P < 0.001$). Early risk factors which correlated significantly with ABR abnormalities present at follow up were hypoxia and hypercapnia (both lasting more than one week) and abnormal ABR results present at discharge ($P<0.005$).

From this study we can conclude that the ABR is time-dependent in relation to the postnatal age and to the risk factors present, which are themselves highly inter-correlated with one another. Risk factors significantly correlated with ABR abnormalities during the first week of life were no longer significant at follow up (e.g. PVH).

We also correlated ABR patterns with the findings on brain ultrasound scan. ABRs were recorded during the first week of life

in 67 preterm infants and assessed in relation to the presence of periventricular haemorrhage, diagnosed by ultrasound scan. All infants with PVH had abnormal ABRs. ABR abnormalities were at times present before PVH was evident on the scan. All infants with normal ABRs also had normal ultrasound scans. There was no correlation between ABR abnormalities and the severity of the PVH. Infants with abnormal ABRs but without changes in the ultrasound scan (non-PVH group) showed more rapid resolution of their abnormal auditory brainstem responses than those with PVH.

This particular part of the study showed the ABR to be a sensitive tool for detecting abnormalities before they appear on the ultrasound scan. ABR abnormalities can clearly reflect disturbances other than gross structural ones.

A final aim was to investigate the use of ABRs in the study of infants with posthaemorrhagic ventricular dilatation. ABRs performed during the period of maximal ventricular dilatation showed various patterns ranging from normality to absent responses. When serial ABRs were studied in parallel with the evolution of PHVD it was found that the ABR abnormalities usually resolved irrespective of the persistence or even progression of the ventricular dilatation. There was no correlation between conduction time through brainstem pathways (as reflected by IPI I-V) and CSF

pressure. In patients with PHVD it was shown that improvement in the ABR might occur when CSF was withdrawn. Intermittent CSF withdrawal (by ventricular tap or lumbar puncture) could be followed by ABR improvement after a period of 24 hours (but not sooner).

Judgements about hearing deficits were not always conclusive when based solely on ABR data obtained prior to discharge. Subsequent ABR testing (at follow up) improved the diagnostic accuracy considerably. Conclusions regarding hearing loss based solely on ABRs elicited in the NICU should be guarded. Behavioural and audiological testing should also be performed before a final diagnosis of hearing loss is made. ABR abnormalities may reflect transient disturbances.

The elucidation of exact pathogenesis is necessary to achieve one of the paediatrician's ultimate goals, namely that of preventing brain lesions and their sequelae. Any attempt to analyse what predisposes to ABR abnormalities must take into account both anatomical and physiological factors which alter the distribution or regulation of the cerebral blood flow, and in particular the effects of such changes upon the auditory brainstem pathway. It is against this background of decreased blood supply, and associated risks that the preterm ABR has to be studied. If, in addition to the above factors there is the additional element of 'immaturity' it is hardly

surprising that the ABR will reflect an inability to generate or transmit electrical impulses.

The audiological implications of abnormal ABRs are now well established. The ABR successfully fulfills the need for early detection of hearing deficits in infants at high risk. Its increasing use for continuous assessment and monitoring of brainstem function is still however in its infancy and the full potential of the ABR in neonatal practice has still to be exploited.

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DECLARATION

This is to certify that all the ABR interpretations were carried out by muself as author of this thesis. The vast majority of the ABRs themselves were also personally performed. A few were carried out by Dr. Lilly Dubowitz, Dr. Helen Skouteli, Dr. George Brassioulis, and Dr. Linda DeVries.

APPENDIX I.

Postnatal complication score (Drillien et al 1980)

Score 0 No complications. Apgar 7-10 at 1 minute. Jaundice less than 150 umol/l

Score 1 Minor complications, initial resuscitation. Apgar 7-10 at 5 minutes. Jaundice less than 200 umol/l, responding to phototherapy. Mild respiratory distress, not requiring specific treatment.

Score 2 Moderate complications. Birth asphyxia requiring intubation, quick recovery less than 3 days. Jaundice more than 200 umol/l. other complications, not severe enough to be included in score 3.

Score 3 Severe complications. Infant's condition causing anxiety for weeks or longer. Repeated apnoeic attacks. Respiratory distress requiring ventilation for more than 3 days. Jaundice requiring exchange transfusion. Cardiac arrest, convulsions.

TABLE A1

POSTNATAL COMPLICATION SCORES IN 'OPTIMAL' INFANTS

NO	SEX	G.A. (wk)	B.W. (gm)	ANTENATAL COMPLICATION	DELIVERY
1.	M	27	1110	PROM	vaginal
2.	F	28	1080	bradycardia	C.S.
3.	F	28	1000	PROM, foetal distress	C.S.
4.	F	29	960	PET	C.S. (elective)
5.	F	29	1160	foetal distress	C.S.
6.	F	29	950	PROM	C.S.
7.	F	30	1215	PET	C.S. (elective)
8.	F	31	1250	PROM,twin pregnancy	C.S.
9.	F	31	1260	PROM " "	C.S.
10.	F	31	1480	PROM	C.S.
11.	F	31	1580	hypertension	C.S.
12.	F	31	1136	hypertension	C.S.
13.	F	31	1630	irritable uterus	vaginal
14	F	31	1140	PET	C.S.
15.	F	32	1210	Multiple pregnancy	C.S.
16.	M	32	1831	" "	C.S.
17.	M	32	1850	PROM	vaginal
18.	M	32	1500	intermittent bleeding	C.S.
19.	F	32	1350	multiple pregnancy	C.S. (elective)
20.	M	32	1210	" "	C.S. "
21.	M	32	1400	PROM	vaginal
22.	M	33	1740	PET	C.S. (elective)
23.	M	33	1640	twin pregnancy	vaginal
24.	M	33	2025	threatened abortion	" (breech)
25.	M	33	1410	uneventful	"
26.	M	33	2080	PET	C.S.
27.	F	33	1500	PET	C.S.
28.	M	34	2450	uneventful	vaginal (breech)
29.	F	35	1650	multiple pregnancy	C.S.
30.	F	35	1810	twin pregnancy	vaginal
31.	F	35	1450	uneventful	C.S.
32.	F	36	2900	polyhydramnios	vaginal
33.	F	36	2220	-	"
34.	M	36	1720	maternal aplastic anaemia	vaginal

TABEL A1 (continue)

NO	SEX	G.A. (wk)	B.W. (gm)	ANTENATAL COMPLICATION	DELIVERY
35.	F	36	2300	foetal distress	C.S.
36.	M	37	3400	-	vaginal
37.	F	38	3100	-	"
38.	M	38	2960	-	"
39.	M	38	3440	-	"
40.	M	38	2500	-	"
41.	F	38	3460	-	"
42.	F	38	2360	-	"
43.	F	39	2860	-	"
44.	F	39	3100	-	"
45.	F	39	3400	-	"
46.	F	39	3520	-	"
47.	F	40	3290	-	"
48.	M	40	3620	-	"
49.	F	40	2980	-	"
50.	F	40	3700	-	"
51.	F	40	3280	-	"
52.	F	40	3700	-	"
53.	F	41	3180	-	"
54.	F	41	3090	-	"
55.	F	41	3280	-	"
56.	F	41	3660	-	"

TABEL A1 (continue)

No	APGAR SCORE ( ) 7-10) 1 min	5 min	INITIAL RESUSCITATION	RDS (mild)	BILIRUBIN (umol/l) <150	150-200	SCORE 0/1
1.	7	9	-	-	-	170	1
2.	8	9	-	-	-	150	1
3.	6	8	+	+	140	-	1
4.	7	9	-	-	120	-	0
5.	3	7	+	+	70	-	1
6.	6	9	-	+	130	-	1
7.	3	9	+	+	-	170	1
8.	3	7	+	-	125	-	1
9.	8	9	-	-	120	-	0
10	6	8	+	-	-	-	0
11.	9	10	+	-	-	-	1
12.	8	9	-	-	-	190	1
13.	5	7	-	-	-	170	1
14.	3	8	-	+	-	170	1
15.	9	10	-	-	-	160	1
16.	6	9	+ (1 min)	-	-	170	1
17.	8	10	-	-	-	-	0
18.	4	7	-	-	140	-	0
19.	7	9	-	-	-	-	0
20.	4	7	+	-	-	160	1
21.	5	9	-	+	-	-	1
22.	8	9	-	-	-	-	0
23.	5	9	+	+	-	180	1
24.	8	10	-	-	130	-	0
25.	3	10	+ (2 min)	-	-	180	1
26.	6	9	+ (2 min)	-	-	160	1
27.	6	10	-	-	140	-	0
28.	8	9	-	+	-	190	1
29.	9	9	-	-	140	-	0
30.	7		-	-	-	-	0
31.	6	8	+ (2 min)	-	140	-	1
32.	9	9	-	-	-	150	1
33.	9	9	-	-	-	-	0
34.	8	9	-	-	-	190	1
35.	9	9	-	-	-	155	1
36.	9	9	-	-	-	-	0
37.	9	9	-	-	-	-	0
38.	8	9	-	-	-	-	0
39.	9	9	-	-	-	-	0
40.	8	9	-	-	-	-	0

TABEL A1 (continue)

No	APGAR SCORE (> 7-10) 1 min	5 min	INITIAL RESUSCITATION	RDS (mild)	BILIRUBIN (umol/l) <150	150-200	SCORE 0/1
41.	9	9	-	-	-	-	0
42.	9	10	-	-	-	-	0
43.	8	9	-	-	-	-	0
44.	8	10	-	-	-	-	0
45.	9	9	-	-	-	-	0
46.	9	9	-	-	-	-	0
47.	9	9	-	-	-	-	0
48.	9	10	-	-	-	-	0
49.	9	9	-	-	-	-	0
50.	8	9	-	-	-	190	1
51.	9	10	-	-	-	-	0
52.	9	9	-	-	-	-	0
53.	9	9	-	-	-	-	0
54.	9	10	-	-	-	-	0
55.	9	10	-	-	-	-	0
56.	8	10	-	-	-	-	0

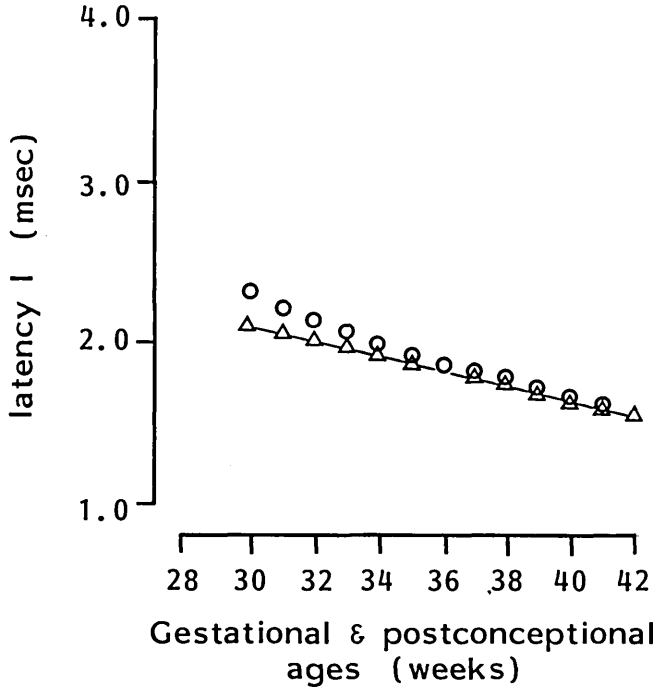
APPENDIX II

COMPARISON OF CROSS-SECTIONAL AND LONGITUDINAL DATA OF WAVE LATENCIES I AND V

To demonstrate both intra and extra-uterine maturation the cross-sectional and longitudinal data were compared (for waves I and V elicited at 80 dB). The cross-sectional and longitudinal data were fitted by quadratic curves and were plotted separately (figures 1 and 2 below, where cross-sectional data are represented by circles and longitudinal data by trianles).

At ages of 31 weeks or less there was a small but insignificant difference between the cross-sectional and longitudinal data (see graphs).

1.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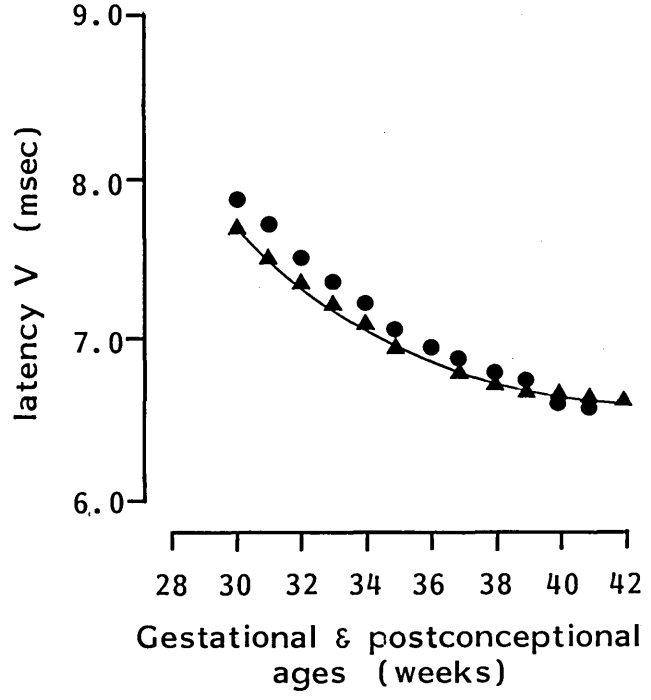
3.0
2.0
1.0
latency I (msec)
28 30 32 34 36 38 40 42
Gestational & postconceptional
ages (weeks)

2.


9.0
8.0
7.0
6.0
latency V (msec)
28 30 32 34 36 38 40 42
Gestational & postconceptional
ages (weeks)

APPENDIX III
THE PROTOCOL

NAME: DOB HOSP NO.

PREGNANCY:

Abnormal pregnancy.....Y=1 N=0
PET.....
hypertension.....
haemorrhage.....

Delivery:
Vaginal:.....Y=1 N=0
vertex.....
breech.....
forceps.....
CS:.....Y=1 N=0

Fetal distress : .....Y=1 N=0
abnormal CTG .....
tachy or bradycardia...
meconium .....

Maternal drugs:.....Y=1 N=0
tocolytics.....
steroids.....
others.....

NEONATAL PERIOD:

Sex: .....M=1 F=2

GA (weeks)
by dates .....
by assessment .....

BW (gms)

Apgar score: 1 min
5 mins

Asphyxia:.....Y=1 N=0

Ventilation:.....Y=1 N=0
at resuscitation only .....
longer .....
duration .....

Acidosis: (pH <7.2):.....Y=1 N=0
No of episodes during 1st week of life
episodes lasting > one week

Hypoxia: (PO2 <5 KPa):.....Y=1 N=0
No of episodes during 1st week of life
episodes lasting > one week

Hypercapnia (PCO2 >8 KPa):.....Y=1 N=0
No of episodes during 1st week of life
episodes lasting > one week
(Severe fluctuation)

Apnea: (early ....,late >1 week...).....Y=1 N=0
with bradycardia .....Y=1 N=0

Jaundice .....Y=1 N=0
peak .....umol/l
date .....
duration .....
phototherapy .....
exchanged .....

