CLINICAL APPLICATIONS OF THE VISUAL EVOKED POTENTIAL:

A COMPARATIVE STUDY OF DIFFUSE FLASH AND PATTERN REVERSAL STIMULATION

GRAHAM EDWIN HOLDER, B.Sc. (Bristol), M.Sc. (Aston)

THESIS SUBMITTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

NEUROPSYCHOLOGY UNIT,

DEPARTMENT OF OPHTHALMIC OPTICS,

THE UNIVERSITY OF ASTON IN BIRMINGHAM

SEPTEMBER, 1979

'Clinical applications of the visual evoked potential: a comparative study of diffuse flash and pattern reversal stimulation'. Thesis submitted for the degree of Doctor of Philosophy. Graham Edwin Holder, September 1979.

SUMMARY

The visual evoked potentials to pattern reversal (PVEP) and diffuse flash (FVEP) stimulation are described in over two hundred patients with disease of the pre-chiasmal, chiasmal or post-chiasmal visual pathways and their diagnostic value assessed.

Patients with demyelinating optic nerve lesions characteristically showed an increased latency of the major positive component of the VEP, the PVEP being more sensitive than the FVEP. In patients with other disease processes affecting the pre-chiasmal visual pathways the findings varied according to the nature of the pathology.

All patients with chiasmal compression showed VEP abnormalities which were, as would be predicted on a purely neuroanatomical basis, maximal over the hemisphere contralateral to the stimulated eye. The importance of using recording electrodes situated away from the midline is stressed.

Patients with post-chiasmal lesions showed VEP abnormalities over the involved hemisphere and therefore contralaterally to any visual field defect. These findings are also in agreement with neuroanatomically based predictions.

The VEP's were generally unremarkable in patients with a significant degree of non-organic visual loss, the main feature being a discrepancy between the patients subjective perception of the stimulus and the objective VEP findings.

Discrepancies between the findings presented and those of previous authors are discussed, the contribution of stimulus and recording parameters to the lateralisation of PVEP abnormalities in patients with chiasmal and post-chiasmal lesions being particularly emphasised.

Comparison between the PVEP and the FVEP suggests that in many cases the complementary nature of pattern reversal and diffuse flash stimulation enables the diagnosis to be correctly established, and that the increasing disuse of diffuse flash as a stimulus in clinical VEP examination is not justified.

Evoked potentials/vision disorders/nervous system diseases/ophthalmology/visual fields.

ACKNOWLEDGEMENTS

I would like to express my sincere thanks to the following: Professor Graham Harding (internal supervisor), Dr. Walter Kennedy and Dr. Cherry Thompson (external) for valuable advice, support and encouragement; Dr. George Harwood and Dr. Asad Khan for advice and assistance with the classification of the multiple sclerosis patients; Greenwich and Bexley A.H.A for financial assistance; and finally, Ms Karen Morrish for conscientiously typing the manuscript.

C O N T E N T S

CHAPTER ONE

INTRODUCTION

1.1 General Introduction

It is well recognised that the electroencephalogram, or EEG, as recorded from the scalp using the normal equipment and techniques, represents only a small sample of the total bioelectrical activity of the brain. There are discrepancies between the EEG as recorded from the scalp and the electrical activity recorded with intracerebral electrodes, and there are many unsolved questions regarding the origins and functions of these electrical phenomena. In spite of the problems, however, the EEG has been the only method available for the direct and continuous recording of the functional happenings and alterations in the brain and has an accepted, well-established role in the diagnosis and evaluation of neurological disease. As Brazier (1964) indicated, the EEG is a most sensitive indicator of brain function, and is the simplest and most precise way of unravelling central nervous system pathways by monitoring the electrical changes that take place.

The EEG, however, is essentially a measure of spontaneous cerebral activity and the more recent technique of recording sensory evoked potentials from the scalp gives a measure of the brain's responsiveness to given stimuli, therefore enabling conclusions to be drawn about the afferent pathways and the response of the cortex.

Changes in the electrical activity of the human brain in response to external stimulation have been recognised ever since Berger (1929) demonstrated that when a subject's eyes were closed a 10 cps alpha rhythm was present in the EEG which disappeared on opening of the eyes. In 1934, Adrian and Matthews showed that responses could be recorded from the occipital cortex following regularly presented flashes of light. This first visual evoked potential (VEP) was of little clinical value, mostly because it was only present in a small proportion of subjects. It is now known that the VEP was not absent in these other subjects but merely

obscured by the higher amplitude spontaneous EEG.

A major advance occurred when Dawson (1947), using the superimposition technique introduced by Galambos and Davis (1943) in studying the auditory system, demonstrated that a potential evoked by electrical stimulation of a peripheral nerve could be detected at the scalp. These records gave a wide base-line due to the random nature of the on-going EEG, but the deflections in response to the stimulus were time-locked, and always appeared at the same point in the trace. It was with this method that Cobb (1950) demonstrated that the early component of the potential evoked by flash stimulation in man occurred with a latency of approximately 35 msec.

The technique of superimposition was rapidly superseded, initially by the electro-mechanical summation of signals (Dawson, 1954) and later by the method of signal averaging. Here the evoked potentials are extracted by averaging a number of EEG traces in fixed time relation to a repetitive stimulus. The spontaneous EEG is unrelated to the stimulus and thus tends to sum to zero, while the evoked potential, being time-locked to the stimulus, becomes (more) evident. In theory it is necessary to sum from zero to infinity but this is clearly impossible and in practice between 50 and 250 summations is normally considered sufficient to provide a reliable measure of the evoked potential. An exception to this is the far-field recording of the auditory brain stem potentials, where, due to their extremely low amplitude, as many as 2000 stimulations are often used.

With rapid advances in technology, evoked potential recording has become increasingly more common, and, despite numerous problems of significance and quantification (e.g Broughton et al., 1969) its application in the clinical field is well-established in the detection of sub-clinical lesions, in the determination of the nature of existing lesions, and in providing objective assessment of a given sensory system.

This thesis is concerned with the neurophysiological study of the visual system, using evoked potential measures, in neuro-ophthalmological patients.

1.2 The Visual Pathways (see Fig. 1.2.1)

The fibres of the optic nerves, estimated at some 10^6 in man (Bruesch and Arey, 1942), are the axons of the retinal ganglion cells, with the macular fibres probably being the most important part of the visual afferent system. In the retina these fibres run from the macula to the temporal side of the optic disc. The optic nerves, which developmentally and histologically are part of the brain, then pass backwards and inwards through the optic foramina.

The two optic nerves unite at the optic chiasm. The nerve fibres from the nasal half of each retina, constituting in humans some 60% of all fibres, cross to mix with uncrossed fibres from the temporal portion of the other eye. The more ventral of these decussating fibres form a short loop extending into the optic nerve on the opposite side before passing back into the optic tract, while the more dorsal fibres form a similarly short loop extending into the ipsilateral optic tract before decussating to the other side. The macular fibres decussate in a similar manner to those from peripheral retina, but decussation occurs in the postero-superior portion of the chiasm (Hoyt and Luis, 1963). The fibres from the temporal portions of the retinae do not decussate but continue backwards in the ipsilateral optic tract.

Each optic tract therefore is composed of fibres from the ipsilateral temporal retina and the contralateral nasal retina. Within the tracts the uncrossed fibres lie dorsolaterally and the crossed fibres ventromedially. Each optic tract sweeps outwards and backwards between the cerebral peduncle and the hippocampal gyrus, and finally inwards. Using electrophysiological criteria Bishop and Clare (1955) have divided the fibres of the optic tracts into four groups. The first two more rapid groups, composed of large fibres carrying information destined for the visual cortex have their synaptic relays in the lateral geniculate bodies, the thinner fibres which mediate the pupillary reflexes are directed to the

Fig. 1.2.1. The visual pathways. The fibres from the maculae, some crossed and some un-crossed are not shown separately in the optic nerves and optic tracts, but their place of arrival at the lateral geniculate body - the intermediate part of its posterior two-thirds - is shown by hatching. The remainder of the posterior two-thirds receives the fibres from non-macular regions of the binocular retinal field. The monocular retinal field is shown projecting into the anterior third of the lateral geniculate body. No attempt has been made to localise the arrival within the striate cortex of fibres from these different regions of the lateral geniculate body. (After Cunningham's Textbook of Anatomy, 1964).

