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FURTHER STUDIES OF THE VISUALLY
EVOKED SUBCORTICAL POTENTIAL IN MAN

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Thesis submitted for the Degree of
Doctor of Philosophy

Clinical Neurophysiology Unit
Department of Vision Sciences
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October 1988

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Summary

The Visually Evoked Subcortical Potential, a far-field signal, was originally defined to flash stimulation as a triphasic positive-negative-positive complex with mean latencies of P21 N26.2 P33.6 (Harding and Rubinstein 1980). Inconsistent with its subcortical source however, the signal was found to be tightly localised to the mastoid.

This thesis re-examines the earlier protocols using flash stimulation and with auditory masking establishes by topographic studies that the VESP has a widespread scalp distribution, consistent with a far-field source of the signal, and is not a volume-conducted electroretinogram (ERG). Furthermore, mastoid localisation indicates auditory contamination from the click, on discharge of the photostimulator.

The use of flash stimulation could not precisely identify the origin of the response. Possible sources of the VESP are the lateral geniculate body (LGB) and the superior colliculus. The LGB receives 80% of the nerve fibres from the retina, and responds to high contrast achromatic stimulation in the form of drifting gratings of high spatial frequencies. At low spatial frequencies, it is more sensitive to colour. The superior colliculus is insensitive to colour and suppressed by contrast and responds to transitory rapid movements, and receives about 20% of the optic nerve fibres.

A pattern VESP was obtained to black and white checks as a P23.5 N29.2 P34 complex in 93% of normal subjects at an optimal check size of 12°. It was also present as a P23.0 N28.29 P32.23 complex to red and green luminance balanced checks at 2° check size in 73% of subjects. These results were not volume-conducted pattern electroretinogram responses.

These findings are consistent with the spatial frequency properties of the lateral geniculate body which is the considered source of the signal.

With further work, the VESP may supplement electrodiagnosis of post-chiasmal lesions.
If a man will begin with certainties, he shall end in doubts; but if he will be content to begin with doubts, he shall end in certainties. The Advancement of Learning, I
v8 (Francis Bacon 1561-1626)

This thesis is dedicated to

My parents, Geshe Kelsang, Jennifer French and Jim Gilchrist
ACKNOWLEDGEMENTS

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CHAPTER ONE
A REVIEW OF ELECTRICAL SIGNALS IN THE VISUAL PATHWAY

1.1 Introduction

The subject of this thesis is the visually evoked subcortical potential (VESp) and the main purpose of this chapter is to put this particular response into the context of other electrical signals arising from the visual pathway.

Section 1.2 describes the anatomy of the visual pathway and is followed by a description of electrical signals which arise from the optic tract and have been found to be useful in non-invasive neuro-ophthalmological investigation (section 1.3). Two sets of responses are introduced in this section: those reflecting retinal function recorded by the electro-oculogram and the electroretinogram; and those reflecting occipito-cortical function, shown by the visually evoked cortical potential (VECP) and recordings made by the electroencephalogram (EEG). The occipito-cortical functions are recorded optimally using scalp electrodes over the occipital cortex. A brief history of the field of electrophysiological work in vision has also been included.

Sections 1.5, 1.6 expand on the flash and pattern electroretinogram and sections 1.7, 1.8 and 1.9 describe the flash and pattern cortical visual evoked potential. These sections have been included to emphasise the development of different research using flash and pattern stimulation in understanding visual function and how this development aids progress in establishing signals as useful research and clinical tools. Section 1.10 describes the literature on subcortical signals in the visual system and introduces the visually evoked subcortical potential (VESp).
1.2 The visual pathway

The visual pathway (Figures 1.1 and 1.2) is probably the major sensory tract in the human brain (Bruesch and Arey 1942) and conforms to the generalised form of afferent tracts carrying impulses to the brain. The neural layer is the retina (Figure 1.1) and the end-organ is the sensory epithelium of the rods and cones. These photoreceptor cells synapse with bipolar cells corresponding to the first order neurones of the sensory pathway.

The second order neurones are the ganglion cells and their axons, of which there are about one million (Arey and Bickel 1935) and which leave the eye as the solid cylindrical mass (Cohen 1967) called the optic nerve to go to the optic chiasma. The chiasma (figure 1.3) is unique in that it is the site at which the nerve fibres from the nasal half of each retina cross to mix with the uncrossed fibres from the temporal half of the retina of the other eye. The fibres from the temporal parts of the retina do not decussate and continue backwards through the chiasma into the ipsilateral optic tract. The ratio of crossed to uncrossed fibres is about 53:47 (Kupfer et al. 1967). The optic tract which leaves the chiasma then splits into two.

Twenty per cent of the visual fibres pass round the lateral geniculate body to the superior colliculus (Figure 1.1). Eighty per cent however, enter the lateral geniculate body (LGB), which is the major relay station in the visual pathway. This subcortical junction is thought not to be just a simple relay station but also to be actively involved in colour and contrast processing (Snodderley 1972). At the lateral geniculate body, the axons synapse with a new relay of third order neurones carrying impulses via the optic radiations to the visual
**FIGURE 1.1**

*Diagram of the visual pathway showing the relative positions of the Lateral Geniculate Body and Superior Colliculus*

*(Lockhart et al. 1974)*
Illustration removed for copyright restrictions
Diagram of the visual pathway illustrating the subcortical positions of the lateral geniculate body in the primary visual pathway.
Nerve fibres from the nasal half of each retina cross to mix with uncrossed fibres from the temporal half of the retina of the other eye. Some inferior peripheral decussating fibres form a short loop (Anterior Knee of Wilbrand) passing forward to the optic nerve of the opposite side. Some of the superior peripheral decussating fibres form a similar loop (Posterior Knee of Wilbrand) passing into the optic tract of the same side before crossing. Macular fibres decussate in the posterio-superior part of the chiasma.
cortex in the occipital lobes, located in the posterior part of the cerebral hemispheres.

The occipital lobes are divided into three areas devised by Brodmann (1909) and are called Brodmann's areas 17, 18 and 19, being delineated by the cellular organisation of each area. The primary visual stimulus is received by area 17 and the impulses are probably integrated in area 18 and co-ordinated with other sensory and motor activities in area 19 (Cogan 1976).

There is a disproportionate representation of the retina both at the lateral geniculate body and the visual cortex. The macular region of the retina, which is the region of highest resolution, is represented in 50% of the lateral geniculate body and about half the total number of nerve fibres in the optic radiation convey solely macular impulses to the visual cortex. Mapping of the human visual cortex has also demonstrated that the macular region is associated with about 50% of the cortical area in Brodmann's area 17 (Drasdo 1977).

1.3 The electrical signals from the visual pathway

Clinically useful electrical signals recorded non-invasively from the pathway can be divided into background activity and evoked responses. In the latter situation, a visual stimulus elicits the signal.

The two prominent background responses are the electro-oculogram (EOG), which is a standing positive potential between the retina and the front of the eye at the cornea, and the electroencephalogram recorded from the occipital
FIGURE 1.4

Diagram showing the sites of recording different signals from the visual pathway.

KEY

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<table>
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<tbody>
<tr>
<td>EEG</td>
<td>-</td>
<td>electroencephalogram</td>
</tr>
<tr>
<td>EOG</td>
<td>-</td>
<td>electro-oculogram</td>
</tr>
<tr>
<td>FLASH</td>
<td>ERG</td>
<td>electoretinogram</td>
</tr>
<tr>
<td></td>
<td>PERG</td>
<td>pattern electoretinogram</td>
</tr>
<tr>
<td>FLASH</td>
<td>VESP</td>
<td>flash visual evoked subcortical potential</td>
</tr>
<tr>
<td>PATTERN</td>
<td>VESP</td>
<td>pattern visual evoked subcortical potential</td>
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<tr>
<td>FLASH</td>
<td>VECP</td>
<td>flash visual evoked cortical potential</td>
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<tr>
<td>PATTERN</td>
<td>VECP</td>
<td>pattern visual evoked cortical potential</td>
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(see text for further details)
cortex.

The use of visual stimulation, eg. by flash or pattern stimulation, has yielded the electroretinogram and the cortical visual evoked potential. The ERG is a measure of retinal integrity and is recorded at the cornea or within the orbital area (Galloway 1981) whilst the VECP as has been mentioned in section 1.1 is optimally recorded by placing scalp electrodes over the visual cortex and provides information about the functional integrity of the visual pathway (Harding 1982).

This thesis also introduces a subcortical evoked potential, the VESP, first described by Harding (1979). It is recorded by scalp electrodes sited more centrally at vertex and paravertex positions. The signals described above are represented on the visual pathway in figure 1.4.

1.4 Historical background

The cornerstone of electrophysiological research in ophthalmology was laid in 1849 by DuBois Reymond. He discovered that the eye demonstrated a potential difference between the cornea and the retina and this led to the concept of the 'resting-potential' of the eye (DuBois Reymond 1849). The electro-oculogram was the recording technique by which slow changes in the corneo-retinal potential or rapid changes produced by eye movements could be demonstrated (Mowrer et al. 1936), and until the 1950s the EOG was used solely to measure eye movements. One of the earliest accounts of its use as a test of retinal function is those of Francois et al. (1955), and subsequent work led to the Arden index being developed to assess the effects of illumination on
the resting potential (Arden and Kelsey 1962) and relating the index to retinal integrity.

Sixteen years after DuBois-Reymond had described the 'resting potential', Holmgren demonstrated in the frog that the resting potential could be modified by the action of light shining on its eye (Holmgren 1865). He had described what is now known as the electroretinogram. In 1877, Dewar published the first observations on the human eye (Dewar 1877). By the 1940s, the ERG waveform was being accurately recorded and analysed and it was clearly recognised that the response being recorded at the cornea reflected retinal activity. Granit (1947) in his classic text 'Sensory Mechanisms of the Retina' was by far the greatest contributor to the research on the retinal origins of the different components of the flash ERG. The ERG is further described in section 1.5 and the ERG to pattern stimulation in section 1.6.

In 1875 Caton described the spontaneous electrical activity of the brain as 'feeble currents which varied in direction' (Caton 1875). His work was done using animals. In 1929 however, the first publications of recordings of brain electrical activity in humans was made by Hans Berger (1929). Berger described two forms of activity as alpha and beta and used the term 'electroenkephalogram' to describe the phenomenon. He observed that sensory stimulation reduced the spontaneous brain activity and concluded that alpha rhythm was seen in the EEG when the subject's eyes were closed and disappeared when the eyes were open (Berger 1932). Adrian and Matthews (1934), having isolated the alpha activity to the occipital cortex, demonstrated electrical responses elicited by regularly repeated flashes of light and recordable over the occipital cortex in the on-going EEG. This was the first
human visual evoked cortical potential, recorded some 57 years after the first human recording of the electroretinogram. This 'following' response was not observed in all normal subjects as it was usually embedded in the much larger amplitude electroencephalogram. The technique of signal averaging first reported in 1951 (Dawson 1951) subsequently improved the definition of the visual evoked cortical potential and led to many systematic studies of the response to flash and pattern stimulation as described in sections 1.7 and 1.8.

1.5 The flash electroretinogram (ERG)

The flash electroretinogram (ERG) is the oldest photically evoked potential and is a graphical representation of the retinal action potential in response to a photic stimulus (Babel et al. 1977). It is usually recorded from the cornea using a contact lens (Karpe 1968) or corneal electrode (Arden et al. 1979), with a reference electrode usually on the temple. The ERG is a polyphasic evoked potential and is a result of the summation of potentials generated at different sites in the retina (Granit 1947; Babel et al. 1977).

The major components are a negative 'a' wave and a positive 'b' wave, (see Figure 1.5). The 'a' wave has a peak latency between 10-20ms amplitude 90-200µV and the 'b' wave latency falls between 30-50ms, amplitude 100-300µV (Babel et al. 1977; Kooi 1979). The amplitude and latencies vary depending on the stimulus conditions and an increase in stimulus intensity decreases the latencies and enhances the amplitudes (Adrian 1945; Burian and Pearlman 1964). The 'a' wave originates in the photoreceptor layer, and the 'b' wave is thought to be generated by the Muller cells (Miller and Dowling 1970). Two slower waves - the 'c' wave, a slow small amplitude response,
FIGURE 1.5

Diagrammatic representation of the human ERG

Scales for latency and amplitude are arbitrary since the waveform is dependent on stimulus parameters and state of retinal adaptation
a : peak of 'a' wave
b : peak of 'b' wave
c : c' wave
d : 'd' wave
e.r.p : early receptor potential
o.p : oscillatory potentials
and the 'd' wave, an off response at the end of a flash stimulus - are thought to originate from the retinal pigment epithelium and have no clinical use.

Using high intensity flash stimulation, various oscillatory potentials can be seen on the ascending branch of the 'b' wave, usually as 4-6 waves about 3-μV in amplitude and at 7ms intervals. They are thought to be independent components from the bipolar cell layer (Adams and Dawson 1971).

The maximum amplitude of the flash ERG occurs at the cornea (Sundmark 1959) and diminishes rapidly as the active electrode moves off the limbus and out of the eye (Nakamura 1978). Using reference sites at Cz and the anterior neck for non-corneal sites, the amplitude of the response at the lower lid was found to be the highest and was 30% of the amplitude of the corneal 'b' wave and 31-16% of the 'a' wave. With more posterior sites, the 'a' wave fell off rapidly whereas a remnant of the 'b' wave persisted as far back as F4. With some subjects, it was present at T4 and T8, although less than 1μV in amplitude and the extent of the field of activity being directly related to the amplitude of the ERG signal. Attenuation of the 'b' wave has been variously recorded at between 10% and 50% of that present at the cornea (Adachi and Chiba 1971; Noonan et al. 1973; Nakamura 1975; Nakamura 1978).

Topographical studies have shown the field of activity spreads up the forehead and down to the cheek ipsilateral to the eye being stimulated, with very little conduction across the median line of the face and minimally along the temple (Nakamura 1975 and Nakamura 1978). This was subsequently confirmed by Rubinstein and Harding (1981) demonstrating abolition of the flash ERG ipsilateral to the occluded eye.
The 'b' wave is used in clinical diagnosis and the reader is referred to Armington (1974), Galloway (1981) and Babel et al. (1977) for relevant information since the area of clinical applications is beyond the scope of this thesis.

1.6 The pattern electroretinogram (PERG)

The ERG to pattern stimulation as opposed to diffuse flash stimulation was first described by Riggs et al. (1964) and Johnson et al. (1966). Pattern reversal stimulation and pattern onset/offset stimulation (Spekreijse, Van der Tweel and Zuidema 1973) using checks and gratings have predominated as the main forms of stimulation (Lawwill 1984). Two forms of stimulation produce waveforms of different characteristics as shown in Figure 1.6. The pattern reversal response has an N10.7 P44.6 N84.7 configuration with mean amplitudes N-P 2µV and P-N 3.2µV (Kirkham and Coupland 1982/1983). Pattern onset/offset stimulation shows a P-N response. The onset wave has a configuration of P30 N70, P-N 7µV, and the offset wave of P50 N100, P-N 10µV, i.e. often larger in amplitude than the onset wave (Korth and Rix 1983).

Improvements in electrode design have produced the gold leaf electrode (Borda et al. 1978; Arden et al. 1979) and the DTL electrode (Dawson et al. 1979). These have improved patient comfort and reduced the optical degradation of the retinal image caused by the contact lens electrode (Dawson et al. 1974), resulting in higher amplitude PERG recordings.
FIGURE 1.6

The Pattern Electroretinogram (PERG) to pattern reversal stimulation and pattern appearance/disappearance

(After Kirkham and Coupland (1982/3); Korth and Rix (1983))
PERG to pattern reversal stimulation using a 30' check size (Kirkham and Coupland 1982, 1983)

PERG to pattern onset/offset using bar gratings 5.5 cycles per degree (Korth and Rix 1983)
PERG research has diversified into inter-related areas which may be described as i) investigations into factors affecting the response, ii) elucidation of the origin of the response and iii) clinical applications.

Studies of stimulus parameters used to elicit the PERG show the pattern reversal response to be essentially photopic, decreasing in amplitude and increasing in latency with reduced luminance. The parameters employed vary between different workers (see Table 1.1) and may be summarised as high contrast 85% achromatic checks or gratings, with a rate of reversal between 2-15 revs/sec, an optimal check size of 15' - 1° (Arden et al. 1980) or grating size 0.62 cycles per degree (Dawson et al. 1982; Dawson and Maida 1983), a field size between 12° - 22° and a background illumination of 30cd/m². The time window of analysis is 100-300ms and the response is averaged to 120-300 sweeps, with a bandpass of 0.1 - 100Hz. The active electrode tends to be placed in the lower canthus usually gold foil or DTL and referred to a silver/silver chloride electrode placed on the temple (Table 1.1).

Responses to pattern onset/offset have been studied by Korth and Rix (1983) and Reimslag et al. (1985). Pattern onset to gratings is sensitive to high luminance, and high contrast, and peaks at 3-4cpd with a field size of 40°. The offset response is more sensitive to lower spatial frequencies as well as lower contrast levels, and it is suggested that the onset response is comparable with the pattern reversal response.

The retinal activity and its source reflected by the PERG is controversial and research is directed towards finding out whether the response is derived from the major flash ERG generators, from a subset of these generators or whether
**TABLE 1.1**

Experimental Parameters used by different laboratories to elicit the pattern

ERG (PERG)
<table>
<thead>
<tr>
<th>AUTHORS</th>
<th>TYPE OF ELECTRODE</th>
<th>BAND PASS IN Hz</th>
<th>TIME WINDOW IN MS</th>
<th>NO OF SWEEPS</th>
<th>CHECK SIZE IN DEGREES &amp; MINUTES</th>
<th>NO OF REVERSALS PER SECOND</th>
<th>PERCENTAGE CONTRAST</th>
<th>FIELD SIZE IN DEGREES</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOKOL AND NADLER 1979</td>
<td>Riggs scleral lens (Riggs 1941) Ref. cheek</td>
<td>1-35</td>
<td>240</td>
<td>100</td>
<td>24'-48'</td>
<td>2</td>
<td>84</td>
<td>13 x 16</td>
</tr>
<tr>
<td>TRICK AND WINTERMEYER 1981</td>
<td>DTL Ref. Outer canthus</td>
<td>0.1-35</td>
<td>120</td>
<td>100</td>
<td>30'</td>
<td>8</td>
<td>74</td>
<td>12.6° x 16.4°</td>
</tr>
<tr>
<td>KIRKHAM AND COUPLAND 1982/83</td>
<td>Gold foil. Ref. mastoids</td>
<td>0.1-100</td>
<td>120</td>
<td>128-256</td>
<td>15'-1°40'</td>
<td>3</td>
<td>80</td>
<td>11° circular</td>
</tr>
<tr>
<td>ARDEN AND VAEGAN 1983</td>
<td>Gold foil. Ref. canthus</td>
<td>0.3-50</td>
<td>120</td>
<td>250-500</td>
<td>30'-1°</td>
<td>4-8</td>
<td>86</td>
<td>16° circular</td>
</tr>
</tbody>
</table>

**TABLE 1.1**  
EXPERIMENTAL PARAMETERS USED BY SOME WORKERS TO ELICIT THE PATTERN ELECTRORETINOGRAM USING CHECKERBOARDS AND PATTERN REVERSAL STIMULATION
it represents an entirely different system (Holden and Vaegan 1983). The spatial tuning of the PERG response, being defined as "when a system responds more vigorously to one frequency of stimulation than to all others" (Armington et al. 1971), has been an intrinsic factor in determining whether the source is pre- or post-receptoral. Furthermore it is necessary to clarify the difference between a pattern specific response ERG resulting from active pattern-processing functions within the retina, and ERG responses to luminance changes.

Lawwill (1974) found the amplitude of the PERG saturated at low levels of luminance and fine gratings, and increased with larger areas of retinal stimulation. However Sokol et al. (1983) in agreement with Armington et al. (1971) were unable to demonstrate spatial tuning at low intensities but showed bandpass effects at higher intensities. Spekreijse, Estevez and Van der Tweel (1973), using a glass contact lens, and Reimslag et al. (1985), using a DTL electrode, felt the response was merely an addition of responses to luminance increase and decrease. Arden and Vaegan (1983) compared two situations - pattern reversal stimulation generating the PERG, and abrupt luminance increase and decrease of a blank screen to evoking a focal ERG or FERG. Although pattern reversal yielded a maximal response to 30' - 1° check size, they felt that PERG responses were due to local luminance changes and not contrasting borders. Hess and Baker (1984), using grating patterns and steady state conditions, found linear and non-linear components to the response. The latter showed a peak amplitude at 2.5cpd irrespective of square or sine wave presentation, or contrast, luminance and temporal frequency conditions. It was felt however, that the results did not reflect different retinal processes to flash or uniform field ERG. Using a
nasopharyngeal electrode, Korth (1984) suggested that the pattern onset response demonstrated spatial selectivity due to stimulation of centre surround receptive fields.

Animal studies have also been undertaken to determine the source of the response. With complete optic nerve section, fall off in PERG amplitude coincided with ganglion cell degeneration but the flash ERG persisted (Maffei and Fiorentini 1981), implying that the response came from the ganglion cell layer. This was subsequently supported by Schuurman and Berninger (1985) and Dawson et al. (1986). Ocular depth profile studies (Holden and Vaegan 1983; Reimslag and Heynen 1984) established the ocular source of the response opposed to a distant CNS site and concluded the retinal response to pattern and unpatterned stimulation represented a common electoretinographic mechanism stimulated by different procedures.

In conclusion, the pattern ERG using corneal electrodes has been established as a low amplitude N20.7 P44.6 N64.7 response to pattern reversal stimulation using black and white checks and gratings of high contrast. It is also evoked by pattern onset-offset stimulation, the onset response possibly corresponding to the pattern reversal response. The issue of luminance driven and pattern driven components within the complex is still being investigated and the sum of evidence so far suggests that the integrity of the ganglion cells is essential for its production.

1.7  The cortical visual evoked potential (VECP)

The non-invasive visual evoked potential can be broadly defined as changes in
potential activity recorded from the brain using scalp electrodes in response to a visual stimulus. The technique of 'signal averaging' introduced by Cobb and Dawson (1960) has become one popular technique used to distinguish the evoked response from other spontaneous background activity. The assumption made when using an averager is that the background EEG is random in its occurrence and over a long enough recording period will be reduced, whereas the evoked response time-locked to the stimulus will emerge as a dominant waveform. Mathematically, the summated samples of the time locked response increase in amplitude in proportion to the number of samples N, whereas the background random activity increases as a function of N.

The potential activity is measured between two electrodes and the format of the VEP depends on where the electrodes are placed. Two common methods of recording the potential differences use common reference (monopolar) or bipolar montages. In reference recording, the potential difference is measured between an electrode placed over the site of activity and an electrode over a relatively inactive site (Harding 1974). In bipolar recordings, both electrodes are placed over the site of activity and are useful for localising the source of VEP activity (Goff et al. 1969). Inter-laboratory comparisons of VEP recordings have been facilitated by the standardisation of scalp electrode sites offered by the 10-20 system (Jasper 1958) (see Figure 1.7).

There are two general types of visual stimuli used to elicit the visual response:

1 Diffuse, unpatterned light:
   a) this may be a flash of light produced by a photostimulator. The flash frequency and intensity can be altered.
Coronal and superior view of the skull showing percentage distances between electrodes

(After Jasper 1958)
b) the light may be sinusoidally modulated, and the intensity of light oscillates about a mean luminance level.

2 Patterned stimuli:

a) Pattern onset-offset-flash elicited.

The subject is presented with a flashed-on pattern. The VER obtained is called a flash elicited transient pattern VEP (Arden et al. 1977) and contains two types of components - those related to the presence of contours in the pattern and those occurring with the increase and decrease of the luminance as the photostimulator flashes on and off.

b) Pattern onset/offset constant luminance.

In any given cycle, the pattern appears once per cycle and then disappears, to be replaced by a blank field of equal mean luminance for the remainder of the cycle.

c) Pattern reversal

Pattern reversal stimulation involves bright and dark pattern elements interchanging rhythmically, the number of reversals being twice the modulation frequency expressed in cycles per second (c.p.s.) or Hertz (Hz). The luminance is once again constant throughout the cycle (Arden et al. 1977).

The resultant VEP depends on the rate at which the stimulus is presented and two types of response have been defined, namely transient and steady state responses (Mackay and Jeffreys 1973; Regan 1975). The transient VEP has
a polyphasic waveform and is displayed as a plot of change in potential against time, the stimulus rate being set so that the visual system responds abruptly and settles down before the next stimulus occurs. However, if the stimulus frequency is higher however, eg. 8-10 flashes per second, the waveform becomes more periodic and is called a steady state VER. In transient VER analysis, the amplitude and latency (or 'implicit time') of each discrete component of the waveform is measured, whilst in steady-state analysis, the amplitude of the signal is measured as a function of the frequency of stimulus presentation.

1.8 The flash VECP

In 1951, Dawson reported the first averager (Dawson 1951) and with variations and improvements on the method of averaging (Clark 1958; Clynnes 1961) the first systematic studies of the VEP to flash stimulation were published in the 1960s.

Using 11 adult subjects, recording potentials around the occiput and supra orbital occipital region, with a bipolar montage and high intensity stimulation, Cobb and Dawson (1960) reported four main components of the cortical VEP (a positive at 20-25ms and a negative at 90-100ms) (Figure 1.8). This is significant to this thesis as averaging had enabled clarification of early components, ie. in the 10-65ms envelope, which were smaller in amplitude and variable in comparison with later components (Contaminin and Cathala 1961). In a study of 75 subjects using midline electrodes Oz referred to Pz, Ciganek (1961) offered a classification of the waves, and although early components were recorded (P28.62 N39.12 P53.4), the most prominent
FIGURE 1.8

Occipital potentials evoked by bright flashes. (Cobb and Dawson 1960)

The top illustration shows simultaneous recording of ERG and occipital potential. The occipital response begins with early deflections at 20-25 m/sec. The middle illustration shows records from different midline electrode pairs. The bottom illustration shows the effects of different intensities, reducing from a to d, early components being better defined at higher intensities. The time scale shows 5 and 20 msec. intervals in all cases (see text for details)
component was a positive component at 95-120ms.

A period of 'taxonomy' (Katzman 1964) ensued in which deflections, polarities, latencies and variability of components were examined as a pre-requisite to using the VER in the important fields of clinical diagnosis and in the understanding of visual physiology. Various classifications emerged (Gastaut and Regis 1965; Dustman and Beck 1969; Harding 1974) all clearly documenting a major positive cortical component between 95-120ms. (Figure 1.9). Research tended to concentrate on this latency envelope at the expense of earlier components which were easily embedded in on-going EEG activity owing to their minute amplitudes and the limits of resolution of the equipment (Contamin and Cathala 1961).

The origins of the components were investigated. Ciganek (1961) felt the primary flash response (55-95ms envelope) was a specific visual response, showing localisation over the visual cortex consistent with retinal stimulation, whilst later components had a more diffuse origin. In a further study of 100 subjects, components before 50ms were more prominent in the parietal regions and dependent on faster flash rates, whilst the later waves attenuated on higher flash rates and predominated over the occipital region. However, all components were felt to be cortical (Kooi and Bagchi 1964).

Various clinical uses of the VECP were identified, for example in objective perimetry, the detection and localisation of lesions within the eye and visual pathway, and the quantitative measurements of visual function (Vaughan and Katzman 1964). However, flash stimulation was seen by some workers to lack precision in localising visual pathology (Copenhaver and Perry 1964;
FIGURE 1.9

Schematic representation of normal VEP to diffuse flash stimulation

Schemes of component labelling are shown above the waveform. The first row (letters) is that of Dustman and Beck (1969); the second row (Roman numerals) is that of Ciganek (1961); the third row is that of Gastaut and Regis (1965); the fourth row is that of Harding (1974) (after Harding 1974).
Ciganek 1969; Rouher et al. 1969). Calloway (1969) felt the flash VER held promise where neurological lesions prevented a subject from responding and Harding (1977) outlined various applications of the flash response using phase reversal techniques, as a useful diagnostic aid in the area of visual field defects in macular diseases and in assessment of retinal integrity in the presence of dense unilateral cataract.