Respiratory disorders: ..... N=0
RDS ..... Y=1
Pnx ..... Y=2
Others .....Y=3

Cardiovascular disorders:.....N=0
PDA .....Y=1
Others .....Y=2

Blood disorders: None.....N=0
Polycythaemia .....Y=1
Anaemia .....Y=2
Others .....Y=3

Infection: .....Y=1 N=0

Drugs: None .....N=0
Aminoglycosides .....Y=1
Others .....Y=2

Convulsions .....Y=1 N=0

US Scan Normal .....N=0
PVH-IVH .....Y=1
Other abnormalities .....Y=2

Grading of PVH None.....N=0
Grade I .....Y=1
" II .....Y=2
" III .....Y=3

Neurological examinations:
1st week
Normal ..... N=0
Abnormal .....Y=1
(abnormality of tone pattern, movement, and/or alertnes)

Discharge
Tone + alertness appropriate for age.....N=0
Difficult to assess/doubtful.....Y=1
Abnormal .....Y=2

TABLE A2
RISK FACTORS ASSESSED IN RELATION TO THEIR POSSIBLE EFFECTS ON THE ABR

ROW	PREGN	DELIVERY	FET DIST	MAT DRUG	SEX
1	1	1	1	1	2
2	1	1	0	1	2
3	0	1	0	1	2
4	0	1	0	1	2
5	1	1	0	1	2
6	1	1	0	1	1
7	1	1	0	*	2
8	1	2	0	1	1
9	1	1	0	1	2
10	1	2	*	1	1
11	1	1	0	2	2
12	1	2	1	1	2
13	0	1	0	1	2
14	1	2	0	1	1
15	0	1	0	1	1
16	1	1	1	1	1
17	1	2	1	1	2
18	1	2	1	1	2
19	1	1	0	1	1
20	1	1	0	1	2
21	0	1	0	0	2
22	1	2	0	2	1
23	1	2	0	1	1
24	1	1	0	1	2
25	1	1	0	1	1
26	1	1	0	0	1
27	1	2	0	1	2
28	1	2	1	1	2
29	1	2	0	1	2
30	1	2	1	1	1
31	1	1	0	1	2
32	1	2	0	1	1
33	1	1	0	1	1
34	1	1	1	0	1
35	1	1	1	1	1
36	0	1	0	0	2
37	1	2	1	1	1
38	0	2	0	0	1
39	1	2	1	1	2
40	1	2	1	1	2
41	1	1	0	1	1

TABLE A2 (continue)

ROW	PREGN	DELIVERY	FET DIST	MAT DRUG	SEX
42	1	2	1	0	1
43	1	2	0	1	1
44	1	1	0	2	2
45	1	1	0	0	2
46	1	2	0	1	2
47	1	2	0	1	1
48	0	1	0	1	1
49	1	2	0	1	1
50	0	1	0	0	1
51	1	1	0	0	1
52	0	1	1	1	1
53	0	1	0	0	1
54	1	1	0	1	1
55	1	2	*	1	1
56	1	2	0	2	1
57	1	2	0	1	1
58	1	1	0	0	1
59	1	2	0	1	1
60	0	2	1	*	1
61	0	2	1	*	2
62	1	2	0	2	2
63	1	1	1	1	1
64	0	1	0	0	1
65	1	2	0	2	2
66	0	1	0	1	1
67	1	1	0	0	2

TABLE A2
RISK FACTORS ASSESSED IN RELATION TO THEIR POSSIBLE EFFECTS ON THE ABR

ROW	PREGN	DELIVERY	FET DIST	MAT DRUG	SEX
1	1	1	1	1	2
2	1	1	0	1	2
3	0	1	0	1	2
4	0	1	0	1	2
5	1	1	0	1	2
6	1	1	0	1	1
7	1	1	0	*	2
8	1	2	0	1	1
9	1	1	0	1	2
10	1	2	*	1	1
11	1	1	0	2	2
12	1	2	1	1	2
13	0	1	0	1	2
14	1	2	0	1	1
15	0	1	0	1	1
16	1	1	1	1	1
17	1	2	1	1	2
18	1	2	1	1	2
19	1	1	0	1	1
20	1	1	0	1	2
21	0	1	0	0	2
22	1	2	0	2	1
23	1	2	0	1	1
24	1	1	0	1	2
25	1	1	0	1	1
26	1	1	0	0	1
27	1	2	0	1	2
28	1	2	1	1	2
29	1	2	0	1	2
30	1	2	1	1	1
31	1	1	0	1	2
32	1	2	0	1	1
33	1	1	0	1	1
34	1	1	1	0	1
35	1	1	1	1	1
36	0	1	0	0	2
37	1	2	1	1	1
38	0	2	0	0	1
39	1	2	1	1	2
40	1	2	1	1	2
41	1	1	0	1	1

TABLE A2 (continue)

ROW	PREGN	DELIVERY	FET DIST	MAT DRUG	SEX
42	1	2	1	0	1
43	1	2	0	1	1
44	1	1	0	2	2
45	1	1	0	0	2
46	1	2	0	1	2
47	1	2	0	1	1
48	0	1	0	1	1
49	1	2	0	1	1
50	0	1	0	0	1
51	1	1	0	0	1
52	0	1	1	1	1
53	0	1	0	0	1
54	1	1	0	1	1
55	1	2	*	1	1
56	1	2	0	2	1
57	1	2	0	1	1
58	1	1	0	0	1
59	1	2	0	1	1
60	0	2	1	*	1
61	0	2	1	*	2
62	1	2	0	2	2
63	1	1	1	1	1
64	0	1	0	0	1
65	1	2	0	2	2
66	0	1	0	1	1
67	1	1	0	0	2

TASBLE A2 (continue)

ROW	GEST AGE	B.W. GRM	APGAR 1M	APGAR 5M	APHYXIA
1	27	1	2	2	0
2	27	1	2	2	0
3	28	2	2	2	0
4	28	2	2	2	0
5	28	1	2	2	0
6	28	2	2	2	0
7	28	1	1	2	1
8	28	1	2	2	0
9	28	1	2	2	0
10	29	1	1	1	1
11	29	2	1	2	1
12	29	1	1	2	1
13	29	2	2	2	0
14	29	2	2	2	0
15	29	3	2	2	0
16	29	2	2	1	1
17	29	2	1	2	1
18	29	1	2	2	0
19	30	1	2	2	0
20	30	2	1	2	1
21	30	2	2	2	0
22	30	2	1	2	1
23	30	3	2	2	0
24	30	2	1	*	1
25	30	2	2	2	0
26	30	3	1	2	0
27	30	2	2	2	0
28	30	2	2	2	1
29	30	2	2	2	1
30	30	2	1	2	1
31	30	2	1	2	0
32	30	1	1	2	0
33	30	3	2	2	0
34	31	3	2	2	0
35	31	3	2	2	0
36	31	3	2	2	1
37	31	1	2	2	0
38	31	3	1	2	1
39	31	2	2	2	0
40	31	2	1	2	1
41	32	2	2	2	0
42	32	2	2	2	0

TABLE A2 (continue)

ROW	GEST AGE	B.W. GRM	APGAR 1M	APGAR 5M	APHYXIA
43	32	3	1	2	1
44	32	3	2	2	0
45	32	3	2	2	0
46	32	2	2	2	0
47	32	3	2	2	0
48	32	3	2	2	0
49	32	2	1	2	1
50	32	3	2	2	0
51	32	3	2	2	0
52	32	2	1	2	1
53	32	3	2	2	0
54	32	3	2	2	0
55	32	3	1	*	1
56	32	2	2	2	0
57	33	2	2	2	0
58	33	2	2	2	0
59	33	3	2	2	0
60	33	3	2	2	0
61	33	2	2	2	0
62	33	2	2	2	0
63	34	3	1	2	1
64	34	3	2	2	0
65	34	3	2	2	0
66	34	3	2	2	0
67	34	2	2	2	0

TABLE A2 (continue)

ROW	VENTILN	PH 1WK	PH >1WK	P02 1WK	P02 >1WK	PC02 1WK
1	*	0	0	0	0	0
2	0	0	0	0	0	0
3	0	*	*	*	*	*
4	1	*	*	*	*	*
5	1	1	0	1	0	1
6	0	0	0	0	0	0
7	1	1	1	1	1	0
8	1	0	0	0	0	0
9	0	0	0	0	0	0
10	1	1	0	1	0	1
11	0	0	0	0	0	0
12	0	1	0	0	0	0
13	1	1	1	1	0	1
14	1	1	0	1	0	0
15	0	0	0	0	0	0
16	0	0	0	0	0	0
17	0	1	0	0	0	1
18	0	0	0	0	0	0
19	0	0	0	0	1	0
20	1	1	0	1	0	1
21	1	1	1	0	0	1
22	1	1	0	0	0	0
23	0	0	0	0	0	0
24	1	1	*	0	*	0
25	0	0	0	0	0	0
26	1	1	0	1	0	1
27	0	0	0	0	0	0
28	0	0	0	0	0	0
29	0	0	0	0	0	0
30	0	0	0	0	0	0
31	0	0	0	1	0	0
32	1	0	0	0	0	0
33	0	0	0	0	0	0
34	1	1	*	0	0	1
35	0	0	0	0	0	0
36	0	1	0	0	0	1
37	0	0	0	0	0	0
38	1	1	*	1	*	1
39	0	0	0	0	0	0
40	1	0	0	0	0	0
41	1	0	0	0	0	0
42	0	0	0	0	0	0

TABLE A2 (continue)

ROW	VENTILN	PH 1WK	PH >1WK	PO2 1WK	PO2 >1WK	PCO2 1WK
43	1	1	0	1	0	1
44	0	0	0	0	0	0
45	0	0	0	0	0	0
46	0	0	0	0	0	0
47	1	0	0	1	0	0
48	0	0	0	0	0	0
49	0	0	0	0	0	0
50	0	0	0	0	0	0
51	0	0	0	0	0	0
52	0	0	0	0	0	0
53	0	0	0	0	0	0
54	0	0	0	0	0	0
55	1	1	0	0	0	0
56	1	1	0	1	0	1
57	1	1	0	0	0	1
58	0	0	0	0	0	0
59	0	0	0	0	0	0
60	1	1	0	1	0	1
61	0	0	0	0	0	0
62	0	0	0	0	0	0
63	0	0	0	0	0	0
64	0	1	0	0	0	0
65	0	0	0	0	0	0
66	0	0	0	0	0	0
67	0	0	0	0	0	0

TABLE A2 (continue)

ROW	PCO2 >1WK	APNEA	+BRADY	JAUNDICE	PEAK	DURATION
1	0	1	1	0	165	4
2	0	1	1	0	170	2
3	*	1	1	0	160	2
4	*	1	1	0	160	2
5	1	1	1	2	240	7
6	0	0	0	0	180	3
7	1	1	1	0	140	7
8	0	1	1	1	220	3
9	0	0	0	0	160	3
10	0	1	1	0	180	5
11	0	0	0	2	240	8
12	0	0	0	0	180	5
13	1	0	0	1	200	7
14	0	1	1	1	230	13
15	0	*	*	1	220	2
16	0	1	1	1	225	3
17	0	0	0	0	70	0
18	0	0	0	0	130	2
19	1	1	1	0	180	3
20	0	1	1	2	245	7
21	1	0	0	2	280	8
22	0	0	0	0	190	2
23	0	0	0	0	190	10
24	*	1	1	1	220	7
25	0	1	1	0	140	2
26	0	1	1	1	210	5
27	0	0	0	0	100	0
28	0	0	0	1	200	2
29	0	0	0	0	190	8
30	0	1	1	0	180	5
31	0	1	1	0	170	4
32	0	0	0	0	150	4
33	0	0	0	1	230	6
34	*	0	0	1	220	2
35	0	0	0	0	150	5
36	0	0	0	2	240	7
37	0	1	0	0	100	0
38	*	1	1	0	180	3
39	0	0	0	0	100	0
40	0	0	0	1	210	7
41	0	1	1	1	200	5
42	0	0	0	2	300	16

TABLE A2 (continue)

ROW	PCO2 >1WK	APNEA	+BRADY	JAUNDICE	PEAK	DURATION
43	0	0	0	0	150	10
44	0	0	0	0	100	0
45	0	0	0	*	*	*
46	0	1	0	0	150	2
47	0	1	1	1	220	5
48	0	0	0	0	100	0
49	0	0	0	0	150	0
50	0	0	0	1	210	5
51	0	0	0	0	180	3
52	0	1	0	0	180	3
53	0	0	0	1	200	*
54	0	0	0	1	230	4
55	0	1	1	1	220	10
56	0	0	0	0	180	4
57	1	1	1	2	240	1
58	0	0	0	2	250	10
59	0	0	0	0	160	2
60	0	1	1	2	240	3
61	0	0	0	1	200	1
62	0	0	0	0	170	2
63	0	1	1	0	175	3
64	0	1	1	2	305	4
65	0	0	0	2	240	14
66	0	0	0	0	185	3
67	0	0	0	1	225	12

TABLE A2 (continue)

ROW	PHOTOTH	EXCHANGE	RESP	CVS	BLOOD	INFECT	DRUGS
1	1	0	1	1	*	2	1
2	1	0	0	0	0	0	1
3	1	0	0	0	0	2	1
4	1	0	3	0	0	1	1
5	1	0	2	1	2	1	1
6	1	0	0	0	2	1	1
7	1	0	1	1	*	1	1
8	1	0	3	0	0	0	2
9	1	0	0	1	2	0	1
10	1	0	1	1	2	0	1
11	1	0	1	0	0	0	1
12	1	0	1	0	0	1	1
13	1	0	2	1	0	1	1
14	1	0	1	0	0	0	1
15	1	0	3	0	0	0	2
16	1	0	3	0	0	0	1
17	0	0	1	1	0	0	1
18	0	0	0	1	2	2	2
19	1	0	0	0	2	1	1
20	1	0	1	0	2	0	1
21	1	0	2	0	0	2	1
22	1	0	1	1	0	2	1
23	1	0	0	0	0	0	1
24	1	0	3	1	2	0	1
25	1	0	1	0	0	0	1
26	1	0	1	1	1	1	1
27	0	0	0	0	0	0	2
28	1	0	0	0	0	1	2
29	1	0	1	1	0	0	2
30	0	0	0	1	0	0	2
31	0	0	1	0	0	0	2
32	1	0	3	0	0	*	2
33	1	0	0	0	0	0	0
34	1	0	1	0	0	0	1
35	0	0	3	0	0	0	0
36	1	0	1	2	0	0	0
37	0	0	0	0	0	1	1
38	0	0	1	0	2	1	2
39	0	0	0	0	0	0	0
40	1	0	0	0	0	0	0
41	1	0	1	2	2	0	1
42	1	0	3	1	0	1	1

TABLE A2 (continue)

ROW	PHOTOTH	EXCHANGE	RESP	CVS	BLOOD	INFECT	DRUGS
43	1	0	2	0	2	0	1
44	0	0	0	0	0	0	0
45	0	0	1	0	0	0	0
46	0	0	0	0	0	0	2
47	1	0	1	0	0	0	1
48	0	0	3	0	0	0	0
49	0	0	0	0	0	1	1
50	1	0	0	0	0	2	2
51	0	0	3	1	0	2	2
52	0	0	0	1	0	1	1
53	0	0	1	0	0	0	0
54	1	0	3	0	0	0	0
55	1	0	3	0	1	0	1
56	1	0	1	0	0	0	2
57	0	0	1	1	2	0	1
58	1	0	0	0	0	0	0
59	0	0	0	0	0	0	0
60	1	0	2	0	0	0	1
61	0	0	0	0	0	0	0
62	1	0	3	0	0	1	2
63	0	0	0	0	0	0	0
64	1	0	0	1	0	0	1
65	2	0	1	0	0	0	0
66	0	0	0	0	0	0	0
67	1	0	0	0	0	0	0

TABLE A2 (continue)

ROW	CNV	OTHER S	U.S.	GRADES	NEURO 1W	NEUR DIS
1	0	1	1	2	1	2
2	0	0	0	0	1	0
3	*	0	1	1	0	0
4	0	0	1	1	1	0
5	3	0	4	2	1	2
6	0	1	1	1	1	2
7	3	1	1	3	1	2
8	0	0	0	0	1	1
9	0	0	2	0	1	1
10	1	1	5	2	1	*
11	3	*	4	1	1	2
12	3	1	6	3	*	2
13	1	0	5	3	1	2
14	0	1	5	1	1	2
15	0	1	0	0	0	0
16	0	0	0	0	0	0
17	0	1	0	0	0	0
18	0	1	0	0	0	0
19	0	1	1	1	1	2
20	0	0	1	1	1	2
21	*	1	1	2	*	2
22	0	0	1	1	1	*
23	0	0	1	1	*	1
24	5	0	1	2	1	1
25	0	0	1	2	1	0
26	3	0	4	3	1	2
27	0	0	0	0	0	0
28	0	1	2	0	1	2
29	0	0	0	0	0	0
30	0	0	0	0	1	2
31	0	0	0	0	0	0
32	0	1	0	0	0	2
33	0	0	2	0	1	*
34	0	1	1	2	0	0
35	0	0	0	0	0	*
36	0	0	0	0	0	0
37	0	0	0	0	0	2
38	1	0	3	0	1	2
39	0	0	0	0	1	0
40	0	0	0	0	0	0
41	0	1	4	1	1	2
42	0	1	1	1	1	2

TABLE A2 (continue)

ROW	CNV	OTHER S	U.S.	GRADES	NEURO 1W	NEUR DIS
43	1	1	4	3	1	2
44	0	0	1	1	0	0
45	0	1	1	0	0	0
46	0	0	0	0	1	0
47	0	0	0	0	0	1
48	0	0	0	0	0	0
49	*	0	0	0	1	2
50	0	0	0	0	0	0
51	0	0	0	0	1	0
52	0	1	0	0	1	0
53	0	0	0	0	*	*
54	0	0	0	0	0	*
55	0	1	0	0	1	2
56	0	0	1	1	1	0
57	0	0	4	3	1	2
58	0	1	0	0	1	0
59	0	0	0	0	1	0
60	0	0	0	0	0	0
61	0	0	0	0	0	*
62	0	0	0	0	1	0
63	0	0	1	1	0	0
64	3	0	4	2	1	2
65	0	0	0	0	0	0
66	0	0	0	0	0	0
67	0	1	0	0	0	0

TABLE A2 (continue)