Ref not in back

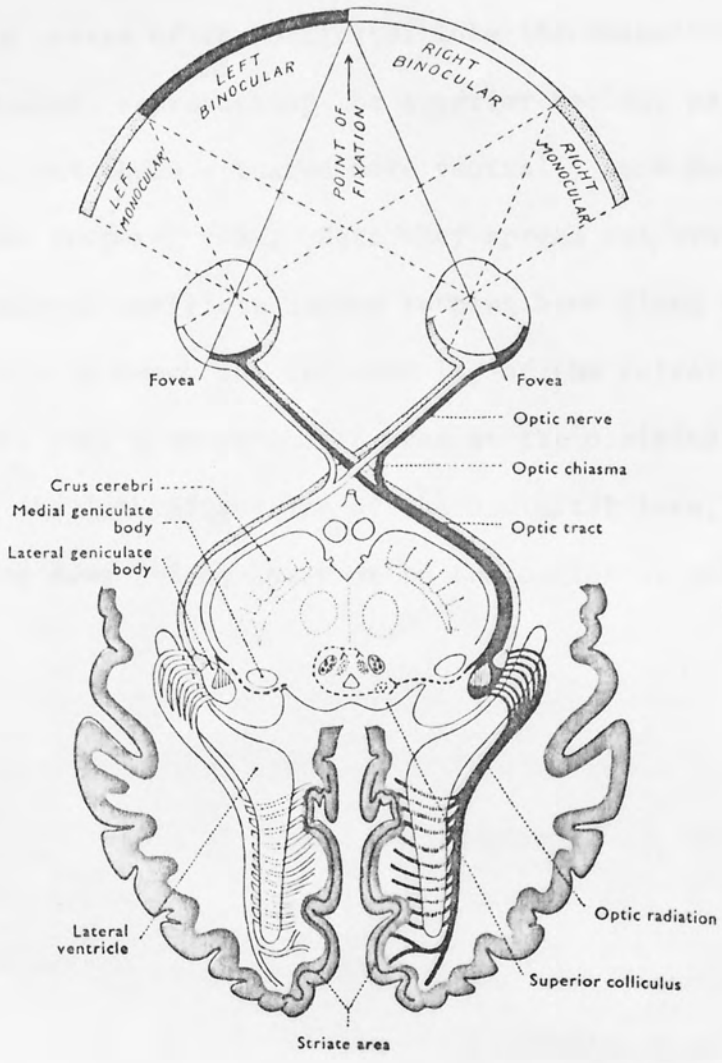

LEFT MONOCULAR
LEFT BINOCULAR
POINT OF FIXATION
RIGHT BINOCULAR
RIGHT MONOCULAR
Fovea
Fovea
Optic nerve
Optic chiasma
Optic tract
Crus cerebri
Medial geniculate body
Lateral geniculate body
Lateral ventricle
Optic radiation
Superior colliculus
Striate area

Fig.1.2.1.

pretectal region, with the thinnest and slowest fibres leading to the mid-brain.

From the geniculate bodies the fibres enter the posterior limb of the internal capsule where they lie posterior to the somatosensory fibres and internal to the fibres of the auditory radiation. They emerge from the capsule as the optic radiation or geniculo-calcarine pathway, which runs to the striate cortex of the occipital lobe (Brodmann's area 17). The more dorsal fibres, representing the superior retina, pass directly to the visual cortex, but those situated more ventrally turn downwards and forwards to the temporal lobe. Here they spread out over the temporal horn of the lateral ventricle before turning back along the inferior aspect of the ventricle to reach the inferior lip of the calcarine fissure. The macula projects onto a wedge-shaped area at the occipital pole, extending slightly onto the lateral surface of the occipital lobe, with the apex of the wedge being some 2-3 cm anterior to the occipital pole.

1.3 Visual Evoked Potentials - Historical Overview

The first systematic studies of the VEP were published in 1960. Cobb and Dawson (1960) using Dawson's superimposition technique, studied the early components (less than 100 msec) evoked by low frequency diffuse flash stimulation. A more thorough analysis of the flash VEP was provided by Vanzulli et al. (1960) who investigated the effects of stimulus intensity, arousal and eye closure and, using much longer analysis times than Cobb and Dawson, were probably the first to stress the extent of the interindividual variability seen in a normal population. These authors used O2 and OZ electrodes referred to a mid-frontal or forehead reference and suggest that the short latency components represent a primary response of the visual cortex but also conclude that afferent visual volleys reach the cortex not only along the specific pathway to area 17 but also through other polysynaptic pathways which are not further defined. They attribute the inter-individual VEP variability to variable projection on the scalp due to the folded areas of visual projection in the medial surface of the hemisphere. These authors did not rely purely on a superimposition technique to extract the evoked potentials, their optimum method being photoelectric analysis with brightness modulation of the signal in successive sweeps (Handler et al., 1960). ← ref not in back!

The first morphologically satisfactory description of the VEP, however, was that of Ciganek (1961). Using bipolar midline occipital-parietal recording he specified a series of waves of alternate polarity with average latencies of approximately 40, 55, 75, 95, 115, 130 and 195 msec, which he labelled I - VII, wave I being surface negative at the occipital electrode. The first three waves he called the primary response, and represented the specific part of the response of the visual cortex. The secondary phase he suggested was due to a non-specific, more diffusely organised system. Ciganek also described a later rhythmic activity which he termed the after-discharge which was best seen with the

eyes closed.

It is of interest that Ciganek based some of his conclusions on recordings obtained with relatively high (16/sec) rates of stimulation which produced a sinusoidal cortical potential of similar frequency. It is now accepted that there are two classes of VEP; the potentials evoked by low frequency stimulation (usually 2/sec or less), often known as the transient VEP, and the sinusoidal type waveform seen with faster rates of stimulation (6/sec or higher) known as the steady-state evoked potential. This overview will concentrate on the transient VEP as this is the measure experimentally used (for a recent review of steady-state evoked potentials the reader is referred to Regan, 1977a).

On further investigating Ciganek's waves I - III, Vaughan et al., (1963), using an occipital-vertex derivation and computer averaging, found slight differences in latency from Ciganek which they attributed to differences in stimulus intensity and electrode placement. They also investigated VEP changes in homonymous hemianopia. This part of their work will be discussed in later sections dealing specifically with clinical VEP findings.

Kooi and Bagchi (1964) again stressed the influence of flash intensity and electrode placement on the morphology of the VEP. These authors also investigated the stability of the VEP, finding correlations of 0.87 - 0.97 for test-retest measurements during the same recording session, and a median value of 0.88 for longer periods of time. No relationships were found between VEP variables and eye colour, colour blindness, refractive error type, pupil size, alpha frequency, alpha amplitude or an alpha persistence index.

Gastaut and Regis (1965) described a model VEP which was similar in form to that of Ciganek (1961). These authors also compared the results obtained by other workers and concluded that, although the VEP morphology reported was highly variable, there appeared to be a relatively consistent

positive component at 100 - 150 msec, the possible effects of stimulus and recording parameters again being stressed. They describe the potential as polyphasic with two recognisable parts followed by a rhythmic after discharge. The early part consisted of four waves (waves 1 - 4) of alternating polarity at approximately 25, 40, 60 and 80 msec, wave 1 being surface positive in the occipital region. The late part consisted of a single positive component, wave 5, with a latency of 130 ± 30 msec. Wave 5 could be monophasic or, more often, triphasic with a positive peak, 5a, at 120 ± 20 msec, a second positive peak, 5c, at 160 ± 30 msec with an intermediate negative wave, 5b, at 140 ± 30 msec. The after-discharge they report as being seen when the subject's eyes were closed. From experiments with light and dark adaptation they concluded that 5a was related to the photopic system and 5c the scotopic system, thereby disagreeing with the non-specific nature of this wave proposed earlier by Ciganek (1961).

This assignment of a specific nature to wave 5 was supported by the work of Rietveld et al. (1965). They investigated the contribution of the fovea and parafovea to the VEP more systematically and concluded that not only the major positive component (wave IV of Ciganek, wave 5 of Gastaut and Regis), but also the preceding negative component were related to the central region of the fovea. Potts and Nagaya (1965) used a 0.06° red target to evaluate foveal function and found that, with this stimulus, the major positivity was preserved, earlier components becoming extinct. Jonkman (1967), using bipolar recording techniques with electrodes positioned according to the 10 - 20 system of electrode placement, described a VEP essentially similar to that of Ciganek (1961) but also concluded that the major positivity at 100 - 120 msec, which Ciganek included in the secondary response, was better regarded as a product of the primary response.

The presence of this major positivity has since been further documented by many authors (e.g Dustman and Beck, 1969; Panayiotopolous et

al., 1970; Harmony, 1973; Harding, 1974). A schematic diagram of the normal VEP to diffuse flash stimulation can be seen in Fig. 1.3.1 along with the notations of Ciganek (1961), Gastaut and Regis (1965), Dustman and Beck (1969) and Harding (1974). As the notation of Harding (1974) is that used by this author all future descriptions will utilise this system.

It is of course of great importance in clinical practice to evaluate the variability of a normal population so that interpretation of the VEP's recorded in an individual patient may be meaningful. Vaughan et al. (1963) using electrodes 3 cm lateral and 1 cm anterior to the inion with a vertex reference, found little absolute difference between traces from the right and left occipital electrodes, but did find a relatively large intersubject variability in both amplitude and latency for the three waves studied (N1, P1 and N2). They also stressed the importance of technical factors such as accurate electrode placement and electrode impedance on the waveform of the VEP, amplitude being more affected than latency. This relative lack of interhemispheric latency asymmetry was confirmed by Kooi et al. (1965). Using electrodes 3 cm anterior and lateral to the inion referred to linked ears, they investigated 80 normal adults in a more comprehensive fashion, examining components N1, P1, N2, P2 and N3. They found little interhemispheric latency asymmetry (never more than 5 msec) but state that interhemispheric amplitude asymmetries were more common. The amplitude asymmetry though was never more than 50%, and this was the figure adopted as their criterion of abnormality. Intersubject peak latency and amplitude variability was also found to be high, more so for the later than earlier components, the standard deviation of the major positive component, P2, being approx 11.0 msec (mean 118 msec). No quantitative assessment was made of the significance of interhemispheric latency asymmetries.

A higher variability of later compared with early components was also described by Jonkman (1967). He investigated the normal interhemispheric asymmetry, though with a relatively small population (10 subjects),

Fig. 1.3.1. Morphology and nomenclature of the normal FVEP. Various schemes of component labelling are shown at the top of the figure. 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); and the last row is that of Harding (1974) which is used throughout this thesis. (After Harding, 1974).