1.9 The pattern VECP

In 1965, Spehlmann introduced the VECP to pattern stimulation. A checkerboard pattern was superimposed on a photostimulator and the VECP evoked by the flashed-on pattern was larger in amplitude than the flash VECP, despite the fact that the luminance had effectively been halved by the presence of the black checks (Spehlmann 1965). Ensuing research was devoted to isolating the pattern specific contribution by the introduction of stimuli which presented pattern at constant luminance. Two main techniques emerged, namely, pattern reversal and pattern onset/offset (terminology adopted by the Brussels Symposium ad-hoc Committee, Arden et al. 1977).

Onset-offset stimulation has been used in studying the physiological significance of pattern VECPs (Jeffreys 1968; Spekreijse, Estevez and Van der Tweel 1973), but the lower variability of the pattern reversal response meant that it became the more popular stimulus. The VECP to pattern reversal stimulation consists of a major positive component with peak latency of 100ms (as shown in Figure 1.10) (Jeffreys 1977; Spekreijse 1980; Reimenslag et al. 1981). In a review of normative studies (Halliday 1980), the major positive component occurred between 90-120ms in 25 studies and 90-110ms
The Visually Evoked Cortical Potential to pattern reversal and pattern appearance/disappearance stimulation.

The pattern reversal response is dominated by a positive component of 100ms - latency (P100).

(After Kriss and Halliday 1980)

The pattern appearance-disappearance response is dominated by a negative CII component. The response is completed by a positive-going off response. (After Spekreijse & Estevez-Uscanga 1972).
PATTERN REVERSAL

P100

0 300ms

PATTERN APPEARANCE/DISAPPEARANCE

CI III OFF

CI II

0 500ms
in 20 studies, despite the widely varying experimental conditions, and earlier components were rarely seen or commented about.

This thesis concentrates on the physiological mechanisms underlying the response to pattern, laying stress on information relating to pattern reversal stimulation as this technique has been the chosen method in eliciting a subcortical pattern response.

Harter and White (1968) investigated the relationship between contour sharpness and stimulus check size and found the pattern VECP amplitude decreased with blur, demonstrating contrast sensitivity and saturated in amplitude with check size. Other workers verified that the pattern VECP was optimal to checks between 10' - 30' check size for all types of pattern stimulation and recording techniques. It was concluded to be essentially a response from the central 3°-5° of the visual field, i.e. the area of highest resolution, (Rietveld et al. 1967; Behrman et al. 1972). Halliday et al. (1979) found a reduction in mean stimulus luminance increased the latency by 15-20ms and a ten fold decrease in luminance reduced the amplitude by 15%, although check contrast had a more marked effect as a two fold contrast change had the equivalent effect of a ten fold luminance change (Van der Tweel 1972).

Checkerboard stimulation was generally preferred to grating stimulation as it was felt that it gave the closest approximation to the radial arrangement of the retinal receptive fields whilst maintaining a simple enough shape for pattern reversal stimulation, and produced a more sharply defined, higher amplitude VECP than that evoked by the grating. One reason offered according to
Fourier theory is that the checkerboard contains a large number of frequencies - two oblique fundamentals and higher harmonics forming the edges. This was supported by Campbell and Maffei (1970) who found the amplitude of steady state VECPs was proportional to the number of spatial frequencies activated and checkerboards evoked a greater amplitude than gratings. Reitveld et al. (1967) had established that the amplitude was maximal when the pattern was composed of right angles or acute angles.

Armington et al. (1971) suggested that the peak of the check size function was probably related to the size of the antagonistic centre surround receptive fields, and this was elaborated by Spekreijse et al. (1977) who established the response was not solely dependent on luminance channels but also on spatial contrast mechanisms, the latter depending on the check size to receptive field diameter.

The reliability of the pattern reversal response amongst normal samples under a variety of experimental conditions enabled various workers to apply the VECP to visual physiology and correlate their findings with psychophysics (Harter et al. 1975). It was also clinically applied as it offered the minimal amount of light scattering and held potential as an objective diagnostic aid, eg. different parts of the visual field could be discretely stimulated and it was an objective tool to assess the integrity of the visual pathway (Halliday and Michael 1970).

The research into the pattern VECP is diverse and beyond the scope of this thesis. The reader is referred to Desmedt (1977) for a comprehensive overview of the area.

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1.10 Subcortical components

In the 1970s, the main thrust of VEP research lay in the cortical response to pattern, and under the clinical and experimental conditions used (Desmedt 1977) components occurring outside a 60-140ms envelope were sparsely described in the literature.

The first suggestion of subcortical potentials was made by Van Hasselt (1972) who described a potential at 10ms recorded around the mastoid region in 4 out of 10 subjects and proposed an optic nerve origin. Cracco and Cracco (1978) proceeded to investigate short latency responses to high intensity flash stimulation, using a series of midline electrodes referred to the ear lobe. The evoked response was described as a series of oscillatory potentials having polarity and latency P21 N25 P30 N34 P39 N45 P52 N48, and a maximal amplitude of 5μV in the midline and parasagittal derivations (see Figure 1.11). The responses to 1000-2000 flashes were averaged and a bandpass 1-2500Hz used to obtain the results. Monocular stimulation reduced the amplitude, and the oscillations in the anterior/frontal regions were thought to originate in the optic nerve and tract as they had a similar configuration to those recorded from the lower lid and outer canthus. However, those responses recorded from the midline and parasagittal derivations with auditory and myogenic contamination eliminated, were thought to be from the lateral geniculate body (LGB) and optic radiation. Fifteen subjects were used and considerable variability in amplitude and configuration was noted both within and across subjects.

Harding and Rubinstein (1981) described a triphasic visual evoked subcortical
FIGURE 1.11

Scalp distribution of early visually evoked oscillatory potentials (Cracco and Cracco 1978)

Using a left ear reference, oscillatory potentials are seen at each scalp electrode location, more prominently in the midline and parasagittal derivations (see text for details)
potential (VESP) to flash stimulation P21 N26.2 P33.6, quite distinct from the ERG and VECP and having a maximal amplitude (2-3μV) near the mastoid (this research will be detailed in Chapter 2). Siegfried and Lukas (1981a, b), however, in a description of five wavelets of latencies N50 P72 N82 P90 N101 predominating around the inion with left ear lobe and vertex as references, could not demonstrate the wavelets between vertex and ear lobe.

In further studies using Cz as reference (Whittaker and Siegfried 1983) the wavelets were widely distributed with no latency changes, were optimal to narrow bandpass filters, and were not volume-conducted from the retina. However, in spite of the wide distribution of these wavelets, the optimal mastoid locations obtained by Harding and Rubinstein (1981) were not verified by this study, and as they reached a maximal amplitude above Oz (1.5μV, as shown in figure 1.12), a visual cortex source was attributed to them.

Using the 7th cervical as a reference, a series of components in the 40-80ms latency range was identified as P47.6 N58.0 P74 P89.4 (Pratt et al. 1982). These components were consistently higher in amplitude at Cz when compared to Oz (see Figure 1.13) which contradicted the findings of Whittaker and Siegfried (1983).

Pratt et al. (1982) felt the large amplitude mastoidal potentials described by Van Hasselt (1972) and Harding and Rubinstein (1981) were a result either of activity from Cz or of insufficient auditory control and it was concluded that components earlier than 40ms had a retinal origin, and components between
Early components obtained by Whittaker and Siegfried (1983)

These components were described as wavelets between 30-70ms
FIGURE 1.13

Distribution of Short Latency Evoked Potentials to high intensity flash
stimulation obtained by Pratt et al. 1982

Key:  
I.O.   Infraorbital
O.C.   Outer Canthus
Mipsi Left Mastoid Process
Common reference: Lower neck
40-70ms were due to overlapping activity of different generators within the optic nerve and tract, summatting at the scalp surface. Table 1.2 summarises these developments in visual subcortical potentials to flash stimulation.

Using checkerboard reversals at 4 reversals/second, a positive potential with a latency band 30-50ms was also elicited (demonstrated in figure 1.14). A maximal amplitude of 0.6-2µV was obtained for binocular viewing conditions and a 14' check size. However, the latency increased to 103ms as check size decreased (Zahn and Matthews 1983). The electrodes were at Oz referred to Cz, and 300-400 averages were taken using a bandpass 1-250Hz and 256ms time window. The peak was thought to be subcortical in origin.

Supporting research of early visual components in the form of depth recordings and animal studies are few. Gastaut (1949) recorded VEPs directly from the visual pathway in man. Recordings from three levels of the visual pathway were investigated from the retina using a contact lens electrode, from the optic radiation using needle electrodes inserted by skull trepanation and from the visual cortex using scalp electrodes. A 'secondary' response having the configuration N20 P30-35 was thought to be due to neural transmission in the optic radiation.

Jouvet and Courjon (1958), having implanted electrodes in six patients prior to neurosurgery, described an optic radiation response to light flashes presented at 1 flash per second as high frequency and polyphasic. VEP components were recorded before and after surgical removal of the occipital pole and early components identified as N23 P28 N40 persisted after occipital pole ablation, findings which were supported by Saletu et al (1971).
Selectively summary of early components of the human visual evoked potential to flash stimulation
<table>
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<tr>
<th>AUTHOR AND YEAR</th>
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<td>VAUGHAN AND KATZMAN (1964)</td>
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Selective summary of early components of the human VEP to flash stimulation.
FIGURE 1.14

Subcortical components obtained to a 14' check size (Zahn and Matthews 1983)

Two examples of subcortical components obtained to checkerboard reversal stimulation using 14' checks (18° field, 80% nominal contrast). Four hundred samples were averaged. A positive potential with a latency band 30-50ms was obtained, with an amplitude of 0.6-2μV. Oz was referred to Cz.
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Electrodes were inserted for diagnostic purposes into septal, thalamic, geniculate, anterior and posterior temporal regions and photic stimulation presented at 2 flashes/second by Hamer et al. (1985).

Averaging 400 responses led to components P28 N36 appearing in the septal and thalamic regions as mirror images of ERG components and were obtained using a surface infra-orbital electrode. Two other components, P40 and N46, were limited to the lateral geniculate electrodes. Pattern reversal stimulation also localised two components P44 and P51 to the lateral geniculate electrodes, having an amplitude range (5-8μV) and being distinct from volume conducted ERG responses. However, no mention of the site of the reference electrode was made.

Some studies of subcortical structures in mammals have been undertaken. Using monkeys, wavelets were elicited by high intensity photic stimulation (Hughes and Mazurowski 1963) and were identified as predominating in the LGB, (latency 16-19ms) and the superior colliculus, (latency 22ms) (Doty et al. 1964). Various studies were done in rabbits. Yokoyama et al. (1966) distinguished pre- and post-synaptic responses of the LGB. The pre-synaptic area gave predominantly positive deflections and the post-synaptic area yielded negative deflections. Other researchers were diffident, suggesting that the wavelets recorded from the rabbit LGB were similar to the wavelets present in the ERG and optic nerve (Yonemura et al. 1967; Yamada 1968).

Vaughan and Gross (1969), studying VEPs in unanaesthetised monkeys before and after surgically induced lesions at various sites along the visual
pathway, described the wavelets as reflecting the post-synaptic geniculate calcarine input to the visual cortex. Honda et al. (1974) allowed several days for stabilisation of electrodes implanted into the LGB and cortex in rabbits, the ERG being recorded using a contact lens electrode. The responses to flash stimulation showed independence of the ERG and cortical VEP from the LGB response. Coagulation of the LGB did not affect the ERG response, and only marginally affected the VEP.

A recent study (Ohzawa and Freeman 1985) using pattern reversal stimulation in the form of sine wave and square wave gratings on cats, examined the electroretinogram and compared it with LGB responses. The retinal and LGB responses were independent in that the sine wave grating elicited a retinal response but no substantial evoked potential from the LGB, whereas the square wave grating produced large responses from the LGB.

In conclusion, the possible generator sites of early components of the visual evoked potential to flash stimulation have yet to be resolved. However the few studies published using pattern stimulation are suggesting a subcortical origin, independent of the electroretinogram.
CHAPTER TWO
INVESTIGATIONS OF THE VISUAL EVOKED SUBCORTICAL
POTENTIAL (VESIP) UNDERTAKEN BY M P RUBINSTEIN AND C
BOYLAN, UNDER THE DIRECTION OF G F A HARDING: A SYNONOPSIS

2.1 Review of Rubinstein's Work

The visual evoked subcortical potential is a triphasic complex of short latency
potentials (Harding and Rubinstein 1980), the composite wave having a mean
latency of P23, N28, P34 (Figure 2.1).

The identification of the VESP developed from the attempt to delineate any
photically evoked activity occurring deep in the visual pathway between the
retina and the visual cortex. Visually evoked potentials having latencies shorter
than 50 milliseconds have been poorly documented, owing to their minute
amplitude, inter-subject variability and the difficulty of their being repeated.
This problem has already been highlighted in Chapter 1, and, in response, one
of the main objectives of this research has been to optimise the conditions for
producing and recording the early components reliably.

The far-field concept, used by Jewett and Williston (1971) to enhance the
components of the brainstem auditory evoked potential (BSAEP), was adapted.
It was found to be appropriate because, as with the BSAEP, the generator sites
of the VESP were thought to be at a considerable distance from the recording
electrodes. Consequently, the decision was made to improve the signal to noise
ratio by using a large number of averages, e.g. about 500-1000 averages for the
VESIP.

A preliminary assessment of electrode sites and their morphology in terms of
latencies and amplitudes of early components to flash stimulation was
FIGURE 2.1

The typical visually evoked subcortical potential recorded in control subjects

The response is a small amplitude, triphasic, positive-negative-positive wave of short latency.

The active electrodes were placed at $T_3^{1/2}$ (left upper mastoid) and $T_4^{1/2}$ (right upper mastoid) and referred to the vertex, Cz.

According to the nomenclature of the 10/20 system (Jasper 1958), $T_3^{1/2}$ is midway between T3 and T5; and $T_4^{1/2}$ is midway between T4 and T6.

(after Rubinstein and Harding 1981)
undertaken (Harding 1979). With a time window of 125ms, a wide bandpass and presentation of 1000 flashes, early visual components were observed in only a few derivations mainly centred around the mastoid area. This finding led to the first organised experimental study on five subjects to assess the extent of the flash ERG and VECP fields of activity of the scalp surface. Two reference sites, the frontal pole Fz and the right ear lobe were used (figure 2.2 shows the montages used). The latencies and peak to peak amplitudes of all components within the 125ms time window were measured manually.

In general, the maximum number of early components was seen in recordings between para vertex electrodes C3 and C4 and the right ear lobe A2, these components being demonstrated at intensities 3939 nits and 9661 nits (intensity levels 8 and 16 on the photostimulator dial). At intensity 16 myogenic artifact was enhanced, and at intensities lower than 8, the early components were variable. Since the activity was noticeable when C3, C4 and T4 were referred to A2, and not seen when Fz was used as a reference, (Figure 2.3), A2 was regarded as the probable site of the early components and, therefore, the active electrode. Six components were identified - N17, P22, N27, P34, N40 and P47. N40 and P47 were considered as N1 and P1, being components of the more conventionally recorded flash VECP and N17 could not be consistently recorded.

Two topographic studies followed to investigate the distribution of the early components. In an anterior-posterior study, seven electrodes were used at FPz, F8, T4, T6 and Oz with half distance electrodes sited at F8½ and T4½ as shown in Figure 2.4. Cz as a common reference was considered to be the best compromise since a more anteriorly sited reference would have been exposed to ERG contamination and a more posterior site would involve the VECP artifact. Furthermore the inter-electrode distance between the active and reference
FIGURE 2.2

Montages used in preliminary pilot study undertaken by Rubinstein 1981

Comprising a number of 'active' sites with common reference sites at Fz and A2 (right earlobe). An ERG was recorded between right lower lid and outer canthus.
FIGURE 2.3

Resultant waveforms using preliminary pilot study montages obtained by Rubinstein 1981.

Using A2 as reference site a number of early components (consisting of P27, N22, P27, N34, P40, N47) are seen mainly in recordings from C3 and C4. These components were not seen in recordings from C3 and C4 when Fz was used as reference site. Recordings from P3, P4 and O2 are dominated by components of the cortical VEP (consisting of a P63-65 component). The ERG is recorded with reversed polarity to all other channels.
Scalp distribution of electrodes used in anterior-posterior topographical study of early components of the VEP by Rubinstein (1981)

Standard 10/20 system sites were Fpz, F8, T4, T6 and Oz. Additional half-distance electrodes were sited at F8½ (mid-way between T4 and F8) and T4½ (mid-way between T4 and T6). All electrodes were referred to a common reference at the vertex, Cz.
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electrodes would be approximately equal. Six flashes per second were presented and 500 averages were the template parameters employed to elicit the VESP.

High amplitude flash ERG predominated at FPz and with reduced amplitude at F8 and F8\(^{1/2}\) without alteration in latency. At T4\(^{1/2}\), a number of early components emerged as a triphasic complex and were distinct from the flash ERG.

There was also an anterior spread of the flash VECP at Oz and T6 from the occiput - these distributions are shown in Figure 2.5. The mean latencies of the triphasic complex was calculated as P21.3 \((\pm\ 1.63)\) N28.1 \((\pm\ 2.07)\) P35.9 \((\pm\ 1.1)\).

For a transverse topographic study, the electrodes were affixed at C4, T4, CP4, CP6, T4 and T4\(^{1/2}\) as illustrated in Figure 2.6. The choice of reference was more difficult: the vertex was chosen because it enabled direct comparison with the anterior-posterior study although it was not equidistant from all the electrodes. However, another reference on the anterior neck was used to satisfy equidistance. With Cz as a reference, the recordings were flat from electrodes close to the vertex but the triphasic complex showed a maximal amplitude at T4\(^{1/2}\) and T3\(^{1/2}\), ie. anatomically on the mastoid process (Figure 2.7). Use of the anterior neck yielded similar results but increased electromyogenic artifact. Thus, the anterior-posterior study served to isolate the VESP from the VER and ERG, and the transverse study localised the response to the mid-mastoid process (Harding and Rubinstein 1981).

Further distinction between the ERG and the triphasic complex was made by monocular and binocular stimulation studies. A simplified montage was used
FIGURE 2.5

Distribution of potentials in anterior-posterior topographical study of early components of the VEP (Rubinstein 1981)

The activity of the frontal pole (Fpz) shows the inverted ERG which is conducted to a number of more posterior sites. At T4\(1/2\), a localised complex of components (N19, P24, N28, P36) is seen. The cortical response dominates the record from Oz.
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Scalp distribution of electrodes used in transverse topographic study of early components of the VEP by Rubinstein (1981)

Standard 10/20 system sites were C4 and T4. Additional electrodes were placed at C6, T8, Cp4, T4\(\frac{1}{2}\) and T8\(\frac{1}{2}\). Two common reference sites were used as comparators sited at the vertex (Cz) and on the anterior neck.
FIGURE 2.7

Distribution of potentials in transverse topographical study of early components of the VEP obtained by Rubinstein (1981)

Using Cz as reference site (Ref.1) a triphasic early component complex (P20-22, N27-29, P33-35) is seen (preceded by a small N17 deflection) of maximal amplitude at electrodes T4½ and T8½. When using an anterior neck reference (Ref.2) as a comparator, the early component complex is still seen at the same sites, but not at any other electrodes.
with temporal electrodes F7½ and F8½, mastoid electrodes T3½ and T4½ and occipital electrodes O1 and O2, all referred to Cz.

On binocular stimulation, the flash ERG was seen at FP1 and FP2, the triphasic complex at T3½ and T4½ and the occipital response at O1 and O2, all the recordings being bilateral and symmetrical in latency and amplitude. With monocular stimulation the ERG at the electrode site closest to the occluded eye was not present. Responses at T3½ and T4½ were still triphasic, the latency being unaffected although the amplitudes were reduced, and there was a similar effect on the VECP at O1 and O2. It was therefore unlikely that the complex was of retinal or pre-chiasmal origin, as monocular stimulation should have resulted in gross unilateral reduction or abolition of the complex ipsilateral to the occluded eye.

An auditory origin for the early complex had to be eliminated as the photostimulator clicked synchronously with flashes from the discharge tube. When the photostimulator was masked, the ERG, the triphasic complex and the VECP were abolished whereas masking the click with white noise did not alter the visual responses.

These initial studies culminated in the complex being called the visual evoked subcortical potential or VESP and the emphasis of the work which followed was to isolate clearly the VESP from the ERG and the VECP.

A further, more detailed investigation of ERG distribution was undertaken as the second positive components of the VESP P35.9 coincided (on occasions) with the peak of the ERG 'b' wave. The scalp and facial topography of the flash ERG of twelve subjects was studied. The same stimulus and analysis parameters used to elicit the VESP were used with electrodes at standard 10/20
sites - FP2 Fz FPz F8 and T4 - with additional electrodes at N2 F12 and T8 as shown in Figure 2.8. The VESP was monitored at the optimal sites of T3½ and T4½. The common reference electrode was put at the vertex Cz, with comparator electrodes at O1 and the anterior neck. Overall, as the distance between the cornea and recording electrode increased, the amplitude of the ERG fell. As was expected from their relative amplitudes, the 'a' wave was abolished earlier than the 'b' wave (Figure 2.9), to a point where the ERG 'b' wave was recorded as a monophasic deflection of less than 1μV at T4 and T8. The VESP, however, assumed the familiar triphasic P-N-P configuration with peak to peak amplitude of the order of 1.5μV and 2.5μV respectively. The distinct difference in morphology between the VESP and the ERG 'b' wave remnant recordable at T4 and T8 strongly suggested that the VESP was not a volume-conducted ERG response (Harding and Rubinstein 1981).

Various pathologies were subsequently examined electrophysiologically during which the ERG, VESP and VECP were recorded simultaneously. These pathologies were carefully selected in order that any differential effects between the ERG, VESP and VECP which depended on their sites could be investigated.

In left unilateral optic nerve trauma there was no light perception in the affected eye and the disc was pale and atrophic. There was a normal photopic ERG but no VESP or VECP from the affected eye whereas the VESP and VECP from the unaffected eye were normal. A similar result was obtained with a suspected optic nerve lesion. A converse situation was presented by retinal detachment involving the macula and consequent reduction in vision. The ERG was abolished from the affected eye but the VESP and VECP were present bilaterally and symmetrically.

Effects of different pathologies directly affecting cortical and subcortical sites
Scalp and facial distribution of electrodes used in topographical study of the ERG by Rubinstein (1981)

Standard 10/20 system sites were Fpz, Fz, Fp2, F8, F4 and T4. Additional electrodes were placed at Nz, F12, T8 (10% lower than Fpz, F8 and T4, respectively) and at M2 and F16 (20% lower than Fp2 and F8, respectively)
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FIGURE 2.9

Scalp and facial distribution of ERG-type signals in five subjects

All electrodes were referred to the vertex (Cz) and the corneal signal was recorded with a GFE at half the gain of all other channels. All subjects showed similar distributions of signals, the extent of the field was in direct proportion to the amplitude of the corneal signal. At electrode sites T4 and T8 a very low amplitude 'b' wave remnant was seen in some cases.
along the visual pathway were examined to establish that the VESP was of subcortical and not cortical origin. In brainstem vascular disturbance, involving subcortical pathways, the VESP was as expected, abolished contralaterally to an existing homonymous hemianopic field defect, although the VECP was only partially affected. In several cases of occipital lesions not involving subcortical sites, normal VESPs concurred with grossly asymmetric VECPs. In two cases of bitemporal hemianopia associated with chiasmal compression, the VESPs were absent over the hemisphere contralateral to the eye stimulated and the VECP was consistent.

The differential effects of optic nerve lesions on the ERG, VESP and VECP having been examined, seven patients presenting with unilateral optic neuritis were studied. The major positive VECP component to flash was delayed, although differences in the flash VESP between the affected and unaffected eyes were not significant. Initially this implied that the optic nerve fibres involved in generating the VESP were unaffected by the optic neuritis. However, Rubinstein (1981) (unpublished PhD thesis) felt that the nature of the stimulus, (ie. high intensity flashes presented at a fast rate) perhaps accounted for the lack of differentiation between the two eyes although this has not been shown conclusively.

The VESP to pattern stimulation

A pilot study was undertaken to elicit the VESP to structured stimulation. Black and white checks were presented at 2 reversals/second and the response to 500 reversals averaged. No response was obtained and it was felt that the VESP was a luminance related response and a high luminance stimulus was perhaps needed. A flashed-on pattern incorporated structured stimulation and a luminance change was therefore adopted, the photostimulator being used at
intensity 8 with grids subtending check sizes of 2°18', 1°42', 1°12' and 36'. Twelve subjects were used and recordings from six channels examined.

Flashed-on pattern did not improve the definition or amplitude of the VESP. Consequently, Rubinstein concluded that the VESP was a luminance and not a contrast related response.

In summary, the investigations below converged to establish the VESP as a subcortical luminance response, distinct from the ERG and the VECP.

1) Standard methods of recording the VECP were successfully modified to record early components and led to the definition of the VESP. The VESP was present in 95% of sixty normal volunteer subjects (30 male, 30 female) aged between 16 and 41 with no significant gender differences.

2) The topographic studies established the localisation of the VESP to T3½ and T4½, (ie. the upper mastoid) and isolated the phenomenon in its distribution over the scalp from the ERG and VER.

3) Monocular and binocular studies indicated a post-chiasmal origin of the early complex.

4) A number of selected case studies examined electrophysiologically strengthened the hypothesis of a subcortical origin.
2.2  Review of the application of the VESP to albinism


Boylan reviewed the evidence for misrouting of the optic nerve fibres along the visual pathway in animals. The studies showed an increase in the number of contralaterally projecting optic nerve fibres in albino animals as compared to their normally pigmented counterparts. In relation to human albinos and scalp recorded evoked potentials, it was proposed that any such misrouting should be reflected in the form of contralateral dominance of the hemispheric responses on monocular stimulation in albino subjects but not in normal pigmented individuals.

A group of 26 oculocutaneous albinos with i) low visual acuity, ii) high incidence of strabismus and iii) nystagmus were investigated and compared with a control group of age matched normally pigmented individuals.

The electrophysiological tests involved in examining lateralisation were the visually evoked cortical potential (VECP) and the VESP. The VECP to both flash and pattern stimulation was examined. Pattern stimulation consisted of black and white checks which were presented in two modes: of pattern appearance-disappearance and of pattern reversal. The VESP to flash stimulation was utilised to provide additional information about the visual pathway. The parameters to evoke it being those outlined by Harding and Rubinstein (1980.)
With the concentration on lateralisation, the 'Cx value' was introduced. Cx defined the average amount that a visual evoked potential component lateralised on monocular stimulation - and was expressed in terms of the latency and amplitude of a component.

The cortical components to flash and pattern stimulation were analysed, and included i) the flash component (P2) which is a consistent and stable positive wave at 80-120ms, ii) the (P100) component for pattern reversal stimulation, indicated by a positive deflection with a peak latency of around 100ms and iii) the CI and CII components elicited by pattern appearance-disappearance stimulation. The CI component is a positive component peaking at 65-80ms, and the CII is a prominent negative wave at 90-120ms.

The flash VECP using reference recording effectively demonstrated monocular contralateral lateralisation in the albinos studied. The latency of the P2 component was consistently earlier contralaterally but the N2P2 amplitude showed more variability. Pattern reversal stimulation was not a useful technique, in agreement with the findings of previous authors (Creel et al. 1981). Boylan concluded that the presence of nystagmus resulted in a poorly formed or absent response. Pattern appearance-disappearance stimulation yielded much better results. A simple waveform mainly consisting of the CI component was produced, the other components being usually absent or poorly defined. With reference recording, both ipsilateral and contralateral lateralisation on monocular stimulation were present among the albino and control groups. Using a bipolar montage however, there was clearer indication of contralateral lateralisation on monocular stimulation when compared to any single measure of the reference recorded response. Half field stimulation was employed to estimate if the full field response in albinism resembled that of the temporal half field response. There was some evidence of this in four subjects but overall the
half field recordings did not contribute much more information.

Group averaging of the results from the albinos revealed clear contralateral lateralisation of the flash VECP both in terms of the P2 latency and the N2P2 amplitudes (figures 2.10 and 2.11). The VECP to pattern appearance-disappearance showed contralaterality on bipolar O1-O2 recording. However, reference recording of full and half field responses did not demonstrate this, effectively confirming previous studies (Apkarian et al. 1983).