ROW	DEATH	ABR 1WK	ABR DIS	ABR OUT	PVH
1	0	1	0	0	1
2	0	1	0	0	0
3	0	1	0	0	1
4	0	1	0	0	1
5	0	1	1	0	1
6	0	1	0	0	1
7	0	1	1	0	1
8	0	1	1	0	0
9	0	1	0	0	0
10	1	1	*	*	1
11	0	1	1	0	1
12	0	1	1	1	1
13	0	1	0	0	1
14	0	1	0	0	1
15	0	1	0	0	0
16	1	1	0	*	0
17	0	0	0	0	0
18	0	0	0	0	0
19	0	1	1	1	1
20	0	1	0	0	1
21	0	1	1	1	1
22	0	1	0	0	1
23	0	1	0	0	1
24	0	1	1	0	1
25	0	1	0	0	1
26	0	1	1	0	1
27	0	1	0	0	0
28	0	0	0	0	0
29	0	0	0	0	0
30	0	1	0	0	0
31	0	0	0	0	0
32	0	0	0	0	0
33	1	0	0	*	0
34	0	1	1	0	1
35	0	0	0	0	0
36	0	0	0	0	0
37	0	0	0	0	0
38	0	1	1	0	0
39	0	1	0	0	0
40	0	0	0	0	0
41	0	1	0	0	1
42	0	1	1	0	1

TABLE A2 (continue)

ROW	DEATH	ABR 1WK	ABR DIS	ABR OUT	PVH
43	0	1	1	0	1
44	0	1	0	0	1
45	0	1	0	0	0
46	0	1	0	0	0
47	0	0	0	0	0
48	0	0	0	0	0
49	0	1	0	0	0
50	1	0	0	*	0
51	0	0	0	0	0
52	0	0	0	0	0
53	0	0	0	0	0
54	0	0	0	0	0
55	0	1	1	0	0
56	0	1	0	0	1
57	0	1	0	0	1
58	0	1	0	0	0
59	0	0	0	0	0
60	0	1	0	0	0
61	0	1	0	0	0
62	0	1	0	0	0
63	0	1	0	0	1
64	0	1	1	0	1
65	0	0	0	0	0
66	0	1	0	0	0
67	0	1	0	0	0

KEY TO ABR CODES:

PREGN : abnormal pregnancy
FET DIST : fetal distress
MAT DRUG : maternal drugs
GEST AGE : gestational age
BW (GM) : birth weight (grams)
APGAR 1M : Apgar score at 1 minute
APGAR 5M : " " " 5 minutes
VENTILN : ventilatory support
PH 1WK : acidosis (pH < 7.2) present during 1st week
PH >1WK : " " " " lasting more than 1 "
PO2 1WK : hypoxia (PO2 < 5 KPa) present during 1st "
PO2 >1WK : " " " " " lasting more than 1 "
PCO2 1WK : hypercapnia (PCO2 > 8 KPa) present during 1st week
PCO2 >1WK: " " " " " lasting more than 1 "
+ BRADY : Apnea + bradycardia
PEAK : peak bilirubin (umol/l)
PHOTOTH : phototherapy
EXCHANGE : exchange transfusion
RESP : respiratory disorders
CVS : cardiovascular disorders
BLOOD : blood disorders
INFECT : infection
DRUGS : drugs (gentamicin)
US : ultrasound scan
GRADES : grades of PVH
NEURO 1WK: neurological findings during 1st week
NEURO DIS: " " at discharge
ABR 1WK : ABR findings during 1st week
ABR DIS : " " at discharge
ABR OUT : " " at follow-up (outcome)
PVH : periventrcular haemorrhage

TABLE A3
RISK FACTORS PRESENT IN THE PVH AND NON-PVH GROUPS

RISK FACTOR*	PVH n=28	(%)	NON-PVH n=39	(%)	TOTAL n=67	(%)
Abnormal pregnancy	23	(82)	29	(74)	52	(77)
Caesarian delivery	09	(32)	21	(54)	30	(45)
Fetal distress	05	(18)	12	(31)	17	(26)
GA (< 30 wks)	19	(67)	14	(36)	33	(49)
BW (< 1000 gm)	06	(21)	06	(15)	12	(18)
(1000-1500 gm)	15	(53)	16	(41)	31	(46)
Abnormal Apgar score						
At 1 minute	10	(36)	09	(23)	19	(28)
At 5 minutes	01	(04)	01	(03)	02	(03)
Asphyxia	09	(32)	11	(28)	20	(30)
Ventilatory support	16	(59)	07	(18)	23	(35)
Acidosis: 1st week	16	(59)	05	(13)	23	(35)
> 1 week	03	(12)	00		03	(04)
Hypoxia: 1st week	09	(35)	04	(10)	13	(20)
> 1 week	02	(08)	00		02	(03)
Hypercapnia: 1st week	10	(38)	04	(10)	14	(21)
> 1 week	06	(25)	00		06	(09)
Apnea (+ bradycardia)	16	(57)	09	(24)	25	(37)
Jaundice	13	(46)	17	(43)	30	(45)
Blood disorders:anaemia	09	(35)	03	(08)	12	(18)
Drugs (gentamicin)	25	(89)	10	(26)	35	(52)

The vaious risk factors are defined in Chapter VI.

TABLE A4

ABR MEASUREMENTS IN PVH STUDY

ROW	GA	PVH	ABR CODE	LAT IL	LAT IR	SC IL	SC IR	LAT VL
1	27	1	6	0.00	0.00	0	0	0.00
2	27	0	5	0.00	2.80	0	2	0.00
3	28	1	3	3.00	3.60	1	1	10.60
4	28	1	3	3.20	3.00	1	1	11.00
5	28	1	6	0.00	0.00	0	0	0.00
6	28	1	5	0.00	0.00	0	0	0.00
7	28	1	5	0.00	0.00	0	0	0.00
8	28	0	3	3.60	3.70	1	1	10.20
9	28	0	4	3.30	4.30	1	2	9.50
10	29	1	3	3.50	3.20	1	1	11.60
11	29	1	3	2.00	2.20	1	1	10.20
12	29	1	6	4.00	0.00	2	0	10.30
13	29	1	5	0.00	2.00	0	1	0.00
14	29	1	5	0.00	3.20	0	1	0.00
15	29	0	3	2.85	2.80	1	1	10.10
16	29	0	3	2.80	2.82	1	1	9.36
17	29	0	1	2.80	2.80	1	1	8.70
18	29	0	1	1.92	2.32	1	1	7.60
19	30	1	6	0.00	0.00	0	0	0.00
20	30	1	5	0.00	0.00	0	0	0.00
21	30	1	6	0.00	0.00	0	0	0.00
22	30	1	3	3.36	2.88	1	1	9.76
23	30	1	3	2.10	2.10	1	1	9.20
24	30	1	3	2.74	2.00	1	1	10.20
25	30	1	4	2.30	4.00	1	2	9.70
26	30	1	3	2.00	2.38	1	1	8.60
27	30	0	4	3.40	4.00	1	2	9.20
28	30	0	1	1.92	2.32	1	1	7.60
29	30	0	1	2.64	2.72	1	1	7.92
30	30	0	3	2.64	2.74	1	1	9.36
31	30	0	1	2.40	2.64	1	1	7.50
32	30	0	1	2.20	2.30	1	1	7.60
33	30	0	1	2.60	2.40	1	1	7.60
34	31	1	3	2.30	2.60	1	1	8.70
35	31	0	1	2.50	2.30	1	1	7.70
36	31	0	1	3.26	3.08	1	1	8.72
37	31	0	1	3.20	2.80	1	1	8.60

TABLE A4 (continue)

ROW	GA	PVH	ABR CODE	LAT IL	LAT IR	SC IL	SC IR	LAT VL
38	31	0	3	1.92	1.94	1	1	9.28
39	31	0	4	2.90	4.40	1	2	8.20
40	31	0	1	2.32	2.72	1	1	7.76
41	32	1	4	3.60	3.20	2	1	10.80
42	32	1	4	2.88	3.20	1	2	9.60
43	32	1	4	2.20	3.50	1	2	9.00
44	32	1	3	2.00	1.60	1	1	7.80
45	32	1	6	2.00	0.00	1	0	8.80
46	32	0	4	3.20	3.28	2	2	8.24
47	32	0	1	2.20	2.60	1	1	7.40
48	32	0	1	2.70	3.08	1	1	8.06
49	32	0	2	3.40	3.80	2	2	8.40
50	32	0	1	2.32	2.32	1	1	7.44
51	32	0	1	2.24	2.40	1	1	7.28
52	32	0	1	1.92	1.84	1	1	7.28
53	32	0	1	2.20	2.10	1	1	7.40
54	32	0	1	2.12	2.12	1	1	7.88
55	32	0	3	2.72	2.16	1	1	8.96
56	32	0	4	2.32	3.12	1	2	7.76
57	33	1	3	2.00	2.00	1	1	8.08
58	33	0	3	2.60	2.60	1	1	8.90
59	33	0	1	2.48	2.72	1	1	8.00
60	33	0	3	2.48	2.22	1	1	7.82
61	33	0	4	2.70	3.30	1	2	8.00
62	33	0	3	2.72	2.56	1	1	8.72
63	34	1	4	5.00	3.60	2	2	11.50
64	34	1	3	1.92	2.00	1	1	7.86
65	34	0	1	3.20	3.20	1	1	7.80
66	34	0	4	4.00	3.20	2	2	10.00
67	34	0	3	1.98	2.08	1	1	8.72

TABLE A4 (continue)

ROW	LAT VR	SC VL	SC VR	IPI L	IPI R	SC IPIL	SC IPIR
1	0.00	0	0	0.00	0.00	0	0
2	10.20	0	2	0.00	7.40	0	2
3	11.80	2	2	7.60	8.20	2	2
4	10.60	2	2	7.80	7.60	2	2
5	0.00	0	0	0.00	0.00	0	0
6	0.00	0	0	0.00	0.00	0	0
7	0.00	0	0	0.00	0.00	0	0
8	9.60	2	2	6.60	5.90	2	1
9	10.80	1	2	6.20	6.50	2	2
10	11.50	2	2	8.10	8.30	2	2
11	10.20	2	2	8.20	8.00	2	2
12	0.00	2	0	6.30	0.00	2	0
13	8.00	0	1	0.00	6.00	0	2
14	10.30	0	2	0.00	7.10	0	2
15	10.80	2	2	7.25	8.00	2	2
16	10.10	2	2	6.56	7.28	2	2
17	8.69	1	1	5.90	5.89	1	1
18	8.00	1	1	5.68	5.68	1	1
19	0.00	0	0	0.00	0.00	0	0
20	0.00	0	0	0.00	0.00	0	0
21	0.00	0	0	0.00	0.00	0	0
22	9.04	2	1	6.40	6.16	2	2
23	8.60	2	1	7.10	6.50	2	2
24	8.60	2	2	7.46	6.80	2	2
25	9.10	2	1	7.40	5.10	2	1
26	8.40	2	1	6.64	6.02	2	2
27	9.20	2	2	5.80	5.20	1	1
28	8.00	1	1	5.68	5.68	1	1
29	8.32	1	1	5.60	5.60	1	1
30	9.88	2	2	6.72	7.14	2	2
31	7.60	1	1	5.12	4.96	1	1
32	7.60	1	1	5.40	5.30	1	1
33	7.50	1	1	5.00	5.10	1	1
34	9.50	1	2	6.20	6.80	2	2
35	7.90	1	1	5.20	5.50	1	1
36	8.78	1	1	5.47	5.70	1	1
37	8.00	1	1	5.40	5.20	1	1
38	9.84	1	2	6.00	7.90	2	2
39	10.40	1	2	5.80	6.00	1	2
40	8.00	1	1	5.44	5.28	1	1
41	10.00	2	2	7.20	6.80	2	2
42	9.16	2	2	6.72	5.96	2	2

TABLE A4 (continue)

ROW	LAT VR	SC VL	SC VR	IPI L	IPI R	SC IPIL	SC IPIR
43	9.50	2	2	6.80	6.10	2	2
44	6.80	1	1	5.80	5.20	2	1
45	0.00	2	0	6.80	0.00	2	0
46	8.08	2	2	5.04	4.88	1	1
47	7.80	1	1	5.20	5.20	1	1
48	8.60	1	1	5.36	5.52	1	1
49	8.50	1	1	5.00	4.70	1	1
50	7.20	1	1	5.12	4.88	1	1
51	7.20	1	1	5.05	4.80	1	1
52	7.28	1	1	5.36	5.44	1	1
53	7.30	1	1	5.20	5.20	1	1
54	7.82	1	1	5.76	5.70	1	1
55	8.12	2	1	6.20	5.96	2	2
56	7.84	1	1	5.44	4.72	1	1
57	8.84	1	2	6.08	6.84	2	2
58	8.70	1	1	5.30	6.10	1	2
59	7.60	1	1	5.52	4.88	1	1
60	7.60	1	1	5.34	5.38	1	1
61	8.60	1	2	5.30	5.30	1	1
62	8.56	2	2	6.00	5.92	2	2
63	10.00	2	2	6.50	6.40	2	2
64	7.88	2	2	5.94	5.88	2	2
65	7.60	1	1	4.60	4.40	1	1
66	8.10	2	1	6.00	4.90	2	1
67	8.32	2	2	6.80	6.24	2	2

TABLE A4 (continue)

ROW	V:I L	V:I R	SC V:IL	SC V:IR	SC V:VIL	SC V:VIR
1	0.00	0.00	0	0	0	0
2	0.00	1.10	0	1	0	2
3	0.40	0.40	2	2	2	2
4	0.36	0.40	2	2	2	2
5	0.00	0.00	0	0	0	0
6	0.00	0.00	0	0	0	0
7	0.00	0.00	0	0	0	0
8	0.70	0.80	1	1	1	1
9	0.70	0.70	1	1	2	1
10	0.57	0.50	1	1	2	2
11	0.35	0.45	2	2	2	2
12	1.50	0.00	1	0	2	0
13	0.00	0.32	0	2	0	1
14	0.00	1.00	0	1	0	2
15	1.80	0.75	1	1	2	2
16	0.60	0.75	1	1	2	2
17	0.60	1.00	1	1	1	1
18	0.50	1.10	1	1	1	1
19	0.00	0.00	0	0	0	0
20	0.00	0.00	0	0	0	0
21	0.00	0.00	0	0	0	0
22	0.60	1.10	1	1	2	1
23	1.00	1.00	1	1	1	1
24	1.60	0.40	1	2	2	2
25	1.00	1.80	1	1	2	1
26	0.40	0.80	2	1	2	1
27	0.50	0.60	1	1	1	1
28	0.50	1.10	1	1	1	1
29	1.90	1.20	1	1	1	1
30	0.60	0.80	1	1	1	1
31	0.75	0.56	1	1	1	1
32	0.70	0.90	1	1	1	1
33	0.60	0.80	1	1	1	1
34	1.10	1.30	1	1	1	2
35	1.20	1.00	1	1	1	1
36	1.10	1.00	1	1	1	1
37	1.60	1.30	1	1	1	1
38	0.27	0.70	2	1	1	1
39	1.40	1.50	1	1	1	1
40	0.90	0.70	1	1	1	1
41	0.38	1.00	2	1	2	2
42	0.56	1.80	1	1	2	2

TABLE A4 (continue)

ROW	V:I L	V:I R	SC V:IL	SC V:IR	SC V:VIL	SC V:VIR
43	0.50	0.59	1	1	2	2
44	0.40	0.50	2	1	2	1
45	0.60	0.00	1	0	2	0
46	0.90	0.40	1	2	1	1
47	0.60	0.60	1	1	1	1
48	0.60	1.10	1	1	1	1
49	1.30	1.00	1	1	1	1
50	1.10	1.60	1	1	1	1
51	1.10	2.50	1	1	1	1
52	0.68	0.70	1	1	1	1
53	0.80	1.00	1	1	1	1
54	0.54	1.30	1	1	1	1
55	1.80	1.00	1	1	2	1
56	0.38	0.70	2	1	1	1
57	0.33	0.37	2	2	1	2
58	0.50	0.60	1	1	1	1
59	0.57	0.53	1	1	1	1
60	0.56	0.57	1	1	1	1
61	0.90	2.00	1	1	1	2
62	0.53	0.89	1	1	1	1
63	0.90	0.70	1	1	2	2
64	0.45	0.50	2	1	2	1
65	1.80	1.00	1	1	1	1
66	0.90	2.70	1	1	1	1
67	0.40	0.70	2	1	1	1

KEY TO THE COMPUTER CODE IN TABLE A4

---

0 absent or severely reduced response
1 normal
2 abnormal

CODE	KEY
GA	Gestational age
PVH	Presence or absence of periventricular haemorrhage on ultrasound scan (0= absent, 1= present).
ABRCODE	1 = normal response, 2 = mild peripheral deficit, 3 = central, 4 = mixed deficit, 5 = severely reduced response, 6 = absent response
LAT IL	Latency of wave I from left ear
LAT IR	" " " " " right "
SC IL	Score " " " " left "
SC IR	" " " " " right "
LAT VL	Latency " " V " left "
LAT VR	" " " " " right "
SC VL	Score " " " " left "
SC VR	" " " " " right "
IPI L	Interpeak interval " left "
IPI R	" " " right "
SC IPIL	Score of interpeak interval from left ear
SC IPIR	" " " " " right "
V:I L	Amplitude ratio V:I from left ear
V:I R	" " " " right "
SC V:IL	Score for amplitude ratio V:I from left ear
SC V:IR	" " " " " " right "
SC V:VIL	Fusion for waves V and VI " " left "
SC V:VIR	" " " " " " " " right "

TABLE A5

ABR MEASUREMENTS IN INFANTS WITH POST-HAEMORRHAGIC VENTRICULAR DILATATION (n=19).