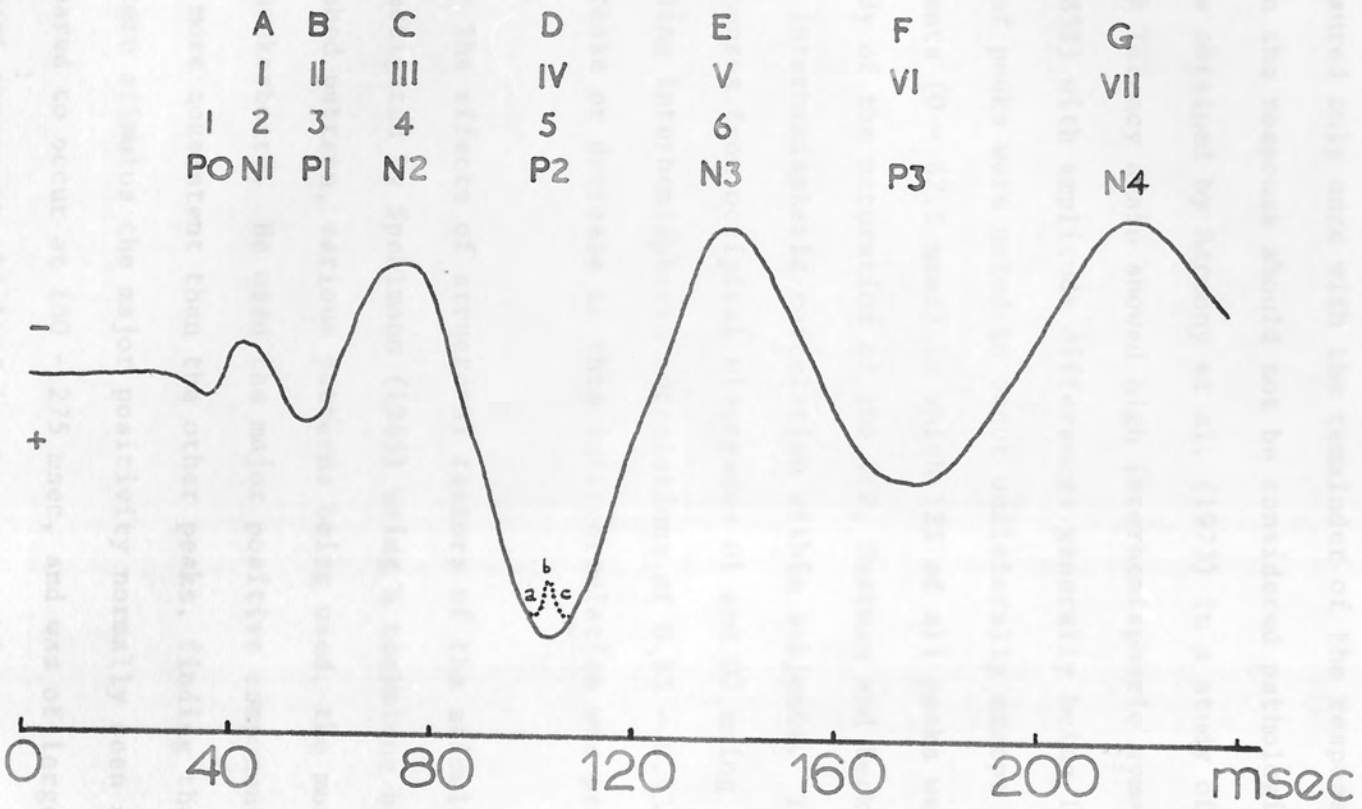

A B C D E F G
I II III IV V VI VII
1 2 3 4 5 6
PO NI PI N2 P2 N3 P3 N4
–
+
a b c
0 40 80 120 160 200 msec

Fig. 1.3.1.

never finding a latency asymmetry of more than 3 msec for peaks N1 - P2, 6 msec being rated as abnormal. The 50% amplitude asymmetry as a criterion of abnormality was accepted by Jonkman, but he qualified this saying that if the asymmetry affected only one component, and was measured only once with the remainder of the response being symmetrical, then the response should not be considered pathological. Similar results were obtained by Harmony et al. (1973) in a study of 139 normal subjects. Peak latency again showed high interhemispheric symmetry (less than 5 msec in 85%) with amplitude differences generally being less than 40%. Only 5% of peaks were noted to occur unilaterally except in the early components (0 - 62.5 msec) in which 12% of all peaks were unilateral. In their study of the maturation of the VEP, Dustman and Beck (1969) also examined the interhemispheric correlation within subjects. They intercorrelated responses from occipital electrodes O1 and O2 using an ear reference, finding interhemispheric correlations of 0.85 - 0.93 in 165 subjects. No increase or decrease in this intercorrelation was present with advancing age.

The effects of structural factors of the stimulus on the VEP were investigated by Spehlmann (1965) using a technique best described as flashed pattern, various patterns being used, the most effective being a checkerboard. He used the major positive component in analysis as this was more consistent than the other peaks, finding that with the flashed pattern stimulus the major positivity normally seen at 100 - 120 msec appeared to occur at 180 - 275 msec, and was of larger amplitude than the largest component elicited in the same subject by diffuse light of the same intensity. An earlier negative component at approximately 100 msec was also usually seen. The pattern specificity of this later positive component was illustrated by the interposition of a 10 dioptre lens between the subject and the stimulus, thus defocussing the pattern, which resulted in a potential similar to that seen with the diffuse flash stimulus.

These pattern related components at approximately 100 msec and 200 msec were investigated more thoroughly by Rietveld et al. (1965) and by Harter and White (1968). Rietveld and his co-workers found that the amplitudes of both the surface negative (at approximately 100 msec) and the surface positive (at approximately 200 msec) components were sensitive to the size of the checks making up the checkerboard. The amplitude of these components was greatest when checkerboard patterns with checks subtending visual angles of 10 - 15 min. of arc were presented, checkerboards with progressively larger or smaller checks resulting in lower amplitudes.

Harter and White (1968) investigated the effects of contour sharpness and check size using patterns with individual check subtenses of 12, 20 and 46 min. of arc viewed through a series of ophthalmic lenses (+6D to -6D), the checkerboards therefore appearing to vary in sharpness of focus under these conditions. Both the negative and positive peaks described by Spehlmann et al. (1965) were found to be sensitive both to the sharpness of focus and the size of the checks, the amplitudes of both components decreasing with increasing dioptre settings. The positive component was found to be of higher amplitude with the smaller checks than the larger. The authors also note that it was possible to determine refractive error by observing the VEP changes which occurred with different lenses. This finding does of course suggest a possible relationship between VEP measures and visual acuity. Further reports of the effects of pattern on the VEP followed (e.g White, 1969; Eason et al., 1970; Harter, 1970 and 1971; Harter and White, 1970; Ciganek, 1971; Uenoyama, 1971) with Dawson et al. (1972) concluding that "as a clinical aid, the VEP and its high frequency correlate the fast occipital potential appear to provide an objective test of the resolving power of the human visual system with an accuracy equal to or exceeding 0.5D sphere". This relationship between visual acuity and the VEP will be further discussed

in later sections of this introduction.

Although various techniques have been described which avoid a luminance component in the stimulus, ranging from the contrast modulation of Millodot and Riggs (1970) and Spekreijse et al. (1972) to the pattern appearance of Jeffreys (1971), the most relevant to this discussion is the technique of pattern reversal. This technique was first described by Cobb and his co-workers (Cobb et al., 1968; Cobb and Morton, 1970) but was more thoroughly investigated by Halliday and Michael (Halliday and Michael, 1970; Michael and Halliday, 1971).

One of the advantages of a stimulus with no overall change in luminance is the ability to selectively stimulate discrete parts of the visual field (largely prevented with luminance-change stimuli due to the light scattering effect of the eye - e.g Brindley and Westheimer's (1965) report that flash stimulation confined to the blind spot can give rise to an electroretinogram). This particular advantage was exploited by Halliday and Michael in their extensive investigation of the VEP's obtained with stimulating fields down to individual octant size.

The pattern reversal stimulus is seen by the subject as a black and white checkerboard pattern which suddenly changes, the black squares appearing to become white and vice-versa. The first reports utilising this technique used either a reversing shutter method (e.g Halliday and Michael, 1970) or a moving mirror method (e.g Cobb and Morton, 1970).

In the reversing shutter method a reversing checkerboard pattern is generated by alternately back-projecting onto a screen, a slide and its negative from two projectors with electronically controlled shutters, the operation of the shutters triggering the averaging computer. In the moving mirror technique a slide of a checkerboard pattern is back-projected onto a screen via a small mirror mounted on the rotating axis of a galvanometer. The mirror is then turned through a small angle causing side-to-side movements of the pattern on the screen.

The potential evoked using the method of pattern reversal is characterised by a major positive component seen at approximately 100 - 120 msec which is seen in all healthy subjects (Halliday and Michael, 1970; Michael and Halliday, 1971; Halliday et al., 1972) and, compared with the relatively high intersubject latency and waveform variability seen with the flash response, is of highly consistent latency and shape within a normal group. The amplitude range for the pattern reversal evoked potential (PVEP) at some 5 - 15μV is similar to that obtained with diffuse flash stimulation (see Fig. 1.3.2 for schematic waveform and description).

Another technique used to elicit the PVEP was described by Behrman et al. (1972). Here a checkerboard screen was constructed out of small squares of Polaroid material arranged so that adjacent squares are polarised in orthogonal planes. This is viewed through an eye piece integral with a second, wheel mounted, polaroid sheet. Rotation of the wheel thus produces a continuously reversing checkerboard of black and white useful at faster stimulus rates (5 - 15 / sec).

More recently television monitors have been used to produce pattern reversal stimulation (e.g Bornstein, 1975; Johnson et al., 1976; Bartl et al., 1978) but this method has been subject to criticism (van Lith et al., 1978). However, if the frame frequency of the television, usually 50 Hz with a resulting total reversal time of 20 msec, is modified to 200 Hz (as suggested by Johnson et al., 1976), a more acceptable reversal time of 5 msec is obtained which may well eliminate the cause for the majority of adverse criticism.

Pattern reversal stimulation has also been achieved using a display of light emitting diodes (LED) linked together in two series so that alternate diodes light simultaneously. The current is switched from one diode chain to the other thus giving an appearance of a pattern reversal (Evans et al., 1974).