The VESP to flash stimulation was recorded in twenty-two albinos and their matched controls. It was pre-supposed that the VESP should also have demonstrated contralateral lateralisation in the albino group. However, on gross observation there were no differences between the control and albino group.

The latency values were not treated to Cx-analysis because in some subjects the response on one recording channel could not be defined. However, on examination of the amplitudes P23-N28 and P28-P34, the Cx values demonstrated that the lateralisation both ipsilaterally and contralaterally was more distinct for the albino group. Both P23-N28 and N28-P34 amplitudes were consistently contralateral or ipsilateral, e.g. an ipsilateral lateralisation of P23-N28 would occur in conjunction with an ipsilateral lateralisation of N28-P34. This was not the case with the control group.

The latency of the flash VECP P2 component was adopted as a yardstick of contralateral lateralisation to compare against VESP lateralisation. Some albinos showed contralateral lateralisation of the flash VECP and ipsilateral lateralisation of the VESP. Moreover, the only two albino subjects demonstrating ipsilateral lateralisation of the VECP showed contralateral lateralisation of the VESP. These results reflected the independence of the two
FIGURE 2.10

The group-average responses of the flash VECPs recorded in the control subjects.

The binocular and monocular group average responses are shown. The latencies of the P1, N2 and P2 components are labelled with the P1N2 and N2P2 amplitudes. The asymmetries and asynchronies between the two hemispheres are of small magnitudes in each case. (After Boylan 1984)
Binocular

1
P41
N64
P104
P1N2 = 2.3 uv
N2P2 = 16.3 uv

2
P40
N63
P110
P1N2 = 1.9 uv
N2P2 = 12.9 uv

Right eye

1
P39
N67
P1N2 = 2.0 uv
N2P2 = 14.7 uv

2
P38
N67
P114
P1N2 = 1.8 uv
N2P2 = 11.7 uv

Left eye

1
P40
N68
P113
P1N2 = 2.0 uv
N2P2 = 12.7 uv

2
P37
N69
P113
P1N2 = 1.0 uv
N2P2 = 9.3 uv

-15 uv
+100 ms
FIGURE 2.11

The group-average responses of the flash VECPs recorded in the albino subjects.

The binocular and monocular group average responses are shown. The binocular response is dominated by a bilateral P2 component. The latency of this component is shorter and the N2P2 amplitude greater over the contralateral compared to the ipsilateral hemisphere on monocular stimulation.

(After Boylan 1984)
Binocular

1. N80
   P40
   P90
   P1
   N2 = 0.15 uV
   N2 = 3.0 uV

2. N41
   P34
   P89
   N2 = 0.15 uV
   N2 = 3.0 uV

Right eye

1. N80
   P40
   P111
   P1
   N2 = 0.2 uV
   N2 = 0.77 uV

2. N32
   P104
   N2 = 3.2 uV

Left eye

1. N40
   P92
   N2 = 4.1 uV

2. N61
   P40
   P109
   P1
   N2 = 0.7 uV
   N2 = 2.0 uV

-2.5 uV
100 ms
responses.

Further evidence for independence of the VECP from the VESP was obtained from topographic studies of the scalp distribution of the VESP. Two albinos were chosen for a study using an anterior-posterior montage and a transverse montage (Figure 2.12). In one subject there was contralateral lateralisation of the VECP and VESP (see Figures 2.14 and 2.16) whereas in the other, contralateral lateralisation of the VECP occurred with ipsilateral lateralisation of the VESP (see Figures 2.13 and 2.15).

Overall, the VESP results showed no statistically significant differences in lateralisation between the albino group and the control group. Furthermore, the majority of albino subjects showed contralateral lateralisation of P2 and in many, ipsilateral lateralisation of the VESP occurred. Topographic studies emphasised the difference further and confirmed Harding and Rubinstein's finding (1981) that the mastoids were the optimal sites for recording the VESP.

Ipsilateral lateralisation of the VESP initially appeared as a contradiction to the anatomical studies into albinism which suggest an increase in the contralaterally projecting fibres along the visual pathway - borne out by the monocular contralateralisation of the P2 of the flash VECP. The failure of the VESP to illustrate misrouting was discussed in terms of the relative positions of the lateral geniculate nucleus (LGN), as a possible source of the VESP, and the visual cortex as a possible source of the VESP. A comparison of the electrodes used for scalp recordings of the VESP and VECP showed that the electrodes at T3½ and T4½ were at a great distance from the closely spaced bilateral generators of the VESP in the midbrain area when compared to electrode sites O1 and O2 which were directly over the visual cortex. It was therefore postulated that even if there was contralateral lateralisation at the LGB, the VESP may still be
Electrode sites used by Boylan (1984) for topographical investigations of the VESP in albinism

(after Boylan 1984)
FIGURE 2.13

The monocular VESPs recorded from a transverse montage in albino 17

The VESP (between dotted lines) lateralises ipsilaterally on monocular stimulation. In addition the later part of the response undergoes polarity reversal about the midline. See text for further details. (Flash intensity 8, 5 flashes per second, 500 sweeps)

(after Boylan 1984)
Subject 17
Right eye
A2 - Cz
T4 1/2 - Cz
CP6 - Cz
CP4 - Cz
CP3 - Cz
CP5 - Cz
T3 1/2 - Cz
A1 - Cz

Left eye
A2 - Cz
T4 1/2 - Cz
CP6 - Cz
CP4 - Cz
CP3 - Cz
CP5 - Cz
T3 1/2 - Cz
A1 - Cz
FIGURE 2.14

The monocular VESPs recorded from a transverse montage in albino 11

The VESP (between the dotted lines) is seen to lateralise contralaterally on monocular stimulation. In addition the later part of the response undergoes polarity reversal about the midline. See text for further details. (Flash intensity 8, 5 flashes per second, 500 sweeps).

(after Böylan 1984)
The monocular VESPs recorded using an anterior posterior montage in albino 17

The VESP (between the dotted lines) shows ipsilateral monocular lateralisation as does the ERG recorded at F7 and F8. However, the occipital late positive shown by the solid line undergoes contralateral lateralisation. See text for further details. (Flash intensity 8, 5 flashes per second, 500 sweeps).

(after Boylan 1984)
FIGURE 2.16

The monocular VESP's recorded using an anterior-posterior montage in albino 11

The VESP (between the dotted lines) undergoes contralateral lateralisation on monocular stimulation. The ERG recorded at electrodes F7 and F8 shows ipsilateral lateralisation while the late positive recorded at O1 and O2 shows contralateral lateralisation (solid line). See text for further details. (Flash intensity 8, 5 flashes per second, 500 sweeps).

(after Boylan 1984)
Subject II

Right eye
F8-Cz
A2-Cz
T6-Cz
O2-Cz
O1-Cz
T5-Cz
A1-Cz
F7-Cz

Left eye
F8-Cz
A2-Cz
T6-Cz
O2-Cz
O1-Cz
T5-Cz
A1-Cz
F7-Cz

-1.25 µV
+ 10 ms
recorded at $T_3^{1/2}$ and $T_4^{1/2}$.

Hence, the lateralisation of the VESP was not predictable based on anatomical misrouting.

2.3 Summary

The development of research into the VESP presented various unresolved issues.

In the initial studies by Rubinstein (1981) the techniques for recording BSAEPs were adapted because like the BSAEP it was thought that the VESP originated from deep, subcortical sites and with a wide bandpass and a large number of averages, it could be elicited. However, the VESP markedly differed from the BSAEP in the following respect. The BSAEP truly reflects evoked potential from a deep source in that, due to the depth of the auditory generators, diffusion of the signal by volume conduction occurs over an extensive area. Thus, the response can be recorded at a wide range of scalp locations without distortion. Within the visual pathway, as discussed by Boylan (1984), there are clear differences in recording the VECP and VESP when examining generator sites and electrode sites. Boylan pointed out that the subcortical generators of the VESP are also at some distance from the electrodes when compared to the occipital electrodes directly over the site of the VECP generators. On this basis, the VESP should not have been so tightly localised to the mastoid area as they found in the initial investigations. Theoretically, $T_3^{1/2}$, $T_4^{1/2}$ and Cz should have been equipotential. Furthermore, the localisation to the mastoid raises the question of auditory contamination of the response. This may well account for the lack of significant contralateral lateralisation of the VESP in albinism.
Due to the nature of flash stimulation, the possible origin of the VESP could not be located with precision and as a pattern response was not elicited by conventional methods, a tectal or lateral geniculate site for the response could not be conclusively elucidated. With pattern reversal, the checks were presented at two reversals per second which are the parameters used to elicit the pattern VECP, but in the same way that flash stimulation parameters used to elicit the VECP result in variable and inconsistent subcortical responses, the pattern reversal response was very poorly defined. Consequently, it was felt that a re-examination of the techniques to present structured stimulation was warranted.

The following objectives emerged from these issues and structured the present study.

1) To investigate further the topography to flash stimulation using a variety of reference recording sites.

2) To investigate the flash VESP with a view to identifying any confounding auditory contamination.

3) To examine the sensitivity of the VESP to structured stimulation in order to locate the source of the response either in the lateral geniculate body or the superior colliculus.
CHAPTER THREE
A RE-INVESTIGATION OF THE FLASH VESP

3.1 Introduction

Early research into the flash VESP has presented various issues relating to the method of stimulation and the scalp distribution of the response. In the initial studies by Harding and Rubinstein (1980), the techniques for recording a deep source response were adapted (as described in chapter 2), and the subsequent identification of a visual response from subcortical structures in the visual pathway implied that the signal should be volume conducted over an extensive area of the scalp. The VESP, however, was found to be tightly localised to the mastoid area when the vertex (Cz) was used as a common reference in various topographic studies. This raised the question of auditory contamination from the click discharge of the photostimulator, and prompted further studies into the topography of the flash VESP using auditory masking and the nature and extent of possible auditory involvement.

Sections 3.2 and 3.3 address the issues of distribution of the VESP over the scalp and the re-examination of different common reference sites. Section 3.4 is a review of auditory evoked potentials with the emphasis on the middle latency auditory evoked response (MLAER) which falls within the same latency envelope as the VESP. Section 3.5 describes the results of a controlled auditory study.

3.2 Pilot topographical study

This pilot study was undertaken to examine the scalp topography of the VESP, having made the assumption that its source is probably deep in the midbrain and therefore the VESP signal should be recorded over an
extensive area.

3.2.1 Materials and methods

The topographic studies were made on twenty normal subjects with an age range of 18-24 years, all subjects having visual acuities of 6/6 or better in each eye. Each subject was seated comfortably in a room of ambient illumination of 100 cd/m² and photic stimulation consisting of flashes of 10μsec duration was delivered from a Grass PS22 photostimulator placed 25 cm from the eye, subtending a field size of 30°. Flashes were delivered at a rate of five flashes/second at an intensity of 3939 cd/m² (intensity 8) and the responses to 500 flashes were averaged. The analysis time was 50 ms and the bandpass filtering was 30-500 Hz. These stimulus parameters had been adjusted to accord with the optimum conditions for recording the VESP described by Harding and Rubinstein (1980). The photostimulator produced a 'click' synchronous with the flash discharge and this was effectively masked by using earphones on each subject.

Seven equally spaced electrodes were placed in a coronal chain from mastoid to mastoid as shown in Figure 3.1 with the central electrode located at the vertex. These electrodes were affixed with collodion and resistances were maintained below 5 KΩ. All the electrodes were referred to a common reference site at the chin.

Across the sample, the results were 'group-averaged' on the Pathfinder 2, using a program which superimposed the raw data from each subject and subsequently averaged the potential activity for the sample of 20. This visual study was part of a larger study of far field responses which included the study of the distribution of early auditory potentials (Clement et al. 1984).
Diagrammatic representation of the electrode sites used in the pilot study of the distribution of the VESP in the coronal plane, using auditory masking.

Seven equally spaced electrodes were placed on the head, and all electrodes were referred to a common reference at the chin.

Electrode 1 was placed at T3\(^{1/2}\) on the left mastoid

Electrode 4 represented the vertex Cz

Electrode 7 was placed at T4\(^{1/2}\) on the right mastoid

Using the nomenclature of the 10/20 system (Jasper 1958), T3\(^{1/2}\) is a site midway between T3 and T5 and T4\(^{1/2}\) is midway between T4 and T6.
3.2.2 Results

The group averaged result showed that a triphasic positive-negative-positive (PNP) complex was obtained at all seven electrode derivations in the coronal plane of latency values in ms: P20.7 N29.5 P35.5 as shown in Figure 3.2. The amplitudes of the P-N and N-P components in microvolts (µV) were as follows:

<table>
<thead>
<tr>
<th>Electrode</th>
<th>Amplitude in µV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left mastoid</td>
<td></td>
</tr>
<tr>
<td>1 P-N</td>
<td>.5</td>
</tr>
<tr>
<td>2 P-N</td>
<td>.45</td>
</tr>
<tr>
<td>3 P-N</td>
<td>.74</td>
</tr>
<tr>
<td>Cz</td>
<td></td>
</tr>
<tr>
<td>4 P-N</td>
<td>.68</td>
</tr>
<tr>
<td>5 P-N</td>
<td>.78</td>
</tr>
<tr>
<td>6 P-N</td>
<td>.62</td>
</tr>
<tr>
<td>Right mastoid</td>
<td></td>
</tr>
<tr>
<td>7 P-N</td>
<td>.47</td>
</tr>
</tbody>
</table>

As can be seen from the above results, there was no clear localisation of the response to the electrode sites at the mastoids, and Cz is clearly active for the VESP signal when the chin is used as a reference.

3.2.3 Summary and conclusions

Using a group of 20 subjects, a widespread distribution of the VESP signal was demonstrated in the form of a P20.7 N29.5 P35.5 complex with amplitudes of P-N .68µV and N-P .78µV at the Cz derivation, when auditory masking of the photostimulator click discharge was employed.
FIGURE 3.2

Pilot study showing the group-averaged distribution of the VESP in the coronal plane for 20 subjects using chin as a common reference and auditory masking

The VESP was a P20.7, N29.5, P35.5 complex present at all seven electrode sites. In accordance with EEG convention, a positive component is indicated by a downward deflection of the pen
COMMON REFERENCE: CHIN
The technique of group-averaging involving superimposition, and subsequent averaging of the waveforms was applied to the raw data of 20 subjects, enabling a study of VESP topography across a large sample. This advantage had to be balanced against the loss of information from individual subjects. However, two important properties of the VESP emerged: the subcortical signal had a widespread distribution in the coronal plane; furthermore the vertex electrode Cz was active for the response. These results did not agree with the findings of Rubinstein (1981) wherein the VESP was anatomically localised to the mid-mastoid process using Cz as a reference.

This pilot study showed that the VESP signal had a widespread distribution when the chin was used as a common reference. These results are more in accordance with the 'far-field' concept initially introduced by Jewett and Williston (1971) to record the subcortical brainstem auditory evoked potential, but which also has relevance to the VESP assuming it has a subcortical origin. In their initial topographies "far field electrode positions, short distances apart showed no significant differences in the waveshape".

This pilot study led to a re-examination of different reference sites to record the VESP.

3.3 Flash topographic studies of the VESP using different reference sites

A study using different reference sites was designed to examine further the distribution of the VESP in the anterior/posterior direction, to complement the coronal study and to compare the VESP with the flash ERG.

Three reference sites were used. These were the chin (employed in the pilot
study in section 3.2), a balanced non-cephalic reference electrode placed on the thorax and the vertex Cz. The vertex was included as it had been used as reference in the initial studies defining the VESP (Harding and Rubinstein 1980).

3.3.1 Materials and methods

Observations were made on 4 male subjects of average age 26 with visual acuities of $6/6$ or better monocularly and full visual fields. Silver/silver chloride electrodes were affixed with collodion and resistances maintained below $5K\Omega$. The electrodes were sited in an anterior/posterior line across the right side of the head, (according to the 10/20 system in a modified form), at FP2, F8, T4, T4$^{1/2}$ and T6 (T4$^{1/2}$ was midway between T4 and T6), with additional electrodes at T3$^{1/2}$ (midway between T3 and T5 on the left side) and Cz (Figure 3.3 demonstrates the montage used). The electroretinogram was recorded monocularly by placing a DTL electrode (Dawson et al. 1979) in the lower canthus of the right eye (Appendix 7).

Throughout the study, the flash ERG was recorded and is diagrammatically presented in an inverted form in accordance with EEG convention such that a positive change at the active electrode results in a downward deflection. This permitted direct comparison of the ERG waveforms with all other recorded waveforms.

Three common reference sites were used - chin, Cz and a balanced non-cephalic reference electrode or BNCRE (Stephenson and Gibbs 1951). The BNCRE consisted of two inter-connected electrodes placed on the upper thorax at the right sternoclavicular junction and the tip of the 7th cervical spine. At this point the electrocardiogram artifact can be effectively cancelled out by a variable
FIGURE 3.3

Scalp distribution of electrodes used in the anterior-posterior
topographical study of the VESP

The electrodes were placed in a temporal array on the right side of
the head at Fpz, F8, T4, T4½ and T6 (10-20 system
nomenclature, Jasper 1958). Additional electrodes were placed at
the vertex, Cz and T3½ (T4½ is midway between T4 and T6
and similarly on the left side of the head T3½ is midway between
T3 and T5).

The flash ERG was recorded from the right cornea using a DTL
electrode (Dawson et al. 1979).

All electrodes were referred to a common reference at the chin and a
balanced non-cephalic reference electrode (BNCRE) on the thorax
(Stephenson and Gibbs 1951)
Illustration removed for copyright restrictions
FIGURE 3.4

Circuit diagram for the balanced non-cephalic reference electrode

(modified from Stephenson and Gibbs 1951)
CV7 = 7th cervical vertebra
RSCN = right sterno-clavicular notch
CE = cephalic electrodes
resistor in each lead (Figure 3.4). This system has been found to be free from any stimulus-locked activity in the visual auditory and somatosensory modalities (Lehtonen and Koivikko 1971), and is therefore thought to be useful as a reference electrode to record the VESP and to compare with the chin reference.

Stimulus and analysis parameters were adjusted to provide the optimum conditions for recording the VESP. The subjects were seated in a slightly darkened room of 100cd/m² and binocular flash stimulation was delivered using a Grass PS22 photostimulator placed 25cm from the eye at intensity 8 (3939 cd/m²) and at a rate of 5 flashes per second. The bandpass was 30-500Hz and the analysis time 50ms. For each reference site, the responses to 500 flashes were averaged. The click discharge from the photostimulator was masked using earphones.

3.3.2 Results

The ERG was recorded at the cornea of the right eye using all three reference sites, i.e. chin, BNCRE and Cz. It did not have the classical flash ERG configuration as the bandpass filters of 30-500Hz were more appropriate for the VESP. Using these filter settings, oscillatory potentials emerged in the flash ERG waveform which is normally recorded using a bandpass of 0.5 to 30Hz.

The 'a' and 'b' components were defined (Galloway 1981) and the most accessible index of the ERG was found to be the 'b' wave amplitude taken from the peak of the 'a' wave to the trough of the 'b' wave. The positive-going 'b' wave frequently demonstrated oscillatory potentials on the N-P component of the response.

Using the chin as a reference, the flash ERG was maximal at the cornea in all
four subjects as shown in Table 3.1a. The negative 'a' wave had a mean latency of 16.78 (± 1.07ms), with mean 'b' wave 40.68 (± 1.8ms), with mean 'b' wave amplitude of 14.44µV (± 4.6). Various oscillatory potentials were also presented which became indistinct at FP2. The amplitude of the 'b' wave rapidly attenuated at a short distance from the cornea, and was difficult to define at F8.

At the temporal chain of electrodes sited at T4, T4½ and T6 and at Cz and T3½, a triphasic complex emerged with mean incidence of P27.28 (± 5.55) N32.82 (±4.18) P37.68 (± 3.29). This complex was also present at T3½ and Cz and the mean amplitudes at these electrodes were:

<table>
<thead>
<tr>
<th>Electrode</th>
<th>P-N</th>
<th>N-P</th>
</tr>
</thead>
<tbody>
<tr>
<td>T4</td>
<td>2.18 (± .9)</td>
<td>1.79 (± .7)</td>
</tr>
<tr>
<td>T4½</td>
<td>2.14 (± .83)</td>
<td>2.1 (± .94)</td>
</tr>
<tr>
<td>T6</td>
<td>2.05 (± .82)</td>
<td>2.05 (± .92)</td>
</tr>
<tr>
<td>Cz</td>
<td>2.14 (± .96)</td>
<td>2.19 (± 1.19)</td>
</tr>
<tr>
<td>T3½</td>
<td>2.21 (± 1.08)</td>
<td>2.22 (± 1.12)</td>
</tr>
</tbody>
</table>

These values showed that the response was not localised to any particular electrode site and was present bilaterally. Figures 3.5 and 3.6 show the distribution of the ERG and VESP in two subjects. The results from all four subjects are given in tables 3.1b and 3.1c.

The BNCRE was used to assess further the distribution of the flash ERG and to investigate whether the chin would be active for the flash ERG. Using the BNCRE, a similar distribution of the flash ERG was found with mean incidence of 'a' 16.4ms (± 1.36), 'b' 38.63 (± 3.46) and 'b' wave amplitude: 8.88µV (± .46) (Table 3.2a).
**TABLE 3.1**

Latency and amplitude results of the anterior-posterior topography study to flash stimulation using chin as the common reference and auditory masking: latency and amplitude values of the flash ERG and flash VESP

**Table 3.1a** Latency and amplitude values of the flash ERG at the DTL electrode on the right cornea

**Table 3.1b** Flash VESP latency values at electrode sites T4, T4\(^{1/2}\), T6, Cz and T3\(^{1/2}\)

**Table 3.1c** Flash VESP amplitude values at electrode sites, T4, T4\(^{1/2}\), T6, Cz and T3\(^{1/2}\)
### TABLE 3.1a

**FLASH ERG: REFERENCE CHIN**

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>LATENCY OF 'a' WAVE IN MS</th>
<th>LATENCY OF 'b' WAVE IN MS</th>
<th>'b' WAVE AMPLITUDE IN uV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.8</td>
<td>41.3</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>17.7</td>
<td>41.9</td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td>15.9</td>
<td>38</td>
<td>12.5</td>
</tr>
<tr>
<td>4</td>
<td>17.71</td>
<td>41.5</td>
<td>9.25</td>
</tr>
<tr>
<td>MEAN</td>
<td>16.78</td>
<td>40.68</td>
<td>14.44</td>
</tr>
<tr>
<td>SD</td>
<td>1.07</td>
<td>1.8</td>
<td>4.6</td>
</tr>
<tr>
<td>† 2SE</td>
<td>1.07</td>
<td>1.8</td>
<td>4.6</td>
</tr>
</tbody>
</table>

### TABLE 3.1b

**FLASH VESP: REFERENCE CHIN**

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>LATENCY IN MILLISECONDS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>'</td>
</tr>
<tr>
<td>1</td>
<td>26.5</td>
</tr>
<tr>
<td>2</td>
<td>34.8</td>
</tr>
<tr>
<td>3</td>
<td>26.4</td>
</tr>
<tr>
<td>4</td>
<td>21.4</td>
</tr>
<tr>
<td>MEAN</td>
<td>27.28</td>
</tr>
<tr>
<td>SD</td>
<td>5.55</td>
</tr>
<tr>
<td>† 2SE</td>
<td>5.55</td>
</tr>
<tr>
<td>SUBJECT</td>
<td>T4 P - N N - P</td>
</tr>
<tr>
<td>---------</td>
<td>---------------</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>3.25</td>
</tr>
<tr>
<td>3</td>
<td>1.07</td>
</tr>
<tr>
<td>4</td>
<td>2.38</td>
</tr>
<tr>
<td>MEAN</td>
<td>2.18</td>
</tr>
<tr>
<td>SD</td>
<td>.9</td>
</tr>
<tr>
<td>+ 2SE</td>
<td>.9</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Anterior/Posterior distribution of the flash ERG and flash VESP using chin as the common reference in subject 1 using auditory masking.

The flash ERG is present at the DTL electrode, and shows two components - an 'a' wave of latency 15.8ms and a 'b' wave, latency 41.3ms.

The VESP emerges at the temporal array of electrodes T4, T4\(1/2\) and T6 as a triphasic complex P26.5 N31.48 P37.6. It is also clearly present at the vertex Cz and T3\(1/2\).
FIGURE 3.6

Anterior/Posterior distribution of the flash ERG and flash VESP using chin as the common reference in subject 2 using auditory masking.

The flash ERG is present at the DTL electrode and Fpz with an 'a' wave at 17.7ms and 'b' wave at latency 41.9ms.

The VESP emerges at the temporal array of electrodes T4, T4\(1/2\) and T6, as a triphasic complex P34.8 N37.6 P41.4. It is also clearly present at the vertex, Cz and T3\(1/2\).
The response was present at FP2 but lower in amplitude. Various oscillatory potentials were again present at the cornea but these wavelets were rapidly attenuated at FP2. The chin was also referred to the BNCRE and no signal was obtained demonstrating that both the chin and BNCRE were equipotential for the flash ERG response. At the temporal array of electrodes on the right side, the triphasic complex of the flash VESP was seen in all four subjects, having a mean incidence of P25 (±3.51) N32.57 (±4.29) P37.3 (±3.12). The ERG and VESP distributions are shown in Figures 3.7 and 3.8, and the results from the sample are shown in tables 3.2b and 3.2c.

The complex was also present on the left side at T3\(\frac{1}{2}\). The mean amplitudes at these electrode sites were:

<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>T4</td>
<td>P-N</td>
<td>2.43</td>
<td>(±.71)</td>
<td>N-P</td>
<td>1.98</td>
</tr>
<tr>
<td>T4(\frac{1}{2})</td>
<td>P-N</td>
<td>2.17</td>
<td>(±.64)</td>
<td>N-P</td>
<td>2.27</td>
</tr>
<tr>
<td>T6</td>
<td>P-N</td>
<td>2.57</td>
<td>(±.74)</td>
<td>N-P</td>
<td>2.53</td>
</tr>
<tr>
<td>Cz</td>
<td>P-N</td>
<td>2.36</td>
<td>(±.63)</td>
<td>N-P</td>
<td>2.24</td>
</tr>
<tr>
<td>T3(\frac{1}{2})</td>
<td>P-N</td>
<td>2.35</td>
<td>(±.75)</td>
<td>N-P</td>
<td>2.41</td>
</tr>
</tbody>
</table>

No clear localisation of the response was present at any electrode site.

Using the vertex (Cz) as a reference, the flash ERG emerged with a mean incidence of a: 15 (±1.67), b: 38.8 (±5.04) and 'b' wave amplitude of 11.19μV (±3.33) (Table 3.3).

The response was still clearly present at F8, the 'b' wave oscillatory potential being volume conducted as far back as T6 in the temporal array of electrodes as shown in Figures 3.9 and 3.10. No subcortical component with a waveform which was distinctive from the flash ERG morphology could be clearly defined.
**FIGURE 3.7**

Anterior/Posterior distribution of the flash ERG and flash VESP using the balanced non-cephalic reference electrode (BNCRE) for subject 1.

The flash ERG is present at the DTL electrode with an 'a' wave at 16.1 ms and 'b' wave at 34.2 ms.

The VESP clearly emerges as a triphasic complex P25.2 N31.52 P36.5 ms at the temporal array of electrodes, T4, T4½, T6, Cz and T3½. Chin is demonstrated as being inactive for the flash ERG.
null
FIGURE 3.8

Anterior/Posterior distribution of the flash ERG and flash VESP using the BNCRE for subject 2.

The flash ERG is present at the DTL electrode with an 'a' wave at 14.9ms and a 'b' wave at 41.8ms.

The VESP clearly emerges as a triphasic complex at latencies P27.9, N37.4, P40.49, at the temporal array of electrodes T4, T4\textsuperscript{1/2}, T6, Cz and T3\textsuperscript{1/2}.