	PCA (wks)	Wave V LATENCY L	R	IPI (I-V) L	R	RATIO (V:I) L	R	ABR CODING
1	33	0	0	0	0	0	0	SI
2	34	6.00	6.88	4.0	4.5	1.2	0.9	DIPI
3	43	0*	0*	0*	0*	0*	0*	NREP
4	35	8.6	7.9	4.4	4.5	1.1	2.0	P(SND)
5	31	9.6	9.6	6.3	5.6	1.9	0.8	C
6	32	8.08	7.68	5.92	5.76	1.2	1.0	C
7	46	6.44	6.28	4.7	4.6	1.0	0.9	N
8	34	6.80	7.8	5.2	5.0	1.0	0.6	N
9	39	7.4	7.4	5.2	5.3	0.9	1.0	N
10	39	7.76	7.52	5.4	5.5	1.1	1.0	P (SND)
11	32	7.38	7.64	5.28	5.0	0.6	2.1	C
12	33	7.0	0	5.4	5.0	0.4	1.3	C
13	35	8.4	8.6	5.6	5.6	1.5	0.8	C
14	43	6.6	6.3	4.6	4.2	1.3	1.0	DIPI
15	36	8.6*	8.2*	5.6*	5.1*	0.7*	0.2*	NREP
16	42	7.12	7.44	4.8	4.96	0.9	0.7	N
17	42	6.64	7.26	4.3	4.4	0.9	0.7	N
18	47	6.90*	6.96*	5.1*	5.0*	0.9*	0.9*	NREP
19	53	0	6.96	0	4.6	0	1.4	SI

KEY TO ABR CODING IN TABLE A5

- C Central impairment
- DIPI Diminished interpeak interval (I-V)
- N Normal
- NREP (*) Non reproducile responses
- P Peripheral impairment of sensorineural type (SND)
- SI Severe impairment

TABLE A6

PHVD infants and the type of study performed:

	A	B	C	D		No of ABRs
				I	S	
1	+	+	-	-	-	3
2	+	-	++	-	+	3
3	+	-	-	-	-	2
4	+	+	-	-	-	2
5	+	+	-	-	-	7
6	+	+	+	-	-	3
7	+	+	+	-	-	7
8	+	-	++	+	-	9
9	+	+	-	+	-	14
10	+	+	-	-	-	7
11	+	-	-	-	-	3
12	+	+	+	-	-	8
13	+	+	++	-	-	7
14	+	+	++	-	+	7
15	+	-	-	+	-	7
16	+	+	-	-	-	8
17	+	-	++	-	+	4
18	+	-	-	+	+	3
19	+	+	++	-	-	10
Total	19	12	+9, ++6	7		114

KEY TO ABR STUDIES:

A PHVD (at time of maximum ventricular dilation) and ABR
B Evolution of PHVD and ABR
C CSF pressure and ABR
  + CSF pressure and ABR recorded
  ++ " " " " " within a couple of hours
D Effect of CSF drainage and ABR
  I = intermittent drainage
  S = shunt

80 dB: Latencies of Waves I and V

No	GA	L Lat I	R Lat I	Left V	Right V
1	28	2.280	2.400	8.120	8.240
2	28	2.200	2.280	7.640	7.760
3	29	2.800	2.640	8.480	8.240
4	29	2.820	3.040	8.800	9.200
5	29	1.920	2.320	7.600	8.000
6	30	2.000	2.080	7.440	7.280
7	31	2.080	2.040	7.480	7.400
8	31	2.640	2.720	8.400	8.320
9	31	2.160	2.440	7.760	7.960
10	31	2.320	2.220	7.680	7.440
11	31	2.240	2.180	8.200	8.200
12	31	2.000	1.840	7.680	7.440
13	32	2.000	2.080	7.180	7.160
14	32	2.400	2.200	7.280	7.160
15	32	1.820	2.400	7.460	8.080
16	32	2.520	1.880	8.080	7.400
17	32	2.080	1.920	7.520	7.360
18	32	2.400	2.480	7.760	7.680
19	33	2.080	1.840	7.440	7.120
20	33	2.240	2.400	7.280	7.200
21	33	2.480	2.080	7.880	7.440
22	33	1.840	2.080	7.280	7.360
23	33	2.720	2.640	8.030	7.600
24	33	1.920	1.840	7.280	7.280
25	34	2.120	2.160	7.320	7.280
26	35	2.000	1.760	7.040	6.880
27	35	1.680	1.840	6.800	7.200
28	36	1.680	1.480	6.680	6.440

80dB Latencies of Waves I and V

No	GA	Left I	Right I	Left V	Right V
29	36	2.000	1.840	6.960	6.880
30	36	2.160	2.080	7.360	7.200
31	36	1.760	1.840	6.960	6.880
32	37	1.600	1.520	6.800	6.560
33	38	2.000	1.740	6.760	6.520
34	38	1.620	1.400	6.220	6.080
35	38	1.600	1.680	6.720	6.720
36	38	1.760	1.920	7.000	7.120
37	38	1.520	1.620	6.780	6.740
38	38	1.680	1.520	6.640	6.720
39	39	1.400	1.480	6.080	6.080
40	39	1.920	1.760	7.200	7.040
41	39	1.520	1.440	6.800	6.880
42	40	1.520	1.520	6.240	6.320
43	40	1.680	1.920	6.640	6.800
44	40	1.680	1.680	6.800	6.800
45	40	1.720	1.880	6.720	6.860
46	40	1.600	1.680	6.640	6.880
47	40	1.840	1.440	6.560	6.560
48	41	2.000	1.920	7.120	6.960
49	41	1.760	1.760	6.800	6.720
50	41	1.600	1.520	6.480	6.320
51	41	1.520	1.600	6.640	6.640
52	30	1.960	2.220	7.600	7.820
53	30	2.320	2.480	7.920	8.000
54	30	2.480	2.240	8.280	8.000
55	30	1.920	1.920	7.440	7.520
56	31	1.800	1.880	7.280	7.400

80 dB: Latencies of Waves I and V

No	GA	Left I	Right	Left V	Right V
57	32	1.760	1.840	7.120	7.200
58	32	2.080	2.320	7.360	7.680
59	33	1.680	1.680	7.040	6.880
60	33	2.000	2.160	7.120	7.360
61	33	1.880	1.840	6.880	6.880
62	33	2.080	1.840	7.280	6.880
63	33	2.000	1.860	7.360	7.220
64	33	2.160	2.280	7.280	7.400
65	34	1.620	1.680	6.820	6.880
66	34	2.000	1.940	7.360	7.220
67	34	2.080	2.200	7.200	7.200
68	34	2.480	1.840	7.600	7.280
69	35	2.080	1.920	7.200	7.120
70	35	2.000	2.000	7.120	7.000
71	35	1.920	1.520	6.800	6.800
72	35	1.800	1.520	7.000	6.800
73	35	1.880	1.920	7.000	7.040
74	37	1.520	1.680	6.560	6.800
75	37	2.060	2.000	7.260	7.200
76	38	2.080	1.920	7.120	7.040
77	39	1.680	1.600	6.720	6.880
78	39	2.000	1.760	7.040	6.720
79	40	1.520	1.520	6.560	6.640
80	40	1.760	1.760	6.880	6.800
81	40	1.560	1.760	6.760	6.880
82	41	1.680	1.520	6.800	6.480
83	42	1.440	1.480	6.180	6.280

80dB IPI

No	Left	Right	No	Left	Right
1	5.840	5.040	29	4.960	5.040
2	5.440	5.480	30	5.200	5.120
3	5.680	5.600	31	5.200	5.040
4	5.980	6.160	32	5.200	5.040
5	5.680	5.680	33	4.760	4.780
6	5.440	5.200	34	4.600	4.680
7	5.400	5.360	35	5.120	5.040
8	5.760	5.600	36	5.240	5.200
9	5.600	5.520	37	5.260	5.120
10	5.360	5.380	38	4.960	5.200
11	5.960	6.020	39	4.680	4.600
12	5.680	5.600	40	5.280	5.280
13	5.180	5.080	41	5.280	5.440
14	4.880	4.960	42	4.720	4.800
15	5.640	5.680	43	4.960	4.880
16	5.560	5.520	44	5.120	5.120
17	5.440	5.440	45	5.000	4.980
18	5.360	5.200	46	5.040	5.200
19	5.360	5.280	47	4.720	5.120
20	5.040	4.800	48	5.120	5.040
21	5.400	5.360	49	5.040	4.960
22	5.400	5.280	50	4.880	4.800
23	5.310	4.960	51	5.120	5.040
24	5.360	5.440	52	5.640	5.600
25	5.200	5.120	53	5.600	5.520
26	5.040	5.120	54	5.800	5.760
27	5.120	5.360	55	5.520	5.600
28	5.000	4.960	56	5.480	5.520

80 dB IPI

No	Left	Right
57	5.360	5.360
58	5.280	5.360
59	5.360	5.200
60	5.120	5.200
61	5.000	5.040
62	5.200	5.040
63	5.360	5.360
64	5.120	5.120
65	5.200	5.200
66	5.360	5.280
67	5.120	5.000
68	5.120	5.440
69	5.120	5.200
70	5.120	5.000
71	4.880	5.280
72	5.200	5.280
73	5.120	5.120
74	5.040	5.120
75	5.200	5.200
76	5.040	5.120
77	5.040	5.280
78	5.040	4.960
79	5.040	5.120
80	5.120	5.040
81	5.200	5.120
82	5.120	4.960
83	4.740	4.800

80dB Amplitude of Waves I and V

No	GA	L I	R I	L V	R V
1	28	260.0	282.0	110.0	142.0
2	28	333.0	430.0	172.0	240.0
3	29	138.0	186.0	128.0	102.0
4	29	175.0	130.0	100.0	130.0
5	29	300.0	150.0	150.0	170.0
6	30	270.0	350.0	200.0	220.0
7	31	220.0	220.0	114.0	110.0
8	31	124.0	112.0	150.0	164.0
9	31	176.0	162.0	126.0	118.0
10	31	184.0	252.0	124.0	128.0
11	31	194.0	178.0	106.0	90.0
12	31	280.0	198.0	144.0	116.0
13	32	224.0	378.0	216.0	268.0
14	32	146.0	140.0	154.0	116.0
15	32	268.0	200.0	134.0	180.0
16	32	102.0	286.0	102.0	162.0
17	32	272.0	230.0	114.0	116.0
18	32	252.0	242.0	164.0	218.0
19	33	186.0	214.0	96.0	108.0
20	33	360.0	170.0	400.0	430.0
21	33	333.0	338.0	134.0	178.0
22	33	350.0	232.0	158.0	156.0
23	33	164.0	206.0	70.0	142.0
24	33	160.0	240.0	110.0	170.0
25	34	152.0	134.0	178.0	126.0
26	35	166.0	276.0	196.0	174.0
27	35	144.0	280.0	188.0	178.0
28	36.0	292.0	278.0	152.0	168.0

80dB Amplitude of Waves I and V

No	GA	L I	R I	L V	R V
29	36	144.0	286.0	98.0	172.0
30	36	114.0	270.0	104.0	216.0
31	36	392.0	398.0	206.0	202.0
32	37	410.0	390.0	146.0	198.0
33	38	210.0	230.0	310.0	400.0
34	38	320.0	314.0	360.0	400.0
35	38	286.0	260.0	186.0	134.0
36	38	435.0	464.0	204.0	186.0
37	38	436.0	470.0	218.0	238.0
38	38	430.0	380.0	235.0	200.0
39	39	314.0	456.0	254.0	278.0
40	39	130.0	200.0	128.0	126.0
41	39	380.0	450.0	260.0	260.0
42	40	382.0	480.0	254.0	300.0
43	40	390.0	390.0	160.0	162.0
44	40	482.0	428.0	198.0	186.0
45	40	422.0	434.0	226.0	236.0
46	40	380.0	300.0	220.0	225.0
47	40	284.0	448.0	184.0	302.0
48	41	354.0	218.0	178.0	174.0
49	41	410.0	398.0	218.0	272.0
50	41	490.0	490.0	200.0	300.0
51	41	150.0	170.0	110.0	190.0
52	30	276.0	314.0	170.0	256.0
53	30	234.0	178.0	138.0	160.0
54	30	224.0	230.0	94.0	168.0
55	30	264.0	238.0	222.0	188.0
56	31	326.0	468.0	268.0	268.0

80dB Amplitude of Waves I and V

No	GA	L I	R I	L V	R V
57	32	366.0	330.0	266.0	166.0
58	32	132.0	80.0	172.0	162.0
59	33	354.0	558.0	214.0	293.0
60	33	194.0	114.0	164.0	138.0
61	33	242.0	360.0	212.0	196.0
62	33	202.0	184.0	204.0	212.0
63	33	256.0	200.0	160.0	198.0
64	33	312.0	164.0	256.0	182.0
65	34	386.0	334.0	296.0	212.0
66	34	256.0	210.0	140.0	122.0
67	34	242.0	282.0	262.0	224.0
68	34	280.0	21.0	200.0	168.0
69	35	182.0	248.0	124.0	136.0
70	35	222.0	276.0	124.0	148.0
71	35	360.0	450.0	310.0	400.0
72	35	232.0	352.0	168.0	198.0
73	35	222.0	470.0	152.0	260.0
74	37	360.0	380.0	180.0	258.0
75	37	136.0	252.0	124.0	158.0
76	38	200.0	214.0	170.0	244.0
77	39	282.0	426.0	150.0	216.0
78	39	232.0	168.0	148.0	166.0
79	40	394.0	214.0	3330.0	382.0
80	40	280.0	264.0	144.0	220.0
81	40	260.0	418.0	146.0	186.0
82	41	334.0	348.0	168.0	180.0
83	42	310.0	226.0	276.0	390.0

80dB Amplitude Ratio V:I

No	GA	L Ratio	R Ratio	No	GA	L Ratio	R Ratio
1	28	0.4231	0.5035	29	36	0.6806	0.6014
2	28	0.5165	0.5581	30	36	0.9123	0.8000
3	29	0.9275	0.5484	31	36	0.5255	0.5075
4	29	0.5714	1.0000	32	37	0.3561	0.5077
5	29	0.5000	1.1330	33	38	1.4760	1.7390
6	30	0.7407	0.6286	34	38	1.1250	1.2740
7	31	0.5182	0.5000	35	38	0.6503	0.5154
8	31	1.2100	1,4640	36	38	0.4690	0.4009
9	31	0.7159	0.7284	37	38	0.5000	0.5064
10	31	0.6739	0.5079	38	38	0.5465	0.5263
11	31	0.5464	0.5056	39	39	0.8089	0.6096
12	31	0.5143	0.5859	40	39	0.9846	0.6300
13	32	0.9643	0.7090	41	39	0.6842	0.5778
14	32	1.0550	0.8286	42	40	0.4103	0.4154
15	32	0.5000	0.9000	43	40	0.4103	0.4154
16	32	1.000	0.5664	44	40	0.4108	0.4346
17	32	0.4191	0.5043	45	40	0.5355	0.5438
18	32	0.6508	0.9008	46	40	0.5789	0.7500
19	33	0.5161	0.5047	47	40	0.6479	0.6741
20	33	1.1110	2.5290	48	41	0.5028	0.7982
21	33	0.4024	0.5266	49	41	0.5317	0.6834
22	33	0.4514	0.6724	50	41	0.4082	0.6122
23	33	0.4268	0.6893	51	41	0.7333	1.1180
24	33	0.6875	0.7083	52	30	0.6159	0.8153
25	34	1,1710	0.9403	53	30	0.5897	0.8989
26	35	1.1810	0.6304	54	30	0.4196	0.7304
27	35	1.3060	0.6357	55	30	0.8409	0.7899
28	36	0.5205	0.6043	56	31	0.8221	0.5726

80dB Amplitude Ratio

No	GA	L Ratio	R Ratio
57	32	0.7268	0.5030
58	32	1.3030	2.0250
59	33	0.6045	0.5251
60	33	0.8454	1.2210
61	33	0.8760	0.5444
62	33	1.0100	1.1520
63	33	0.6250	0.9900
64	33	0.8205	1.1100
65	34	0.7668	0.6347
66	34	0.5469	0.5810
67	34	1.0830	0.7943
68	34	0.7143	0.8000
69	35	0.6813	0.5484
70	35	0.5586	0.5362
71	35	0.8611	0.8889
72	35	0.7241	0.5625
73	35	0.6847	0.5532
74	37	0.5000	0.6789
75	37	0.9118	0.6270
76	38	0.8500	1.1400
77	39	0.5319	0.5070
78	39	0.6379	0.9881
79	40	0.8376	1.7850
80	40	0.5143	0.8333
81	40	0.5615	0.4450
82	41	0.5030	0.5172
83	42	0.8903	1.7260