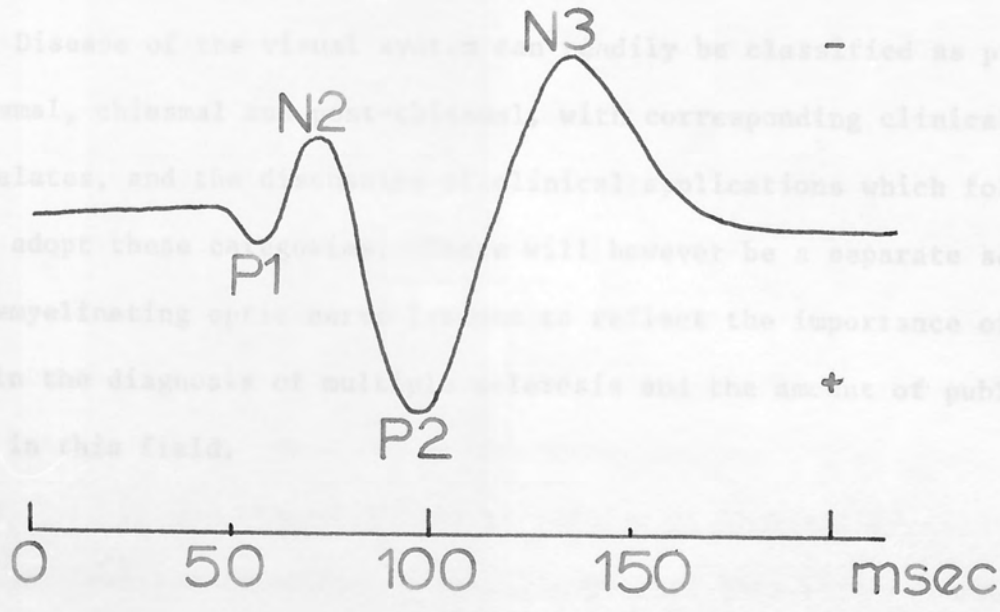


Fig. 1.3.2. The normal PVEP

Following the pioneering work by Halliday and his colleagues (Halliday et al., 1972, 1973) on the use of PVEP in the diagnosis of demyelinating disease, the technique has become an important and well-established weapon in the clinician's diagnostic armament, and clinical PVEP applications will be considered in ensuing sections. Important work has also been published on half-field stimulation in normal subjects (e.g Barrett et al., 1976a, b; Blumhardt et al., 1977), but as this is particularly relevant to the clinical findings in patients with bitemporal and homonymous visual field defects, this again will be discussed in the relevant clinical sections.

Disease of the visual system can readily be classified as pre-chiasmal, chiasmal and post-chiasmal, with corresponding clinical correlates, and the discussion of clinical applications which follows will adopt these categories. There will however be a separate section on demyelinating optic nerve lesions to reflect the importance of the VEP in the diagnosis of multiple sclerosis and the amount of published work in this field.

1.4 The VEP in Demyelinating Optic Nerve Lesions

The first report to describe increased latency of the VEP in demyelinating disease is that of Richey et al. (1971) although a previous paper had reported amplitude reduction in acute optic neuritis (Rouher et al. 1969). Using diffuse flash stimulation Richey and his colleagues recorded the VEP in 50 patients with multiple sclerosis (MS) and compared these with the findings in 50 normal control subjects. The criteria used for the diagnosis of MS is not specified. 40% of the patients were found to have abnormal VEP's, the characteristic abnormality being an increased latency (by 6 - 16 msec) of the major VEP components. No significant amplitude changes were detected. Possibly the most important observation however was that 8 patients had abnormal VEP's out of 17 with symptoms or signs confined to the spinal cord, thus suggesting sub-clinical optic nerve demyelination. The presence of delayed flash VEP's (FVEP's) in optic nerve demyelination was confirmed (Namerow and Enns, 1972) in 20 MS patients all of whom had had at least one episode of retrobulbar neuritis, and all of whom showed abnormally delayed VEP's. Unfortunately the authors do not comment on the proportion of abnormal findings obtained from the asymptomatic eye, but do note that patients whose visual acuity had returned to normal could still show abnormalities in the VEP.

Perhaps the pioneering work in this field though was that of Halliday and his co-workers (1972) who first described the use of pattern reversal as a stimulus in the clinical VEP assessment of optic nerve function. Nineteen patients with unilateral optic neuritis were compared against seventeen normal controls, all except one displaying an increase in latency of the major positive (P2 see Fig. 1.3.1) component. The magnitude of this delay was substantial (normal mean 121 msec; optic neuritis mean 155 msec) with a delay of some 80 msec being recorded in one patient. The mean amplitude value was reduced by some 50%. The authors noted that delayed VEP's could be recorded even up to 5 years

after an episode of optic neuritis and that a persistently increased latency may be present with normal fundi and visual fields. These workers also used flash stimulation and stress the enormous advantages of pattern reversal. The major positive component characteristically seen in the PVEP (pattern reversal evoked potential) in normal eyes was clearly recognisable in the abnormal responses and delays could be clearly evaluated. Also, the spread of latencies from normal eyes was small thus enabling an increase in latency to be detected with confidence in individual cases. The efficiency of the PVEP compared with the FVEP (flash visual evoked potential) was clear in that although slight FVEP delays were noted in some patients, others showed no such delay even where PVEP latency was markedly abnormal.

Halliday and his colleagues then investigated the value of the PVEP in multiple sclerosis (Halliday et al., 1973). They examined 73 patients, 51 of whom satisfied McAlpine's (McAlpine et al., 1972) criteria for 'definite', 'probable' or 'possible' MS. These criteria are described in section 3.3. Of these 51 patients, 49 had a delayed major positive (P2) component including 25 patients with no previous history of optic neuritis. Delays were uniocular in 14 cases and binocular in 35. The outstanding features of this report though are firstly the very high percentage of MS patients who had delayed PVEP's, and secondly that even amongst patients with normal discs and no previous history of optic neuritis the incidence of delayed responses was 86%. These authors then further extended this work (Halliday et al., 1974b) reporting that 48% of patients with progressive spastic paraplegia (13/27) had delayed PVEP's. They conclude that a delayed PVEP, by establishing the presence of a sub-clinical optic nerve lesion, may obviate the need for myelography in certain cases of progressive spastic paraplegia. The same group of workers (Halliday et al., 1974a) had also demonstrated that, in the delayed PVEP of demyelination, there was a significant correlation between visual acuity and the amplitude of

the pattern response but not with the latency, latency delays appearing to persist indefinitely.

This high incidence of PVEP delay in both clinical and sub-clinical optic nerve demyelination has been confirmed by numerous subsequent authors (e.g Asselman et al., 1975; Bornstein, 1975; Hume and Cant, 1976; Lowitzsch et al., 1976; Mastaglia et al., 1976; Wildberger et al., 1976a; Bynke et al., 1977; Celesia and Daly, 1977; Hennerici et al., 1977; Matthews et al., 1977; Zeese, 1977; Hoeppner and Lolas, 1978; Nilsson, 1978; Shahroki, 1978), the more important of which are detailed in Fig. 1.4.1. Although the percentage VEP abnormality in patients with 'definite' MS varies relatively little from group to group (75 - 97%), in the 'probable' and 'possible' categories no subsequent authors have been able to replicate the initial findings of Halliday et al. (1973) of 100% and 92% respectively, and indeed the range of percentage PVEP abnormality in these groups is substantial (33 - 100% for 'probable'; 21 - 92% for 'possible'). This may reflect differences in patient groups and stimulus parameters, but the diagnostic criteria of McAlpine et al. (1972) are rather imprecise, more recent classification schemes (McDonald and Halliday, 1977) being more stringent. Clearly any differences in classification may be expected to be reflected in the PVEP abnormality figures.

Despite the apparently clear advantage of PVEP over FVEP in MS diagnosis (Halliday et al., 1972) some workers have continued to report FVEP findings with varying results. Use of a 5^{o} flashing red stimulus on a blue background was described (Adachi-Usami et al., 1972) as eliciting a marked delay in the response from the affected eye in a patient with acute unilateral optic neuritis. Feinsod and Hoyt (1975) following the earlier work of Feinsod et al. (1973), used a conventional diffuse flash stimulus and report abnormal early components in all of 25 patients with MS, 15 of whom had no visual symptoms or signs.

	Definite		Probable		Possible		Total	P.H.O.N
		%		%		%		
Halliday et al. (1973)	33/34	97	5/5	100	11/12	92	49/51	24/24
Asselman et al. (1975)	26/31	84	5/6	83	3/14	21	34/51	15/15
Hume and Cant (1976)	6/7	86	4/5	80	5/10	50	15/22	5/5
Lowitzsch et al. (1976)	60/73	82	25/42	60	13/20	65	98/135	-
Mastaglia et al. (1976)	19/23	83	3/9	33	12/36	33	35/68	-
Celesia and Daly (1977)	29/37	78	2/6	33	6/10	60	37/53	22/23
Hennerici et al. (1977)	13/16	81	12/18	66	10/23	43	35/57	100%
Matthews et al. (1977)	46/61	75	14/24	58	10/28	36	70/113	30/36
Nilsson (1978)	15/19	79	8/9	89	3/10	30	26/38	13/14
Shahroki et al. (1978)	49/60	82	24/46	52	12/43	28	85/149	54/62
TOTAL %		82		60		41		

(P.H.O.N. - Past history of optic neuritis)

Fig. 1.4.1 Incidence of PVEP Abnormalities in Patients with Multiple Sclerosis

Wildberger et al. (1976a) although using higher frequency (4/sec) stimulation in their comparative study of FVEP and PVEP in optic neuritis, were unable to confirm the high percentage FVEP abnormality reported by Feinsod and Hoyt (1975). Using 15 patients with optic neuritis, 14 were found to have normal FVEP's to total retinal stimulation, 9 with macular stimulation. However the early components studied by Feinsod and Hoyt are not seen with higher frequency stimulation, valid inter-report comparison therefore being difficult. Only 4 of Wildberger's 15 patients had normal PVEP's (8/sec stimulation) again confirming the superiority of pattern reversal stimulation in the detection of optic nerve demyelination.