Chin is demonstrated as being inactive for the flash ERG.
TABLE 3.2

Latency and amplitude results of the anterior-posterior topography to flash stimulation using the balanced non-cephalic reference electrode and auditory masking: latency and amplitude values of the flash ERG and flash VESP

Table 3.2a  Latency and amplitude values of the flash ERG at the DTL electrode on the right cornea

Table 3.2b  Flash VESP: latency values at electrode sites T4, T4½, T6, Cz and T3½

Table 3.2c  Flash VESP: amplitude values at electrode sites T4, T4½, T6, Cz and T3½
### TABLE 3.2a
LATENCY AND AMPLITUDE VALUES OF THE FLASH ERG REF. BNCRE

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>LATENCIES IN MS</th>
<th>AMPLITUDE IN µV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a wave b wave</td>
<td>b wave</td>
</tr>
<tr>
<td>1</td>
<td>16.1 34.2</td>
<td>8.5</td>
</tr>
<tr>
<td>2</td>
<td>14.9 41.8</td>
<td>8.5</td>
</tr>
<tr>
<td>3</td>
<td>16.4 37.6</td>
<td>9.45</td>
</tr>
<tr>
<td>4</td>
<td>18.2 40.9</td>
<td>9.05</td>
</tr>
<tr>
<td>MEAN</td>
<td>16.4 38.63</td>
<td>8.88</td>
</tr>
<tr>
<td>SD</td>
<td>1.36 3.46</td>
<td>.46</td>
</tr>
<tr>
<td>± 2SE</td>
<td>1.36 3.46</td>
<td>.46</td>
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</table>

### TABLE 3.2b
LATENCY VALUES OF THE FLASH VESP REF. BNCRE

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>LATENCIES IN MS</th>
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<tr>
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<td>3.51</td>
</tr>
<tr>
<td>± 2SE</td>
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</tbody>
</table>
**TABLE 3.2c**

AMPLITUDE VALUES IN \( \mu V \)

<table>
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<tr>
<th>SUBJECT</th>
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<th>T3½</th>
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<tr>
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<td>1.49</td>
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</tr>
<tr>
<td>± 2SE</td>
<td>.71</td>
<td>.62</td>
<td>.64</td>
<td>.64</td>
<td>.74</td>
</tr>
</tbody>
</table>
FIGURE 3.9

Anterior/posterior topography of the flash ERG and flash VESP using the vertex, Cz as the common reference electrode and auditory masking for subject 1.

The flash ERG was delineated by an 'a' wave at 14.2 ms and a 'b' wave at 44.1 ms.

The VESP was difficult to define.
FIGURE 3.10

Anterior/posterior topography of the flash ERG and VESP using the vertex, Cz, as the common reference and auditory masking in subject 2.

The flash ERG was clearly defined: the latency values for the 'a' and 'b' waves were a: 14.08ms and b: 42.1ms

The VESP could not be defined clearly
TABLE 3.3

Latency and amplitude results of the anterior-posterior topography study to flash stimulation using Cz and auditory masking

The flash ERG was clearly identifiable in all four subjects. There was no clear VESP response.
**TABLE 3.3**

**LATENCY AND AMPLITUDE VALUES OF THE FLASH ERG**

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>LATENCIES IN MS</th>
<th>AMPLITUDE IN uV</th>
</tr>
</thead>
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<tr>
<td></td>
<td>a wave</td>
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<tr>
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<tr>
<td>SD</td>
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<td>5.04</td>
</tr>
<tr>
<td>+ 2SE</td>
<td>1.67</td>
<td>5.04</td>
</tr>
</tbody>
</table>
within the VESP latency envelope.

3.3.3 Summary and conclusions

The flash ERG was recorded monocularly using a DTL electrode from the cornea of the right eye and with three reference sites: the chin, a BNCRE and the vertex or Cz. The ERG was present as a negative 'a' wave of mean latency 16.34ms and a positive 'b' wave of mean latency 37.2ms and with an amplitude of 11.69μV at the cornea referenced to chin with similar results obtained for the other reference sites.

Using a chin reference and the BNCRE, the flash ERG rapidly attenuated beyond the frontal pole, and in the temporal array of electrodes on the right side at T4 and T4¼ and T6 a triphasic complex clearly emerged of mean incidence P27.28 N32.82 P37.68 and mean amplitudes for the P-N component ranging from 2.05μV to 2.21μV and N-P 1.79 to 2.22μV. The signal was also present at Cz and T3¼.

These values showed no localisation of the response and supported the wide spread distribution found in the pilot study (section 3.2). Similar results were obtained using the BNCRE which also verified the inactive nature of the chin reference.

With Cz used as a reference, subcortical components with the distinct PNP configuration of the VESP could not be as clearly defined.

Rubinstein (1981) had investigated the anterior-posterior distribution of the flash VESP using similar electrode derivations as the present study and Cz as a reference. High amplitude flash ERG with oscillatory potentials predominated
at the cornea and rapidly attenuated at F8. At T4½, although remnants of the 'b' wave of the ERG were still present, a triphasic complex of PNP polarity was recorded with mean latencies P21.30 N28.1 P35.9 and mean amplitudes P-N 1.09µV N-P 2.05µV. This response was tightly localised to T4½ and was not present at either T4 or T6 (Figure 2.5).

In the present study using auditory masking, the VESP was demonstrated as a triphasic complex P27.28 N32.82 P37.68, when the chin was used as a reference. The VESP response was found to have a widespread scalp distribution in the anterior-posterior direction, being present in a temporal array of electrodes on the right side of the head at T4, T4½ and T6. The signal was also clearly identifiable at Cz and T3½. The VESP was found to be independent of the ERG which was recorded at the cornea using a DTL electrode (Dawson et al. 1979) and was present at frontal electrodes. Similar results were obtained using a BNCRE.

Using Cz as a reference, the ERG was clearly recorded at the cornea, although the VESP however was difficult to define.

Both the chin and the BNCRE have emerged as more appropriate common reference sites, being inactive for the flash ERG, whilst Cz is too active for the VESP. The results of this anterior-posterior study, together with the pilot study, raise the question of discrepancy with the distributions found by Rubinstein (1981) where no mention of auditory masking was made in the methods sections of the corresponding topographic studies. Indeed, following an initial study with and without masking, no further mention of auditory masking was made.

In the following studies the field of activity of the VESP, the signal has been
recorded from three electrode sites - at T3\(^{1/2}\), Cz and T4\(^{1/2}\) using the chin as a common reference to assess the extent of auditory involvement.

3.4 Review of auditory evoked potentials

The most common method of classifying auditory evoked potentials is by the latency of the response, and the following main categories have been proposed: early components spanning 0-8ms; middle latency components from 8 to 50ms; and long latency responses over 50ms (see Figure 3.11).

The early latency components consist of the cochlear microphonic, the electrocochleogram and the brainstem auditory evoked potential. The cochlear microphonic has no measurable latency and threshold. It is of non-neural origin and its waveform exactly replicates that of the stimulus. It is thought to originate from the sensory hair cells of the organ of corti within the cochlea and reflect the receptor or generator potential produced by the mechanical distortion of the hair cells in response to sound stimulation. The electrocochleogram has a neural origin and measures the response of the auditory nerve to sound stimulation. It is recorded using a fine stainless steel needle as an active electrode passed through the tympanic membrane to rest on the promontary of the cochlea within the middle ear cavity (Gibson 1978).

The brainstem auditory evoked potential (BSAEP) is a surface recorded composite potential of extremely low amplitude reflecting activity at several different levels of the subcortical auditory pathway following an appropriate auditory stimulus, and the whole BSAEP is complete within 10ms post stimulus (Jewett and Willison 1971; Stockard et al. 1980) Following depth recordings and lesion studies in animals (Jewett 1970; Buchwald and Huang 1975) and clinical studies on patients with known brainstem lesions (Starr and
FIGURE 3.11

Diagrammatic representations of auditory evoked potentials
(redrawn after Gibson 1980.

a): Components of the Brainstem Auditory Evoked Potential (BSAEP) after Jewett (1971)

b): Typical components of the Middle Latency Auditory Evoked Potential (MLAER)

c): Components of the slow cortical potentials (gains were not included)
a) 70dB

IPSLATERAL

CONTRALATERAL

BRAINSTEM POTENTIALS

b) 60dB

Pa

No  Na  Nb

SLOW CORTICAL POTENTIALS

REFERENCE: VERTEX

161
Hamilton 1976; Sohmer and Zuckerman 1979), the BSAEP is thought to reflect the activation of the auditory nerve and brainstem nuclei. The BSAEP has now been established as a useful objective measure of the functional integrity of the subcortical auditory pathway (McCandless 1978; Stockard et al. 1980).

The middle latency range of auditory evoked potentials falls within the same latency range as that of the VESP.

Following the initial discovery by Davis (1939) of evoked potentials to sound stimulation within the spontaneous EEG, the first auditory evoked potentials obtained by averaging techniques were reported by Geisler et al. (1958). These potentials occurred with latencies of 20-30ms and were maximal in the inion region. He concluded that the responses were of cortical origin on the basis of their consistency within each subject, their wide scalp distribution, their onset latencies (comparable to those of somatosensory and visual evoked potentials), and their similarity to auditory responses recorded from animals. However, the enhancement of these responses with increased muscle tone led Bickford et al. (1964) to suspect a myogenic origin and he described them as somomotor responses. This was corroborated by Cody et al. (1964) and Borsanyi and Blanchard (1964).

A more localised response to auditory stimulation arising from the post auricular region was reported by Kiang et al. (1963). This response originated from the reflex activity which was initiated in the cochlea and mediated by brainstem auditory nuclei and the post auricular branch of the facial nerve. It was found to be a myogenic potential which depended on the post auricular muscle tone and showed a marked enhancement in amplitude and shortening in response latency with increased muscle tone (Kiang et al. 1963; Yoshie and Okudaira 1969). The response was bilateral, the most prominent and stable
components being the negative-positive component occurring between 11-20ms active at the mastoid when referred to the vertex (Picton et al. 1974; Jones 1979).

With the appropriate relaxation of scalp musculature, Goldstein and Rodman (1967) and Mendel and Goldstein (1969) reported neurogenic components consisting of a positive at 13ms, a negative at 22ms, positive at 34ms and a negative at 44ms, having amplitudes of 0.5-3μV. This response was stable with time and with sleep and arousal, the most stable components being the negative at 22ms and the positive component at 34ms. This middle latency response (Geisler et al. 1958) had a fairly widespread distribution over the scalp with a maximum in the fronto central regions (Picton et al. 1974; Streletz et al. 1977). It was normally recorded with an active electrode at the vertex and reference electrodes on the mastoids or earlobes - the earlobes being preferable in order to reduce possible contamination by the post auricular myogenic potential. The MLAER could be elicited by any stimulus with a fairly abrupt rise time, i.e. by clicks, tone bursts or tone pips. It was reported to be identifiable down to levels of 30dB in adults, children and neonates and stable in natural or drug induced sleep (Mendel and Goldstein 1971; Kupperman and Mendel 1974). A great variety of bandpass filters have been used, extending from 0.1 - 5000Hz by Arslan et al. (1984) down to narrow bandpasses in the region of 5-150Hz frequently used by Mendel, et al. (1969) Volk (1983). Table 3.4 summarises the stimulus parameters and components documented by various workers in the field.

There is controversy regarding the neural generators of the MLAER. Picton et al. (1974) suggested possible sources in the thalamus, primary auditory cortex and association cortex. Recordings made from subdural electrodes in humans (Lee et al. 1984) suggest possible sources in the primary auditory cortex and in
TABLE 3.4

Components of the middle latency auditory evoked response identified by different researchers.

The stimuli and bandpasses used have also been included. Nomenclature of the different components has been adopted from Mendel and Goldstein (1969)
<table>
<thead>
<tr>
<th>AUTHORS</th>
<th>STIMULUS</th>
<th>BAND PASS FILTERS IN Hz</th>
<th>COMPONENTS OF RESPONSE IDENTIFIED IN MS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>MENDEL AND</td>
<td>50dB Click</td>
<td>5 - 150</td>
<td>-</td>
</tr>
<tr>
<td>GOLDSTEIN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1969</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PETERS ET AL.</td>
<td>10 - 150</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>1974</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THORNTON ET AL.</td>
<td>Tone bursts</td>
<td>25 - 175</td>
<td>-</td>
</tr>
<tr>
<td>1974</td>
<td>60dB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STRELETZ ET AL.</td>
<td>60dB click</td>
<td>1 - 10000</td>
<td>8-12</td>
</tr>
<tr>
<td>1977</td>
<td></td>
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<td>PICTON ET AL.</td>
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<td>8.9</td>
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<tr>
<td>1974</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCHERG AND VOLK</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>1983</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARSIAN ET AL.</td>
<td>80dB click</td>
<td>-</td>
<td>5.7</td>
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<td>1984</td>
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</tr>
<tr>
<td></td>
<td>60dB click</td>
<td>-</td>
<td>6.0</td>
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</table>
the inferior colliculus of the brainstem.

Summary

Taking into account the electrode sites and recording parameters for the neurogenic middle latency auditory evoked response, there may be a possibility of contamination of the VESP with an auditory component. The Grass photostimulator used to deliver the flash stimulus produces a clearly audible click well above subjective threshold levels, and indicated the need for investigation of any auditory evoked components present when auditory masking is not included in the experimental design.

3.5 Controlled auditory study

The topographic studies outlined in sections 3.2 and 3.3 demonstrated that the use of the chin as reference was preferable when recording the flash VESP. With auditory masking, the results did now show localisation of the VESP to the mastoid process and prompted the undertaking of a control study to investigate any possible auditory contamination from the photostimulator discharge.

3.5.1 Materials and methods

Observations were made on 25 normal male volunteer subjects with a mean age of 26 years. All had visual acuities of 6/6 or better in each eye and full visual fields. Silver/silver chloride EEG electrodes were placed at T3½, Cz and T4½ with collodion and the resistances maintained below 5KΩ. All three electrodes were referred to the chin.
Each subject was seated in a slightly darkened room of 100 cd/m² and was exposed to three different modes of stimulation and to one non-stimulus situation. Two properties of the grass PS22 photostimulator, namely the flash discharge and the incurred synchronous click were used. The modes of stimulation were:

1) The flash discharge, presented at 6 flashes/second with the synchronous click masked by earphones, giving a visual response.

2) The click, heard at 6 clicks/second but with flash discharges masked, giving an auditory signal.

3) The flash with the synchronous click, presented 6 flash/clicks per second.

4) The fourth, non-stimulus condition masked both flash and click but the photostimulator was still running and the background responses were still averaged.

In all four modes, the photostimulator was 25cm from the subject and level with the subject’s eyes. The flashes were delivered at intensity 8 or 3939 nits and at the rates described above. With the use of an audiometer, the level of the click was assessed independently by ten subjects within the sample and the average subjective level of the click was found to be 50dB.

The four modes were presented in random order between subjects. Two runs were recorded for each mode and the waveforms superimposed to identify common components. For each run, 500 stimulations were presented and
averaged on the Pathfinder II, the time window being 50ms and the bandpasses 30-500Hz. The data was stored and analysed manually with latency and peak to peak amplitudes being made of all components within the time window used. Across the sample of 25, the results were group averaged for each of the four modes to give an overview of the waveforms, latencies and amplitudes.

3.5.2 Results

The group-averaged responses of the waveforms on the Pathfinder II displayed clear triphasic PNP complexes as shown in figures 3.12, 3.13, 3.14 and 3.15. The latencies and amplitudes at the Cz derivation were:

Flash: P26.4 N33.1 P37.8 P-N 0.9µV N-P 0.81µV
Click: P24.5 N31.2 P35.8 P-N 0.56µV N-P 0.47µV
Click/Flash: P27.7 N32.8 P37.2 P-N 0.56µV N-P 0.93µV

There was no evoked response to the non-stimulus run.

This group-averaging procedure enabled initial inspection of the data, which was subsequently investigated further by statistical analysis as will be described.

For each of the three modes of presentation, ie. 1) flash 2) click 3) flash/click, the mean latency and mean amplitudes were calculated. The mean latency was calculated from the scored values for each of the components of the PNP complex, and where a signal was not obtained to a given stimulation, (ie. there was no clear difference between the potential activity of the stimulus and non-stimulus runs), it was excluded from the calculation. The mean amplitudes for the P-N and N-P components of the waveform were also found for each
FIGURE 3.12

Group-averaged results for the flash VESP using the flash discharge of the photostimulator, with auditory masking.

The responses are shown at electrode derivations T3$^{1/2}$, Cz and T4$^{1/2}$ referred to the chin.
FIGURE 3.13

Group-averaged results for the auditory evoked potential obtained using the click stimulus of the photostimulator in the auditory control study, with visual masking

The responses are shown at T3$^{1/2}$, Cz and T4$^{1/2}$, referred to chin
FIGURE 3.14

Group-averaged results for the flash/click mode of stimulation in
the auditory control study

The signal is shown at electrode sites T3\(^{1/2}\), Cz and T4\(^{1/2}\)
referred to chin
FIGURE 3.15

Grouped results for the three modes of stimulation shown at the Cz derivation for the auditory control study.

The results demonstrate the similarity in latency and overall response configuration to the flash, click and flash/click modes of presentation.

The signals are shown for the Cz derivation referred to chin.
mode, across the sample. Where no response was elicited, the amplitude was
designated zero and included in the manual averaging. Standard errors were
also calculated to indicate the 95% confidence intervals of the sample.

Two subjects out of twenty-five did not give an evoked response to any of the
modes of presentation. Twenty subjects gave a response to flash stimulation,
ie. mode 1) – two examples are shown in Figures 3.16, and 3.17. The
remaining three gave a triphasic response to the click discharge and two of these
gave a signal to the flash/click mode. For pure flash stimulation, the mean
latency was P26.62 (±2.04) N33.53 (±1.96) P38.37 (±2.1) and mean
amplitudes in μV.

T3¹/²: P-N .97 (±.26) N-P .93 (+.3)
Cz: P-N .9 (±.24) N-P .89 (±.28)
T4¹/²: P-N .92 (±.24) N-P .84 (±.26)

Fifteen subjects out of 23 responded to mode 2, ie. the click discharge and two
examples of the auditory signals are shown in Figures 3.18 and 3.19. The
mean latency was P26.32 (+1.02) N32.52 (+1.7) P38.61 (+2.4) and mean
amplitudes were as follows:

T3¹/²: P-N .71 (+.26) N-P .59 (+.2)
Cz: P-N .72 (+.26) N-P .57 (+.2)
T4¹/²: P-N .74 (+.28) N-P .64 (+.26)

Eight subjects did not respond to the click stimulus. However, five subjects
showed an evoked response to both the flash and the flash/click modes, and the
remaining three responded to flash only.
Example of the flash VESP obtained at T3\(1/2\), Cz and T4\(1/2\),
common reference chin, using auditory masking: subject 11
FIGURE 3.17

Example of the flash VESP obtained at T3½, Cz and T3½, referred to chin, using auditory masking: subject 12
FIGURE 3.18

Example of the middle latency auditory evoked response (MLAER) at T3\(\frac{1}{2}\), Cz and T4\(\frac{1}{2}\) referred to chin, using visual masking; subject 1
Example of the middle latency auditory evoked response (MLAER) at T3\(1/2\), Cz, and T4\(1/2\), referred to chin, using visual masking: subject 19
FIGURE 3.20

Example of the response to flash/click stimulation at T3 1/2, Cz and T4 1/2, common reference chin: subject 12
FIGURE 3.21

Example of the response to flash/click stimulation at T3½, Cz and T4½, common reference chin: subject 18
Sixteen subjects showed a triphasic complex to flash/click stimulation, two examples of which are shown in Figures 3.20 and 3.21. Mean latencies were P25.81 (±1.18) N33.5 (±0.84) P40.34 (±1.18) and mean amplitudes at the three derivations were as follows:

\[
\begin{align*}
T3^{1/2}: & \quad P-N \quad 0.83 (±.3) \quad N-P \quad .76 (±.32) \\
Cz: & \quad P-N \quad 0.82 (±.3) \quad N-P \quad .83 (±.34) \\
R4^{1/2}: & \quad P-N \quad .8 \quad (±.3) \quad N-P \quad .76 (±.32)
\end{align*}
\]

Out of the seven non responders, two subjects showed a pure visual response and two gave a pure auditory response, and the remaining three responded to both the pure flash and pure click modes of stimulation. Tables 3.6 and 3.7 summarise the data described above.

A chi squared test was undertaken on the frequency of non response to a signal under the three modes of stimulation as shown in Table 3.5. It was found that there was no significant difference in the occurrence of a triphasic complex in any of the three modes \( (X^2 = 3.00 \quad p > .05) \).

Only ten subjects out of twenty-three gave a triphasic complex to all three modes (figure 3.22) and a further seven subjects showed evoked responses to two modes of stimulation (figure 3.23).

Using this group of seventeen, paired t-tests were carried out across the group for the corresponding latencies of the P-N-P components and corresponding P-N and N-P amplitudes between the three modes of stimulation at the three electrode sites of T3\(^{1/2}\), Cz and T4\(^{1/2}\). For example, in considering the latency and amplitude results for electrode site T3\(^{1/2}\), the group data for the latency of the negative component and the P-N amplitude for flash were compared with the
FIGURE 3.22

Example of the configuration of the responses to flash, click and flash/click stimulation: subject 5

Responses to all three modes of stimulation are shown for the Cz derivation referred to chin, and illustrate that the signals have similar latencies
FIGURE 3.23

Example of subject responding to two out of three modes of stimulation: subject 12

The responses to flash, click and flash/click stimuli are shown for the Cz derivation referred to chin.

The auditory response was poorly defined in this subject
TABLE 3.5

Chi-squared test on the responders to non-responders using 3 modes of stimulation in the auditory control study.

The table demonstrates that there were no significant differences in the ratio of responders to non-responders for the three stimulus modes.
### TABLE 3.5

**FREQUENCY OF OCCURRENCE OF THE**

**RESPONSES TO THREE MODES OF STIMULATION**

<table>
<thead>
<tr>
<th>MODE</th>
<th>FLASH</th>
<th>CLICK</th>
<th>FLASH/CCLICK</th>
</tr>
</thead>
<tbody>
<tr>
<td>RESPONDERS</td>
<td>20</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>NON-RESPONDERS</td>
<td>5</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>TOTAL</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
</tbody>
</table>

**CHI-SQUARED \( \chi^2 (2) = 3.00 \) \( P > 0.05 \) NS
corresponding group data for the latency and amplitude values for click and flash/click. The results of these tests are detailed in tables 3.8 and 3.9 and demonstrated there were no significant differences in incidence of the triphasic complex at T3½, Cz and T4½ (p > 0.05) between the three modes of presentation.

When the amplitudes were considered, no significant differences were found (p > 0.05) for the P-N and N-P components when pure flash was compared to click and flash/click. However, when the click response (mode 2) was compared to flash/click (mode 3), the N-P component was found to be significantly higher in amplitude for the flash/click response at the electrode sites Cz and T4½. (For Cz p = .014, and T4½ p = .02, ie. p < 0.05).

As previously mentioned, the group averaging procedures showed clear triphasic complexes. These confirmed the statistical analysis using paired t-tests, in demonstrating similar waveform latencies for the three modes (see Figure 3.15) and showing that the N-P component of the flash/click mode was larger in amplitude (0.93μV at Cz), than the N-P component of the auditory response (0.47μV at Cz). These group results were reconfigured to the Cz reference in order to allow investigation of any lateralisation of the response to either T3½, Cz or T4½ when the chin was used as a reference. This involved subtraction of the signal at Cz from that at T3½ and at T4½. For the VESP, subtraction resulted in a flat line indicating no lateralisation of the response. For mode 2) ie. the auditory response, a broad negative component emerged, delineated at T3½ by P18.24 N25.84 P34.32 P-N .47μV and N-P 62μV, and for T4½ by P18.4 N26.2 P37.2 and P-N .33μV and N-P .49μV. Mode 3) ie. flash/click reconfigured to Cz showed lateralisation to T3½. The signal had latencies of P19.04 N25.68 P34.64 and amplitudes P-N .68μV and N-P .34μV. These results (figure 3.24) suggested that stimulation of the auditory
TABLE 3.6

Auditory Control Study: Mean latencies of the PNP complex to three modes of stimulation

TABLE 3.7

Auditory Control Study: Mean amplitude values for the P-N and N-P components to three modes of stimulation and at the three electrode sites T3\(1/2\), Cz and T4\(1/2\)
### TABLE 3.6

<table>
<thead>
<tr>
<th>STIMULUS TYPE</th>
<th>P</th>
<th>N</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flash</td>
<td>$26.26,^{\pm}1.74$</td>
<td>$33.53,^{\pm}1.96$</td>
<td>$38.37,^{\pm}2.1$</td>
</tr>
<tr>
<td>Click</td>
<td>$26.32,^{\pm}1.02$</td>
<td>$32.52,^{\pm}1.7$</td>
<td>$38.61,^{\pm}2.4$</td>
</tr>
<tr>
<td>Flash/Click</td>
<td>$25.81,^{\pm}1.18$</td>
<td>$33.5,^{\pm}.84$</td>
<td>$40.34,^{\pm}1.18$</td>
</tr>
</tbody>
</table>

### TABLE 3.7

<table>
<thead>
<tr>
<th>ELECTRODE</th>
<th>T3½</th>
<th>Cz</th>
<th>T4½</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>P-N</td>
<td>N-P</td>
<td>P-N</td>
</tr>
<tr>
<td>Flash</td>
<td>.97(±.26)</td>
<td>.93(±.3)</td>
<td>.9(±.24)</td>
</tr>
<tr>
<td>Click</td>
<td>.71(±.26)</td>
<td>.59(±.2)</td>
<td>.72(±.26)</td>
</tr>
<tr>
<td>Flash/Click</td>
<td>.83(±.3)</td>
<td>.76(±.32)</td>
<td>.82(±.3)</td>
</tr>
</tbody>
</table>
TABLE 3.8

Auditory Control Study: Results of the paired t-tests on latencies

T tests were used to compare the mean latency values for the PNP components between the three modes of stimulation.

The probability values in this table are all greater than 0.05 indicating no significant differences between the latencies of each component.

TABLE 3.9

Auditory Control Study: Results of the paired t-tests on amplitudes

The mean values of the P-N and N-P components for one mode of stimulation were compared with the corresponding values of another mode. This comparison was undertaken for the three electrode sites T3\(1/2\), Cz and T4\(1/2\).

The probability values indicate that there were no significant differences between the mean amplitudes when flash was compared against flash/click stimulation. However significant differences between amplitudes for the N-P at Cz and T4\(1/2\) were obtained when the click and flash/click modes of stimulation were compared (p<0.05). These values are marked with an asterisk.
### TABLE 3.8

<table>
<thead>
<tr>
<th>GROUP 1</th>
<th>GROUP 2</th>
<th>P</th>
<th>N</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLASH</td>
<td>CLICK</td>
<td>0.32</td>
<td>0.8</td>
<td>0.58</td>
</tr>
<tr>
<td>FLASH</td>
<td>FLASH/CLICK</td>
<td>0.92</td>
<td>0.6</td>
<td>0.18</td>
</tr>
<tr>
<td>CLICK</td>
<td>FLASH/CLICK</td>
<td>0.92</td>
<td>0.54</td>
<td>0.22</td>
</tr>
</tbody>
</table>

### TABLE 3.9

<table>
<thead>
<tr>
<th>ELECTRODE SITES:</th>
<th>T3½</th>
<th>Cz</th>
<th>T4½</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P-N</td>
<td>N-P</td>
<td>P-N</td>
</tr>
<tr>
<td>GROUP 1</td>
<td>GROUP 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FLASH</td>
<td>FLICK</td>
<td>0.42</td>
<td>0.16</td>
</tr>
<tr>
<td>FLASH</td>
<td>FLASH/CLICK</td>
<td>0.78</td>
<td>0.6</td>
</tr>
<tr>
<td>CLICK</td>
<td>FLASH/CLICK</td>
<td>0.06</td>
<td>0.06</td>
</tr>
</tbody>
</table>
Reconfigured group-averaged waveforms for flash, click and flash/click referred to Cz

For each mode of stimulus presentation, the waveforms at Cz were subtracted from the waveforms at T3½ and T4½.

The flash response is a flat line indicating responses were equal in amplitude at T3½, Cz and T4½ showing up no differences on subtraction.

For the auditory response, and the response to flash click stimulation - there was lateralisation indicating a differential response at T3½, Cz and T4½ when the auditory pathway is involved.
pathway had a differential effect on the three electrode sites of T3 1/2, Cz and T4 1/2 in terms of amplitude when the chin was used as a reference, and the subsequent reconfiguration of the waveforms to Cz, demonstrated these differences by showing localisation of the responses to the mastoid area.