60dB: Latencies of waves I and V

No	GA	Lat. I L	Lat. I L	Lat. V R	Lat. V R
1	28	3.120	2.960	9.000	8.840
2	28	2.680	2.440	8.220	7.920
3	29	3.200	3.120	8.880	8.640
4	29	2.560	3.040	8.240	9.040
5	30	2.400	2.640	7.520	7.600
6	30	2.800	2.840	8.400	8.420
7	30	3.040	2.960	8.640	8.480
8	30	3.200	3.180	9.040	8.880
9	30	2.480	2.400	8.000	7.920
10	31	2.680	2.160	8.080	7.600
11	31	2.240	2.480	7.600	7.840
12	31	2.920	2.880	8.400	8.320
13	31	2.880	2.800	8.720	8.480
14	31	2.560	2.600	8.080	8.120
15	31	2.640	2.560	7.840	7.840
16	31	2.440	2.400	8.600	8.480
17	1	2.560	2.400	8.160	8.080
18	32	2.200	2.240	7.400	7.360
19	32	3.040	2.160	7.840	7.360
20	32	2.700	3.400	8.060	9.080
21	32	2.880	2.680	8.360	8.160
22	32	2.400	2.560	7.840	8.000
23	32	3.000	2.800	8.280	8.000
24	32	2.600	2.080	7.960	7.520
25	32	2.400	2.560	7.760	7.760
26	32	2.320	2.320	7.520	7.680
27	32	3.120	2.720	8.000	7.920
28	33	2.560	2.000	7.840	7.280

60dB: Latency of Waves I and V

No	GA	Lat. I L	Lat. I L	Lat. V R	Lat. V R
29	33	2.480	2.560	7.680	7.680
30	33	2.200	2.220	7.320	7.480
31	33	2.160	2.240	7.200	7.240
32	33	3.040	2.640	8.000	7.680
33	33	2.320	2.320	7.760	7.760
34	33	2.560	2.560	7.680	7.600
35	33	2.400	2.240	7.680	7.520
36	33	3.040	2.640	7.760	7.920
37	33	2.720	2.400	8.000	7.760
38	33	2.480	2.720	8.000	7.600
39	33	3.280	3.600	8.560	8.560
40	33	2.560	2.400	7.860	7.840
41	34	2.440	2.680	7.720	7.800
42	34	2.320	1.960	7.520	7.080
43	34	2.240	2.160	7.600	7.520
44	34	2.400	2.460	7.580	7.580
45	34	2.640	2.640	7.760	7.680
46	35	2.240	2.320	7.280	7.280
47	35	2.400	2.220	7.520	7.520
48	35	2,400	2.520	7.480	7.480
49	35	2.400	1.920	7.280	7.200
50	35	2.500	2.320	7.700	7.640
51	35	2.320	2.560	7.580	7.600
52	35	2.160	2.400	7.200	7.520
53	35	2.560	2.560	7.600	7.680
54	35	2.240	2.320	7.280	7.600
55	36	2.200	2.160	7.160	7.040
56	36	2.080	2.560	7.040	7.520

60 dB: Latencies of Waves I and V

No	GA	Lat. I L	Lat. I L	Lat. V R	Lat. V R
57	36	2.560	2.400	7.600	7.600
58	36	2.080	2.000	7.280	6.960
59	37	1.840	1.760	7.120	6.720
60	37	2.000	1.880	7.040	7.000
61	37	2.480	2.280	7.600	7.400
62	37	2.360	2.400	7.520	7.600
63	38	2.400	2.400	7.520	7.520
64	38	2.240	2.160	6.960	6.960
65	38	1.740	2.160	6.480	6.480
66	38	2.320	2.160	7.360	7.280
67	38	1.920	2.240	7.120	7.440
68	38	2.000	2.180	7.200	7.380
69	38	1.840	1.760	6.960	6.960
70	39	1.860	1.820	6.860	6.780
71	39	1.840	2.160	6.720	7.120
72	39	2.320	2.320	7.440	7.360
73	39	1.680	1.680	6.280	6.400
74	39	2.240	2.000	7.120	6.880
75	9	2.340	2.320	7.520	7.280
76	39	2.320	2.640	7.360	7.680
77	40	1.760	1.840	6.480	6.720
78	40	2.080	2.000	7.120	6.880
79	40	1.680	1.920	6.720	6.880
80	40	1.840	1.920	6.920	6.960
81	40	2.240	2.320	7.120	6.880
82	40	2.000	2.400	6.720	6.880
83	40	2.000	2.280	6.560	7.240
84	40	2.320	2.360	7.360	7.040

60 dB: Latencies of Waves I and V

No	GA	Lat. I L	Lat. I L	Lat. V R	Lat. V R
85	40	2.320	2.240	7.440	7.280
86	40	1.920	1.760	7.040	6.960
87	41	1.760	1.920	6.720	6.880
88	41	1.840	2.160	6.720	6.640
89	41	2.080	2.160	7.200	7.220
90	41	2.080	1.840	6.960	6.800
91	41	1.920	1.840	6.960	6.720
92	42	1.920	1.920	6.620	6.720

60dB IPI

No	L	R	No	L	R
1	5.880	5.880	28	5.280	5.280
2	5.540	5.480	29	5.200	5.120
3	5.680	5.520	30	5.120	5.260
4	5.680	6.000	31	5.040	5.000
5	5.120	4.960	32	4.960	5.040
6	5.600	5.580	33	5.440	5.440
7	5.600	5.520	34	5.120	5.040
8	5.840	5.700	35	5.280	5.280
9	5.520	5.520	36	4.720	5.280
10	5.400	5.440	37	5.280	5.360
11	5.360	5.360	38	5.520	4.880
12	5.480	5.440	39	5.280	4.960
13	5.840	5.680	40	5.300	5.440
14	5.520	5.520	41	5.280	5.120
15	5.200	5.280	42	5.200	5.120
16	6.160	6.080	43	5.360	5.360
17	5.600	5.680	44	5.180	5.120
18	5.200	5.120	45	5.120	5.040
19	4.800	5.200	46	5.040	4.960
20	5.360	5.680	47	5.120	5.300
21	5.480	5.480	48	5.080	4.960
22	5.440	5.440	49	4.880	5.280
23	5.280	5.200	50	5.200	5.320
24	5.360	5.440	51	5.260	5.040
25	5.360	5.200	52	5.040	5.120
26	5.200	5.360	53	5.040	5.120
27	4.880	5.200	54	5.040	5.280

60dB IPI

No	L	R	No	L	R
55	4.960	4.880	83	4.560	4.960
56	4.960	4.960	84	5.040	4.680
57	5.040	5.200	85	5.120	5.040
58	5.200	4.960	86	5.120	5.200
59	5.200	4.960	87	4.960	4.960
60	5.040	5.120	88	4.880	4.480
61	5.120	5.120	89	5.120	5.060
62	5.160	5.200	90	4.880	4.960
63	5.120	5.120	91	5.040	4.880
64	4.720	4.800	92	4.700	4.800
65	4.740	4.320			
66	5.040	5.120			
67	5.200	5.200			
68	5.200	5.200			
69	5.120	5.200			
70	5.000	4.960			
71	4.880	4.960			
72	5.120	5.040			
73	4.600	4.720			
74	4.880	4.880			
75	5.120	4.960			
76	5.040	5.040			
77	4.720	4.880			
78	5.040	4.880			
79	5.040	4.860			
80	5.080	5.040			
81	4.880	4.560			
82	4.720	4.480			

60dB Amplitude

No	L.I	R.I	L.V	R.V
1	120.0	208.0	144.0	150.0
2	204.0	278.0	128.0	168.0
3	132.0	196.0	104.0	86.0
4	192.0	100.0	134.0	124.0
5	204.0	254.0	152.0	134.0
6	136.0	192.0	190.0	184.0
7	160.0	76.0	100.0	88.0
8	86.0	112.0	102.0	154.0
9	184.0	124.0	176.0	168.0
10	162.0	224.0	158.0	220.0
11	154.0	160.0	106.0	162.0
12	122.0	82.0	86.0	136.0
13	76.0	176.0	150.0	136.0
14	116.0	70.0	106.0	72.0
15	162.0	192.0	96.0	136.0
16	202.0	186.0	122.0	94.0
17	180.0	162.0	94.0	108.0
18	100.0	232.0	134.0	210.0
19	146.0	190.0	158.0	212.0
20	146.0	118.0	80.0	100.0
21	64.0	118.0	82.0	128.0
22	182.0	148.0	98.0	150.0
23	126.0	116.0	188.0	140.0
24	218.0	250.0	196.0	194.0
25	134.0	88.0	144.0	122.0
26	106.0	80.0	144.0	162.0
27	175.0	170.0	120.0	290.0
28	254.0	276.0	238.0	182.0

60dB Amplitude

No	L. I	R. I	L. I	R. I
29	178.0	134.0	224.0	206.0
30	134.0	98.0	154.0	148.0
31	100.0	228.0	134.0	222.0
32	130.0	132.0	96.0	170.0
33	150.0	168.0	100.0	96.0
34	150.0	152.0	96.0	148.0
35	110.0	140.0	86.0	88.0
36	200.0	120.0	34.0	310.0
37	240.0	136.0	120.0	148.0
38	196.0	180.0	112.0	96.0
39	96.0	102.0	76.0	106.0
40	100.0	77.0	102.0	66.0
41	170.0	152.0	110.0	102.0
42	246.0	252.0	138.0	288.0
43	154.0	142.0	78.0	84.0
44	184.0	198.0	162.0	240.0
45	154.0	102.0	160.0	188.0
46	162.0	118.0	142.0	126.0
47	132.0	174.0	94.0	120.0
48	146.0	174.0	192.0	102.0
49	170.0	270.0	290.0	370.0
50	216.0	162.0	118.0	166.0
51	156.0	204.0	128.0	204.0
52	146.0	194.0	168.0	130.0
53	62.0	114.0	100.0	112.0
54	120.0	162.0	204.0	128.0
55	186.0	142.0	152.0	118.0
56	94.0	180.0	132.0	116.0

60dB Amplitude

No	L. I	R. I	L. V	R. V
57	136.0	168.0	116.0	138.0
58	198.0	248.0	128.0	158.0
59	156.0	318.0	172.0	250.0
60	306.0	250.0	232.0	200.0
61	130.0	126.0	78.0	100.0
62	116.0	122.0	150.0	166.0
63	148.0	152.0	158.0	136.0
64	290.0	180.0	230.0	200.0
65	202.0	174.0	280.0	272.0
66	130.0	160.0	78.0	134.0
67	270.0	242.0	262.0	148.0
68	190.0	142.0	216.0	102.0
69	240.0	240.0	180.0	180.0
70	376.0	362.0	244.0	264.0
71	196.0	250.0	168.0	172.0
72	120.0	112.0	134.0	124.0
73	222.0	238.0	238.0	284.0
74	160.0	204.0	160.0	216.0
75	168.0	160.0	188.0	144.0
76	140.0	240.0	140.0	220.0
77	310.0	290.0	308.0	188.0
78	260.0	198.0	228.0	188.0
79	268.0	222.0	148.0	190.0
80	268.0	22.0	158.0	248.0
81	170.0	170.0	220.0	240.0
82	182.0	460.0	134.0	310.0
83	164.0	170.0	226.0	180.0
84	156.0	190.0	150.0	280.0

60 DB AMPLITUDE

No	L. I	R. I	L. V	R. V
85	138.0	142.0	192.0	228.0
86	162.0	198.0	154.0	132.0
87	276.0	72.0	160.0	162.0
88	240.0	350.0	270.0	180.0
89	198.0	200.0	174.0	232.0
90	186.0	348.0	158.0	406.0
91	270.0	350.0	140.0	180.0
92	152.0	140.0	218.0	282.0

60dB Amplitude RATio V:I

No	L	R	No	L	R
1	1.2000	0.7212	29	1.2580	1.5370
2	0.6275	0.6043	30	1.1490	1.5100
3	0.7879	0.4388	31	1.3400	0.9737
4	0.6979	1.2400	32	0.7385	1.2880
5	0.7451	0.5276	33	0.6667	0.5714
6	1.3970	0.9583	34	0.6400	0.9737
7	0.6250	1.1580	35	0.7818	0.6286
8	1.1860	1.3750	36	1.7000	2.5830
9	0.9565	1.3550	37	0.5000	1.0880
10	0.9753	0.9821	38	0.5714	0.5333
11	0.6883	1.0120	39	0.7917	1.0390
12	0.7049	1.6590	40	1.0200	0.8571
13	1.9740	0.7727	41	0.6471	0.6711
14	0.9138	1.0290	42	0.5610	1.1430
15	0.5926	0.7083	43	0.5065	0.5915
16	0.6040	0.5054	44	0.8804	1.2120
17	0.5222	0.6667	45	1.0390	1.8430
18	1.3400	0.9052	46	0.8765	1.0680
19	1.0820	1.1160	47	0.7121	0.6897
20	0.5479	0.8475	48	1.3150	0.5862
21	1.2810	1.0850	49	1.7060	1.3700
22	0.5385	1.0140	50	0.5463	1.0250
23	1.4920	1.2070	51	0.8205	1.0000
24	0.8991	0.7760	52	1.1510	0.6701
25	1.0750	1.3800	53	1.6130	0.9825
26	1.3580	2.0250	54	1.700	0.7901
27	0.6857	1.7060	55	0.8172	0.8310
28	0.9370	0.6594	56	1.4040	0.6444

60dB Amplitude Ratio V:I

No	L	R	No	L	R
59	1.1030	0.7862	87	0.5797	0.5956
60	0.7582	0.8000	88	1.1250	0.5143
61	0.6000	0.7937	89	0.8788	1.1600
62	1.2930	1.3610	90	0.8495	1.1670
63	1.0680	0.8947	91	0.5185	0.5143
64	0.7931	1.1110	92	1.4340	2.0140
65	1.3860	1.5630			
66	0.6000	0.8375			
67	0.9704	0.6116			
68	1.1370	0.7183			
69	0.7500	0.7500			
70	0.6489	0.7293			
71	0.8571	0.6880			
72	1.1170	1.1070			
73	1.072	1.1930			
74	1.000	1.0590			
75	1.1190	0.9000			
76	1.000	0.9167			
77	0.9935	0.6483			
78	0.8769	0.9495			
79	0.5522	0.8559			
80	0.5896	1.1170			
81	1.2940	1.4120			
82	0.7363	0.6739			
83	1.3780	1.0590			
84	0.9615	1.4740			
85	1.3910	1.6060			
86	0.9506	0.6667			

40 dB: Latencies of waves I and V and IPI

NO	GA	I		V		I-V	
		L	R	L	R	L	R
1	28	0	0	10.6	10.5	0	0
2	28	3.36	3.36	8.80	8.88	5.44	5.52
3	29	0	0	10.3	0	0	0
4	29	-	-	-	-	-	-
5	29	3.36	0	9.44	0	6.08	0
6	30	3.76	3.84	8.48	8.80	4.72	4.96
7	31	3.28	3.42	8.68	8.78	5.40	5.36
8	31	3.36	3.28	8.88	8.64	5.48	5.36
9	31	0	3.92	9.52	9.68	0	5.76
10	31	3.28	0	8.80	0	5.52	0
11	31	3.76	3.44	8.96	8.96	5.20	5.52
12	31	3.28	0	9.38	10.2	6.10	0
13	31	3.28	3.20	8.80	8.80	5.52	5.60
14	32	3.04	2.64	8.08	7.80	5.16	5.18
15	32	9.00	3.68	8.80	8.32	4.80	4.64
16	32	-	-	-	-	-	-
17	32	0	0		9.12	0	0
18	32	3.68	2.88	9.12	8.2	5.44	5.44
19	32	-	-	-	-	-	-
20	33	3.20	3.12	8.40	8.32	5.20	5.20
21	33	0		9.20	9.25	0	0
22	33	3.20	3.20	8.88	8.52	5.68	5.32
23	33	-	-	-	-	-	-
24	33	N.A.		N.A.		N.A.	
25	33	4.56	3.28	10.1	8.48	5.60	5.20
26	33	3.44	0	9.12	8.32	5.68	0
27	34	3.76	0	9.12	9.12	5.36	0
28	35	3.12	2.96	8.16	8.00	5.04	5.04
29	35	2.78	3.12	7.80	8.40	5.12	5.28

40 dB: Latencies of waves I and V and IPI

No	GA	I		V		I-V	
		L	R	L	R	L	R
30	35	3.60	3.60	8.80	8.64	5.20	5.04
31	36	3.00	2.88	8.00	7.84	5.00	4.98
32	36	3.68	2.96	8.72	7.84	5.04	4.88
33	36	3.44	3.12	8.56	8.24	5.12	5.12
34	36	2.64	2.48	7.92	7.36	5.28	4.88
35	38	2.64	2.48	7.92	7.28	5.28	4.80
36	38	2.88	2.80	7.28	7.04	4.40	4.24
37	38	3.52	2.88	8.40	8.00	4.88	5.12
38	38	2.48	3.12	7.68	8.16	5.20	5.12
39	38	3.12	2.88	8.24	8.16	5.12	5.28
40	38	3.12	3.20	7.92	7.84	4.80	4.64
41	38	2.64	2.80	6.96	6.72	4.32	3.92
42	39	2.32	2.24	6.64	6.72	4.32	4.48
43	39	2.80	2.56	7.92	7.36	5.12	4.80
44	39	3.36	2.96	8.48	8.08	5.04	5.12
45	39	2.32	2.64	8.40	8.32	6.08	5.68
46	40	2.56	2.32	7.04	7.12	4.48	4.80
47	40	2.96	2.88	8.08	7.84	5.12	4.96
48	40	2.90	2.84	7.28	7.36	4.88	4.72
49	40	2.48	2.80	7.52	7.84	5.04	5.04
50	40	3.52	2.96	8.00	7.76	4.48	4.80
51	40	2.48	2.24	7.12	7.04	4.64	4.80
52	41	2.32	2.72	7.58	7.76	5.26	5.04
53	41	3.04	2.32	7.92	7.36	4.88	5.04
54	41	2.56	2.88	7.44	7.36	4.88	4.48
55	41	2.24	2.16	7.52	7.44	5.20	5.36