The early flash components were also studied by Ellenberger and Ziegler (1977). They found abnormal FVEP's in 97% of patients with previous visual symptoms and 56% of visually asymptomatic patients. Neither the presence nor the magnitude of the latency delay correlated with the degree of visual impairment.

Perhaps the most surprising report is that of Hennerici et al. (1977) who compared foveal illuminated rectangle (45' subtense) stimulation with pattern reversal stimulation in 57 patients with MS. Rectangle stimulation (an on-effect of illuminating the rectangle against a uniform background) was found to be more sensitive than pattern reversal with abnormal findings of 94%, 94% and 78% of patients with 'definite', 'possible' and 'probable' MS respectively. Although their check size may be a relevant factor for the PVEP's, a check size of $1^{o}10'$ being thought to provide extrafoveal stimulation, it is of interest that the percentage rectangle VEP abnormalities are closer to the findings initially reported by Halliday et al. (1973) than those of other subsequent authors.

Abnormalities of the steady-state PVEP have also been described in MS (e.g Milner et al., 1974; Regan et al., 1976; Wildberger et al., 1976a).

1.5 The VEP in Non-Demyelinating Pre-Chiasmal Lesions

i) Amblyopia and the VEP assessment of visual acuity

Following the early work of Harter and White (1968) and Millodot and Riggs (1970) a number of authors have examined the relationship between the VEP and visual acuity, both in search of techniques for objective refraction assessment and in the evaluation of amblyopia. This work will be considered in some detail for it is considered important that the nature of any possible VEP abnormalities that can be produced by e.g inadequate refraction should be thoroughly documented to prevent possible misinterpretation in the clinical diagnostic field.

Early results with diffuse flash stimulation were generally equivocal (e.g Nawratzki et al., 1966; Fishman and Copenhaver, 1967) and indeed Lombroso et al. (1969) found normal FVEP's and abnormal flashed pattern VEP's in amblyopic eyes and therefore postulated a specific inhibition of pattern vision in amblyopia. However, Potts and Nagaya (1969), using their 0.06^{o} flashing red stimulus, reported diminished or absent foveal VEP's in strabismic amblyopia, and Tsutsui et al. (1973) found no significant differences between diffuse flash and flashed pattern in various types of amblyopia. These latter authors, who found abnormal VEP's in all cases of stimulus deprivation amblyopia and a high incidence of abnormality in strabismic amblyopia (including some patients with delayed VEP), did however use a low intensity stimulus in contrast to previous investigators.

A more recent comparative study using diffuse flash and flashed pattern stimuli (Levi, 1975) confirmed the results of Lombroso et al. (1969). Normal VEP's were found with diffuse flash stimulation but the flashed pattern VEP's were of significantly reduced amplitude in amblyopic eyes (see also Spekreijse et al., 1972). Although Lombroso and his co-workers only found a 50% incidence of abnormality with the flashed pattern, they used 60' checks in a 60^{o} horizontal, 40^{o} vertical field, Levi using 11' checks in a field of unspecified size. One would expect smaller checks to be more sensitive to reduced visual acuity, and this may well account f

the apparent discrepancy between the two reports.

The majority of recent work has used pattern stimuli with no luminance change. Spekreijse et al. (1972) observed an amplitude reduction to 20' check pattern appearance in one amblyopic patient, no latency change being apparent. Arden and his colleagues (Behrman et al., 1972; Arden et al., 1974) using the steady-state response (6 - 16/sec) to pattern reversal stimuli, observed significant amplitude reductions in 22/36 cases of amblyopia, but also observed phase changes (equivalent to latency changes) in 17 patients, mostly those in whom there was an absence of binocular vision. Amplitude reductions in amblyopic eyes have also been observed by Sokol and Bloom (1972) and Freeman and Thibos (1975); both groups using steady-state evoked potential measures.

A more systematic study was performed by Sokol and Shaterian (1976) again utilising steady-state EP's (12/sec). Normal eyes were found to have maximum amplitude responses to 7.5' and 15' reversing checks (in agreement with the findings of other workers, e.g Harter and White, 1970; Regan and Richards, 1973), but the amblyopic eyes peaked at check sizes of 30' or larger. The authors also note that occasionally the response amplitude was larger in the amblyopic eye for a given check size and suggest that VEP's recorded from amblyopic eyes to a single check size should be treated with caution.

More recently Wanger and Nilsson (1978) examined the PVEP in 10 patients with amblyopia. An initial trial with 14/sec stimulation failed to elicit significant differences between their normal group and the patient group; subsequent recordings used 1.4 reversals/sec. Interocular amplitude asymmetries were observed in 4 patients (occasionally the amblyopic eye producing the larger response) but significant latency delays were also observed in 4 patients. Two of these showed an interocular latency asymmetry of abnormal magnitude and in the other two patients the latencies from the amblyopic eyes fell outside the normal range.

Visual acuity assessment using evoked potential measures has also been reported (e.g Sokol and Dobson, 1976; Marg et al., 1976; Regan, 1977b).

ii) Other pre-chiasmal lesions

Rather surprisingly in view of the amount of work published recently in optic nerve demyelination, there are relatively few reports dealing with other forms of optic nerve disease, many of the reports that do exist examining only a few cases. Because of the important contribution of the macula to the VEP (e.g Regan and Heron, 1969) macular lesions will also be discussed in this section.

Of the early workers using diffuse flash stimulation, Vaughan and Katzman (1964) reported that patients with severe retinal disease or optic nerve disease show loss, alteration or suppression of the VEP from the affected eye, also stressing the value of the ERG (electroretinogram). Copenhaver and Perry (1964) using a 2.5^{o} stimulus demonstrated VEP amplitude reduction of greater than 50% in 14/18 patients in a 'neural' group consisting of macular scars, tumours and degenerations, optic neuritis, etc, those patients with reduced acuity displaying greater percentage reduction compared with the fellow eye. Jacobsen et al. (1968) found variable amplitude reduction in 8 patients with retinitis pigmentosa (2 patients with absent VEP); 13 cases of 'optic atrophy or optic neuritis' displaying reduced amplitude occasionally accompanied by latency delay. The prognostic value of the FVEP in amblyopia and cataract, prior to therapy or surgery, has also been investigated (Arnal et al., 1972; Thompson et al., 1977).

Following the introduction of the PVEP to the clinical field (Halliday et al., 1972), the majority of more recent reports have utilised this type of stimulus. Wilson (1978) studied 15 patients with ischaemic optic neuropathy. Using 60' check pattern reversal and diffuse flash stimulation 4 patients were found to show minor latency delays (less than 10 msec), whereas 13 patients showed a significant amplitude reduction

(assessed as less than 50% of the normal mean amplitude). The extent of the amplitude reduction was thought to be related both to the degree of involvement of central vision and to the extent of the visual field defect. Normal findings were always obtained in the unaffected eye (c.f.optic nerve demyelination) and no significant differences were observed between pattern reversal and diffuse flash stimulation. PVEP abnormalities in ischaemic optic neuropathy had previously been noted by Asselman et al. (1975) who found that 3 patients had 'delayed' PVEP's and by Hennerici et al. (1977) who found that 5 patients had delayed PVEP's, this delay also occurring with their rectangular foveal flash stimulus. Unfortunately neither of these authors supply any further information. Ikeda (1978) describes 6 patients with ischaemic optic neuropathy as having delayed PVEP's of subnormal amplitude, but in a case report the PVEP from the affected eye was delayed by only 2 msec with respect to the normal controls. There was, however, a significant interocular asymmetry of 20 msec, the affected eye also showing an amplitude reduction of some 40% compared with the unaffected eye.

VEP changes have also been noted in optic nerve compression. Pre- and post-operative recordings were taken by Feinsod and Auerbach (1971) in two patients with tuberculum sellae meningiomata using a diffuse flash stimulus. Prior to decompression the FVEP was reduced or absent from the affected eye, a post-operative improvement in one patient being parallelled by an improvement in the FVEP. Asselman et al. (1975) found 'delayed' VEP to pattern reversal stimulation (PVEP) in two patients but no further information is provided.

A more detailed description of PVEP changes in optic nerve compression has been provided by Halliday and his co-workers (Halliday, 1976; Halliday et al., 1976). The finding of delayed PVEP was confirmed in these studies, the authors noting that the maximum delay seen (33 msec with a pituitary tumour and suprasellar extension) is less than the mean delay seen

in optic nerve demyelination. Amplitude reductions and gross distortion of the waveform were also thought to be more characteristic of compression than demyelination. Uniocular delays, possibly accompanied by amplitude reduction and waveform distortion have since been described by subsequent authors (Hume and Cant, 1976; Ikeda et al., 1978) in suprasellar extensions of pituitary tumours, but this work, together with a more detailed discussion of Halliday's findings will be considered in the section dealing with lesions of the optic chiasm.

VEP abnormalities have also been described in optic nerve trauma. Arden (1973) reported a case of facial injury resulting in a fracture of the inferior plate of the orbit. Although the visual acuity was only reduced to 6/18 in the affected eye the steady-state VEP to a 9' check reversing pattern was virtually absent. The FVEP was also abnormal, but the authors note that the pattern response was clearly more sensitive.

Use of the FVEP as an indicator of optic nerve damage following major trauma to the eye has been described (Crews et al., 1975), absence of the FVEP in complete avulsion of the optic nerve also being reported (Hillman et al., 1975).