3.5.3 Summary and conclusions

Three different stimulus properties of a Grass PS22 photostimulator were isolated to investigate auditory evoked potentials falling in the same latency range as the triphasic VESP recorded at T3 1/2, Cz and T4 1/2, referred to the chin. Examples of the results given for the Cz derivation are as follows:

MODE 1  Flash Int.8    P26.26   N33.53   P38.37   P-N   .9    N-P   .89
MODE 2  Click 50dB    P26.32   N32.52   P38.61   P-N   .72    N-P   .57
MODE 3  Flash/Click   P25.81   N33.5   P40.34   P-N   .82    N-P   .83

A chi-squared test showed there was no significant difference in the occurrence frequency of a response to the three modes of stimulation (p > 0.05) - (Table 3.5).

Seventeen subjects responded to more than one mode of stimulation and paired t-tests were used across this group to test for any significant differences in the corresponding latencies of the P-N-P components and corresponding P-N and N-P amplitudes between the three modes of stimulation and at the three electrode sites of T3 1/2, Cz and T4 1/2. No significant differences (p > 0.05) were found in the latency values of the P-N-P complex between the three modes of stimulation. With reference to amplitudes, no significant differences were found (p > 0.05) when the pure flash mode was compared to click and flash/click. However, when the amplitudes of the click response (ie. Mode 2) were
compared to the amplitudes of the flash/click (i.e. Mode 3) signal, the N-P component was found to be significantly higher for the flash/click response at electrode sites Cz and T4\(^{1/2}\) (for Cz: \(p = 0.014\), i.e. \(p < 0.05\); for T4\(^{1/2}\): \(p = .02\), i.e. \(p < 0.05\)).

The group-averaged waveforms confirmed the statistical analysis of the data in demonstrating clear triphasic complexes for the three modes of stimulation and in showing that the N-P component of the flash/click mode was larger in amplitude (0.47\(\mu\)V at Cz). These grouped results were reconfigured to the Cz reference, i.e. for each mode, the signal obtained at Cz was subtracted from the signal at T3\(^{1/2}\) and T4\(^{1/2}\). For flash stimulation, subtraction resulted in a flat line showing no lateralisation of the response. However, for the auditory response, a broad negative component emerged, delineated by P18.24 N25.84 P34.32 at T3\(^{1/2}\) and T4\(^{1/2}\). For the flash/click mode there was lateralisation to T3\(^{1/2}\) with a signal having latencies of P19.04 N25.68 P34.64. These results suggested that stimulation of the auditory pathway resulted in a differential effect on the three electrode sites of T3\(^{1/2}\), Cz and T4\(^{1/2}\) when the chin was used as a reference.

It can be concluded that without auditory masking of the click discharge of the photostimulator, there may be a substantial auditory response and this signal will contaminate the VESP. Such a contamination may cause a false localisation of the response to the mastoid area. This is the most likely explanation for the localisation of the VESP signal reported by Rubinstein (1981).

3.6 Discussion

In the initial studies on the flash VESP, 'far-field' recording techniques (Jewett and Williston 1971) were adapted to accentuate early subcortical components in
the visual pathway (Rubinstein 1981). A triphasic complex of early components was detected having maximal amplitude around the upper mastoid processes, i.e. at T3^{1/2} and T4^{1/2}, the mean latencies of the peaks of the complex being P21 N26.2 P33.6 when referred to Cz. Boylan et al. (1984) in a discussion of the possible subcortical generator sites pointed out that these sites were at a large distance from the scalp electrodes when compared to occipital electrodes directly over the site of the VECP generators. Theoretically therefore, the VESP should have had a widespread field of activity and T3^{1/2}, T4^{1/2} and Cz should have been equipotential. Furthermore, the mastoidal location for early wavelets was not verified by other workers (Siegfried and Lukas 1983), and Pratt et al. (1982) suspected that large amplitude responses at the mastoid perhaps indicated some auditory contamination.

The photostimulator used for the flash VESP produces a 'click' on discharge, audible to the subjects and synchronous with the presentation of the flash stimulus.

Masking of this 'click' in early topographic studies (Harding and Rubinstein 1981) is ambiguous. In the present studies, a reinvestigation of the flash VESP using auditory masking was undertaken, with a view to establishing appropriate reference sites and studying the distribution of the response.

Two flash topographic studies covering the transverse distribution and anterior posterior spread of the signal demonstrated that the flash VESP had a wide field of activity and Cz in both situations appeared to be active for the subcortical signal. The most appropriate reference sites were the non-scalp derivations at the chin and a BNCRE at the level of the 7th cervical vertebra posteriorly and the sterno-clavicular joint on the thorax. With these electrodes, the VESP was found to be independent of the flash ERG recorded monocularly from the right
eye both in its morphology and bilateral distribution. That is, it was not only recorded from a temporal array on the right side of the head at T4, T4½, T6, but also at T3½ and Cz as a P26.94 N32.38 P37.15 complex using the chin reference. This bilateral distribution is significant as a monocularly recorded flash ERG rarely crosses the median line of the head (Nakamura 1975, 1978; Harding and Rubinstein 1981). These topographies contradict the results obtained by Rubinstein (unpublished thesis) and prompted a study to assess the possible degree of auditory contamination.

An auditory control study using the two properties of the photostimulator to present three different modes of stimulus presentation was designed, and the visual and auditory signals obtained are shown in figure 3.15. All three modes of stimulation produced a P-N-P complex of similar latency for each of the three components. From the group averaged responses the latency and amplitude values were as follows at the Cz derivation:

Mode 1: Flash  P26.4  N33.1  P37.8  P-N  .9µV  N-P  .81µV
Mode 2: Click  P24.5  N31.2  P35.8  P-N  .56µV  N-P  .47µV
Mode 3: Flash/Click  P27.7  N32.8  P37.8  P-N  .57µV  N-P  .93µV

The data was reconfigured to Cz, that is, the waveforms at T3½ and T4½ for the group and each stimulus mode were subtracted from the grouped waveform at Cz.

There were no differences in amplitude at the three electrode derivations for the flash response, i.e. the subtractions produced flat lines. However, there were differences in amplitude for the auditory response (mode 2) and for the flash click response. For the pure auditory response, a broad negative component emerged at T3½ and T4½ delineated by P18.24 N25.84 P34.32ms. This
indicated that as Cz was subtracted from T3½ and T4½, the amplitudes for the negative component were larger at the mastoids. For the flash/click mode, the response lateralised to T3½ with latencies of P19.04 N25.68 P34.64. Figure 3.24 summarises these results. It is of interest to relate these findings to the middle latency auditory evoked response (MLAER) well established in the literature. Mendel and Goldstein (1969) found its most stable neurogenic components were a negative at 22ms and a positive at 34ms. The amplitudes were at a maximum at the fronto-central regions with the active electrode at the vertex referred to the earlobe. The MLAER was elicited by any stimulus with an abrupt rise time such as a click, and identifiable at stimulus levels of 30dB and above. With reference to the auditory control study, the click discharge was subjectively assessed to be 50dB by ten subjects and it is proposed that a middle latency auditory response of neurogenic origin was being evoked. Reconfiguration to Cz of the group-averaged waveforms has effectively inverted the wave as Cz is normally used as the active electrode in middle latency studies. For the pure auditory response, the N25.84 and P34.32 would correspond to P25.84 and N34.32 if phase inverted to relate to the literature.

These studies suggest that as differences in amplitudes were obtained when the click was audible, the earlier research on the VESP undertaken by Rubinstein (1981) was perhaps contaminated by an auditory response which would explain the localisation to the mastoid area. The study however, could not assess the percentage contribution of auditory and visual potential activity in the flash/click (mode 3) signal for any given individual, but it is likely that for many subjects there is a marked contribution from the auditory pathway.

It is therefore suggested that further studies on the flash VESP should be designed to incorporate an auditory masking procedure and to include a reference electrode not sited on the scalp.
CHAPTER FOUR
REVIEW OF THE RECEPITIVE FIELD PROPERTIES OF THE LATERAL GENICULATE BODY AND SUPERIOR COLLICULUS

4.1 Introduction

The possible subcortical sources of the VESP are the lateral geniculate body and the superior colliculus and the purpose of this chapter is to present the anatomy and visual physiology of these structures. There are several paradigms within which visual processing can be discussed, and with reference to the macroelectrode recordings of the VESP, the most appropriate framework is to be found in the visual receptive fields properties of the two structures.

The history of receptive field studies has been included to introduce the classification and terminology used in describing the visual properties of these fields. Primates have been mainly considered as their anatomy and projections differ least significantly from humans (Cooper et al. 1965; Szentagothai 1973).

4.2 Structure of the Lateral Geniculate Body (LGB)

The lateral geniculate body can be described as a neuronal relay station, being a major synaptic junction between the retina and visual cortex (Lockhart, et al. 1974). About 80% of the visual fibres enter the lateral geniculate body, after partial decussation at the optic chiasma, the rest passing round it to reach the superior colliculus via the superior brachium (figure 4.1 and 4.2).

Direct studies of the LGB in man are sparse, although histology of the organisation and distribution of the cells at a quantitative level has been done on autopsy material using trans-neuronal atrophy techniques (Kupfer 1962; Balado
FIGURE 4.1

Left side of brainstem illustrating the anatomical relationship between the lateral geniculate body and the superior colliculus

(Lockhart et al. 1974)
Illustration removed for copyright restrictions
FIGURE 4.2

Brainstem Dissected in Skull

Viewed from behind demonstrating the lateral geniculate body
and the superior colliculus (Lockhart et al. 1974)
Illustration removed for copyright restrictions
and Franke 1937; Chacko 1948; Sullivan et al. 1958).

Within the LGB are six layers or laminae of cells classically described and numbered by Chacko (1949). Layers 1 and 2, the more ventral layers, contain large cells and are called the magnocellular layers, the four dorsal layers being described as parvocellular layers (figure 4.3). Within a range of primates, the magnocellular layers are nearer the outer surface of the thalamus. Clark (1932) suggested that the ventral location of the magnocellular laminae in higher primates (monkeys, apes and man) allowed for the strong development of the parvocellular laminae in these species. Confirming this idea, Rakic (1977) has described how the LGN of the rhesus monkey rotates during gestation, in essentially the pattern that Clark had anticipated. The cells that form the magnocellular layers are born earliest from the ventricular zone of the thalamus, migrate outwards and collect at the pial surface of the thalamus. The cells forming the parvocellular laminae are born later and as they migrate outward they accumulate inside the magnocellular layers. After the LGB has rotated, they are found in their adult location, i.e. dorsal to the magnocellular layers.

Each retinal point is represented in several laminae (Kupfer 1962) and corresponding points of the retina of the two eyes are represented in a linear manner in all six laminae of the LGB (figure 4.4). Each point on the retina is represented by a wedge shaped area in the LGB, thus producing a point to sector representation. The laminae are therefore stacked in a visuotopic continuity of a given point of the visual field between adjacent laminae (Allman 1977). The central 15° of the visual field is estimated to be represented in over 50% of the geniculate volume (Hickey and Guillery 1979). On examination of stained sections from 57 human brains of neurologically normal individuals, the laminar arrangement was found to be quite variable, although the dorsal parvocellular section within which foveal vision is represented showed the least
FIGURE 4.3

The Lateral Geniculate Nucleus (LGN) of the normal human

A diagrammatic representation of a frontal section through the LGN of a normal human illustrating its laminar nature. Layers 1 to 6 (L1-L6) are labelled. Layers 2, 3 and 5 received fibres from the ipsilateral eye; 1, 4 and 6 from the contralateral eye.

(After Chacko 1949)
FIGURE 4.4

The neuronal connections within the lateral geniculate body

(Kupfer 1962)
variability (Hickey and Guillery 1979).

A few quantitative studies of the number of nerve fibres in the visual system have been made. The figure usually cited is one million (Arey and Bickel 1953; Oppel 1963; Kupfer et al. 1967) and of these over 800,000 are thought to innervate the LGB, the ratio of crossed to uncrossed fibres being 53% : 47%.

4.3 History of receptive field studies in vision

In 1938, Hartline introduced the concept of the visual receptive field by exploring a frog's retinal surface using a spot of light (Hartline 1938). Single optic nerve fibres were dissected from the axon bundle layer of the retina and the retinal surface examined with a spot of light to find regions of the retina which could alter or modulate the spike activity of the particular optic nerve axon under study. Hartline described three categories of cells:- those responding to the onset of the light stimulus showing an "on" response, those responding to the offset of the stimulus, ie. an 'off' response, and those excited by either the onset or offset of the light, ie. an "on-off" response. Hartline noted that the region of the retina to which a particular nerve axon showed sensitivity was limited, and the mapped area for each fibre was called the 'receptive field'.

Kuffler (1953) initiated similar studies in mammals, using the cat. He developed a technique for recording responses from the intact eye and employed the optics of the eye in the presentation of the stimuli. Recordings from ganglion cells in the cat demonstrated that the receptive fields could be subdivided into two concentric zones - a circular central zone of high sensitivity yielding either "on" or "off" responses to a light spot, surrounded by a peripheral annular zone of lower sensitivity yielding the opposite response to the centre. Thus, if a cell had a centre demonstrating an "on" response, the
periphery was sensitive to the offset of the light spot. Kuffler (1973) subsequently showed interactions between the centre and surround of a receptive field when both regions were simultaneously stimulated (figure 4.5). They were described as functionally antagonistic, and Hartline's 'receptive field' was redefined as 'receptive field centre'.

Two further major observations were reported by Wiesel (1960). The ganglion cells in the macular region had markedly smaller receptive field centres than those in the peripheral retina. Furthermore, the antagonistic effect of the surround varied from cell to cell, being weaker when the centre region was large. These findings supported the idea that receptive field centre size was an important determinant of visual acuity. Hubel and Wiesel (1960) noted the presence of colour sensitive cells in the retina of monkey and that the smaller receptive fields of monkey ganglion cells matched the higher spatial resolution of which the monkey is capable and the monkey's ability to discriminate between colours.

Various workers had explored different properties of the centre-surround organisation principally in the cat (McIlwain 1964; Rodieck and Stone 1965; Rodieck 1965) without proposing that any particular properties were of primary significance. The first systematic classification of receptive field properties of retinal ganglion cells in the cat was drawn by Enroth-Cugell and Robson (1966) and was based on the response of receptive fields of individual ganglion cells to grating stimuli of threshold and suprathreshold contrast. The grating form of stimulus was adopted because it had been used in psychophysical studies of human vision to characterise the human contrast sensitivity function (Campbell and Green 1965). The human ability to detect the presence of a grating stimulus depends on the spatial frequency of the grating (very fine gratings becoming indistinguishable from a uniform background even at high contrast levels) and
FIGURE 4.5

On-centre receptive field in cat.

A. Spot of light directed into centre causes vigorous discharges

B. Surround illuminated by ring of light inhibits background discharge and causes responses when light is turned off

C. Light covering entire receptive field has relatively small effect when turned on and off because in this example antagonistic actions in centre and surround almost cancel each other out

Illumination, indicated by dark line lasts to 0.5 second (from Kuffler 1973)
on the contrast between black and white bars (the greater the contrast, the finer the grating which can be resolved). A plot of the minimum contrast needed for the detection of a grating against the spatial frequency of the grating is known as a contrast sensitivity function.

Enroth-Cugell and Robson (1966) succeeded in obtaining contrast sensitivity functions for individual ganglion cells. A grating pattern was drifted across a given receptive field at a constant velocity. The velocity was varied with the spatial frequency of the grating so that at any particular spatial frequency, four black and white bars crossed the receptive field every second. The grating evoked a discharge in an on-centre cell each time a light bar crossed the centre of a receptive field. The cell’s discharge was therefore modulated in synchrony with the cycle-by-cycle passage of the grating, and the modulation could be reduced to zero by either reducing the contrast or increasing the spatial frequency of the grating. The cell then fired at a rate and in a manner indistinguishable from its firing when the screen was of uniform luminance.

Approximately 25% of the ganglion cells behaved in this “linear” way. The majority of cells behaved in a "non-linear" way. In these cells the modulated pattern of firing was replaced by an unmodulated increase in firing rate when the spatial frequency of the grating was reduced. When the border between bright and dark bars was centred on a "linear" type cell, the cell gave no response, determining what was called the "null position" of the cell. With the "non-linear" cell type, no null position for the stimulus could be found (figure 4.6).

The linear cells were called X cells and the non-linear cells Y cells, and two other important differences were also noted. The receptive field centres of Y cells were generally larger than those of X cells, and X cells were encountered
FIGURE 4.6

The linearity test of Enroth-Cugell and Robson (1966).

The original caption reads:
"Responses of an off-centre X-cell (A) and an off-centre Y-cell (B) to the introduction and withdrawal of a stationary sinusoidal grating pattern. The contrast (0.32) was turned on and off at 9.45Hz. Downward deflexion of the lowest trace in both A and B indicates withdrawal of the pattern (contrast turned off), upward deflexion indicates introduction of the pattern (contrast turned on). The upper line in each pair is the pulse density of the ganglion cell discharge (scale at left: pulses/sec); the length of the zero line represents a duration of 2 sec. The 'phase angle of the pattern', i.e. the angular position (in degrees) of the (cosine) grating relative to the mid point of the receptive field centre, is given at the right of the figure and is illustrated by the sketches. A: X-cell (no.84); spatial frequency 0.13c/deg. B: Y-cell (no.13); spatial frequency 0.16c/deg."

Compare the two histograms in the second row; the left-hand histogram shows almost no response while the right-hand histogram shows two peaks. The same difference is apparent between the bottom two histograms. The two-peaked response obtained from the Y cell is the evidence of its nonlinearity.
more frequently near the area centralis of the cat retina (the homologue of the primate's macular region).

These findings have been widely confirmed and interpreted as evidence that X cells subserve high resolution pattern vision and Y cells subserve movement or low resolution pattern vision in mammals (Stone 1983). Fukada (1971) and Cleland et al. (1971) independently reported correlations between receptive field properties and axonal conduction velocities of cat retinal ganglion cells and both suggested that Y cells had faster axons than X cells.

A third type of receptive field, or 'W' cell was described (Rodieck 1973). The receptive fields had on-off centres (Stone and Fabian 1966) and were "suppressed by contrast" (Rodieck 1967). The ganglion cells also had slower conducting axons than the X and Y cells (Stone and Hoffman 1972).

These observations began a long and continuing series of studies of the properties of W/X/Y cell systems in different animals along the primary visual pathway at the retina, lateral geniculate body, visual cortex and other visually associated areas such as the superior colliculus. The following sections will be devoted to the receptive field studies in monkeys with the emphasis on the lateral geniculate body (LGB).

4.4 Receptive field studies in primates

The retina

The first physiological classification of monkey ganglion cells allowing comparison with the classification developed for the cat was proposed by Gouras (1969), who reported that ganglion cells in the foveal region could be
described as either 'tonic' or 'phasic'. Tonic cells responded to a flashing light stimulus with a tonic pattern of firing, i.e. a burst of spikes which was sustained as long as the spot was presented. 'Phasic' cells, however, gave only short transient bursts of spikes which died away before the stimulus was removed. The tonic cells were more concentrated in the fovea, had slower conducting axons (2ms) compared to 4ms for phasic cells, and had smaller receptive fields than phasic cells. In these properties, tonic cells differed from phasic cells in the same way as X cells differed from Y cells in cats. In addition, many of the tonic cells were colour coding, i.e. their responses varied with the wavelength of the stimulus, whilst phasic cells did not show this specificity. This work was confirmed and expanded in ensuing studies. De Monasterio and Gouras (1975) described three groups of monkey ganglion cells: one group as concentric and colour-coding, a second group as concentric and broad-band, i.e. spectrally insensitive, and a third as non-concentric. The broad band/concentric cells resembled the phasic cells described by Gouras (1969) and being more common in the peripheral retina they were independent of stimulus colour, gave phasic responses to standing contrast stimuli and had larger receptive fields. The colour-coding cells resembled the Gouras' tonic cells, giving sustained responses to standing contrast stimuli, having small receptive fields and being found more frequently in the fovea. The non-concentric cells were a newly recognised group comprising only 9% of the sample. They had on-off centres and were movement sensitive. Schiller and Malpeli (1977) also proposed three broad groupings. Most of their sample fell into two groups, a broad band group and colour coding group, which the authors noted closely resembled the Y and X cells. The third group was termed 'rarely-encountered' and were like W cells in that they had on-off centre regions, were suppressed by stimuli with contrast, showed no colour specificity and had slow conducting axons. They were subsequently called 'W-like' cells (Schiller et al. 1979) and were found to comprise the major component of the retinal input to the superior colliculus.
De Monasterio et al. (1976) extended the analysis of monkey ganglion cells to include their axonal conduction velocity and the linear/non-linear spatial properties described as a distinguishing feature of cat X and Y cells by Enroth-Cugell and Robson (1966). Their results indicated that broad band cells further resemble Y cells in the non-linearity of their spatial summation and faster conduction velocities, whilst colour coding cells resembled X cells by being linear and slow conducting. Marrocco (1978) felt however there was more overlap between the groups than was the case for the cat's retina. Stone (1983) summarised the differences between the groupings of retinal ganglion cells between cats and monkeys by saying that X cells are more numerous and W cells less numerous in monkeys than in cats.

4.5 Receptive field properties of the primate LGB

The classification of the relay cells in the LGB of monkeys into X-like and Y-like cells has emerged even more clearly than the classification for the retina (Dreher et al. 1976; Sherman et al. 1976; Schiller and Malpeli 1978). The parvo/magno cellular division of the LGB has been found to correlate more strongly with an X/Y division of function, i.e. relay cells in the parvocellular laminae relay the activity of X-like ganglion cells to the visual cortex whilst the magnocellular layers relay Y-like activity (Dreher et al. 1976). The cells in the parvocellular laminae had smaller receptive fields, gave sustained or tonic responses to standing contrast and received the input from the retina via slow conducting afferents. The cells in the magnocellular laminae had larger receptive fields, gave phasic responses to contrast stimuli and were responsive to high stimulus velocities. Dreher et al. (1976) commented on the striking X/Y distinction at the LGB and that every LGB cell studied could be classified as
either X-like or Y-like on the basis of tonicity, responsiveness to fast moving stimuli and afferent conduction velocity.

Throughout these studies, the chromatic properties of the X-like cells clearly emerged (Dreher et al. 1976; Sherman et al. 1976). It is interesting to note, however, that investigations of the colour properties of the receptive fields at the LGB had been initiated in the 1950's.

In 1958, DeVlois et al. observed geniculate cells in the monkey which were excited by one set of wavelengths and inhibited by others when the eye was stimulated with flashes of monochromatic light equated for luminance (De Valoils et al. 1958). The optimum stimulus for the cells was emphasised and the majority of cells which demonstrated such colour opponency were in great profusion in the parvocellular layers. Approximately 70% of the cells in the parvocellular layers relating to the fovea were found to be spectrally opponent (DeValois et al. 1966) and fell into one of two categories. One category consisted of two classes of cells: those giving a maximum excitatory response to around 500nm and maximum inhibition to 630nm, named green excitatory, red inhibitory cells or (+G - R) cells and those giving a (-G + R) response. This category predominated and was called the red/green system. The other class was the blue/yellow system which showed a maximum excitation to 440-nm and maximum inhibition to 600nm (+B - Y) and vice-versa.

Wiesel and Hubel (1966), offering a classification dependent on receptive field organisation and cone inputs to the LGB, found that 84% of their cells in the parvocellular laminae were colour opponent. Again, predominantly red and green spectral hues gave optimal responses. Using small spots and annuli of light, the chromatic and spatial receptive field properties were explored and three types of receptive fields were described as types I, II and III. Seventy-seven
percent of the receptive fields were type I. The fields were concentrically organised but the centre had a different spectral sensitivity from the surround. For example, a cell might have a centre excited by a red light and a surround inhibited by a green light or vice-versa. There were four possibilities of combined spatial and spectral interactions. For "on"-centre cells the centre could be red or green excitatory, whilst for "off"-centre cells a red light would inhibit the centre and a green light excite the surround, or vice-versa. Very few cells were found with a blue excitatory centre and yellow inhibitory surround and none for the reverse situation. Type I cells had the smallest field centres recorded, at 30°. Only 7% of the cells fell into the type II category. These cells were spectrally opponent in that the cells received inputs from two opposing cone types but the two cone inputs had identical spatial distributions as there was no centre-surround structure, i.e. the fields were spatially coextensive. The remaining cells had a type III structure which involved a centre-surround organisation with no spectrally opponent organisation (figures 4.7 and 4.8).

Many workers explored this classification further. De Monasterio and Gouras (1975) found that in the parvocellular area representing the foveal region up to 5° eccentricity there were more green on-centre fields than red on-centre fields. The introduction of structured stimulation to look at chromatic properties of the parvocellular layers yielded other characteristics. Creutzfeldt et al. (1979) introduced a different classification of the spectrally sensitive cells in the parvocellular layers based on a series of chromatic slits moved over the receptive field, finding that the majority of cells were excited by a wide range of wavelengths from 575-675nm and suppressed by wavelengths below 500nm. In a study comparing colour opponency to moving slits with large field flashes, the colour specificity was more effectively demonstrated using large field chromatic flashes (Gouras and Kruger 1979). Using Mondrian stimulus patterns, with field sizes of 15° x 15° and 20° x 20°, Nothdurft and Lee (1982a,
FIGURE 4.7

Responses of a dorsal layer geniculate cell to white and monochromatic light.

Left: illumination of field centre with 0.5° spot
Right: illumination of whole receptive field

Coloured spots were produced by placing an interference filter in the beam of white light. They therefore contain far less energy than the white stimuli. Light adapted state. Field centre 19° from the fovea, 6° below the horizontal meridian

(Wiesel and Hubel 1966)
Illustration removed for copyright restrictions
4.8a) **SPECTRAL SENSITIVITY OF A RED ON-CENTRE CELL**

Relative sensitivities obtained by determining log reciprocal thresholds. Crosses = on responses. No responses to 540 mpi, at any intensity. Light adapted state; stimuli are superimposed on a 1 cd/m² steady diffuse white background.

4.8b) **SPECTRAL SENSITIVITY OF A GREEN ON-CENTRE CELL**

Green on centre, red off surround. Field centre 10-12' in diameter, situated 10° from the fovea

(From Wiesel and Hubel 1966)
Illustration removed for copyright restrictions
b) showed that the responses to monochromatic stimuli at the level of individual receptive fields were a reliable guide to a cell's responsiveness to mixed colours. It was noted that with a wide range of colours the neurones in the parvocellular layers did not show any "off" responses. Using drifting sine wave gratings, Hicks et al. (1983) found that at a temporal frequency between 10-20Hz, the parvocellular response to chromatic gratings increased with low spatial frequencies. In agreement, Derrington et al. (1984) proposed that the spectral sensitivity of the parvocellular neurones changed with the spatial frequency of the stimulus, as raising the spatial frequency of a stationary chromatic grating from a spatially unstructured field to 4-5Hz reduced the response to chromatic stimulation. Their findings were supported by Ingling and Martinez-Uriegas (1985).

More studies concentrating on the achromatic properties of the X-like cells have been directed to the spatial resolution and contrast sensitivity properties of the parvo/magno cellular divisions of the LGB, using achromatic sine wave gratings.

The spatial resolution of a receptive field at the LGB has been defined in terms of the discharge response of an LGB neurone to a sine-wave grating which is either drifted across the receptive field or presented as a pattern reversal with the light and dark bars repeatedly interchanged. As the spatial frequency was increased the response finally disappeared into noise and the grating frequency at which this happened has been called the spatial resolution of the neurone (Kaplan and Shapley 1982) or the 'neuronal acuity' (Blakemore and Vital-Durand 1979).

At any given eccentricity, the ability of X cells to resolve gratings has been found to be greater than that of Y-cells. Using stationary gratings of high
contrast, optimal stimulus values of 2-8cpd for X cells compare with 0.5-1cpd for Y cells (Dreher et al. 1976); and with drifting gratings, optimal values for X cells of 4-5cpd and for Y cells of 0.5-1cpd (Derrington and Lennie 1984) have been obtained.

In terms of spatial resolutions, values of 35-40cpd for LGB receptive fields representing the foveal projection have been found (Blakemore and Vital-Durand 1979; Derrington and Lennie 1984). The spatial resolution has been expressed as being inversely proportional to the receptive field size and at any given eccentricity three times larger for Y- cells than X- cells (Irvin et al. 1986).