40 dB: Latencies of Waves I and V and IPI

No	GA	I		V		I-V	
		L	R	L	R	L	R
55	30	0	0	9.28	10.3	0	0
56	30	3.84	4.24	9.52	9.92	5.68	5.68
57	30	-	-	-	-	-	-
58	30	3.36	3.28	9.28	8.64	5.92	5.36
59	31	3.52	2.96	8.94	8.48	5.42	5.52
60	32	3.36	2.96	8.78	8.32	5.42	5.52
61	32	3.68	0	9.04	8.56	5.36	0
62	32	3.12	3.04	8.40	8.40	5.28	5.36
63	32	3.42	3.20	9.04	8.72	5.12	5.52
64	33	3.36	2.96	8.64	8.16	5.28	5.52
65	33	3.28	0	8.56	8.64	5.28	0
66	33	3.00	2.80	8.18	8.00	5.18	5.20
67	33	2.80	2.60	7.80	7.68	5.00	5.08
68	33	3.76	3.44	8.32	8.32	4.56	4.88
69	33	3.12	2.96	8.48	8.48	5.36	5.52
70	33	3.68	3.12	8.80	8.24	5.12	5.12
71	34	2.96	2.48	8.24	7.60	5.20	5.12
72	34	2.80	2.80	8.24	8.16	5.44	5.36
73	34	4.00	3.80	8.98	8.80	4.98	5.00
74	34	3.30	0	8.96	8.48	5.60	0
75	35	3.28	2.80	8.00	7.76	4.72	4.96
76	35	3.00	2.80	7.88	8.16	4.88	5.36
78	35	3.46	3.97	8.52	9.00	5.08	5.08
79	35	3.00	2.16	7.92	7.92	4.92	5.76
80	35	3.52	3.20	8.56	8.48	5.04	5.28
81	35	3.28	3.20	8.48	8.32	5.20	5.12
82	37	2.40	2.40	7.44	7.44	5.04	5.04
83	37	2.96	3.16	8.00	8.36	5.04	5.20

40 dB: Latencies of waves I and V and IPI

No	GA	I		V		I-V	
		L	R	L	R	L	R
84	37	3.20	3.04	8.46	8.24	5.26	5.20
85	38	3.20	2.88	8.32	8.00	5.12	5.12
86	39	2.20	2.32	7.20	7.28	5.00	4.96
87	39	2.40	2.80	7.36	7.68	4.96	4.88
88	39	3.20	2.80	8.32	7.92	5.12	5.12
89	40	2.48	2.48	7.04	7.52	4.56	5.04
90	40	2.64	3.36	7.68	7.84	5.04	4.48
91	40	3.20	2.88	8.24	7.92	5.04	5.4
92	40	2.40	2.96	7.84	7.84	5.44	4.88
93	41	2.56	2.48	7.28	7.20	4.72	4.72
94	42	2.46	2.56	7.16	7.36	4.70	4.80

40 dB: Amplitudes of waves I and V Ratio V:I

No	GA	Left I	Right I	Left V	Right V	Left V:I	Right V:I
1	28	0	0	144	82	-	N.A.
2	28	124	158	136	82	1.09	0.51
3	29	0	0	108	0	-	-
4	29	-	-	-	-	-	-
5	29	-	0	-	0	-	0
6	30	0	0	0	0	-	-
7	31	98	228	98	120	1.00	0.52
8	31	96	110	86	0	0.84	
9	31	80	0	82	88	1.00	
10	31	114	0	114	0	1.00	
11	31	104	106	96	88	0.92	0.83
12	31	142	0	72	0	0.50	
13	31	128	0	110	56	0.86	
14	32	180	128	212	182	1.17	1.42
15	32	114	132	88	90	0.77	0.68
16	32	-	-	-	-	-	-
17	32	-	-	-	-	-	-
18	32	164	114	100	72	0.61	0.63
19	32	-	-	-	-	-	-
20	33	84	86	80	114	0.95	1.32
21	33	-	-	-	-	-	-
22	33	-	-	-	-	-	-
23	33	-	-	-	-	-	-
24	33	102	-	68	44	0.66	-
25	33	-	-	-	-	-	-
26	34	78	-	118	80	1.51	-
27	35	105	136	124	146	1.18	1.07
28	35	66	120	74	124	1.12	1.03

40 dB: Amplitude of waves I and V and Ratio V:I

No	GA	Left I	Right I	Left V	Right V	Left V/I	Right V/I
29	35	76	118	84	128	0.87	1.08
30	36	142	142	144	118	0.84	0.83
31	36	44	122	80	156	1.82	1.28
32	36	88	116	112	128	1.27	1.10
33	36	94	144	148	106	1.57	0.74
34	37	86	184	136	160	1.58	0.87
35	38	230	174	212	202	0.92	1.16
36	38	78	110	64	116	0.82	1.05
37	38	252	252	156	186	0.50	0.74
38	38	120	86	166	138	1.38	1.60
39	38	156	136	176	202	1.13	0.67
40	38	210	260	220	280	1.28	1.08
41	39	118	160	164	262	1.39	1.64
42	39	122	152	194	256	1.59	1.68
43	39	106	134	86	178	0.81	1.33
44	39	202	152	144	136	0.71	0.89
45	40	148	184	170	184	1.15	1.00
46	40	104	182	144	230	1.38	1.26
47	40	195	182	134	168	0.68	0.92
48	40	132	190	164	138	1.24	0.73
49	40	160	160	244	184	1.52	1.15
50	40	160	194	102	194	0.64	1.00
51	41	190	110	180	90	0.95	0.82
52	41	140	230	126	334	0.90	1.45
53	41	152	324	152	224	1.00	0.69
54	41	124	100	144	176	1.16	1.76

40 dB: Amplitude of Waves I and V and Ratio V:I

No	GA	Left I	Right I	Left V	Right V	Left V/I	Right V/I
55	30	92	0	136	128	1.48	N.A.
56	30	98	108	118	80	1.20	0.74
57	30	-	-	-	-	-	-
58	30	68	72	74	108	1.08	1.50
59	31	126	146	146	206	1.16	1.41
60	32	134	206	106	190	0.79	0.92
61	32	-	-	-	-	-	-
62	32	76	46	174	106	2.29	2.30
63	32	182	144	182	192	1.00	1.33
64	33	128	162	124	172	0.97	1.06
65	33	-	-	-	-	-	-
66	33	134	64	160	152	1.19	2.37
67	33	160	124	216	182	1.35	1.46
68	33	82	158	136	102	1.65	0.64
69	33	136	192	166	164	1.22	0.85
70	33	112	98	152	98	1.36	1.63
71	34	164	244	134	220	0.82	0.90
72	34	170	152	84	78	0.50	0.51
73	34	110	96	192	172	1.74	1.79
74	34	76	0	112	148	1.47	N.A.
75	35	-	-	-	-	-	-
76	35	140	160	88	110	0.62	0.69
77	35	-	-	-	-	-	-
78	35	160	98	160	92	0.96	0.94
79	35	-	-	-	-	-	-
80	35	-	-	-	-	-	-
81	35	98	126	170	170	1.73	1.35
82	37	166	110	164	118	1.00	1.07

40 dB: Amplitude of Waves I and V and Ratio V:I

No	GA	Left I	Right I	Left V	Right V	Left V/I	Right V/I
83	37	-	-	-	-	-	-
84	37	144	98	116	110	0.80	1.12
85	38	150	134	144	162	0.96	1.20
86	39	170	158	148	136	0.87	0.86
87	39	154	226	94	114	0.61	0.50
88	39	148	100	134	126	1.90	1.26
89	40	-	-	-	-	-	-
90	40	142	102	222	216	1.56	2.12
91	40	156	202	158	182	1.01	0.90
92	40	122	134	82	118	0.50	0.88
93	41	174	162	128	176	0.73	1.09
94	42	128	175	130	200	1.01	1.14

80 dB: Latencies of waves III and VI and IPI III-VI

No	GA	III		VI		III-VI	
		L	R	L	R	L	R
1	28	5.04	5.26	11.1	10.3	6.06	4.96
2	28	4.40	4.48	9.12	8.24	4.72	3.76
3	29	5.44	4.88	10.0	9.76	4.56	4.96
4	29	6.32	6.40	10.7	0	5.25	0
5	29	4.72	5.52	10.0	10.3	5.28	4.78
6	30	4.80	4.56	9.20	8.80	4.40	4.24
7	31	4.28	4.72	9.20	9.00	4.92	4.28
8	31	5.68	6.16	10.3	10.6	4.64	4.48
9	31	4.88	5.84	9.44	0	4.56	0
10	31	5.12	4.80	10.2	0	5.12	0
11	31	5.92	5.52	0	10.4	0	4.88
12	31	5.12	4.64	9.84	0	4.72	0
13	32	4.40	4.16	8.00	8.00	3.60	3.84
14	32	4.96	4.96	8.80	8.48	3.84	3.52
15	32	5.28	5.68	0	9.52	0	3.84
16	32	5.60	5.68	0	0	0	0
17	32	4.64	4.32	0	9.36	0	5.04
18	32	5.28	5.12	9.20	9.28	3.92	4.16
19	33	4.72	4.64	9.12	0	4.40	0
20	33	4.96	4.88	9.20	8.88	4.34	4.00
21	33	5.36	5.20	9.52	9.28	4.16	4.08
22	38	3.92	3.76	7.52	7.60	3.60	3.84
23	33	5.12	4.96	9.52	9.20	4.40	4.24
24	33	5.28	5.76	9.52	8.88	4.24	3.12
25	33	4.56	4.72	8.56	8.72	4.00	4.00
26	33	4.48	4.96	9.44	0	4.96	0
27	35	4.72	4.24	8.80	8.00	4.08	.76
28	35	4.48	4.96	8.00	9.60	3.52	4.64

80 dB: Latencies of Waves III and VI an^ IPI III-VI

No	GA	III		VI		III-VI	
		L	R	L	R	L	R
28	35	4.48	4.96	8.00	9.60	3.52	4.64
29	36	4.32	4.32	0	8.00	0	3.68
30	36	4.80	4.64	8.32	8.24	3.52	3.60
31	36	4.80	4.80	8.96	8.80	4.76	4.00
32	36	4.48	4.64	8.48	8.56	4.00	3.92
33	37	4.56	4.32	8.08	7.84	3.52	3.52
34	38	4.16	3.92	7.68	7.44	3.52	3.52
35	38	4.48	4.48	8.32	8.32	3.84	3.84
36	38	4.32	4.24	8.40	8.72	4.08	4.48
37	38	4.42	4.80	0	8.64	0	3.84
38	38	4.24	4.08	8.40	8.24	4.16	4.16
39	39	4.00	3.92	7.94	7.60	3.44	3.68
40	39	4.96	4.72	8.72	8.96	3.76	4.24
41	39	4.08	4.32	0	8.16	0	3.84
42	40	4.00	3.92	7.60	7.68	3.60	3.76
43	40	4.32	4.40	8.32	8.16	4.00	3.92
44	40	4.16	4.16	8.16	8.08	4.00	3.92
45	40	4.00	4.16	8.16	8.40	4.16	4.24
46	40	4.24	4.40	8.96	8.56	4.72	4.16
47	40	4.08	3.92	7.92	8.08	3.84	4.16
48	41	4.56	4.90	8.64	8.90	4.08	4.00
49	41	4.32	4.48	8.32	8.32	4.00	3.84
50	41	4.12	4.24	7.52	7.68	3.40	3.44
51	41	4.08	4.24	7.46	8.24	3.38	4.00

80 dB: Latencies of Waves III and VI and IPI III-VI

No	GA	III		VI		III-VI	
		L	R	L	R	L	R
52	30	4.48	5.18	9.40	10.0	4.72	4.80
53	30	4.64	4.48	9.52	9.12	4.88	4.64
54	30	5.44	5.12	0	10.4	0	4.08
55	30	4.64	4.80	9.36	9.04	4.72	4.24
56	31	4.22	4.40	9.44	8.80	5.22	4.40
57	32	4.80	4.26	9.12	8.96	4.32	4.40
58	32	-	-	-	-	-	-
59	32	4.88	5.68	9.20	9.28	4.32	3.60
60	32	-	-	-	-	-	-
61	33	4.44	4.08	8.80	8.72	4.16	4.64
62	33	-	-	-	-	-	-
63	33	4.32	4.32	8.70	9.04	4.38	4.72
64	33	4.32	3.80	8.16	8.24	3.84	4.44
65	33	4.96	4.64	8.60	8.64	3.64	4.00
66	33	4.40	4.16	9.20	9.12	4.80	4.96
67	33	4.80	5.28	8.96	9.20	4.16	3.92
68	34	4.48	4.20	8.64	8.52	4.16	4.16
69	34	4.40	4.16	9.20	9.12	4.80	4.96
70	34	4.36	4.28	8.64	8.80	4.28	4.52
71	34	5.44	4.64	9.12	8.72	3.68	4.08
72	35	3.82	4.44	8.26	8.62	4.44	4.18
73	35	4.36	4.20	8.66	8.64	4.30	4.44
74	35	4.72	4.48	8.72	8.32	4.00	3.84
75	35	4.40	4.32	8.56	8.40	3.16	4.08
76	35	4.40	4.32	9.20	9.60	4.80	5.28
77	37	4.00	4.22	8.40	8.40	4.24	4.08
78	37	4.80	4.64	9.28	8.80	4.48	4.16
79	38	4.64	4.56	8.80	8.72	4.16	4.16

80 dB: Latencies of waves III and VI and IPI III-VI

No	GA	III		VI		III-VI	
		L	R	L	R	L	R
79	38	4.64	4.56	8.80	8.72	4.16	4.16
80	39	4.00	4.08	8.08	8.48	4.08	4.40
81	39	4.64	4.48	8.80	8.80	4.16	4.32
82	40	-	-	-	-	-	-
83	40	4.48	4.48	8.62	8.00	4.14	3.52
84	40	4.20	4.20	8.20	8.80	4.00	4.00
85	40	4.40	4.32	8.08	8.32	3.68	4.00
86	41	4.16	4.16	8.16	8.24	4.00	4.08
87	42	3.68	3.84	7.68	7.84	4.00	4.00

60 dB: Latencies of waves III-VI and IPI III-VI

No	GA	III		VI		III-VI	
		L	R	L	R	L	R
1	28	6.48	6.24	0	11.3	0	4.48
2	28	5.12	5.36	9.36	9.28	4.24	3.92
3	29	5.84	5.28	10.4	9.92	4.56	6.64
4	29	5.36	5.84	0	0	0	0
5	30	5.28	5.04	9.44	9.28	4.16	4.24
6	31	4.78	5.36	8.96	9.20	4.18	3.84
7	31	6.08	5.84	0	10.8	0	4.96
8	31	6.00	6.44	10.4	11.5	4.48	5.06
9	31	5.76	5.20	9.68	0	3.92	0
10	31	5.44	5.36	0	0	0	0
11	31	5.52	6.00	10.7	0	5.20	0
12	31	5.52	5.60	0	9.92	0	4.32
13	32	4.80	4.48	8.32	8.32	3.52	3.84
14	32	5.60	5.28	9.20	9.24	3.60	4.56
15	32	5.44	6.72	0	0	0	0
16	32	6.00	5.58	0	0	0	0
17	32	5.20	4.32	9.74	9.36	4.54	5.04
18	32	5.48	5.36	9.68	9.20	4.20	3.84
19	33	5.04	4.88	9.28	0	0	0
20	33	5.44	5.36	0	9.52	0	4.14
21	33	5.36	5.60	9.52	9.52	4.16	3.92
22	38	4.29	3.92	7.24	7.12	2.95	3.20
23	33	5.36	5.20	10.0	9.36	4.36	4.16
24	33	6.24	5.92	9.92	10.2	3.68	4.32
25	33	5.28	5.44	9.32	0	4.04	0
26	34	5.36	6.40	9.80	10.8	4.44	4.40
27	35	4.88	4.96	9.52	9.36	4.64	4.40
28	35	4.92	4.92	0	9.00	0	4.08
29	35	5.60	5.44	9.76	9.84	4.16	4.40