Leber's and other heredo-familial optic atrophies have so far received little attention. Halliday (1976) describes a replacement of the PVEP major positivity by a negativity in patients with central scotomata, Leber's optic atrophy being included in this category. Dorfman et al. (1977) recorded serial PVEP's in two brothers with Leber's optic atrophy during the active phase of the disease. Prior to the onset of the disease PVEP's were normal, the earliest abnormalities to appear being prolongation of latency or an unusual morphology characterised by a double positive peak. During the subsequent deterioration in visual acuity, there was a parallel increase in PVEP latency accompanied by a less consistent amplitude reduction. Eventually the PVEP became extinct. Asymptomatic family members were all found to display no PVEP abnormality. The difference

between these findings and those suggested by Halliday (1976) may be related to the larger check size (1^{o} 50' compared with Halliday's 50') used by Dorfman and his colleagues.

A similar finding of delayed PVEP was recently described by Carroll and Mastaglia (1978) who thoroughly investigated, both clinically and electrophysiologically, 54 members of a family with Leber's optic neuropathy. In the 14 patients with definite disease, 8 patients had absent PVEP's from both eyes, 3 patients displaying uniocular PVEP absence. Delayed responses were recorded in 4 eyes and a widened response with a normal latency was observed from one asymptomatic eye. Of interest, and in disagreement with the findings of Dorfman et al. (1977), is that atypical or mildly abnormal VEP changes, either mildly delayed, widened or atypical bifid positivities, were recorded in asymptomatic family members, some 'at risk', some 'not at risk'. The findings were thought to indicate demyelination with axonal degeneration.

There has also been little published work on toxic or nutritional amblyopia. Van Balen (1971) found an absent FVEP in the late stages of optic nerve damage caused by iodochlorhydroxyquinoline. Halliday (1976) describes one case of tobacco/alcohol amblyopia in whom the PVEP changes were typical of the changes they associate with central scotomata - the normal major positivity being replaced by a negative wave of similar latency. Changes in the FVEP with anti-malarial drugs are described by Paty et al. (1976) in 18 patients using white, red and blue stimulation. Fifteen patients were on long-term treatment with quinoline derivatives for chronic disease (rheumatoid arthritis or S.L.E), 3 receiving prophylactic anti-malarial treatment only. Large interindividual variations were observed but marked delays associated with amplitude reduction are described in 8 patients. The effects of the different wavelength stimuli are obscure, and clinical findings (? any reduction in visual acuity) not reported.

Contrary to the findings of both Halliday (1976) and Paty et al. (1976),

Ikeda et al. (1978) describe PVEP findings of bilaterally reduced amplitude but with no latency delay in 17 patients (1 West Indian amblyopia, 1 quinine amblyopia and 15 tobacco/alcohol amblyopias). However it is noticeable in the detailed results table that both eyes of one tobacco/alcohol patient displayed markedly improved (by 18 msec) latencies following B12 injections. Delayed PVEP's have also been reported in myxoedema (Mastaglia et al., 1978) and more recently in Parkinsonism (Bodis-Wollner and Yahr, 1978), the magnitude of the latter delays being reduced by dopamine therapy.

Delayed PVEP's in glaucoma (Cappin and Nissim, 1975 - steady-state PVEP; Bartl, 1978) have also been reported, the latter authors also describing amplitude reductions strongly related to the value of intraocular pressure.

Normal PVEP's were found by Asselman et al. (1975) in two patients with papilloedema, presumably, though not specified by the authors, without secondary optic atrophy and reduced visual acuity.

The effects of unilateral disciform degeneration of the macula on the FVEP were studied by Roper-Hall et al. (1971), FVEP abnormalities having previously been reported in macular disease (Fishman and Copenhaver, 1968). Stimulation of the affected eye produced, apart from a generally reduced amplitude response, a marked suppression in the major positive (P2) component. In the cases of bilateral disciform degeneration, the response from the more affected eye was worse, with an intact P1 component but virtually absent P2.

Absence of the steady-state PVEP (10' checks) was described by Behrman et al. (1972) in a patient with a macular cyst and visual acuity of 1/60. Use of 30 - 40' checks however, said to stimulate the paramacular retina, resulted in findings similar to those in the unaffected eye. A similar absence of the steady-state PVEP in macular disease was reported by Sokol (1972). A reduced PVEP amplitude with normal latency is described by

Sanders (1976) in a patient thought to have suffered an acute maculopathy. Sandberg et al. (1977) however report absent or out of phase VEP's in 6 patients with macular degenerations. These authors used a 1.5^{o} flickering (5/sec) stimulus superimposed on a steady 10^{o} background in a stimulator ophthalmoscope.

1.6 The VEP in Chiasmal Lesions

Muller (1962) studied the flash response in 10 patients with bitemporal hemianopia, 5 patients showing an increased latency of the cortical response. Vaughan and Katzman (1964) studied a single patient with an asymmetrical bitemporal hemianopia (O.D> O.S). Stimulation of the left eye showed a reduced FVEP amplitude over the right hemisphere, stimulation of the right eye displaying a bilaterally reduced response. FVEP changes in a single patient with bitemporal hemianopia are also reported by Jacobsen et al. (1968). They found a small FVEP over the hemisphere ipsilateral to the stimulated eye, with a much reduced or absent contralateral response. A single patient with a traumatic split of the optic chiasm is described by Fisher et al. (1968). This patient exhibited a normal positive going potential over the hemisphere ipsilateral to the stimulated eye whereas the hemisphere contralateral to the stimulated eye always showed an inverted response. An analysis of the potential distributions in this patient indicated that the potential evoked from each eye could be accounted for by a single generator in the ipsilateral cortex, confirming loss of the contralateral component (Lehmann et al., 1969).

A patient with bitemporal hemianopia from a craniopharyngioma was studied by Kooi et al. (1973). Confirming previous reports the response over the hemisphere ipsilateral to the stimulated eye corresponded to that commonly observed in normal adults, the contralateral response being distinctly different, particularly in the first 100 msec. Topographic field analysis showed ipsilateral voltage maxima for all major components, only their wave VI (approximately 190 msec) appearing to have a bilateral field distribution.

Steady-state pattern reversal stimulation was used by Wildberger et al. (1976) in their study of 6 patients with bitemporal hemianopia from chiasmal compression. Using 30' checks in a 24^{o} field and using O2 - C4,

O1 - C3 derivations, stimulation of the right eye resulted in reduced amplitude left hemisphere responses; stimulation of the left eye produced a reduced right hemisphere response. No definite phase changes are noted by these authors, purely the amplitude reduction contralateral to the stimulated eye.

In the same year a thorough study was published by Halliday et al. (1976) of PVEP changes in 10 patients with chiasmal compression (9 pituitary tumours, 1 craniopharyngioma). These authors used 50' checks in a 32^{o} field and recorded the PVEP from electrodes situated 5 cm anterior and 5 cm lateral to the inion referred to a mid-frontal reference. PVEP abnormalities of amplitude reduction, latency delay and/or waveform distortion were seen in all patients but, rather surprisingly, the abnormalities were localised ipsilaterally to the stimulated eye and therefore ipsilaterally to the visual field defect. The contralateral response was less abnormal, the degree of abnormality being determined largely by the extent of optic nerve involvement in suprasellar extension. This ipsilateral abnormality localisation, not reported by previous authors, clearly does not correspond with the findings that would have been predicted on a purely neuroanatomical basis. In one patient with a pituitary adenoma, abnormal responses were recorded following stimulation of a clinically normal eye indicating that, as in MS, optic nerve dysfunction may be detected with PVEP prior to its clinical appearance. It is of interest here that Hume and Cant (1976) also describe an ipsilateral abnormality localisation in a single patient with bitemporal hemianopia from a pituitary adenoma. These authors used 40' checks in a 20^{o} field, the PVEP being recorded from O2 and O1 referred to linked ears. The authors suggested that their findings indicated lesions of the non-crossing fibres, though examined in the light of the findings of Halliday et al. (1976), this clearly may not be the case.

The nearest experimental model we have to patients with hemi-field defects is the use of half-field stimulation in normals. Although the use

of luminance change stimuli is fraught with difficulties due to light scatter within the eye, Eason and White (1967) reported that FVEP's from the right occipital area were greater in amplitude when the temporal retina was stimulated than when the nasal retina was stimulated. They suggested that this was probably due to the anatomical absence of fibres projecting from the right nasal retina to the right occipital cortex. Recording over both hemispheres Eason et al. (1967) found that the occipital area receiving primary projections from the retinal area stimulated produced larger amplitude FVEP's than that in the other hemisphere. These findings were supported by Andreassi et al. (1975) who, using X's as stimuli via a computer display terminal found that when stimuli appeared in the left visual field the right occipital area produced latencies shorter than those simultaneously recorded over the left and vice-versa for stimuli presented in the right visual field.

PVEP findings with hemi-field stimulation have however been less consistent. Cobb and Morton (1970) reported that the occipital PVEP to half-field stimulation was maximal contralaterally to the stimulated half-field using a transverse bipolar chain of electrodes. Subsequent work (Barrett et al., 1976a) has however suggested that this contralateral localisation is in fact an artefact of the recording technique. Using the same electrodes referred to a mid-frontal reference these latter authors found the PVEP to be maximal ipsilaterally to the stimulated half-field.