Using fine sine wave gratings, the distribution of the linear X-like cells and non-linear Y-like cells has been reappraised. Kaplan and Shapley (1982) agreed with Blakemore and Vital-Durand (1981) in finding that 99% of cells in the four dorsal parvocellular layers and 75% of the cells in the two magnocellular layers were X-like cells. This finding has led to the suggestion that a close homology exists between the X and Y cells of the magnocellular laminae and the X and Y cells of the cat LGN which are not separated into distinct laminae. The parvocellular laminae in monkey is seen as forming a separate visual neural pathway only distinctive in higher primates. However, other parameters such as axonal conduction velocity and velocity selectivity have not been considered (Stone 1983). Leventhal et al. (1981) have demonstrated the morphologies of ganglion cells projecting to the parvo and magnocellular laminae and their data support the earlier interpretation of parvocellular cells as X-like and magnocellular cells as Y-like (Dreher et al. 1976; Sherman et al. 1976; Schiller and Malpeli 1978).

With reference to contrast sensitivity, the magnocellular units had much higher contrast sensitivities than parvocellular units (Kaplan and Shapley 1982; Schein
and de Monasterio 1986), and the higher sensitivities of the magnocellular units
gave saturated responses to gratings of high contrast whereas the parvocellular
units were rarely saturated, (figure 4.9), the magnocellular units being 5-10
times more sensitive (Derrington and Lennie 1984).

4.6 **Summary of the receptive field properties of the LGB**

The X-like cells in the LGB represent the foveal projections to the LGB and as
many as 90% of this projection fall into the type I category of Hubel and
Wiesel's classification (Lennie 1980). These X-like cells predominating in the
parvocellular laminae have a concentric centre-surround receptive field structure,
are preferentially sensitive to high spatial frequencies, have low contrast
sensitivities, respond with a sustained discharge and have long conduction
velocities. They are spectrally sensitive, with most cells responding to the
red-green section of the spectrum.

The Y-like channel projects mainly from the peripheral retina to the magnocellular
layer and has units with relatively larger receptive fields, has high
contrast sensitivity functions, shows short conduction times and is insensitive to
colour.

It was originally proposed that colour and luminance processing were
segregated functions. The parvocellular layers were thought to process colour
information and the magnocellular units to process contrast at low to medium
contrasts (Hubel and Wiesel 1966; Shapley 1982). It is now thought, however,
that the parvocellular units have a dual role, in that they respond well to the
modulation of chromaticity at low spatial frequencies and to the modulation of
luminance at high spatial frequencies, and provide signals about both the
chromatic and spatial properties of stimuli (Ingling and Martinez-Uriegas 1985;
FIGURE 4.9

Contrast sensitivity functions of monkey LGB neurones

The filled symbols are from magnocellular neurones; the open symbols are from parvocellular neurones. Contrast sensitivity was the reciprocal of the contrast require to give a response of 5 impulses/second. The parvo-cell indicated by the upright triangles (Δ) was among the most sensitive parvocellular neurones. More typical results are represented by the other two parvocellular cells.

(Shapley 1982)
The magnocellular units were thought to mediate the achromatic mechanisms (De Monasterio and Schein 1980; Kaplan and Shapley 1982) but their large receptive fields and sparse coverage of the fovea makes this unlikely. They are substantially more sensitive than parvocellular units to stimuli of higher temporal frequency and their large receptive fields and high contrast sensitivity are more suited to detecting movement. Moreover, there is a fairly direct projection from their site of termination in the visual cortex to the mid temporal region where receptive fields extracting information about the movement of objects are present (Derrington et al. 1984).

4.7 The Superior Colliculus

Introduction

The mammalian superior colliculus lies on the dorsal surface of the midbrain and is the homologue of the optic tectum in the lower vertebrates. In non-mammals the optic tectum is the major end point of visual fibres of the optic tract, and as it also receives acoustic, proprioceptive, somesthetic and tactile information, it is the highest centre for integration of the various senses, co-ordinating complex movements and functions of the animal. However, as the phylogenetic scale is ascended, the cerebral cortex of the higher vertebrates has taken on the integration of sensory and motor functions. This transferral process, known as 'telecephalisation', has resulted in the midbrain area of mammals undergoing a great reduction in size and functional significance. The primate visual pathway is a classic example of this process, since only about 20% or less of the optic fibres leaving the optic chiasma go to the superior colliculus.
4.8 Structure of the superior colliculus and connections of the superficial layers

The most striking cytoarchitectural feature of the mammalian superior colliculus has been the presence of alternating fibrous and cellular layers running approximately parallel to the collicular surface. This feature has led to the division of the superior colliculus into seven layers (Duke-Elder 1961) which is used by anatomists and neurophysiologists as their foundation for research on the colliculus (figure 4.10). The fundamental seven layers from superficial to deep are:

1. Stratum zonale
2. Stratum griseum
3. Stratum opticum
4. Stratum griseum intermediate
5. Stratum album intermediate
6. Stratum griseum profundum
7. Stratum album profundum

Further subdivision of the superior colliculus into superficial and deep sections was first suggested by lesion studies on the tree shrew (Casagrande et al. 1972; Harting et al. 1973; Casagrande and Diamond 1974). When lesions were restricted to the superficial layers, tree shrews were unable to discriminate visually between objects, and larger lesions extending into the deep layers resulted in an additional failure to orientate towards stationary objects. Electrophysiological experiments on non-anaesthetised monkeys also emphasised the differences between the superficial and deep layers. The cells of the superficial layers are primarily visual, while cells in the deeper layers
Alt: FIGURE 4.10

Coronal section through the superior colliculus

Alternating fibre and cell layers of monkey superior colliculus.

The seven layers indicated on the right are divided into three layers designated as the superficial division and four layers designated as the deep division. I.C.: Inferior Colliculus, C.G.: Central Grey Matter
Stratum Zonale
Stratum Griseum Superficiale
Stratum Griseum Intermediate
Stratum Album Intermediate
Stratum Griseum Profundum
Stratum Album Profundum

Superficial
Deep
discharge in relation to eye movements. Moreover, activity between the parts is not necessarily co-ordinated; visual stimulation in the superficial layers does not necessarily lead to eye movement activity in deeper layers and conversely movement activity in deeper layers does not require visual responses in the superficial layers (Mohler and Wurtz 1976; Sparks and Pollack 1977; Mays and Sparks 1979). The superior colliculus will therefore be described in terms of its superficial and deep sections.

**Superficial**

The first three layers of the superior colliculus, i.e. stratum zonale, stratum griseum and stratum opticum are regarded as the superficial layers and these are the layers receiving afferent fibres predominantly from the retina and the visual cortex (figure 4.11). Afferent fibres from the frontal eye fields, and the parabigeminal and pretectal nuclei of the midbrain, are also thought to be sources of fibres, although the latter two have not been demonstrated, as such, in primates (Wurtz and Albano 1980).

In relation to the retinotectal input, Apter (1945) was the first worker to demonstrate a retinotopic organisation in mammals. The visual field projection to the superior colliculus in primates has been found to be fundamentally different from that of other mammals. In subprimates, nearly the complete contralateral retinal input is represented, whereas in primates, the contralateral retinal input to the colliculus arises only from the nasal hemi-retina (Lane et al. 1971, Lane et al. 1973; Harting and Guillery 1976). Opinions concerning the projection of the central visual fields have varied. Wilson and Toyne (1970) concluded, using fibre degeneration techniques, that there was little or no projection of the central visual fields and this was corroborated by Tigges and O'Steen (1974). However, electrophysiological techniques have shown that in
The main connections of the superior colliculus in monkey
species possessing a retina with a clearly specialised region, eg. the cat's visual streak and the primate's fovea, there is a correspondingly disproportionate representation of that region in the colliculus (Lund 1972). In primates, one-third of the collicular surface represents the central 10° of the visual field (Cynader and Berman 1972; Hubel et al. 1975). Early workers thought that only the contralateral retinal fibres projected to the monkey colliculus (Schiller and Stryker 1972) but direct uncrossed retinal input is present and has been found to be quite extensive (Hubel et al. 1975).

The mapping or projection of the visual field across the superficial layers of the primate superior colliculus is orderly (Cynader and Berman 1972). The central visual field is represented at the anterior pole and lateral margin, and the peripheral visual field is represented at the posterior pole (figure 4.12). The projection of the contralateral hemi-retina includes the entire colliculus whereas the projection of the ipsilateral hemi-retina is represented only in the anterior portion of the colliculus (Hubel et al. 1975).

**Cortico tectal input**

The projection of visual cortex to the superficial layers is well established in primates and numerous other species (Wilson and Toyne 1970; Lund 1972; Finlay et al. 1976). The projections arise from a specific group of pyramidal cells from layer 17 (Finlay et al. 1976) and terminate ipsilaterally throughout the superficial layers (Lund et al. 1975; Powell 1976). The corticocollicular projections like the retinotopical map are topographically arranged and end in a tight visuotopic register such that the area of cortex receiving fibres from one retinal area projects to an area of the superficial colliculus receiving fibres from the same retinal area (Schiller 1978). Surprisingly, removal of the cortical input, either by ablation or by cooling, has little or no effect upon the visual responses
Comparison of the projection of the visual field upon the monkey and cat superior colliculus

(Schiller et al. 1972)
of cells in the superficial layers of the primate colliculus (Schiller et al. 1974). Observed changes are limited to an increase in monocularly dominated receptive fields, and although the foveal representation from the primary visual cortex is more clearly demonstrable than the corresponding retinal input (Goldberg and Robinson 1978), the visual responses of these cells are not especially affected by interruption of striate-tectal inputs.

The frontal eye fields project to the superficial layers and also to the dorsal part of the intermediate layers (Kuypers and Lawrence 1967; Kunzle and Akert 1974; Kunzle et al. 1976). The exact contribution of these cells is unknown but it is thought that the visual neurone in the frontal eye fields provides some modulation of visual receptive field responses in the superior colliculus.

**Efferent connections**

In keeping with the visual character of afferent connections to the superficial layers, the efferent fibres project to known visual nuclei of the thalamus and to two other visual structures found in the midbrain, i.e. the pretectal complex and the parabigeminal complex.

**Thalamus**

The superficial layers project to three visual thalamic nuclei: - the dorsal lateral geniculate, the pregeniculate nucleus and the inferior pulvinar (Mathers 1971; Harting et al. 1973; Benevento and Fallon 1975; Graham 1977; Harting et al. 1978). The nature of the tectal input to these visual structures has yet to be elucidated.
Midbrain

It is thought there are various reciprocal connections between the colliculus and the pretectal complex and parabigeminal complex. However, they have not been clearly established (Berman 1977; Benevento et al. 1977; Graham 1977).

4.9 Visual receptive field properties of the superficial layers

Of the three major categories of retinal ganglion cells (ie. X,Y,W) only two have been shown to project to the colliculus of the monkey (de Monasterio and Gouras 1975; Schiller and Malpeli 1977; de Monasterio 1978a,b). The 'W' cells form a substantial proportion of the ganglion cells projecting from the retina to the superior colliculus. The 'W' ganglion cells had originally been named and identified in the cat retina (Stone and Fabian 1966). They were described as having receptive fields with on-off centres, i.e. they would respond equally briskly to the onset and offset of a stationary flash of light, they were suppressed by contrast (Rodieck 1967); they had large receptive fields; they were slow conducting and were predominant in the retinal projection to the superior colliculus. With reference to monkey, 91% of the retinal input to the superior colliculus comes from slow conducting W fibres (Marrocco 1978), the remaining 9% comes from rapidly conducting 'Y' cells.

A few early gross electrophysiological experiments supported the idea that slower conducting fibres project to the superior colliculus. Bishop and O'Leary (1942) described a large slow negative potential produced by stimulation of the stratum opticum. Altman and Malis (1962) found in cats that flash stimulation produced a response at latency 36.5ms from the superior colliculus and 27ms from the visual cortex.
The visual receptive fields of superficial layer cells consist of a central activating region surrounded by a zone capable of suppressing the response of the centre (Humphrey 1968; Schiller and Koerner 1971; Cynader and Berman 1972; Marrocco and Li 1977; Moors 1978). The majority of these cells respond transiently to the onset and/or offset of spots of light with a latency of about 40-80ms. There is a gradient of response strength across the activating centre; responses to small flashes are greater towards the central portion of the field and are weaker towards the periphery (Goldberg and Wurtz 1972). The activating centre exhibits-the property of internal summation, that is, a progressively greater number of spikes up to 5 spikes/second are elicited as a function of increasing stimulus diameter (Kadoya et al. 1971). The summation effect has two components: there is an increase in response, reaching a maximum at some stimulus diameter smaller than the activating centre, and the response latency is also reduced with larger stimuli (Moors 1978). When the diameter of the spot exceeds the boundaries of the central activating region, and infringes upon the surround, the centre response is suppressed. The size of the central activating region varies from 0.25° foveally to 5° at a point representing the visual field 40° from the fovea (Kadoya et al. 1971; Cynader and Berman 1972). The optimal diameter of the exploring light stimulus to maximise spike discharge is 1° - 1.3° (Cynader and Berman 1972).

The relative strength of the centre surround interaction is variable, and stimulation of the suppressive surround of collicular cells alone does not evoke a discharge (Schiller and Koerner 1971; Goldberg and Wurtz 1972; Cynader and Berman 1972), whereas the antagonistic surrounds of some retinal ganglion cells can be independently excited by annuli (Dreher et al. 1976). The term 'suppressive surround' is therefore used to describe receptive fields of superior colliculus cells to distinguish them from the antagonistic surrounds found in other parts of the visual pathway.
Most cells of the superficial layers also respond to moving stimuli. In contrast to the cat (Sterling and Wickelgren 1969), few sampled cells are selective for the direction of movement (Goldberg and Wurtz 1972). Cells are also non-selective for stimulus velocities (Goldberg and Wurtz 1972; Marrocco and Li 1977; Moors 1978).

Three types of response patterns to moving stimuli have been described (Marrocco and Li 1977). One type consists of two sets of 'leading and lagging' edge responses resulting from the passage of the stimulus edge through the initial and final receptive field borders. A second response pattern consists of a single set of leading and lagging edge responses occurring only at the initial receptive field border; an inhibitory effect resulting from the initial discharge eliminates the leading and lagging edge response at the second receptive field border. A third type of pattern field is elicited by a small moving stimulus. There is possibly a fourth kind of visually responsive cell termed the "jerk" detection which responds strongly to abrupt changes in stimulus velocity but these cells are either quite deep in the superficial layers or in the intermediate layers and have only been seen in paralysed preparations (Schiller and Koerner 1971; Cynader and Berman 1972).

The use of non-anaesthetised monkeys has allowed examination of the visual responses of these cells when the animal actively responds to the visual stimuli. Two types of modulation of the visual response have been found: one that leads to an enhanced visual response when the monkey uses the visual stimulus as a target for a saccadic eye movement, and another that reduces the response of the cell to stimulus falling on the retina during a saccade.

Goldberg and Wurtz (1972) noticed that for some cells, the visual response was
more vigorous when a trained monkey was required to make a rapid or saccadic eye movement from a fixation point to a visual stimulus lying within the central activating region. The enhancement on-response was not evident on initial trials when the monkey was first required to make a saccade to the visual stimulus, but it occurred on subsequent trials when the monkey could expect to make a rapid eye movement to the receptive field stimulus (Wurtz and Mohler 1976). The second type of modulation found in some visual cells produced a suppression of their discharge rate following saccades. The suppression occurred with saccades in many directions and was only slightly influenced by saccadic amplitude. The effect of the suppression was to reduce sensitivity to all visual input during an eye movement (Wurtz and Albano 1980).

There is no sensitivity to contour or contrast (Cynader and Berman 1972; Schiller 1978) and no response selective to changes in wavelength of light (Marrocco and Li 1977). Schiller and Malpeli (1977) found that there were no colour sensitive receptive fields at all in the superior colliculus of monkey which was to be expected given the colour insensitive properties of the 'W' and 'Y' projection from the retina (Stone 1983).

4.10 Connections of the deep layers

Afferent fibres

Whereas the superficial layers of the colliculus receive fibres mainly from visually associated areas, the deeper layers are less visually orientated with somatic and auditory projections becoming more significant. The patterns of connections are far more complex with subcortical projections involving nearly all regions of the brainstem and cortical regions from prefrontal to occipital cortex. Afferent connections which have been well documented, come from
neck muscle and extraocular muscle proprioceptors (Abrahams and Rose 1975),
pre-frontal cortex (Goldman and Nauta 1976), substantia nigra (Rodieck 1979)

The deep efferent connections are also concerned with non-visual sensory areas.
Further details can be found in the work by Wurtz and Albano (1980) and
Grantyn and Grantyn (1976).

4.11 The visual receptive field properties of the deep layers

The receptive fields are considerably larger ranging from 1° to 7° diameter, are
circular or ellipsoidal, and respond to stimuli suddenly presented rather than
continual presentation which results in adaptation (Gordon 1975). With
increasing depth, the receptive fields size increases and responses are elicited to
visual and non-visual stimuli. The fields are not sensitive to shape, contrast or
colour (Gordon 1975; Chalupa 1984).

4.12 Summary of the possible functions of the Superior Colliculus

The integration of sensory modalities in the deep layers of the superior colliculus
of primates, means that orientation of the head and limbs is possible (Goldberg
and Robinson 1978). Wurtz and Albano (1980) however, felt that it was
important to reiterate that the visual projection from the retina to the superior
colliculus decreases in significance as the phylogenetic table is ascended, ie. as
the visual cortex becomes more highly developed.

Pathological considerations point to the probability in man that the superior
colliculus still retains some importance in the direction of saccadic movements
(Alpers 1945; Apter 1945; Zee 1976).
4.13 Summary of the visual receptive field properties of the LGB and superior colliculus

In summary, the visual receptive fields of the LGB and superior colliculus differ significantly in their properties. The LGB is divided into two magnocellular layers and four parvocellular layers. The parvocellular layers predominate and their visually receptive units are sensitive to high contrast achromatic gratings presented as drifting gratings or in pattern reversal mode. The optimal stimulus size for eliciting responses has been found to be 4.25 cpd (approximately 14') (Derrington and Lennie 1984). These units also respond to chromatic stimulation in the form of red/green spatially unstructured fields or chromatic gratings of low spatial frequencies (Hicks et al. 1983).

In contrast, the superior colliculus responds to flashes of light and movement and very rapidly becomes unresponsive to sustained stimulation (Wurtz and Albano 1980). It is also suppressed by contrast and is unresponsive to colour (Marrocco and Li 1977). Table 4.1 summarises these properties.

These properties governed the form of stimulation used to elucidate the origins of the VESP as described in Chapter 5.
TABLE 4.1

Visual receptive field properties of the lateral geniculate body (LGB) and superior colliculus
## SOME VISUAL RECEPTIVE FIELD PROPERTIES OF THE LATERAL GENICULATE BODY AND SUPERIOR COLLICULUS

<table>
<thead>
<tr>
<th>PROPERTIES</th>
<th>LATERAL GENICULATE BODY</th>
<th>SUPERIOR COLLICULUS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PARVOCELLULAR</td>
<td>MAGNOCELLULAR</td>
</tr>
<tr>
<td>LOCATION OF RECEPTIVE FIELDS</td>
<td>Foveal</td>
<td>Peripheral</td>
</tr>
<tr>
<td></td>
<td>(Gratings: 4.5cpd)</td>
<td>(grating 0.5-1cpd)</td>
</tr>
<tr>
<td></td>
<td>Chromatic unstructured fields</td>
<td>1°</td>
</tr>
<tr>
<td>OPTIMAL* STIMULUS SIZE</td>
<td>Achromatic 14'</td>
<td>30' - 1°</td>
</tr>
<tr>
<td></td>
<td>(Chromatic unstructured fields)</td>
<td>(grating 0.5-1cpd)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1°</td>
</tr>
<tr>
<td>COLOUR SPECIFICITY</td>
<td>Red/green concentric opponent</td>
<td>Weakly opponent</td>
</tr>
<tr>
<td></td>
<td>Blue/yellow</td>
<td></td>
</tr>
<tr>
<td>CONTRAST SENSITIVITY</td>
<td>Low</td>
<td>High</td>
</tr>
</tbody>
</table>

Cynader & Berman 1972
Derrington & Lennie 1984
Dreher et al. 1976
Hicks et al. 1983

*Size of stimulus evoking the highest frequency of spike discharge from the receptive fields
CHAPTER FIVE
STUDIES OF THE VESP TO STRUCTURED STIMULATION

5.1 Use of patterned stimulation in this study

Since the possible origins of a VESP are likely to be in either the lateral geniculate body or the superior colliculus, stimulus presentations had to be carefully designed to activate optimally one or other of the two structures in order to identify the source of the VESP.

As described in section 4.5, the LGB has receptive fields responding, in unit electrophysiology research, to high contrast achromatic gratings of high spatial frequencies approximately 12' - 14' and to chromatic stimulation in the form of red/green unstructured fields or chromatic gratings of low spatial frequencies. The superior colliculus responds to flashes of light and to movement but very rapidly becomes unresponsive to sustained stimulation and is suppressed by contrast and is unresponsive to colour (section 4.9).

It was felt therefore that structured stimulation introducing contour and colour was one method that may effectively isolate the response to an LGB rather than a collicular source but in relation to gross scalp electrode recordings various other considerations have to be taken into account.

With reference to the scalp VECP, high contrast black and white checkerboard stimulation has been generally preferred to grating stimulation. Rietveld (1967) felt that check stimulation was the simplest and closest approximation to the radial arrangement of receptive fields, giving maximal amplitudes when the pattern was composed of right angles. One reason offered for the more sharply defined, higher amplitude VECP than that evoked by the grating was the
presence of a large number of frequencies forming the edges (Campbell and Maffei 1970). The peak of the check size function was thought to be related to the receptive fields size (Armington 1971) and elaborated by Spekreijse et al. (1977) who established that the pattern VECP response was dependent on spatial contrast mechanisms.

In this study, a form of stimulation which presented pattern at constant luminance was important to avoid producing responses confounded by overall luminance changes to which the superior colliculus would respond. Pattern reversal stimulation was therefore adopted for the achromatic studies, since it has been established as a reliable technique in VEP studies (Halliday 1980) and also enabled comparison with the pattern electroretinogram for which it is the more popular form of stimulation (Lawwil 1984).

Various physiological properties of the retina and LGB determine the nature of the colour stimulation. The retina has about 7 million cones in each eye (Davson 1980) and 6 million of these are red and green cones predominating in the foveal, (Gouras and Zrenner 1982), with their ganglion cells projecting to the parvocellular layers of the LGB. At the LGB, optimal responses to colour stimulation are contained by using red and green gratings of low spatial frequency and unstructured red and green fields (Hicks et al. 1983).

Clynnes et al. (1964) reported that scalp potentials could be evoked by abruptly changing the colour of the stimulus without changing its subjective brightness. These responses were reported to be more clearly colour dependent than responses to flashes of white light, and large unstructured fields (11° - 25°) of red interchanging with green were found to produce the best colour VEPs (Shipley et al. 1966; Ciganek and Ingvar 1969).
However, Regan (1972) commented that where two colours interchanged, the VEP resulted from a decrease in luminance of the first colour, an increase in the luminance of the second colour and a change in the wavelength of the stimulus; thus, the luminance and chromatic components of a VEP were mixed. As transient VEPs had been successfully elicited by pattern stimulation offering black and white contrast in the form of checkerboards, it was thought that equiluminant red and green checks using pattern reversal would give VEPs responding to chromatic contrast as distinct from luminance related VEPs (Regan 1977).

Kelly, (1974), using two colour stimulation found that the response magnitude was least when flickering stimuli were patternless and greatest when a checkerboard of two alternating colours was present.

Red and green checks produced better VEPs than stimuli designed to activate the blue cone mechanism. Less than 19% of the cones in primate retina are blue sensitive, and Marc and Sperling (1977) and Klingamen and Moskowitz-Cook (1979) found in trying to isolate the blue cone mechanism that the VEPs were poorly defined.

Gouras and Zrenner (1979) felt that colour opponent fields were not stimulated by flashes of short duration as 19ms, longer presentations being necessary, and Zrenner and Gouras (1983) and Paulus et al. (1984) found that an opponent X type unit would react better to chromatic contrast.

Pattern reversal stimulation using black/red, black/green and black/white checks all gave very similar VEP responses in a recent study and luminance balanced red and green checks gave distinctly different responses (Grall et al. 1984). Mattiello et al. (1984) emphasised the importance of equiluminance and constant
luminance, noting the large inter and intrasubject variability in evoked potentials to colour presentation. Estevez and Dijkhuis (1983) recommended caution when demonstrating VEPs to colour pointing out that not all interactions between cone systems are necessarily colour interactions.

In view of the above findings, red and green luminance balanced checks were used in the mode of pattern reversal presentation to investigate the VESP sensitivity to colour.

5.2 Objectives

The main objectives of the following studies presented as laboratory reports were:

1) To assess the sensitivity of the VESP to structured stimulation in the form of a checkerboard reversing pattern, using black/white checks and red/green checks.

2) To identify the optimal check sizes for achromatic and chromatic stimulation.

3) To determine whether the results of this stimulation distinguish the LGB from the SC in terms of the possible source of the response.

4) To isolate the response from possible retinal sources in the form of the pattern electroretinogram.
5.3 The VESP to achromatic pattern reversal stimulation

5.3.1 Materials and methods

Fifteen normal male volunteer subjects were used, having a mean age of 25 years and corrected monocular visual acuities of 6/6 or better. Silver/silver chloride electrodes were placed according to the 10-20 system at T3½, Cz and T4½. These electrode locations were adopted in the original studies on the flash VESP (Harding and Rubinstein 1981). However, in the current studies all three electrodes were referred to the chin (figure 5.1).

The subjects were comfortably seated in a room of average luminance of 100cd/m². The visual stimulator was placed 30cm in front of the eyes.

Pattern reversal stimulation was produced by the back-projection of transparencies of black and white checks onto a translucent screen, with pattern reversal being produced by the oscillation of a silvered mirror, mounted on a pen motor which moved the checkerboard abruptly through one check width and back at a rate of 6 reversals per second (Drasdo 1976, 1982). Binocularly viewed checkerboards, with subtended check sizes of 8', 12', 24', 36', 48' and 1° were used within a 30° diameter field. The mean luminance of the checkerboard was 1050cd/m² and the contrast 0.85. For each check size, two separate runs were performed and the order of presentation of the different check sizes randomised.

Each run consisted of the average of 500 responses to 500 reversals delivered at a rate of 6 reversals per second. The responses averaged using a Nicolet
Diagram showing the electrode montage used to record the pattern VESP to checkerboard reversal stimulation using i) black and white checks and ii) red and green luminance balanced checks.

The electrode positions are labelled according to the 10/20 system (Jasper 1958)
Pathfinder II. The bandpass was 30Hz - 500Hz and analysis time 50ms.

From each subject, latency and amplitude measurements were taken for components consistently present when the two runs taken for each check size were superimposed.

Two non-stimulus runs were also set up wherein the subject viewed a blank lenticular 30° field of mean luminance equal to that of the checkerboard field. This ensured that in both stimulus and non-stimulus conditions, the scattered light within the eyes was retained at a constant luminance throughout the study.

5.3.2 Results

Fourteen subjects out of the sample of fifteen gave a response to the achromatic pattern reversal stimulation and the signal was obtained from all three derivations, i.e. T3\(\frac{1}{2}\), Cz and T4\(\frac{1}{2}\), in the form of a positive-negative-positive (P-N-P) complex. The one remaining subject was defined as a non-responder since the potential activity of the stimulus runs was not different from the response to the equiluminant unstructured field.

As this method of eliciting the VESP to pattern reversal stimulation had never previously been employed, the waveforms were ranked by two independent observers to identify the maximum amplitude response. Kendall’s coefficient of concordance enabled the assessment of the extent of agreement between the two observers. They carried out a blind ranking on the amplitude of the P-N and N-P components of the triphasic complex in relation to check size across the sample, and a high measure of concordance was obtained (P-N: Kendalls W = .37, p = 0.01; N-P Kendalls W = .37, p = 0.01).
The peak-to-peak amplitudes of the P-N and N-P components were subsequently measured and the latencies of the P-N-P complex scored (appendix 3 and 4).