60 dB: Latencies of waves III and VI and IPI III-VI

No	GA	III		VI		III-VI	
		L	R	L	R	L	R
30	35	4.88	4.72	8.56	0	3.68	0
31	36	5.04	5.44	0	8.80	0	3.36
32	36	5.20	4.96	9.20	8.64	4.00	3.68
33	36	4.64	5.04	8.80	8.80	4.16	3.84
34	37	4.80	4.48	8.56	8.16	3.76	3.68
35	38	4.56	4.64	8.08	7.84	3.52	3.20
36	38	4.64	4.88	8.48	8.48	3.84	3.60
37	38	4.60	5.04	8.80	9.20	4.16	4.16
38	38	5.12	5.20	8.96	8.56	3.84	3.36
39	38	4.56	4.56	8.24	8.24	3.68	3.68
40	39	4.48	4.48	7.76	7.76	3.28	3.28
41	39	5.52	4.88	8.56	8.08	3.04	.20
42	39	5.36	5.12	9.36	9.12	4.00	4.08
43	39	4.96	4.88	8.24	8.32	3.28	3.44
44	40	4.32	4.16	7.92	7.76	3.60	3.60
45	40	4.72	4.72	8.72	8.80	4.00	4.08
46	40	4.48	4.40	8.16	8.16	3.68	3.76
47	40	4.40	4.72	8.48	8.64	4.08	3.92
48	40	4.88	4.96	8.88	8.48	4.00	3.52
49	40	4.16	4.08	8.24	8.24	4.08	4.16
50	41	4.96	4.88	8.96	8.56	4.00	3.68
51	41	4.96	4.64	8.96	8.40	4.00	3.76
52	41	4.48	4.88	7.72	8.16	3.24	3.28
53	41	4.96	4.48	8.24	8.48	3.28	4.00

60 dB: Latencies of waves III and VI and IPI III-VI

No	GA	III		VI		III-VI	
		L	R	L	R	L	R
54	30	5.22	5.44	9.00	9.02	3.78	4.32
55	30	5.68	4.88	0	9.52	0	4.64
56	30	5.84	6.00	0	11.0	0	5.00
57	30	5.20	5.28	10.4	0		0
58	31	5.20	5.20	9.84	9.36	4.64	4.16
59	32	5.52	4.68	9.68	9.36	4.16	4.08
60	32	5.28	5.12	9.60	9.48	4.32	4.36
61	32	5.12	5.68	9.12	9.28	4.00	4.08
62	32	5.44	5.6	9.48	9.22	4.04	3.86
63	33	5.00	4.96	9.76	9.44	4.64	4.48
64	33	5.04	5.04	8.80	9.20	3.76	4.16
65	33	5.04	5.20	9.28	9.40	4.24	4.20
66	33	4.48	4.50	8.80	8.24	4.32	3.74
67	33	5.52	5.60	0	9.20	0	3.60
68	33	5.00	4.88	9.00	9.58	4.00	4.20
69	33	5.28	5.12	9.20	9.28	3.92	4.16
70	34	4.88	4.40	9.20	8.72	4.32	4.16
71	34	5.20	4.56	9.44	9.20	4.24	4.64
72	34	5.00	4.80	9.00	9.20	4.00	4.40
73	34	5.60	5.52	9.52	9.36	3.92	3.84
74	35	4.72	4.60	8.80	8.48	4.08	3.88
75	35	4.44	4.78	8.80	9.12	4.36	4.34
76	35	4.80	4.68	8.74	9.00	3.94	4.32
77	35	5.28	5.04	8.96	8.72	3.68	3.68
78	35	4.96	5.04	9.12	0	4.16	0
79	35	4.96	5.28	9.36	9.68	4.46	4.40
80	37	4.72	4.40	8.40	8.48	3.68	4.08
81	37	4.96	4.88	8.72	9.04	3.76	4.16

60 dB: Latencies of Waves III and VI and IPI III-VI

No	GA	III		V		III-IV	
		L	R	L	R	L	R
82	37	5.28	5.20	9.60	9.44	4.32	4.24
83	38	5.20	5.20	9.20	9.28	4.06	4.08
84	39	4.40	4.22	8.32	8.32	3.92	4.10
85	39	4.32	4.64	8.24	8.48	3.92	3.84
86	39	5.60	4.96	9.76	9.12	4.16	4.16
87	40	4.32	4.40	0	0	0	0
88	40	4.80	4.88	0	8.72	0	3.84
89	40	4.64	4.70	8.48	8.64	3.89	3.94
90	40	5.04	4.80	0	0	0	0
91	41	4.40	4.48	8.64	8.24	4.16	3.76
92	42	4.32	4.32	7.76	7.84	3.44	3.52

1. HEARING THRESHOLDS IN PRETERM AND FULL TERM INFANTS

No	GA	HEARING THRESHOLD		No	GA	HEARING THRESHOLD	
		Left	Right			Left	Right
1	27	60	40	29	33	20	20
2	28	40	40	30	33	30	30
3	28	30	30	31	33	40	40
4	29	40	45	32	33	30	30
5	29	40	40	33	33	30	25
6	30	40	40	34	34	30	30
7	30	40	40	35	34	30	30
8	30	30	40	36	34	40	40
9	30	40	40	37	34	30	30
10	31	30	30	38	34	30	40
11	31	40	30	39	35	20	30
12	31	40	40	40	35	30	30
13	31	40	40	41	35	30	30
14	31	40	40	42	35	25	25
15	31	40	40	43	35	30	30
16	31	40	30	44	35	30	35
17	31	40	30	45	35	30	30
18	31	40	40	46	36	30	30
19	32	30	30	47	36	25	30
20	32	30	30	48	36	20	20
21	32	40	40	49	36	20	25
22	32	30	20	50	37	30	30
23	32	30	30	51	37	20	25
24	32	40	30	52	37	20	20
25	32	30	25	53	37	25	25
26	33	30	30	54	37	20	20
27	33	30	20	55	38	20	20
28	33	30	30	56	38	20	20

No	GA	HEARING THRESHOLD	
		Left Ear	Right Ear
56	38	20	20
57	38	20	20
58	38	20	20
59	39	30	20
60	39	20	20
61	39	10	10
62	39	20	10
63	39	15	20
64	40	20	20
65	40	20	20
66	40	10	10
67	40	15	10
68	40	20	10
69	41	20	20
70	41	15	10
71	41	15	20
72	42	20	20

Latency Intensity Function (continue)

80dB

	28-32 50	33-37 62	38-42 54
1	8.120	7.440	7.120
2	7.640	7.280	6.760
3	8.480	7.880	6.220
4	8.800	7.280	6.720
5	7.600	8.030	7.000
6	7.440	7.280	6.780
7	7.600	7.040	6.640
8	7.920	7.120	6.080
9	8.280	6.880	7.200
10	7.440	7.280	6.800
11	7.280	7.360	6.720
12	7.480	7.280	7.040
13	8.400	6.820	6.240
14	7.760	7.360	6.640
15	7.680	7.200	6.800
16	8.200	7.600	6.720
17	7.680	7.320	6.640
18	7.180	7.040	6.560
19	7.280	6.800	7.120
20	7.460	7.200	6.800
21	8.080	7.120	6.480
22	7.520	6.800	6.640
23	7.760	7.000	6.560
24	7.120	7.000	6.880
25	7.360	6.680	6.760
26	8.240	6.960	6.800
27	7.760	7.360	6.180
28	8.240	6.960	7.040

Latency Intensity Function (continue)

80dB

	28-32 50	33-37 62	38-42 54
29	9.200	6.800	6.520
30	8.000	6.560	6.080
31	7.280	7.260	6.720
32	7.820	7.120	7.120
33	8.000	7.200	6.760
34	8.000	7.440	6.700
35	7.520	7.360	6.080
36	7.400	7.600	7.040
37	7.400	7.280	6.880
38	8.320	6.880	6.880
39	7.960	7.360	6.720
40	7.600	6.880	6.320
41	8.200	6.880	6.800
42	7.440	7.220	6.8090
43	7.160	7.400	6.860
44	7.160	6.880	6.880
45	8.080	7.220	6.560
46	7.400	7.200	6.960
47	7.360	7.280	6.720
48	7.680	7.280	6.320
49	7.200	6.880	6.640
50	7.680	7.200	6.640
51		7.120	6.800
52		7.000	6.880
53		6.800	6.480
54		6.800	6.280
55		7.040	
56		6.440	

Latency Intensity Function (continue)

	80dB		
	28-32 50	33-37 62	3842 54
57		6.880	
58		7.200	
59		6.880	
60		6.560	
61		6.800	
62		7.200	

Latency Intensity Function in realtion to GA and PCA

	40dB			60dB		
	28-32 44	33-37 68	38-42 62	28-32 54	33-37 70	38-42 60
1	10.600	8.400	6.960	9.000	7.840	7.520
2	10.500	8.320	6.720	8.220	7.680	6.960
3	8.800	9.200	7.280	8.880	7.320	6.480
4	8.880	9.250	7.040	8.240	7.200	7.360
5	10.300	8.880	8.400	7.520	8.000	7.120
6	9.440	8.520	8.000	8.400	7.760	7.200
7	8.480	10.100	7.680	8.640	7.680	6.960
8	8.800	8.480	8.160	9.040	7.680	6.860
9	9.280	9.120	8.240	8.000	7.760	6.720
10	9.520	8.320	8.160	8.080	8.000	7.440
11	9.280	8.640	8.320	7.600	8.000	6.280
12	10.300	8.520	8.000	8.400	8.560	7.120
13	9.920	8.160	7.920	8.720	7.860	7.520
14	8.640	7.800	7.840	8.080	7.720	7.360
15	8.680	8.320	6.640	7.840	7.520	6.480
16	8.780	8.480	6.720	8.600	7.600	7.120
17	8.880	8.800	7.920	8.160	7.580	6.720
18	8.640	8.160	7.360	7.400	7.760	6.920
19	9.520	8.640	8.480	7.840	7.280	7.120
20	9.680	8.000	8.080	8.060	7.520	6.720
21	8.800	7.680	8.400	8.360	7.480	6.560
22	8.960	8.320	8.320	7.840	7.280	7.350
23	8.960	8.480	7.040	7.280	7.700	7.440
24	9.380	8.240	7.120	7.960	7.580	7.040
25	10.200	9.120	7.200	7.760	7.200	6.720
26	8.800	9.120	7.360	7.520	7.600	6.720
27	8.800	8.240	7.280	8.000	7.280	7.200
28	8.940	8.240	7.680	8.840	7.160	6.960

Latency Intensity Function in rellation to GA and PCA

	40dB			60dB	
	28-32	33-37	38-42	28-32	33-37	38-42
	44	68	62	54	70	60
56		7.840	7.360		7.480	6.640
57		8.560	7.520		7.600	7.220
58		8.240	7.440		7.520	6.800
59		7.920	7.280		7.680	6.720
60		7.360	7.200		7.600	6.720
61		7.920	7.160		7.040	
62		7.280	7.360		7.520	
63		7.440			7.600	
64		8.000			6.960	
65		8.460			6.720	
66		7.440			7.000	
67		8.360			7.400	
68		8.240			7.600	
69					7.200	
70					7.640	

Latency Intensity Function of wave V in relation to to GA and PCA

	20dB			30dB		
	28-32	33-37	38-42	28-32	33-37	38-42
	3	16	28	20	24	4
1	9.600	8.880	8.880	10.300	9.120	7.960
2	11.000	8.800	8.880	9.400	9.520	7.440
3	8.640	9.000	8.800	11.200	8.800	8.080
4		8.480	9.360	9.360	8.400	8.240
5		9.760	9.520	9.120	9.120	
6		9.740	9.840	11.000	9.360	
7		9.860	7.520	9.720	9.440	
8		10.700	8.960	9.520	8.960	
9		10.000	7.760	9.840	8.880	
10		9.840	8.720	10.000	9.040	
11		10.600	9.840	9.760	8.560	
12		10.600	9.360	9.440	8.240	
13		8.400	9.560	9.000	9.120	
14		9.360	10.800	8.560	9.760	
15		9.240	8.640	9.200	9.240	
16		8.400	8.000	8.640	8.960	
17			8.640	9.120	8.720	
18			7.360	8.720	9.240	
19			7.640	8.640	9.960	
20			9.360	8.960	9.880	
21			7.880		9.120	
22			9.520		9.120	
23			8.640		8.240	
24			8.640		7.920	
25			8.560			
26			8.640			
27			8.080			
28			7.960			

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Hearing threshold in preterm and term infants by auditory brainstem response

Hearing thresholds were established in preterm and term newborn infants by auditory brainstem responses in the first week of life. The presence of wave V was the criterion for threshold sensitivity in infants considered neurologically optimal on the basis of stringent clinical criteria and sequential ultrasound examination. The hearing threshold was found to be at 40 dB in preterm infants between 28 and 34 weeks gestational age, at 30 dB in infants between 35 and 38 weeks, and below 20 dB in term infants. This study confirms that the thresholds of newborn infants diminish with increasing age, and there is no apparent difference whether maturation occurs inside or outside the uterus. The data should provide a baseline for objective and quantitative assessment of hearing loss early in the neonatal period. (J PEDIATR 1985;107:593-599)

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AUDITORY BRAINSTEM RESPONSES provide an objective method for quantifying the functions of both the peripheral auditory apparatus (middle ear and cochlea) and the central auditory pathway as it courses through the brainstem. The method is particularly useful in newborn infants, in whom traditional methods of behavioral audiometry are difficult to interpret.[1-3] Other methods of auditory assessment, such as the crib-o-gram[4] and the cradle,[5] are of diagnostic value only in infants with high levels of hearing loss, and will pick up only severe bilateral deafness.[5]

The prevalence of hearing deficits among the "graduates" of intensive care units has been estimated to be as high as 2% to 4%,[6-9] indicating the urgent need for accurate and quantitative procedures for screening hearing.[10]

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Early resort to hearing aids and special education is needed as soon as possible,[11] because the earlier the management is instituted the better are speech and language development.[12]

Although ABRs have been used in many centers to screen populations at risk, very limited data are available on the hearing capacity of normal preterm infants. Moreover, inconsistencies in selection of "normal" preterm infants have led to wide variations in the reported normal values for different components of the ABR at various gestational ages. In addition there has, to date, not been a systematic study of the hearing threshold in these preterm infants. This gap in the literature has created major difficulties in estimating hearing deficits and elevated thresholds in high-risk neonates before discharge from the neonatal unit.

ABR	Auditory brainstem response
HL	Hearing level

Our aim was to draw up maturation curves for the hearing threshold as determined by ABR in a population of neurologically optimal newborn infants, who had no apparent neurologic deficit on very stringent clinical grounds and cranial ultrasound imaging.

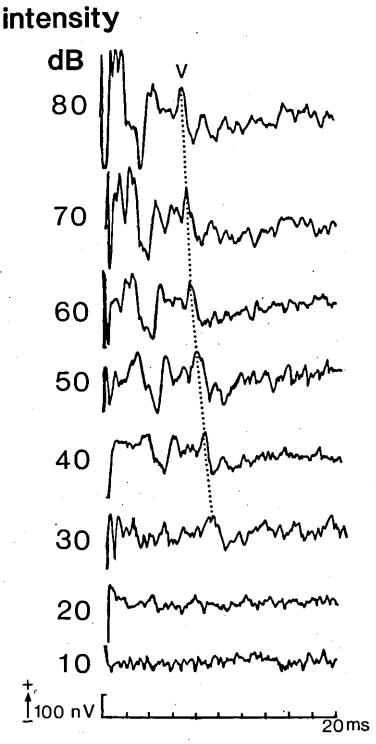

Fig. 1. ABR (normal infant gestational age 33 weeks) as a function of stimulus intensity (10 to 80 dB HL). There is a gradual shift of wave *V* as intensity is reduced. Presence of wave *V* at minimum intensity (30 dB) is hearing threshold. Stimuli were clicks at repetition rate of 10/sec.

METHODS

During a 1-year period (September 1983 to September 1984), ABRs were performed in all neurologically optimal preterm infants admitted to the Neonatal Unit at Hammersmith Hospital during the first week of life and weekly until discharge. Additional term babies from the postnatal wards were also included, informed consent having been obtained from the parents. Infants were classified as "optimal" if they were at low risk of developing neurologic complications and normal according to the following criteria:[13] (1) a postnatal complication score of 0 or 1 on a scale adopted from Drillien et al.[14]; (2) normal results on sequential neurologic examination, according to the protocol of Dubowitz and Dubowitz[15]; (3) absence of intracranial pathologic findings according to independent sequential ultrasound examination performed in all preterm and term infants in the Neonatal Unit.[16]

During this period of the study we reviewed data from some 300 infants. Although many of them were considered potentially suitable for the study, only 42 infants met the above criteria. Their gestational ages ranged from 27 to 42 weeks (mean 34.5 weeks), and their birth weights from 950 to 3700 gm (mean 1962 gm).