This paradoxical lateralisation of the PVEP to half-field stimulation was further described (Barrett et al., 1976b). With the relevant electrodes situated 5 cm anterior and 5 cm lateral to the inion referred to a mid-frontal electrode, the PVEP was recorded to 50' checks contained in a 16^{o} semi-circular field extending 16^{o} out from the fixation point. The maximum response was invariably recorded over the hemisphere ipsilateral to the stimulated field. The authors suggest that this may be due to the positioning of the visual cortical generator areas on the medial and

postero-medial surface of the hemisphere, where the neurones are transversely oriented. The ipsilateral electrodes are therefore optimally situated to 'view' the cortical surface of the opposite hemisphere. The authors predict on the basis of these results that patients with hemifield defects will display, to full field stimulation, the abnormality ipsilaterally to the field defect, and indeed their work on chiasmal compression (Halliday et al., 1976) which has previously been discussed appears to confirm these predictions. It should be noted however that when Barrett et al. (1976b) confine their stimulation to the macular area, the response "becomes less well lateralised, and may even have a contralateral predominance". The authors suggest that this is compatible with the cortical representation of the macula at the occipital pole with the generator neurones facing posteriorly rather than medially. Further investigations by these authors (Blumhardt et al., 1977) have confirmed this paradoxical lateralisation of the half-field response.

The effects of half-field stimulation in normals have also been thoroughly investigated by Shagass et al. (1976), obtaining results somewhat comparable with those found by Lehmann et al. (1969) in their split chiasm patient. The PVEP's recorded contained four peaks, 1) a major positivity at approximately 95 msec seen contralaterally to the stimulated field, negativity occurring ipsilaterally; 2) a predominantly ipsilateral positive component at approximately 125 msec; 3) a predominantly ipsilateral negative component at approximately 165 msec; and 4) a midline positivity at approximately 225 msec. Recording with a transverse bipolar electrode chain resulted in largely contralateral PVEP's due to the effects of potential gradient confirming the findings of Barrett et al. (1976a). The authors stress the importance of stimulus and recording parameters on the potentials obtained.

The FVEP, using stimulators under the eyelids, has also been used to monitor optic nerve and chiasmal function during parasellar surgery (Wilson et al., 1976).

1.7 The VEP in Post-Chiasmal Lesions

In addition to those lesions specifically involving the posterior visual pathways, the findings in patients with more diffuse conditions, or with specific lesions not directly involving the anterior visual pathways, will be discussed in this section.

Cohn (1963) using 3 - 10/sec flash stimulation reported a prominent interhemispheric amplitude asymmetry in all patients with homonymous hemianopia, in some patients the lower amplitude potentials evoked in the affected hemisphere showing only a second harmonic component. The author noted that these changes were more reproducible than findings obtained using 1/sec stimulation. Vaughan et al. (1963) studied the FVEP (1.5/sec, eyes closed) from electrodes placed 1 cm anterior and 3 cm lateral to the inion referred to a vertex electrode in 19 patients with unilateral cerebral lesions with no visual field defect and in 30 patients with homonymous visual field defects. These authors confined their analysis to waves I, II and III of Ciganek (1961), i.e N1, P1 and N2 in this author's nomenclature. Significant interhemispheric asymmetries were observed in both the hemianopic and the non-hemianopic groups, component P1 being most useful as component N1 was not seen in some 33% of their normal control group. This amplitude asymmetry was of greater magnitude in the hemianopic group, latencies also being significantly extended in the patients with visual field defects. The mean interhemispheric amplitude asymmetry in the normal control group was some 20% with an amplitude asymmetry of greater than 50% being considered as abnormal. None of the non-hemianopic controls fell outside the 50% abnormality criterion but 16 of the 25 hemianopic patients in whom component P1 could be identified exceeded this limit. Those patients with macular sparing were most likely not to show a significant amplitude reduction, the authors emphasising the contribution of the central visual field to the FVEP and concluding that visual defects only involving peripheral areas of the field may not be

reflected as abnormalities in the FVEP. Of the 18 patients with homonymous visual field defects involving the central 10^{o} studied by Vaughan and Katzman (1964), 15 showed a unilateral amplitude reduction of greater than 50% in component P1, the abnormality occurring on the side of the lesion.

Kooi et al. (1965) examined the FVEP (eyes open) in 29 patients with homonymous visual field defects and 19 patients with a unilateral hemisphere lesion but no visual involvement. All of the 23 patients with hemianopic defects showed an asymmetrical response, the presence or absence of macular involvement not particularly influencing the findings. Two of the 6 patients with quadrantanopias had symmetrical FVEP's. The most characteristic abnormalities in visual pathway damage were delayed latency of components N1 and P1, and amplitude reduction of component N3. Seven patients were examined in whom previously documented visual field defects had resolved, all showing symmetrical FVEP's. Contrary to the findings of Vaughan et al. (1963), an absence of component P1 was not thought indicative of visual pathway involvement as this absence was observed in the left hemisphere traces of 2 normal subjects and in the right hemisphere traces of 3 normal subjects.

The effects of surgically induced occipital lobe lesions on the FVEP were studied by Crighel and Botez (1966) in 9 patients following surgical treatment of intracranial space-occupying lesions. The FVEP was usually found to be absent or reduced, but in 2 patients an amplitude increase on the side of the lesion was seen in recordings from the parietal areas.

The FVEP changes in patients with posterior visual pathway involvement, and in patients with space-occupying lesions not directly involving these pathways, were comprehensively studied by Jonkman (1967) in a large number of neurological patients with varying neurological disease. Differing from the consistent abnormalities reported by some previous workers (e.g Kooi et al., 1965), some patients with homonymous hemianopia were found to display no significant FVEP asymmetry. Conversely some cerebral lesions were

accompanied by highly asymmetrical responses even though there was no clinical visual pathway involvement. Of the 39 patients in whom VEP asymmetry was observed, 29 showed an amplitude asymmetry of greater than 50% in one or several components. In 19 cases there was a difference in latency of more than 5 msec in one or more of the components up to and including P2, and 24 of these 39 patients showed marked asymmetry in response morphology which could not be expressed in terms of amplitude or latency asymmetries. In some cases this asymmetry was so gross as to preclude amplitude or latency evaluation. An asymmetry of the rhythmic after activity (reduced on the side of the lesion) was also seen in some patients. It is of interest that in some frontal or fronto-temporal tumours an increased amplitude was observed on the side of the lesion, occasionally the response also being of shorter latency. FVEP changes in intracranial space-occupying lesions were also observed by Bergamini and Bergamasco (1967), who found that in all cases of visual pathway involvement the ipsilateral FVEP was altered in comparison with that of the unaffected hemisphere.

Schneider (1968) also noted the relevance of the site of the lesion on the FVEP changes as previously reported by Jonkman (1967). The more posteriorly situated the tumour, the more marked the effects on the FVEP, and the earlier these effects appeared. Unilateral reduction or abolition of the rhythmic after activity on the side of the lesion was also noted in some patients. An interhemispheric FVEP asymmetry in patients with sub-thalamic lesions but no visual field defect was reported by Crighel and Poilici (1968). No such asymmetry was seen in medullary or midbrain lesions but late components were bilaterally increased.

Jacobsen et al. (1968) examined the FVEP in 7 patients with homonymous hemianopia and macular sparing. Component N1 was usually normal, components P1 and N2 showing amplitude reductions or latency delays, N2 being affected to a greater degree than P1. Gross interhemispheric FVEP asymmetry was

thought to be characteristic. Some patients with partial hemianopic defects displayed no significant asymmetry but in one patient the sensitivity of the technique was increased by the use of sinusoidally modulated as opposed to square wave flash stimulation.

The effects of cerebrovascular disease on the FVEP were examined by Oosterhuis et al. (1969). They studied 30 patients, 6 of whom had a hemianopic visual field defect. Contrary to the findings of Vaughan et al. (1963) and in agreement with those of Kooi et al. (1965) these authors did not consider the absence of components N1 and P1 as pathological. They found that the primary (60 - 100 msec) and secondary (100 - 300 msec) responses, and the VEP as a whole, were more frequently abnormal in patients with severe pathology than in those with moderate pathology. An abnormal asymmetry of the secondary response only occurred in patients with visual field defects, confirming the findings of Jonkman (1967), but in two patients with homonymous hemianopia and macular sparing the FVEP was normal. The authors report the possibility of loss or attenuation of the rhythmic after activity on the side of the lesion, but also quote two patients in whom an ipsilateral increase in rhythmic after activity (the after discharge of Ciganek) was observed. They also concluded that the FVEP from parieto-occipital areas appeared to provide a better indicator of cerebral disturbances than the occipital to ear derivations.

The relevance of recording parameters was also stressed by Harding et al. (1969) who recommended the EEG technique of phase reversal to localise the VEP to the relevant occipital electrode in patients with homonymous visual field defects. They conclude that this technique is an efficient means of eliminating some of the interpretative problems caused by the large FVEP variability in a normal population. In the patients there was an absence of phase reversal at the occipital electrode contralateral to the visual field defect.

Bergstrom and Nystrom (1970) examined the FVEP in 32 patients with

varying cerebral pathology. Half the patients were fully conscious, half being comatose. No significant differences were seen between the comatose and non-comatose groups. FVEP's were frequently abnormal (interhemispheric amplitude asymmetry greater than 50% or response absence) either unilaterally or bilaterally, the presence of an asymmetrical response always indicating a predominantly unilateral lesion. Seven patients had asymmetrical rhythmic after activity, always reduced or absent on the side of the lesion. The authors also raise the question as to whether abolition or severe distortion of the FVEP represents the greater degree of abnormality.

Further studies of the FVEP in cerebrovascular disease were performed by Crighel and Sterman-Marinchescu (1971). They examined 19 patients (46 - 72) between the 2nd and 5th day following a severe stroke. Normal responses were seen in 7 patients, absent responses in three. An interhemispheric asymmetry occurred in 6 patients, 5 with sylvian artery thrombosis, 1 with carotid thrombosis. The authors conclude that the FVEP is an indicator of the background cerebral functional state as a result of cerebral atherosclerosis; only in a few cases was the FVEP thought to be influenced by the acute lesion.