In terms of ranking of the raw data, eleven subjects gave a maximal amplitude response to a 12' check size and two examples of these signals are shown in figures 5.2 and 5.3. Out of the remaining three responders, one subject gave equal amplitude responses to both 8' and 12' check sizes and two subjects gave a maximal response at 36' check size.

Across the sample, the mean latency values in ms were calculated from the scored results for each component of the P-N-P complex and for each check size, and the standard errors (± 2SE) included to define the upper and lower limits of the sample within the 95% confidence interval. For a given check size, if the P-N-P complex was not obtained for a particular subject, the result was excluded from the calculation. The results for 8', 12' and 24' were treated in this way as most of the subjects responded to these check sizes. There were only two responders to a 36' check and one response to 60'.

The mean amplitude values in microvolts (μV) (±2SE) were calculated for the P-N and N-P components at T3½, Cz and T4½ and for 8', 12' and 24' check sizes. The means were expressed for the total sample of fifteen and where the response had not been obtained, the amplitude was scored as zero.

Thirteen subjects gave a VESP response at the 12' check size (figures 5.2, 5.3 and 5.4). The mean latency values were P24.2 (± 1.48ms) N29.09 (± 1.46) and P33.52 (±1.78). In terms of amplitude, eleven subjects gave their maximum response at 12' and the overall mean values at the three derivations were:
FIGURE 5.2

VESP to black/white checkerboard reversal stimulation showing a maximal response to a 12' check at the Cz derivation: reference chin; subject 1

A triphasic complex was obtained to check sizes of 8', 12' and 24'. The responses are taken for the vertex (Cz) derivation, reference chin. A P20.7 N28.1 P31.2 complex was obtained with a maximum amplitude to the 12' check size
FIGURE 5.3

VESPs to achromatic pattern reversal stimulation showing a maximal response to a 12' check size at the Cz derivation; reference chin; subject 12

The VESP to a black and white checkerboard pattern was present as a triphasic complex P26.8 N29.6 P34.2. The waveforms have been shown for the electrode derivations T3½, Cz and T4½.
FIGURE 5.4

VESP to achromatic pattern reversal stimulation using a 12' check size demonstrating the response at T31/2, Cz and T41/2;
reference chin; subject 3

The VESP was present as P25.8 N32.8 P37.5.

There were no significant differences in amplitude at T31/2, Cz and T41/2.
T3\(^{1/2}\): P-N 0.8 (±0.26) N-P 0.75 (±0.22)
Cz: P-N 0.76 (±0.2) N-P 0.77 (±0.22)
T4\(^{1/2}\): P-N 0.78 (±0.24) N-P 0.74 (±0.22)

Within the sample, seven subjects gave a triphasic response at 24' with mean latency values of P24.1 (±2.54) N28.97 (±1.82) P32.46 (±1.86) and mean amplitudes of:

T3\(^{1/2}\) P-N: 0.35 (±0.22) N-P 0.36 (±0.22)
Cz: P-N 0.34 (±0.22) N-P 0.34 (±0.22)
T4\(^{1/2}\): P-N 0.34 (±0.22) N-P 0.36 (±0.22)

In all seven subjects, the amplitudes at 24' were lower than the amplitudes at 12' as shown for two subjects in figures 5.21 and 5.3. Figure 5.5 shows the responses at all three derivations.

Only five subjects gave a response at 8' with mean latencies P22.96 (±2.7) N27.86 (±2.16) P32.72 (±2.8) and mean amplitudes of:

T3\(^{1/2}\): P-N 0.23 (±.2) N-P 0.23 (±.2)
Cz: P-N 0.24 (±.18) N-P 0.24 (±.22)
T4\(^{1/2}\): P-N 0.22 (±.18) N-P 0.2 (±.2)

Table 5.1 summarises the mean latency values for the three check sizes of 8', 12' and 24' and shows that the confidence intervals overlap for each component of the P-N-P complex at the three check sizes, demonstrating a consistent incidence of the evoked responses. However, in relation to amplitudes (summarised in
TABLE 5.1

Mean latency values for the achromatic VESP at 8', 12' and 24' check sizes

The latency values in milliseconds (ms) are for the positive-negative-positive complex (P-N-P) obtained at 8', 12' and 24' using black and white checks.

TABLE 5.2

Mean amplitude values for the achromatic VESP at 8', 12' and 24'

The amplitude values are given in microvolts (μV) for the P-N and N-P components and demonstrate maximum values for the 12' check size at the electrode sites T3½, Cz and T4½ common reference chin.
### Table 5.1
(LATENCIES IN MILLISECONDS)

<table>
<thead>
<tr>
<th>CHECK SIZE</th>
<th>POSITIVE</th>
<th>NEGATIVE</th>
<th>POSITIVE</th>
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</tr>
<tr>
<td>(-2SE)</td>
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<td>2.16</td>
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</tr>
<tr>
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<tr>
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<tr>
<td>(-2SE)</td>
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### Table 5.2
(AMPLITUDE IN MICROVOLTS)

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<tr>
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<td>.42</td>
</tr>
<tr>
<td>(-2SE)</td>
<td>.22</td>
<td>.22</td>
<td>.22</td>
</tr>
</tbody>
</table>
FIGURE 5.5

Example of the achromatic pattern VESP response to a 24'
check size at electrode sites T3$\frac{1}{2}$, Cz and T4$\frac{1}{2}$ referred to
chin: subject 13

The P19.1 N27.6 P32.6 complex had similar amplitude
responses at T3$\frac{1}{2}$, Cz and T4$\frac{1}{2}$
table 5.2), the figure 5.6 expresses graphically a clear maximal response at 12' for the P-N and N-P components at the electrode site Cz.

In order to study the overall wave morphology of the sample, a group averaging of the raw data was undertaken for each of the three check sizes 8', 12' and 24' and for the individual electrode sites T3½, Cz and T4½. The results shown in figures 5.7 and 5.8 supported those results obtained by manual averaging, in that a triphasic complex was obtained of latency P25.52 N30.24 P35.36. The amplitude was highest for the 12' check size having values at the Cz derivation of P-N 0.54µV N-P .49µV. Figure 5.7 shows the responses at 24' were still clearly present but were lower in amplitude - P-N .22µV and N-P .2µV, whereas the signal to an 8' check size produced a group response which was more variable.

The grouped response showed no lateralisation of the amplitudes to T3½ or T4½ and this was verified by the mean amplitudes obtained by manual averaging and recorded in tables 5.2. The amplitude values for the grouped data were lower than those obtained by manual averaging. In group averaging, the peak responses were not all at exactly the same latencies, so that two peaks superimposed then averaged by the program did not exactly coincide. Therefore the averaged result of this slight imperfect alignment due to different latency values might give a reduced averaged amplitude.

5.3.3 Summary and conclusions

Using a sample of 15 subjects a triphasic VESP complex was most clearly defined to a high contrast black and white reversing checkerboard and was optimally evoked for a 12' check size in accordance with a ranking procedure. This signal had mean latency values of P24.2 N29.09 P33.52 and mean
FIGURE 5.6

Graph showing a maximum amplitude VESP response at 12’

using black and white checks

The values for amplitude at the check sizes 8’, 12’ and 24’
were taken for the Cz derivation (reference chin).

The dotted line represents the P-N values in microvolts, and
the solid line represents the N-P values.

The standard error values (±2SE) have also been included
FIGURE 5.7

VESP to pattern reversal stimulation: group averaged responses to black and white checks for the Cz derivation referred to chin

The group averaged achromatic response shows a maximal amplitude for the 12' check size
FIGURE 5.8

Group averaged response to achromatic stimulation shown to

a 12' check size at T3\(\frac{1}{2}\), Cz and T4\(\frac{1}{2}\), reference chin
amplitude values at Cz of P-N .76μV and N-P .77μV. A lower amplitude response was obtained at the larger check size of 24' with mean values of P-N .34 and N-P .34μV and at 8' having mean values of P-N .24μV and N-P .24μV at the Cz derivation.

For each check size, the mean amplitudes did not differ significantly at the three electrode sites T3½, Cz and T4½, i.e. there was no localisation of the response. The mean incidence of the response at the three check sizes was also consistent as the 95% confidence intervals overlapped.

Subsequent group averaging of the raw data on the Pathfinder II was carried out, which involved superimposition and averaging of the amplitude. This resulted in lower group amplitude values due to slight latency differences between the waveforms, but nevertheless demonstrated a maximal response for a 12' check size, falling off for 24', and showing reasonable responses to a 8' check size when the responses could not be delineated from background potential activity.

This study demonstrates that a VESP complex was formed at similar latencies to those signals which had been obtained in the original studies defining the VESP to flash stimulation P23 N28 P34 (Harding and Rubinstein 1980). In the studies undertaken by Rubinstein (1981), a response could not be obtained to pattern reversal stimulation using check sizes of 2° and 56' presented at 2 reversals/second, or to flashed on pattern using grids of 2°18', 1°42', 1°12' and 36'.

This study, however, suggests that the VESP can be elicited to pattern reversal stimulation using the chin as reference, with electrodes at T3½, Cz and T4½. Under the conditions applied of presenting the checks at 6 reversals per second,
the VESP is optimally elicited to a 12' check size falling off in amplitude to 24'
and not readily obtained to the larger check sizes of 36', 48' and 1° which offer
a higher luminance component in relation to pattern detail. It is also suggested
that as the VESP elicited to 12' is a pattern related response, it is necessary to
compare it to the pattern electroretinogram in order to establish that the
distribution of the pattern VESP is independent from the pattern
electroretinogram (PERG).

5.4 Spatial distribution of the PERG: pilot study

5.4.1 Introduction

The VESP response has been established to achromatic pattern reversal
stimulation as a P21 N25 P29.4 complex. In order to demonstrate the
independence of these components from the (PERG), the following pilot study
to investigate the spatial distribution of the PERG was undertaken.

The PERG has been reviewed in chapter one section 1.6 and the technique
adopted in this study was that outlined by Arden and Vaegan (1983). It was
developed as a clinical technique after it had been established that the largest
responses were obtained to high contrast black and white checks with an optimal
check size of 30' and field size 16° x 22°. A major positive was obtained at
about 35-40ms with an amplitude of 2-4μV using pattern reversal stimulation.

5.4.2 Materials and methods

Five male subjects with a mean age of 26 years with corrected acuities of 6/6 or
better were used in the study. Recordings were made monocularly from the
right eye from four sites - the cornea, the lower lid, a supra orbital site and FP2
(figure 5.9). In order to record from the cornea, a DTL electrode (Dawson et al. 1979) was placed in the lower fornix of the right eye and silver/silver chloride electrodes used in the usual way at the other three sites. All four active electrodes were referred to a common reference electrode at the chin.

Each subject was seated in a slightly darkened room of 100cd/m² and the projector was placed 30cm in front of the eyes. The stimulation consisted of black and white checks of angular subtense 28' and 56' at the eye within a circular field of 30°. The mean luminance of the checkerboard was 1050cd/m² and the contrast 0.83. The checks were presented at 4 reversals/second.

All the responses were averaged to 200 reversals on the Pathfinder II and time windows of 50ms and 100ms were used. The 100ms time window enabled latency and peak to peak amplitude measurements to be made across the complete PERG configuration, and the 50ms time window allowed a direct comparison of the PERG waveform with that of the pattern VESP.

5.4.3 Results

The PERG was effectively recorded from the cornea in all five subjects. Throughout this study the ERG has been illustrated in an inverted form in accordance with the EEG convention that a positive potential change at the active electrode should result in a downward deflection allowing direct comparison of the PERG waveforms with the VESP complex.

For the 28' and 56' check sizes, a clear N-P-N configuration emerged at the DTL electrode and at the sub-lid electrode in all five subjects as shown in tables 5.3 and 5.4 and figures 5.10 and 5.11. The latencies of the individual components were scored, and the peak-to-peak amplitudes were measured, and
FIGURE 5.9

Diagram showing the electrode sites used to study the distribution of the pattern electroretinogram (PERG)
FIGURE 5.10

Distribution of the pattern electroretinogram (PERG) to a 27"
check size and pattern reversal stimulation: reference chin.
subject 1.

The PERG has an N-P-N configuration N15.7 P39.5 N60
FIGURE 5.11

Distribution of the PERG to a 56' check size and pattern
reversal stimulation: reference chin; subject 4

The PERG has an N-P-N configuration N16.1 P36.5 N58.9
TABLE 5.3

Latency values of the PERG to check sizes of 28', 56' using pattern reversal stimulation

The latency values for the negative positive negative N-P-N complex at the cornea given in milliseconds, ms, for five subjects used in a pilot study to examine the distribution of the PERG. A DTL electrode (Dawson et al. 1979) was used to record the PERG from the cornea.
<table>
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<th>COMPONENT:</th>
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<th>( 56' )</th>
<th>( 28' )</th>
<th>( 56' )</th>
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<th>( 56' )</th>
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<tbody>
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</tr>
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<td>1.84</td>
<td>1.34</td>
<td>2.87</td>
<td>4.28</td>
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**TABLE 5.4**

Amplitude values of the N-P and P-N components of the PERG response in microvolts (µV) to check sizes of 28' and 56' using pattern reversal stimulation

The amplitude values demonstrate that the response for 28' and 56' rapidly attenuates beyond the cornea in five subjects used in a pilot study to examine the spread of the PERG signal.
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<th>ELECTRODE:</th>
<th>AMPLITUDES IN MICROVOLTS</th>
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</tr>
<tr>
<td>CHECK SIZE:</td>
<td>28' *</td>
</tr>
<tr>
<td>AMPLITUDE:</td>
<td>N-P</td>
</tr>
<tr>
<td>SUBJECTS:</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3.1</td>
</tr>
<tr>
<td>2</td>
<td>2.5</td>
</tr>
<tr>
<td>3</td>
<td>1.75</td>
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<tr>
<td>4</td>
<td>3.75</td>
</tr>
<tr>
<td>5</td>
<td>2.50</td>
</tr>
<tr>
<td>MEAN</td>
<td>2.72</td>
</tr>
<tr>
<td>SD</td>
<td>.75</td>
</tr>
<tr>
<td>± 2SE</td>
<td>.66</td>
</tr>
</tbody>
</table>
the mean latencies and mean amplitudes were calculated for the DTL electrode and the sub-lid site. For both check sizes, only one subject showed a response at the supra orbital electrode and no PERG was recorded for any subject at FPz.

For both the 28' and 56' check sizes, the PERG response showed a clear major positive component at the cornea with early and late negative components. For the 28' check size, the mean latencies at the cornea were N18.56 (±1.52) P37.19 (±1.84) N66.1 (±2.87) and mean amplitudes N-P 2.72 (±.66μV) and P-N 3.85 (±3μV). The amplitude of the response fell sharply beyond the margin of the orbit, the response at the sub-lid showing mean amplitudes of N-P 1.16 (±.44) and P-N 1.65 (±.48) with only one subject showing a response at the supra orbital site and no subject showing a signal at FPz.

For the 56' check size, a similar distribution was obtained. At the cornea, all five subjects showed the N-P-N configuration with mean latencies N19.2 (±1.84) P39.14 (±1.34) N62.06 (±4.28) and N-P 2.36μV (±.32) and P-N 4.1μV (±.36μV). These amplitudes were reduced beyond the orbit being measured at the sub-lid electrode as N-P 1.01 (±.32)μV and P-N 1.98 (±.25)μV and again no response was recorded at FP2.

5.4.4 Summary and conclusions

Using clinically resilient techniques, the PERG was clearly elicited at the cornea to a reversing checkerboard pattern using check sizes of 28' and 56'. For 28' the mean incidence was N18.56 P37.19 N66.1 and mean amplitudes N-P 2.72μV and P-N 3.85μV with the response falling off sharply beyond the orbit. At the sub-lid electrode, the amplitudes were N-P 1.16μV and P-N 1.65μV, which represented an amplitude attenuation of 57%. Only one subject gave a PERG response at the supra orbital electrode with amplitudes of N-P
1.2µV and P-N 1.1µV, and no response was recorded within the sample at FP2. Similar results were obtained for the 56’ check size.

These findings supported the results obtained by Adachi-Usami et al. (1983) which showed that the PERG could not be recorded at a mid frontal electrode on monocular stimulation using eight subjects, and that a marked reduction of the PERG was found at a site corresponding to FPz (a 72% reduction in amplitude of the N-P component and a 67% reduction in the P-N component).

In this study, the PERG was found to be limited in its distribution essentially to the cornea and surrounding orbital area, rapidly attenuating at frontal electrode sites. Moreover, the PERG had an N-P-N configuration of latency N18.3 P37.19 N66.1 - a fundamentally different wave morphology to that of the pattern VESP, which in study one emerged as a P24.2 N29.09 P33.52 complex recorded more temporally at T3½, Cz and T4½.

On the basis of wave morphology, latency values and the tight distribution of the PERG around the orbit, it was concluded that the signal obtained to achromatic pattern reversal stimulation at T3½, Cz and T4½ was subcortical potential activity to structured stimulation and was described as the achromatic pattern VESP.

5.5 The VESP to chromatic pattern reversal stimulation

5.5.1 Materials and methods

Fifteen normal male volunteer subjects were used, having a mean age of 25 years and corrected monocular visual acuities of 6/6 or better. Silver/silver chloride electrodes were placed according to the 10-20 system at T3½, T4½
and Cz, and all three electrodes were referred to the chin. The subjects were comfortably seated in a room of average luminance 100cd/m².

Pattern reversal stimulation was produced using red and green luminance balanced checks of mean luminance 500cd/m² with an overall field diameter of 30°. A range of check sizes from 12' to 3° was used.

The stimulus was viewed binocularly - and for each check size two separate runs were performed and the order of check presentation randomised.

For each subject and check size, latency and amplitude measurements were taken for components consistently present on superimposition of the two sets of responses.

All responses were averaged with the use of a Nicolet Pathfinder II. The bandpass was 30Hz - 500Hz and analysis time 50ms. In order to maximise the signal, the response to 500 reversals delivered at 6 reversals/second was averaged.

5.5.2 Results

Thirteen subjects out of the sample of fifteen gave a response to chromatic pattern reversal stimulation. The signals were in the form of a P-N-P complex and were obtained from all three derivations, ie. T3¹/₂, Cz and T4¹/₂. Two subjects showed no difference in response to the stimulus and non-stimulus runs.

As this was the first time the VESP had been elicited by this method, the waveforms were ranked by two independent observers on the basis of the
amplitudes of the P-N and N-P components of the complex against check size, and, using Kendall's coefficient, a very high measure of concordance was obtained P-N: Kendall \( W = .35 \) \( p = .01 \); N-P: Kendalls \( W = .37 \), \( p = .01 \). The latencies of the P-N-P complex were subsequently scored and the peak to peak amplitudes of the P-N and N-P components were measured.

From the rankings, eleven subjects out of the thirteen responders gave a maximal amplitude response for a 2° check size as is shown by the two examples in figures 5.12 and 5.13. The remaining two subjects gave an optimal response at 1°.

The mean latency values were calculated from the scored results for each component of the P-N-P complex and for each check size, and the standard errors (±2SE) being included to define the 95% confidence intervals of the sample. For a given check size where the P-N-P complex was not identifiable, the data were excluded from the calculation. The responses to 1°, 2° and 3° were treated in this way as no results were obtained on either side of this range of check sizes (appendix 5 and 6).

The mean amplitudes in \( \mu V \) (±2SE) were calculated for the total sample of fifteen and where the VESP was not defined for a given check size, the amplitude was scored as zero and included in the calculation of the mean.

Eleven subjects out of the thirteen responders gave a VESP response as shown in figures 5.12, 5.13 and 5.14 at a 2° check size with mean latencies being \( P24.43 \) (±1.38) \( N28.29 \) (±1.4) and \( P32.03 \) (±1.4). For all eleven subjects, the optimal response was obtained for the 2° check, the mean amplitudes in \( \mu V \) being:
FIGURE 5.12

VESP to red/green pattern reversal stimulation showing a maximum amplitude response to a 2° check size at the Cz derivation: reference chin; subject 14

The VESP was present as a triphasic complex defined at 2° as P23.4 N29.26 P32.2. The response has been shown at check sizes of 1°, 2° and 3°
FIGURE 5.13

VESP to red/green pattern reversal stimulation showing a maximum amplitude response to a check size of 2° at the Cz derivation: reference chin: subject 10

The VESP is in the form of a triphasic P24.2 N26.6 P29.9 complex. The waveforms have been shown for check sizes of 1°, 2° and 3°
FIGURE 5.14

VESP to chromatic pattern reversal stimulation using a $2^\circ$ check size and demonstrating the response at $T3^{1/2}$, Cz and $T4^{1/2}$; reference chin; subject 13

The VESP was present as P25.5 N29 P31.6, with no significant differences in amplitude at the three electrode derivations of $T3^{1/2}$, Cz and $T4^{1/2}$
Within the sample, five subjects gave a triphasic complex at 1° with mean latencies of P24.06 (±3.8) N27.48 (±3.72) P31.52 (±3.58). Two of the subjects gave a higher amplitude at 1° compared to 2°. The mean amplitudes for the sample at 1° were:

\[
\begin{align*}
T3^{1/2}: & \quad P-N \quad .75 \quad (±.28) \quad N-P \quad .75 \quad (±.28) \\
Cz: & \quad P-N \quad .76 \quad (±.28) \quad N-P \quad .74 \quad (±.32) \\
T4^{1/2}: & \quad P-N \quad .75 \quad (±.28) \quad N-P \quad .73 \quad (±.32)
\end{align*}
\]

Five subjects gave a response at 3° and in all cases the amplitudes were lower than those values at 2° with mean latencies P24.52 (±1.88) N28.08 (± 1.78) P31.85 (±2.64) and mean amplitudes of:

\[
\begin{align*}
T3^{1/2}: & \quad P-N \quad .29 \quad (±.24) \quad N-P \quad .29 \quad (±.26) \\
Cz: & \quad P-N \quad .3 \quad (±.26) \quad N-P \quad .29 \quad (±.26) \\
T4^{1/2}: & \quad P-N \quad .28 \quad (±.24) \quad N-P \quad .26 \quad (±.22)
\end{align*}
\]

Table 5.5 summarises the mean latency values for the three check sizes of 1°, 2° and 3° and shows that the confidence intervals overlap for each component of the P-N-P complex for the three check sizes demonstrating consistency in the incidence of the response to colour. In relation to amplitude however, the table 5.6 and graph 5.15 for the P-N and N-P amplitudes at Cz for each check size express a clear maximal response at 2°.
**TABLE 5.5**

Mean latency values for the chromatic VESP at 1°, 2° and 3° check sizes

The latency values in milliseconds are given for the positive-negative-positive complex

**TABLE 5.6**

Mean amplitude values for the chromatic VESP at 1°, 2° and 3°

The amplitude values are given in microvolts (μV) for the P-N and N-P components and demonstrate a maximum value for the 2° check size at the electrode sites T3½, Cz and T4½
### TABLE 5.5

LATENCIES IN MILLISECONDS

<table>
<thead>
<tr>
<th>CHECK SIZE</th>
<th>POSITIVE</th>
<th>NEGATIVE</th>
<th>POSITIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1°</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>MEAN</td>
<td>24.06</td>
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<tr>
<td>SD</td>
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<td>3.72</td>
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</tr>
<tr>
<td>2°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEAN</td>
<td>24.43</td>
<td>28.29</td>
<td>32.03</td>
</tr>
<tr>
<td>SD</td>
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<td>2.95</td>
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<td>(−2SE)</td>
<td>1.78</td>
<td>1.78</td>
<td>2.64</td>
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### TABLE 5.6

AMPLITUDE IN MICRO VolTS

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<thead>
<tr>
<th>CHECK SIZE</th>
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<th>T4½</th>
</tr>
</thead>
<tbody>
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</tr>
<tr>
<td>MEAN</td>
<td>.29</td>
<td>.3</td>
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<tr>
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<td>.46</td>
</tr>
<tr>
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<td>.24</td>
</tr>
<tr>
<td>2°</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>MEAN</td>
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<td>.75</td>
</tr>
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<td>SD</td>
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<td>.56</td>
<td>.55</td>
</tr>
<tr>
<td>(−2SE)</td>
<td>.28</td>
<td>.28</td>
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</tr>
<tr>
<td>SD</td>
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<td>.29</td>
<td>.29</td>
</tr>
<tr>
<td>(−2SE)</td>
<td>.14</td>
<td>.14</td>
<td>.14</td>
</tr>
</tbody>
</table>
**FIGURE 5.15**

Graph showing a maximum amplitude VESP response at 2° using red and green luminance balanced checks at the Cz derivation.

The average values for amplitude at 1°, 2° and 3° check sizes were taken for the Cz derivation (reference chin).

The dotted line represents the P-N values in microvolts and the solid line represents the N-P values.

The standard values (±2SE) have also been included.
FIGURE 5.16

Group-average of rank 1 VESP responses to chromatic stimulation

The signals were ranked by two independent observers. The result of the group average are shown for the electrode sites T3$^{1/2}$, Cz and T4$^{1/2}$ referred to chin after normalisation (see text)
FIGURE 5.17

Group-averaged VESP results to chromatic stimulation using red/green checkerboard reversal stimulation.

The raw data was group-averaged on the Pathfinder II after normalising the latencies.

The results show a clear triphasic response to a 2° check size.

The results are shown for the Cz derivation - reference chin.
FIGURE 5.18

Group-averaged chromatic VESP response to 2° check size
using luminance balanced red and green checks and pattern
reversal stimulation.

The group-average demonstrated that the response had the
same amplitudes at T3½, Cz and T4½ when referred to the
chin
Group averaging of the raw data on the Pathfinder II produced low amplitude responses initially for all three check sizes although a very high measure of concordance of the response had been established on first inspection of the data and for this reason the latencies were normalised. All the amplitudes of rank one were group averaged at arbitrary latency values and the results are shown in figure 5.16. These values served as a template for subsequent group averaging of the data at 1°, 2° and 3° check sizes and the results are illustrated in figures 5.17 and 5.18. Group-averaging demonstrated variable responses at 1° and 3° but a clearly defined triphasic complex at 2° of amplitude P-N 0.51μV and P-N 0.49μV, which supported the results obtained by manual averaging.

5.5.3 Summary and conclusions

Thirteen out of fifteen subjects gave a clear triphasic P-N-P response to chromatic pattern reversal stimulation. In assessing the raw data, two independent observers showed a high measure of concordance when evaluating the amplitudes against check size (W = .37, p= 0.01).

The P-N-P response was clearly delineated to a 2° check size at latencies P24.43 N28.29 P32.23 with mean amplitudes at the Cz derivation of P-N .76μV, N-P .74μV. These amplitude values were attenuated for 1° and 3°, reaching values of P-N .3μV N-P .29μV for 1°, representing a 61% reduction in amplitude, and for 3°: P-N .19μV N-P .21μV corresponding to a 73% reduction when compared to the amplitudes at 2°.

A normalised group averaging procedure showed a clear response at 2°, with the results at 1° and 3° not clearly distinguishable from the background.
This study demonstrates that the VESP can be evoked by colour stimulation in the form of red/green luminance balanced checks and at 6 reversals per second, the VESP being optimally elicited for a 2° check size.

5.6 Discussion

In the initial studies undertaken by Rubinstein (1981), the flash VESP as a P21 N26.2 P33.6 complex appeared to be quite distinct from the flash ERG and the flash VECP, and it was concluded that the signal was subcortical. Pattern reversal techniques were adopted using check sizes of 56' and 2° presented at 2 reversals/second, which were the same parameters used by the Neurophysiology Unit to elicit the cortical visual potential to pattern. But, in the same manner as the flash stimulation parameters used to produce the flash VECP resulted in variable and inconsistent flash subcortical responses (Contamin and Cathala 1961), the subcortical pattern response was also found to be poorly defined under the conditions used to elicit the pattern VECP.

Thus, the VESP could not be precisely located and the source of the response was thought to be from either the lateral geniculate body or the superior colliculus - two synaptic junctions in the visual pathway.

In this study, a re-examination of the techniques of presenting structured stimulation was felt to be warranted in order to assess the sensitivity of the VESP to pattern. The choice of stimulation depended on the visual processing being undertaken by the LGB and superior colliculus.

The LGB receives about 80% of first order neurones from the retina and is the major synaptic junction in the visual pathway to the cortex. It has receptive fields in the parvocellular layers, occupying a large section of the structure and
are sensitive to high contrast achromatic gratings. The optimal spatial frequency for achromatic gratings was found to be 4.25 cpd (14') (Derrington and Lennie 1984). The parvocellular layers also respond to chromatic stimulation in the form of red/green unstructured fields or chromatic gratings of low spatial frequencies (Hicks et al. 1983).