Gestational age of all infants was determined according to the Dubowitz score.[17] If this differed from maternal dates by more than 1 week, an estimate derived from motor nerve conduction velocity was taken as an additional index of gestational age.[18]

All ABRs were recorded on a Medelec Sensor machine. Three standard EEG silver disk electrodes were applied to the scalp, the negative electrodes being on the ipsilateral mastoid, the positive on the vertex, and the neutral on the contralateral mastoid. Interelectrode impedances were all below 6 KΩ, and typical impedance was below 2 KΩ. Rarefaction acoustic phase signals (clicks) of square waves 100 μsec duration at a rate of 10/sec were generated and delivered via a TDH-39 earphone held to each of the infant's ears in turn (the other ear lying on the mattress). A total of 1024 to 2048 responses was averaged through bandpass of 300 to 3000 Hz. To determine the hearing threshold, a stimulus of 40 dB* normal hearing level† was applied initially, and depending on the responses, the stimuli were increased or decreased to determine the threshold of the response. The hearing threshold was defined as the minimum intensity needed to elicit wave V. Each trial was repeated two or three times to ensure reproducibility. The test could usually be completed within an hour. All hearing thresholds were assessed jointly by two observers.

The acoustic milieu (air and incubators) in the Neonatal Intensive Care Unit and in the postnatal wards was measured by a Bruel and Kjaer Sound Pressure Level Meter (2203). The sound level weighting scale was set at A, which covers the spectrum of frequencies of normal hearing. Noise levels in air were in the range of 58 to 62 dB sound pressure level (mean 60 ± 2 dB). In incubators (Vickers model 142) the noise level was 50 to 54 dB sound pressure level (mean 52 ± 3 dB).

RESULTS

In the 42 infants classed as optimal, 144 ABR examinations were performed in both ears. The minimum hearing thresholds were analyzed with respect to gestation and

*The hearing level of the click stimulus at intensity 40 dB corresponds to 73 peak equivalent sound pressure level (re: 0.0002 dynes/cm²) as determined by Bruel & Kjaer Sound Level Meter (type 2209), Bruel & Kjaer artificial ear (type 4152), and condenser microphone (type 4144).

†The calibration was done by Medelec Ltd. They tested a number of their employees (clinically examined and found to be neurologically and otologically normal, with no history of noise exposure). Their hearing thresholds were set as the zero (0 dB HL).

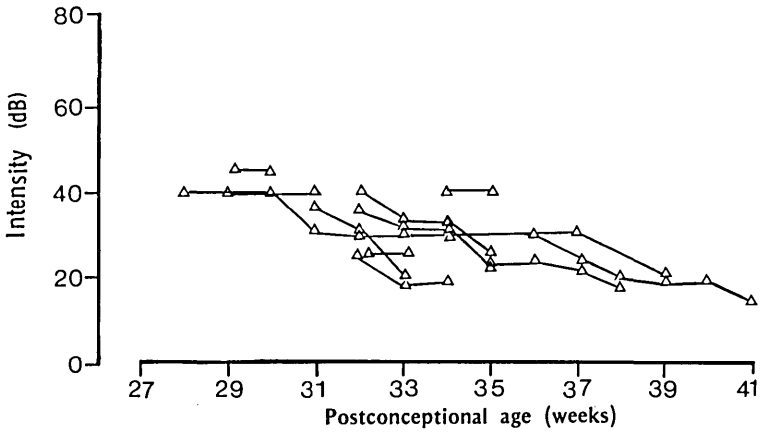

Fig. 2. Longitudinal study of 11 infants showing maturational trend in threshold reduction. The lower the gestational age, the higher the response threshold.

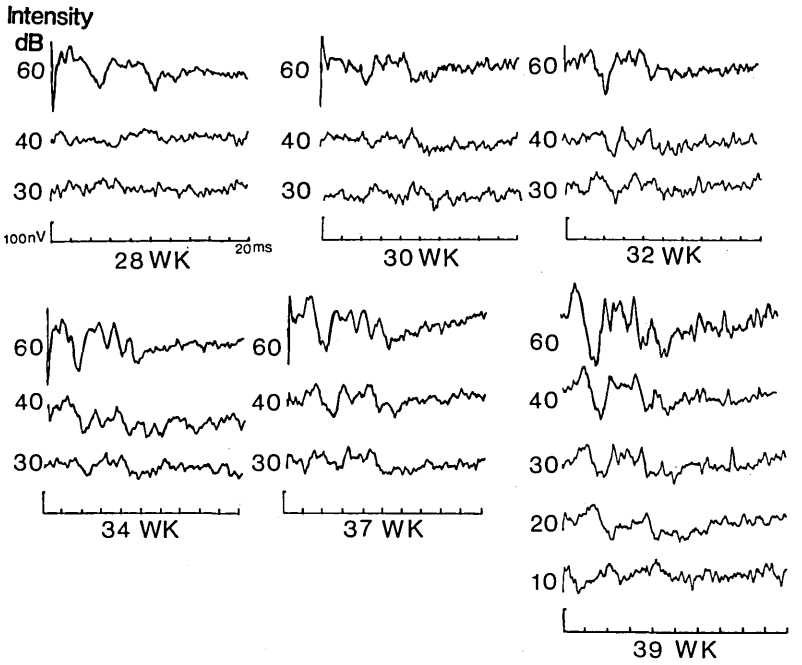

Fig. 3. Longitudinal changes in ABR waveforms and threshold reduction in a preterm newborn infant of 28 weeks gestation.

postconceptional age. Hearing threshold level determination is illustrated in Fig. 1.

Thresholds for infants of appropriate gestational age and for infants small for gestational age were plotted separately, as were longitudinal and cross-sectional data. Eleven infants were studied longitudinally; their progressive reduction in threshold is shown in Fig. 2. The ABR complexes appeared initially as a poorly defined waveform, with an elevated threshold. As the infant approached term, well-defined waveforms and lower thresholds appeared. Fig 3 illustrates the longitudinal changes in threshold reduction for one infant. The longitudinal follow-up in these infants paralleled the cross-sectional data (Fig. 4).

Inasmuch as there seemed to be complete overlap between these groups, the data were subsequently pooled for statistical analysis.

The hearing threshold decreased steadily with increasing gestational age, and because the thresholds appeared to

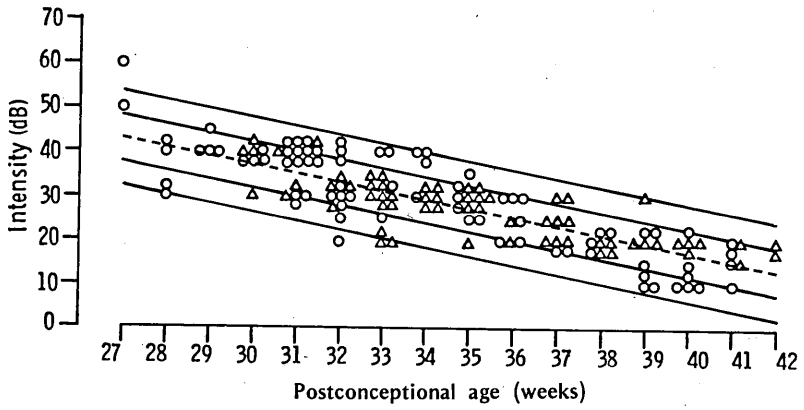

Fig. 4. Regression lines and confidence limits for hearing threshold in preterm infants. o, Cross-sectional data (84 ears); △, longitudinal data (60 ears) (144 ABRs in 42 infants).

Table. ABR hearing threshold in relation to gestational age and conceptional age

Gestational age and conceptional age (weeks at test)	*n*	*Hearing threshold (intensity level of wave V in dB)*				
		Mean	*+1 SD*	*−1 SD*	*+2 SD*	*−2 SD*
27	2	43.4	48.8	38.0	54.1	32.6
28	4	41.4	46.8	36.0	52.1	30.6
29	4	39.4	44.8	34.0	50.2	28.6
30	8	37.4	42.8	32.0	48.2	26.6
31	18	35.4	40.8	30.0	46.2	24.7
32	14	33.4	38.8	28.0	44.2	22.7
33	16	31.4	36.8	26.1	42.2	20.7
34	10	29.4	34.8	24.1	40.2	18.7
35	14	27.5	32.8	22.1	38.2	16.7
36	8	25.5	30.8	20.1	36.2	14.7
37	10	23.5	28.9	18.1	34.2	12.7
38	8	21.5	26.9	16.1	32.2	10.7
39	10	19.5	24.9	14.1	30.3	8.7
40	10	17.5	22.9	12.1	28.3	6.7
41	6	15.5	20.9	10.1	26.3	4.8
42	2	13.5	18.9	8.1	24.3	2.8

have linear relationship with gestational age, straight lines were fitted by least square.

Because of the imprecision of the SD estimated at single weeks of gestation, a single pooled estimate was used. If the threshold reading for one ear at a particular age can be written as the sum of two points, y = y1 + y2, when y1 is the same for both ears of a given baby and has variance σ_1^2, and y2 differs between the two ears and has variance σ_2^2. Then this model allows for the observed correlation between the two threshold measurements made in each baby. If a one-way analysis of variance[19] provides mean squares of A and B between and within babies, respectively, σ_1^2 and σ_2^2 can be estimated by (A − B)/2 and B, and the variance appropriate to a measurement in a single ear is then $\sigma_1^2 + \sigma_2^2$. The mean threshold and values 1 and 2 SD above and below the mean are plotted against gestational age in Fig. 4 and are given numerically in the Table.

From these curves we would expect neurologically optimal preterm infants with gestational ages ranging from 28 to 34 weeks to have a hearing threshold at 40 dB, and infants with gestational ages of 35 to 39 weeks a threshold of 30 dB or less. Fig. 5 demonstrates the presence of hearing threshold levels at different gestational ages (29 to 38 weeks).

Ambient noise levels seemed to have no effect on hearing thresholds measured in the same infants in the different environment in which the recordings were performed (air or incubators, in the neonatal intensive care unit or

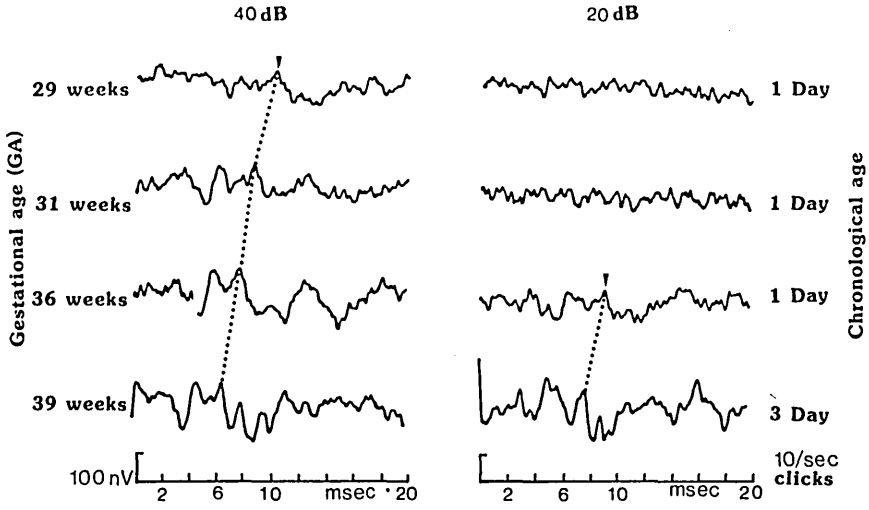

Fig. 5. Auditory brainstem responses recorded from four infants, three preterm on day 1 and one term on day 3, at intensities 40 and 20 dB. Note appearance of wave V at 20 dB at 36 weeks gestational age and definite presence of hearing threshold at 40 dB at all gestational ages (from 29 weeks).

postnatal wards). Similar thresholds were obtained in all these environments.

DISCUSSION

The hearing threshold in term newborn infants has been thought to be within the range of normal adult levels.[12] Schulman-Galambos and Galambos[20] estimated a difference of 10 dB, and Mokotoff et al.[21] thought the difference to be no greater than 20 dB. Kaga and Tanaka[22] reported that by the age of 5 months practically all normal infants had auditory brainstem responses at 20 dB, and that only at the age of 3 to 4 years did the threshold fall to adult levels of 10 dB.

There is controversy concerning thresholds in preterm infants, and gestational age is the main factor determining the presence or absence of responses. Although Starr et al.[7] reported the presence of ABRs in preterm infants of 28 weeks gestational age, Stockard and Stockard[23] found that absence of responses in preterm infants of 30 weeks gestation was common, whereas with gestational age of more than 32 weeks the thresholds appeared at 85 or 75 dB sound pressure level.[24] Recently, Salamy[25] found that in infants of less than 30 weeks conceptional age, 50% had recognizable waves at 60 dB HL.

Galambos and Hecox[26] believed that the ABR first appeared from 26 to 28 weeks gestation at a strong stimulus of 70 dB above adult level; this was confirmed by Hecox and Burkhard.[27]

Our studies suggest that neurologically optimal preterm newborn infants have a much lower hearing threshold than previously reported. Having selected an optimal population, we were able to define with accuracy lower than previously recorded hearing thresholds in all infants down to 28 weeks gestation.

We have been unable to identify any neurologically optimal infants (by our criteria) under 27 weeks. In our experience with neurologically nonoptimal infants at this low gestation, the ABRs have been consistently absent.[28] However, the auditory apparatus is structurally mature by 6 months gestation,[29] and Starr et al.[7] had noted that an ABR can be recorded from preterm infants as young as 25 weeks gestation, if the signal is sufficiently intense.

Our longitudinal and cross-sectional data also confirmed that there was no difference in maturation of the auditory pathway inside and outside the uterus.[30]

In the present neurologically optimal population, we found no case in which a threshold could not be determined. This suggests that difficulties experienced by earlier authors in obtaining hearing thresholds may be related to abnormalities in the patients (audiologic, neurologic, or both), to environmental causes (ambient noise levels), or to inadequate sensitivity of the equipment.

Fawer and Dubowitz[13] had failures of 50% at 40 dB, and Roberts et al.[9] found the same in preterm infants at 40 weeks postconceptional age. These were attributed to immaturity and ambient noise. In the present study, ambient noise did not prove to interfere with threshold, and technical improvement in our equipment compared with that used earlier on this unit by Fawer and Dubowitz[13] resulted in higher sensitivity.

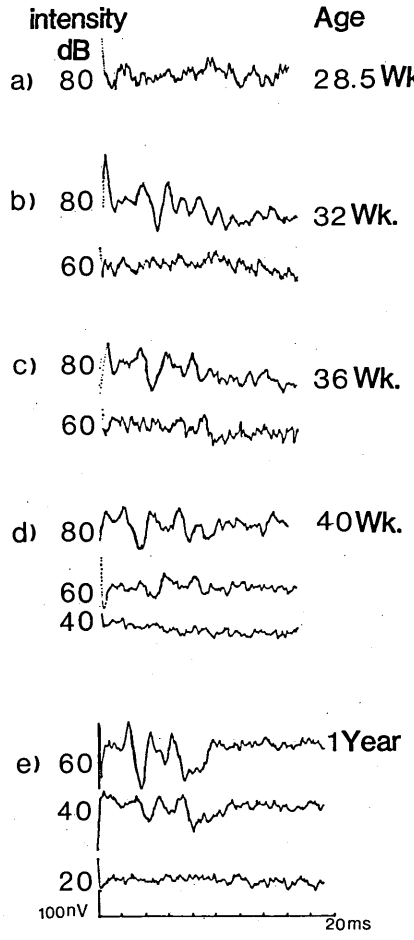

Fig. 6. Longitudinal study of premature infant (gestational age 27 weeks) with periventricular hemorrhage. ABR recorded at postconceptional age of 28.5 weeks *(a)* showed absent response at 80 dB. Subsequent ABRs showed elevated threshold and delayed development in threshold reduction compared with others of same age group (compare Fig. 3). Note that at postconceptional age of 32 weeks *(b)* 60 dB was absent; at 36 weeks *(c)* threshold appeared at 60 dB; and by term *(d)* 80 and 60 dB were present but 40 dB absent. At 1 year of age *(e)* ABR was absent at 20 dB. This baby was followed up at a Hearing and Speech Centre. Normal hearing was audiologically confirmed at 2.7 years; but there was delay in expressive language and articulation. Similar findings were found in two other infants with periventricular hemorrhage (one, the patient's twin brother). All showed delayed speech.

Mjøen et al.[31] reported thresholds of 0 to 32 dB HL to be present in 83% of their high-risk neonates of gestational age 27 to 44 weeks, but ages were not specified for given thresholds.

Difficulties in obtaining a hearing threshold may be associated with neurologic problems. Such problems were seen in some infants with high-risk factors such as severe asphyxia, hyperbilirubinemia, or periventricular hemorrhage. Some of the babies with periventricular hemorrhage had elevated hearing thresholds and delayed development of the lower thresholds appropriate to their ages (Fig. 6). Follow-up studies for hearing and speech in these babies at the ages of 2 and 3 years showed delay in language development, suggesting that hearing threshold may predict later problems with language development and that elevated hearing thresholds may be more significant than previously assumed.

The determination of hearing thresholds may prove to be useful in neonatal screening. For clinical purposes, a threshold of 20 dB above what it should be for the infant's age should raise suspicion of hearing loss.

By using stringent criteria of selection and appropriate statistical analysis, this study provides normal thresholds in relation to gestational age and may be used for screening of hearing in a population of high-risk preterm infants.

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