The superior colliculus receives about 20% of the neurones from the retina. Its receptive fields respond to flashes of light and movement, very rapidly become unresponsive to sustained stimulation, are suppressed by contrast and are unresponsive to colour.

It was felt therefore that structured stimulations introducing the properties of high contrast and colour were two methods that might effectively locate the signal to the LGB or superior colliculus and furthermore, that the use of stimulation offering constant luminance throughout its presentation avoided the production of responses confounded by luminance changes. As pattern reversal stimulation has been established as a reliable technique in VEP studies (Desmedt 1977) and enabled comparison with the pattern ERG (Arden and Vaegan 1983), it was the adopted mode of presentation.

In these studies, the VESP was elicited by high contrast black and white checks presented at 6 reversals per second. The response was found to be clearly independent of the pattern ERG and was maximal for a check size of 12' as a P24.2 N29.09 P33.52 complex of amplitudes P-N .76 N-P .77. The response was present but attenuated at 24' and 8'.

Under these conditions, since the signal was optimal to 12', it was considered to be a contour and not a luminance related response. The VESP was also obtained to red and green luminance balanced checks as a triphasic complex of
latency P24.43 N28.29 P32.03ms and amplitudes P-N .76µV and N-P .74µV at a 2° check size.

These achromatic and chromatic responses were present at electrode derivations T3½, Cz and T4½ referred to the chin, and were not localised to any derivation.

Where black and white checks are used, the findings suggest that the VESP was probably arising from the LGB. Furthermore, the ability to elicit VESPs to colour at the same latencies using luminance matched red and green checks of 2° suggests that the signal cannot originate from the colour insensitive superior colliculus. The results showing an optimal check size of 12' for black and white stimulation and 2° for red/green stimulation support both the findings of Hicks et al. (1983) and the proposal by Derrington et al. (1984) that the spectral sensitivity of the parvocellular layers changes with spatial frequency of the stimulus, and that raising the spatial frequency of the stimulus impairs the response to chromatic stimulation whilst increasing the responsiveness to high contrast achromatic stimulation.
CHAPTER SIX
DISCUSSION AND CONCLUSIONS

The research described in this thesis has examined the visually evoked subcortical potential using scalp electrodes, and the studies undertaken can be divided into two sections: the VESP to flash stimulation and the VESP to pattern reversal stimulation.

The studies using flash stimulation have their genesis in the earlier work of Harding and Rubinstein which was carried out at the Clinical Neurophysiology Unit, Aston University, between 1978 and 1981 (Harding and Rubinstein 1980; Rubinstein 1981). By adapting 'far-field' techniques, a triphasic complex of early components was detected in "95% of normal subjects and scalp topographical studies revealed this to be of maximal amplitude around the upper mastoid process" (Rubinstein 1981). To record the signal, active electrodes sited at T3 ¹⁄₂ and T4 ¹⁄₂ (representing the left and right mastoids respectively) were referred to the vertex or Cz, and the complex of early components detected had a positive-negative-positive waveform with mean peak latencies in milliseconds of P21 N26.2 P33.6. Various studies isolated this complex from the cortical visual evoked potential and the flash electroretinogram, and also indicated a post-chiasmal source for the signal. This evidence led to the signal being described as the visually evoked subcortical potential or VESP (Harding and Rubinstein 1980).

Various issues however, were subsequently raised about the flash VESP. Boylan et al. (1984) in a discussion of the anatomical arrangement of the visual pathway with reference to scalp electrodes pointed out that the subcortical generator sites of the VESP were at a large distance from the scalp electrodes when compared to occipital electrodes which are placed directly over the generator sites of the cortical visual evoked potential (figure 6.1). The
The electrodes T3½ and T4½ are at a large distance away from the source of the VESP when compared to the distance of O1 and O2 from C1 and C2.
KEY:  
L1  L2 : Lateral Geniculate Bodies:  
       (generator sites of the VESP)  

C1  C2 : Visual Cortices (generator 
sites of the VECP)
implication was that the VESP should have had a widespread field of activity and should not have been so tightly localised bilaterally to the mastoid areas. Furthermore, this mastoid location had not been verified by other workers studying subcortical visually evoked activity (Whittaker and Siegfried 1983; Polo et al. 1985; Gambi and Rossini 1985), and Pratt et al. (1982) suspected that responses obtained in the mastoid areas indicated some auditory contamination. This explanation was feasible as the photostimulator used in researching the flash VESP produces a 'click' on discharge which is synchronous with the flash, and descriptions of masking for the click in the early topographic studies of the flash VESP are ambiguous. It was felt therefore that a re-examination of the flash VESP was necessary.

In Chapter 3 of this thesis, three studies of the flash VESP using auditory masking have been described. The first study was a pilot transverse topographic study on twenty subjects. Seven equally spaced electrodes were placed in a coronal plane from left mastoid to right mastoid, with the central electrode at the vertex and the common reference electrode at the chin. The technique of group-averaging, involving superimposition and subsequent averaging of the waveforms, was applied to the new data and enabled a study of the VESP across the sample.

The subcortical signal had a widespread distribution in the transverse plane as a P-N-P complex of group latency values P20.7 N29.5 P35.5ms. The group amplitudes in microvolts at the individual electrode sites were:
<table>
<thead>
<tr>
<th>Electrode</th>
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<th>N-P (µV)</th>
</tr>
</thead>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>.5</td>
<td>.78</td>
</tr>
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<td>2</td>
<td>.45</td>
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<td>3</td>
<td>.74</td>
<td>.84</td>
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<td>VERTEX</td>
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</tr>
<tr>
<td>4</td>
<td>.68</td>
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<td>5</td>
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<td>6</td>
<td>.62</td>
<td>.81</td>
</tr>
<tr>
<td>RIGHT MASTOID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>.47</td>
<td>.62</td>
</tr>
</tbody>
</table>

The main complication of the widespread activity was that Cz, which was used as the common reference site throughout Rubinstein's thesis (Rubinstein 1981), was clearly active for the VESP signal and a more appropriate common reference site had to be found.

The second study was designed to examine different reference sites, to investigate further the distribution of the flash VESP in the anterior/posterior direction and to compare the VESP with the distribution of the flash ERG.

The most appropriate common reference sites were found to be non-scalp derivations at the chin and a balanced non-cephalic reference electrode (BNCRE) placed on the upper thorax (Stephenson and Gibbs 1951). Using the chin as a reference, and a DTL electrode on the right eye the flash ERG was recorded as an 'a' wave at 16.34 ms and 'b' wave 37.2 ms, with mean 'b' wave amplitude being 11.69 µV, (Dawson et al. 1979). The 'b' wave rapidly attenuated in amplitude at a short distance away from the cornea and was difficult to define beyond the frontal electrodes. However, at a temporal chain of electrodes on the right side of the head at T4, T4½ and T6, a triphasic complex emerged of mean incidence P27.28 N32.82 P37.68. This complex was also present at
additional electrodes placed on the left mastoid at T3½ and at the vertex at Cz.

The mean amplitudes at these electrodes were:

<table>
<thead>
<tr>
<th></th>
<th>P-N µV</th>
<th>N-P µV</th>
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<tbody>
<tr>
<td>T4</td>
<td>2.18</td>
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</tr>
<tr>
<td>T4½</td>
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</tr>
<tr>
<td>T6</td>
<td>2.05</td>
<td>2.05</td>
</tr>
<tr>
<td>Cz</td>
<td>2.14</td>
<td>2.19</td>
</tr>
<tr>
<td>T3½</td>
<td>2.21</td>
<td>2.22</td>
</tr>
</tbody>
</table>

A similar distribution was found when a BNCRE on the upper thorax was used. These findings showed that the VESP had a widespread distribution in the anterior/posterior direction when the chin and a BNCRE were used. The vertex (Cz) was also used as a reference and the ERG was clearly recorded at the cornea. However, the VESP was difficult to define.

The results of this anterior/posterior study together with the pilot study were not in concordance with the distributions found by Rubinstein (1981) and prompted a further study to assess the extent of possible auditory involvement in Rubinstein's work in which no mention of auditory masking was made in the topographical studies.

Twenty-five subjects were used in an auditory control study in which each subject was exposed to four different modes of stimulation using two properties of a Grass PS22 photostimulator, namely the flash discharge and the incurred synchronous 'click'. The four modes of stimulation involved: i) presenting the flash with the click masked by earphones, thus eliciting a visual response, ii) allowing the click to be heard with the flash discharge masked, giving an auditory signal, iii) presenting both the flash and click, iv) setting up a
non-stimulus condition whereby the flash and click were masked but the photostimulator was still operated and the background responses were still averaged. A modified electrode montage was used whereby active electrodes at T3 1/2 Cz and T4 1/2 were referred to the chin. The results were group averaged and the following latency and amplitude levels were obtained.

Statistically within the sample of 25 subjects, twenty subjects gave a flash VESP with a mean latency of P26.62 N33.53 P38.37 and mean amplitudes at Cz of P-N .9 and N-P .89μV. Similar amplitude values were obtained for the signals at T3 1/2 and T4 1/2. Fifteen subjects gave an auditory signal to the click discharge of mean latency P26.32 N32.32 P38.61 and mean amplitude at Cz of P-N .72μV and N-P .56μV. Ten subjects from the sample subjectively assessed the click at 50dB (mean). Sixteen subjects showed a signal to the flash/click stimulation with mean latencies P25.81 N33.5 P40.34 and mean amplitudes at Cz of P-N 0.82μV N-P 0.83μV. A chi-squared test showed that there were no significant differences in the frequency of occurrence of the response between the three modes of stimulation (p >0.05).

Seventeen subjects responded to more than one mode of stimulation. Within this group no significant differences (p >0.05) were found in the latency values of the P-N-P complex between the three modes of stimulation. Furthermore, the amplitudes of the flash VESP when compared to the click response and the flash/click signal were not significantly different either (p > 0.05). However, when the amplitudes of the click response were compared to the amplitudes of the flash/click signal, the N-P component was found to be significantly higher for the flash/click response at electrode sites Cz and T4 1/2 (for Cz: p = 0.014, for T4 1/2: p = 0.02, i.e. p < 0.05).

The group-averaged waveforms confirmed the statistical analysis of the data in
demonstrating clear triphasic complexes for the three positive modes of stimulation. These grouped results were reconfigured to the Cz reference, i.e. for each mode of stimulation, the signal obtained at Cz was subtracted from the signal at T3\(^{1/2}\) and T4\(^{1/2}\). For flash stimulation, subtraction resulted in a flat line showing no lateralisation of the response, i.e. there were no differences in latency and amplitude values at the three electrode derivations. However, there were differential effects when the auditory pathway was involved. For the purely auditory response, a broad negative component emerged at T3\(^{1/2}\) and T4\(^{1/2}\) delineated by P18.24 N25.84 P34.32 and P-N 0.47\(\mu\)V and N-P 0.62\(\mu\)V at T4\(^{1/2}\) and P18.4 N26.2 P37.2 and P34.32 and P-N 0.33\(\mu\)V and N-P 0.49\(\mu\)V. This indicated that as Cz was subtracted from T3\(^{1/2}\) and T4\(^{1/2}\), the amplitudes for the negative component were larger at the mastoids. For the flash/click mode, the response lateralised to T3\(^{1/2}\) with latencies of P19.04 N25.68 P34.64 and amplitudes P-N 0.68\(\mu\)V and N-P 0.34\(\mu\)V, again implying a response which was greater in amplitude and more negative at T3\(^{1/2}\).

It was of interest to relate these findings to the middle latency auditory evoked response - the MLAER (Geisler et al. 1958). Mendel and Goldstein (1969) found that its most stable neurogenic components were a negative at 22ms and a positive at 34ms. The amplitudes were at a maximum in the fronto-central regions with an active electrode at the vertex referred to the earlobe or mastoid and elicited by any stimulus with an abrupt rise time such as a click. The response was identifiable at levels of 30dB and above. With reference to the auditory control study, the click discharge was subjectively assessed to be 50dB and the studies suggest that when the auditory pathway was stimulated, some components of the middle latency auditory evoked potential were being elicited resulting in different amplitude values at the three electrode sites T3\(^{1/2}\), Cz and T4\(^{1/2}\). These differences on reconfiguration to Cz showed up as broad negative components apparently localised in subtraction to the mastoid area.
Although this study could not assess the percentage contribution of auditory and visual potential activity in the flash/click signal for each individual, it is likely that for many subjects there is a marked contribution from the auditory pathway.

From these studies it was concluded that:

1) Further studies on the flash VESP should be designed to incorporate an auditory masking procedure.

2) The reference electrode should be of a non-scalp derivation, eg. the chin, or be a balanced non-cephalic reference electrode used at the level of cervical 7 and the sterno-clavicular junction.

Owing to the very nature of flash stimulation, the possible origin of the VESP could not be located with precision. However, Harding and Rubinstein (1981) concluded that "as its lateralisation was not changed by the occlusion of an eye, its origin was not pre-chiasmal from either the retina or optic nerve and must arise from post-chiasmal centres. The most obvious choice would be the lateral geniculate bodies". The lateral geniculate bodies (LGB) are major subcortical relay station of the visual pathway in the thalamic area. Eighty per cent of the optic nerve fibres from the retina synapse in the LGB with third order neurones which subsequently carry impulses via the optic radiation to the visual cortex. The other possible sources of the VESP were the superior colliculi - which are synaptic junctions receiving about 20% of the optic nerve fibres from the retina and projecting to other midbrain areas.

The LGB is divided into two magnocellular and four parvocellular layers (Chacko 1949). The parvocellular layers predominate and within these layers
the central 15° of the visual field is represented in over 50% of the geniculate volume (Hickey and Guillery 1979). The visual receptive units of the parvocellular layers are sensitive to high contrast achromatic gratings (black/white drifting gratings) and the optimal stimulus size for eliciting a response has been found to be 4.25 cycles per degree or 14 minutes (Derrington and Lennie 1984). These units also respond to chromatic stimulation in the form of red/green unstructured fields or chromatic gratings of low spatial frequencies (Hicks et al. 1983).

The superior colliculus, however, responds to flashes of light and movement, and very rapidly becomes unresponsive to sustained stimulation. It is also suppressed by contrast (Schiller 1978) and is unresponsive to colour (Marrocco and Li 1977).

It was felt therefore that structured stimulation introducing the properties of high contrast and colour were two methods which could effectively locate the source of the signal to the LGB or superior colliculus. Furthermore, stimuli offering constant luminance throughout their presentation avoided the production of responses which were confounded by luminance changes. Pattern reversal stimulation using black and white checks and luminance-balanced red and green checks was the method of choice, as pattern reversal techniques are now well established in the visual evoked potential field and enabled direct comparison with the pattern reversal ERG waveform (Arden and Vaegan 1983). Chapter 5 describes studies of the pattern VESP to achromatic and chromatic stimulation and its relation to the pattern ERG.

Using a sample of fifteen subjects a triphasic VESP complex was most clearly defined to a high contrast black and white reversing checkerboard and was optimally evoked at the electrodes T3 1/2, Cz and T4 1/2 which were referred to
the chin for a 12' check size. This signal had mean latency values of P24.2 N29.09 P33.52 and mean amplitude values at Cz of P-N .76µV and N-P 0.77µV. A lower amplitude response was obtained at the larger check size of 24' with mean values of P-N 0.34µV and N-P 0.34µV and also at 8' with mean values of P-N 0.25µV and N-P 0.23µV at the Cz derivations. For each check size, the mean amplitude did not differ significantly at the three electrode sites T3⁵⁄₂, Cz and T4⁵⁄₂, ie. there was no localisation of the response. These findings are similar to those of Harner et al. (1985) who found a response at 14'.

The present study demonstrated that a VESP complex was formed at similar latencies to those signals obtained by flash stimulation in the original studies defining the VESP as a P23 N28 P34 complex (Harding and Rubinstein 1980). In his thesis, Rubinstein (1981) tried to obtain a signal to pattern reversal stimulation using check sizes of 2° and 56' presented at 2 reversals per second, and also to flashed-on patterns using grids superimposed on the photostimulator. The studies were not successful and led Rubinstein to conclude that the VESP was simply a luminance related response. The findings in this thesis however suggest that the VESP can in fact be elicited to pattern reversal stimulation using the chin as a common reference, and at a rate of presentation of 6 reversals per second. The signal was optimally elicited to a 12' check size, indicating that the VESP was a contour related response and it was felt necessary to compare it with the pattern electroretinogram (PERG) in order to establish that the distributions of the PERG and pattern VESP were different and independent.

When techniques established by Arden and Vaegan (1983) were employed, the PERG was clearly elicited at the cornea. A DTL electrode was used (Dawson et al. 1979) and the checkerboard had check sizes of 28' and 56'. In terms of its
distribution, the PERG was found to be limited essentially to the cornea and surrounding orbital area, rapidly attenuating at frontal electrode sites on the forehead (supporting the findings of Adachi-Usami 1983). The PERG had an N-P-N configuration of latencies - N18.5 P37.19 N66.1 - and had a fundamentally different wave morphology to that of the pattern VESP which has emerged as a P24.2 N29.09 P35.52 complex more posteriorly at T 3\(\frac{1}{2}\), Cz and T4\(\frac{1}{2}\). On the basis of wave morphology, latency values and the distribution of the pattern ERG being tightly localised to the orbital area, it was concluded that the signal obtained to achromatic pattern reversal stimulation at T3\(\frac{1}{2}\), Cz and T4\(\frac{1}{2}\) reflected subcortical potential activity and was described as the achromatic pattern VESP.

A protocol similar to that of the achromatic study was adopted to elicit a subcortical signal to colour stimulation. Using luminance balanced red and green checks, a clear triphasic P24.43 N28.29 P32.03 response with mean amplitudes of P-N .76\(\mu\)V and N-P 74\(\mu\)V at the Cz derivation was clearly delineated to a 2\(^\circ\) check size. These amplitudes were attenuated for 1\(^\circ\) and 3\(^\circ\), reaching values of P-N 0.3\(\mu\)V N-P 0.29\(\mu\)V for 1\(^\circ\) and P-N .19\(\mu\)V and N-P .21\(\mu\)V for 3\(^\circ\). For each check size, the mean amplitudes did not differ significantly at the three electrode sites T3\(\frac{1}{2}\), Cz and T4\(\frac{1}{2}\).

The ability to obtain a VESP signal to chromatic stimulation suggested that the signal could not be arising from the superior colliculus, which is colour insensitive.

Overall, the pattern VESP results - showing an optimal check size of 12\' for high contrast achromatic stimulation and 2\(^\circ\) for red/green stimulation (figure 6.2). These results support the findings of Hicks et al. (1983) and the proposal by Derrington et al. (1984) relating to visual receptive field properties at the
FIGURE 6.2

Graph showing the optimum check sizes for the achromatic and chromatic VESP to checkerboard reversal stimulation for the N-P component at the Cz derivation, reference chin

For a black/white checkerboard pattern at 6 reversals per second, the optimum stimulus size was 12' check.

For a red/green luminance balanced checkerboard reversal stimulation, the optimum stimulus size was a 2' check.
LGB.

These properties demonstrate that the spectral sensitivity of the parvocellular layers of the LGB changes with the spatial frequency of the stimulus, as raising the spatial frequency of the stimulus impairs the response to chromatic stimulation and increases the responsiveness to high contrast achromatic stimulation.

It was therefore concluded that:

1) The signal evoked by high contrast achromatic pattern reversal stimulation was a subcortical response independent of the ERG.

2) The optimal stimulus size of 12' for eliciting the achromatic VESP implied the response was contour related and the source could be located in the LGB and not the superior colliculus.

3) The responses to chromatic stimulation provided further evidence for the LGB source of the VESP.

4) Moreover, the optimal stimulus size of 12' for the achromatic VESP and 2° for the chromatic VESP supported the findings that the visual receptive fields of the parvocellular layers of the LGB are more responsive to high contrast achromatic stimuli at higher spatial frequencies.

It is interesting to speculate whether the flash VESP also reflects subcortical activity from the LGB or whether it has a more diffuse origin in the visual
pathway. Harding and Wright (1986) have suggested that the pattern and flash sub-systems in the visual pathway may be quite independent.

Supporting evidence came from a study of one of the pre-senile dementias called Alzheimer's disease (Wright et al. 1986) in which the flash cortical response is markedly delayed whilst the pattern reversal cortical component P100 remains well within normal limits. In acute optic neuritis, the reverse situation prevails, ie. there is a marked effect on the pattern response but an entirely normal flash cortical response (Harding and Wright 1986). It has previously been suggested that the pattern reversal technique simply reflects the integrity of the primary visual pathway, ie. the geniculocortical pathway (Blumhardt and Halliday 1981) and is insensitive to any cortical destruction that spares this pathway and the primary visual projection to Brodmann's area 17 - see Figure 6.3.

The flash and pattern VESP represent subcortical, post-chiasmal responses from the visual pathway and as such could add to information about the integrity of the visual pathways between the retina and visual cortex which may not be offered by the electroretinogram and the cortical visual evoked potential. Although Rubinstein (1981) had applied the flash VESP to various clinical conditions, it is suggested by this thesis that the results could have been confounded by stimulation of the auditory pathway.

It is therefore proposed that the protocols described in this thesis for eliciting the flash and pattern VESP form a basis for developing clinically robust techniques which can be subsequently used to further the understanding of the pattern and flash sub-systems and thereby offer more diagnostic information about visual pathway integrity in various pathologies such as optic neuritis.
FIGURE 6.3

Three different conditions and their effect, or lack of effect, on flash and pattern visual evoked potentials

The normal subject shows normal latency pattern responses presumably from area 17, and normal flash responses mainly generated by areas 18 and 19. In the patient with acute optic neuritis there is a marked effect on the pattern systems, producing a delayed response at area 17 but an entirely normal flash response either produced by parallel processing through area 17 or via a separate non-geniculate pathway at area 19. In Alzheimer's disease, the primary visual pathway is unaffected and therefore both systems subserving pattern produce normal responses but, since the pathology affects area 19 but spares area 17, the flash response is markedly delayed. (After Harding and Wright 1986).
APPENDIX 1

AUDITORY CONTROL STUDY
LATENCIES OF THE TRIPHASIC PNP COMPLEX TO
THREE MODES OF STIMULATION
# AUDITORY CONTROL STUDY

## LATENCIES OF THE PNP COMPLEX TO

### THREE MODES OF STIMULATION

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### Auditory Control Study

#### Latencies of the PNP Complex

#### Three Modes of Stimulation (contd)

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APPENDIX 2

AUDITORY CONTROL STUDY

AMPLITUDES IN MICROVOLTS OF THE P-N AND N-P COMPONENTS OF THE TRIPHASIC COMPLEX AT ELECTRODE SITES T3½, Cz AND T4½ (REFERRED TO CHIN) FOR A SAMPLE OF 25 SUBJECTS AND THREE MODES OF STIMULATION
### Controlled Flash Study-Amplitudes

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Note: The table includes amplitudes for different conditions across subjects, with columns for P-N, N-P, and T3 1/2, Cz, T4 1/2 for flash and click conditions individually and together.
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|----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 14       | 1.27| .59 | 1.08| .45 | 1.0 | .71 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 15       | .93 | .78 | 1.37| .99 | 1.03| .82 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 16       | 1.15| .86 | 1.17| 0.8 | 1.17| .87 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 17       | .8  | .7  | .49 | .67 | 1.09| .81 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 18       | 1.04| .82 | 0.97| .75 | 1.00| .72 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 19       | 1.17| 1.27| 1.3 | 1.08| 1.37| 2.04|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 20       | .96 | 1.31| 1.17| 1.58| 2.31| 2.5 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 21       | 1.56| 1.11| 1.64| 1.23| 1.55| 1.19|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 22       | 1.07| 1.0 | 1.1 | 1.01| 1.05| .98 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 23       | 1.64| 1.24| 1.64| 1.18| 1.66| 1.27|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 24       |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 25       | .82 | 1.18| .73 | 1.08| .77 | 1.23|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| MEAN     | .97 | .93 | .9 | .89 | .92 | .84 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| SD       | .64 | .76 | .61 | .72 | .62 | .66 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
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APPENDIX 4

VESPTO ACHROMATIC PATTERN REVERSAL STIMULATION

AMPLITUDES OF P-N AND N-P COMPONENTS IN MICROVOLTS
| SUBJECTS | 8° | | 12° | | 24° |
|----------|----|----|----|----|----|----|----|----|----|----|----|
|          | T3 ½ | Cz | T4 ½ | T3 ½ | Cz | T4 ½ | T3 ½ | Cz | T4 ½ | T3 ½ | Cz | T4 ½ |
| 1        | .85  | 1.19 | 1.1 | 1.39 | .97 | .77 | 1.92 | 1.73 | 1.64 | 1.72 | 1.95 | 1.79 | 1.34 | 1.27 | 1.29 | 1.26 | 1.34 | 1.33 |
| 2        |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |
| 3        |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |
| 4        |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |
| 5        |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |
| 6        |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |
| 7        | .45  | .53 | .46 | .53 | .45 | .54 | .73  | .89 | .71  | .9 | .78 | .79 | .52  | .7 | .58 | .61 | .56 | .6 | 52  | .58 |
| 8        | .84  | .56 | .91 | .5 | .33 | .6 | .9 | .7 | .68 | .67 | .72 | .81 | .52  | .59 | .52 | .6 | .52 | .61 |
| 9        |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |
| 10       |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |
| 11       |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |     |      |     |
| 12       | .57  | .58 | .57 | .61 | .66 | .55 | .91  | .93 | .84 | .96 | .85 | .91 | .76  | .59 | .7 | .61 | .73 | .68 |

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BLACK AND WHITE AMPLITUDES (cont'd)
APPENDIX 5

VESPM TO CHROMATIC PATTERN REVERSAL STIMULATION
LATENCIES OF THE PNP COMPLEX IN MILLISECONDS
# Latencies of Red and Green Study

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| Mean     | 24.06| 27.48| 31.52| 24.43| 28.29| 32.03| 24.52| 28.08| 31.85|
| SD       | 4.16 | 4.17 | 4    | 2.35 | 2.31 | 2.29 | 2.11 | 1.99 | 2.95 |
| SE       | 1.9  | 1.86 | 1.79 | .71  | .7   | .7   | .94  | .89  | 1.32 |

359
APPENDIX 6

VESPE TO CHROMATIC PATTERN REVERSAL STIMULATION

AMPLITUDES OF P-N AND N-P COMPONENTS IN MICROVOLTS
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**Amplitudes Across All Derivations Red/Green in $\mu V$**
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APPENDIX 7

METHODS OF APPLYING AND SECURING THE DTL ELECTRODE
The DTL electrode may be stabilized on the cornea by three methods:

a. The DTL tip may be placed on or under the lower lid. Signal amplitude will be about 75% of normal (below).

b. It may be captured between the limbus and pupil under a plano soft contact lens. Signals will be 95-100% of those recorded with a Burian-Allen monopolar electrode.

c. The tip of a long DTL may be attached (adhesive or petroleum jelly is good) at the inner canthus as well as at the outer canthus and the excess in corneal contact between the pupil and limbus. Signal level will be as in 'B' above.

This electrode is NOT STERILE.

Gas sterilization is recommended. Excess DTL fiber material is provided. Some fibers may be removed (cut) for additional comfort. The conductive thread may be shortened.
APPENDIX 8

ABSTRACTS AND PUBLICATIONS
SOURCE DERIVATION OF THE BRAIN-STEM AUDITORY EVOKED POTENTIAL

Clinical Neurophysiology Unit, Department of Vision Sciences, Aston University, Aston Triangle, Birmingham B4 7ET (U.K.)

(Accepted for publication: June 27, 1985)
P18.06 THE VISUAL EVOKED SUBCORTICAL POTENTIAL TO PATTERN REVERSAL STIMULATION.

G.F.A. Harding and U. Dhanesha

(Birmingham, UK)
THE VISUAL EVOKED SUBCORTICAL POTENTIAL TO PATTERN REVERSAL STIMULATION

G. F. A. Harding and U. Dhanisha
Department of Vision Sciences, Aston University, Aston Triangle, Birmingham B4 7ET, England

(Arrived 27 June 1986)


(in press)
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