The presence of a VEP in a patient with severe bilateral occipital lobe damage following a gunshot wound was found by Feinsod and Auerbach (1973) to indicate a good prognosis for visual recovery even though clinical examination predicted cortical blindness. No interhemispheric asymmetry assessment was possible due to the use of midline recording electrodes. Duchowny et al. (1974) reported 6 cases of 'cortical blindness' in children following trauma or bacterial meningitis. Their findings suggested that the short latency components (less than 100 msec) correlated with the level of visual function, component P1 being most sensitive. In one case with homonymous hemianopia there was selective FVEP reduction at the occipital electrode contralateral to the visual field defect. Abraham et al. (1975) studied patients with occipital blindness from basilar artery occlusion.

Responses of normal morphology and amplitude were followed by complete visual recovery. An absent FVEP correlated with permanent blindness and the authors report that "unequal and subnormal VEP's obtained after monocular stimulation and even small responses reached after binocular stimulation accompanied permanent occipital lobe damage resulting in homonymous hemianopia". It is interesting that an interocular asymmetry should be reflected as a hemianopic visual field defect, mid-line recording only being used! A single case of occipital blindness had previously been reported (Jayle et al., 1971) where the FVEP displayed an inter-hemispheric asymmetry and the patient was left with an homonymous hemianopia.

The FVEP in 4 patients, with lesions in varying parts of the post-chiasmal visual pathways was studied by Feinsod et al. (1975). They concluded that optic radiation involvement was indicated by a delay in the initial FVEP component; that striate cortical involvement obliterated both early and late FVEP components; and that suprastriate involvement was indicated by selective loss of late components over the affected hemisphere. A suprastriate involvement leading to 'suprastriate hemianopia' had previously been described (Feinsod et al., 1974).

Kooi et al. (1975) reported post-traumatic FVEP changes. Of particular note being one patient in whom there was virtual absence of the FVEP over one hemisphere but without any evidence of a visual field defect. Similar patients have also been studied by Feinsod et al. (1976) confirming Kooi et al.'s (1975) suggestion that the FVEP can be used to distinguish between organic and non-organic post-traumatic visual impairment.

The FVEP was studied in 28 patients with homonymous visual field defects by Galkina et al. (1975), 21 of whom had 'complete' homonymous hemianopia. All of these 21 patients had abnormal FVEP's, being characterised by unilateral absence of the FVEP, a decrease in amplitude of some or all of the FVEP components or an increased latency. This uni-lateral abnormality was observed over the hemisphere contralateral to the

visual field defect. Of particular interest though is that of patients with lesions predominantly affecting the mediobasal areas of the temporal lobe, and with hemianopic field defect due to involvement of the optic radiation, responses in half of these were of increased amplitude on the affected side.

The first use of patterned stimuli was reported by Regan and Heron (1969). Using their technique of simultaneously stimulating both half-fields with stimuli of similar but not identical frequency (e.g 18.0, 18.5/sec) and separating the responses to each half-field by means of Fourier analysis, they found that in a patient with homonymous hemianopia and macular sparing following posterior cerebral artery occlusion, that the response to sinewave modulated flash stimulation in the affected field was reduced, the response to pattern stimulation being normal. The authors attribute this difference to the dependency of the pattern response on central vision.

Wildberger et al. (1976) using 8/sec stimulation studied the steady-state PVEP (30' checks) in 6 patients with homonymous hemianopia. There was a reduction in VEP amplitude over the affected hemisphere in all cases, but no apparent difference between patients with or without macular sparing. Hemi-field stimulation was also found effective by these authors.

The PVEP in a single patient with left homonymous hemianopia following removal of an arteriovenous malformation at the right occipital pole is described by Blumhardt et al. (1977), using 50' checks in a 32^{o} field. On the side of the lesion the PVEP was normal whereas over the normal hemisphere, where neuroanatomy would predict the normal PVEP to occur, a channel 5 cm from the midline showed only a small positive deflection, a further laterally placed channel showing no response. Recordings from patients with more extensive occipital lobectomies (no further details supplied) also showed paradoxical lateralisations where although the PVEP was recorded over one hemisphere, it was clearly being generated in the other. These findings are consistent with those predicted from half-field

stimulations in normals (Barrett et al., 1976a, b) and from full-field stimulation in patients with bitemporal hemianopia (Halliday et al., 1976) which have previously been reported by the same authors.

Reports have also appeared of the VEP in a number of other conditions e.g Usher's syndrome (Abraham et al., 1977); hyperoxia (Crighel et al., 1966); frontal lobe tumours (Crighel et al., 1976); in epilepsy (Crighel et al., 1974) in coma ((Ogashiwa and Saito, 1973; Kawamura et al., 1975) and in late infantile neuronal lipidosis (Harden and Pampiglione, 1972).

1.8 The VEP in Non-Organic Visual Loss

The nature of the visual evoked potential, in providing objective assessment of the function of the afferent visual pathways, has been used to evaluate the reliability of patients' claims of impaired vision in the absence of physical signs. The relevant findings are those of completely normal VEP's when symptoms reported by the patient would suggest otherwise.

Potts and Nagaya (1969) reported that patients with hysterical amblyopia displayed completely normal foveal VEP's (0.06^{o} red flashing stimulus), whereas, in their study, all patients with strabismic amblyopia showed diminished or absent foveal VEP's. The use of the FVEP in hysterical amblyopia was also described by Adams et al. (1969) but these authors also warn against the unequivocal acceptance of VEP criteria, citing the case of one patient with almost certain hysterical amblyopia in whom scotopic FVEP anomalies were observed.

Subsequent reports, though mostly using only a few patients, have confirmed this FVEP normality in non-organic visual loss (e.g Harding, 1974; Lazurus, 1974; Beck et al., 1975; Behrman and Levy, 1975). The use of the FVEP in disclosing the non-organic basis of suspect symptoms following trauma has also been described (Kooi et al., 1975; Feinsod et al., 1976).

Halliday (1973) describes the use of the PVEP in hysterical visual loss, normal PVEP's being recorded from both eyes in patients with markedly asymmetrical (down to no perception of light) visual acuities. Clearly one would expect to see a marked interocular PVEP asymmetry in the presence of such a marked interocular visual acuity asymmetry. The technique was thought to be most useful with uniocular visual loss where there is a good eye to act as a control. The author also stresses that the PVEP, despite strongly suggesting non-organic visual loss, does not preclude the existence of some organic disease.

1.9 Resume

From the large amount of published work reviewed in the preceding sections of this introduction, the use of the visual evoked potential can readily be seen to be well-established in the confirmation or determination of the nature of existing lesions; in the detection of sub-clinical lesions; and in the objective demonstration of intact retino-cortical transmission despite subjective reports implying the contrary. Clearly though there are areas of contention and areas where there is little published work. In addition, the astute reader has undoubtedly noticed that, since the introduction of the PVEP to the clinical field (Halliday et al., 1972) the number of reports using flash stimulation has decreased, most recent work concentrating on pattern reversal stimulation.

The purpose of this study is to compare the FVEP and the PVEP in a variety of neuroophthalmic and neurological conditions to determine whether the increasing disuse of the FVEP is justified. The study will also hopefully expand our knowledge in those fields where there is either a lack of published research or where those findings that are published are in contention.

CHAPTER TWO

METHODOLOGY

2.1 Subject Matter

2.1.i Patients

The patients who form the experimental material for this study all attended for VEP examination between April 1975 and December 1978 at the South East Thames Regional Department of Clinical Neurophysiology, situated at the Brook General Hospital. The majority of these patients were referred either by the Consultants of the Regional Neurological and Neurosurgical Units based at the same hospital or by the Consultant Ophthalmologists based at nearby Greenwich District Hospital. VEP examination was performed either on an out-patient or an in-patient basis. No referrals were accepted from General Practitioners. All patients therefore received thorough investigation and in a high proportion of the patients in this study the diagnosis was established with a high degree of certainty. In those few cases where doubt remains the diagnosis was generally established by exclusion methods. Undiagnosed cases have, for the large part, not been considered.

In some patients the final diagnosis was independent of the VEP findings. It is inevitable though that in other patients the VEP was involved in the diagnostic process since a clinical VEP service was available and a large number of the patients described in this thesis were referred for VEP examination as a routine investigation. Further details of VEP involvement in the final diagnosis will be discussed where relevant.

An exception to the unselected nature of most of the subject matter for this study are the patients who form the optic nerve demyelination group. The finding of delayed PVEP, and to a lesser extent delayed FVEP, is now well-established in the diagnosis of both clinical and sub-clinical optic nerve demyelination. However there is some discrepancy between authors as to the percentage of abnormal findings in multiple sclerosis (MS) - see section 1.4 and Fig. 1.4.1 - and it was therefore decided to

investigate this aspect of the VEP in optic nerve demyelination. The patients selected for inclusion in this group were the first one hundred patients under the age of 60 referred for in-patient VEP examination at the Brook Hospital in 1978 with a possible diagnosis of MS (?MS). Although this selection precludes a long follow-up period during which the appearance of further symptoms or signs may have altered the degree of certainty with which the diagnosis had been established, it was felt that the degree of certainty at the time of VEP examination should be the relevant factor. In-patients were selected rather than out-patients because 1) the thorough nature of the initial neurological examination at the time of admission and its full documentation in the case notes; 2) the (relative) ease of obtaining these case notes following discharge from hospital; and 3) the comprehensive range of investigative procedures available at the Brook Hospital, particularly in the neuroradiological field, which enabled the presence and nature of possible alternative pathology to be accurately determined.

Throughout the thesis it is proposed that the 'results' and 'discussion' sections will be combined according to the anatomical site of the lesion as used in the introduction. Further clinical details of all patients studied will be included in the relevant sections for ease of reference.

2.1.ii Normal Controls

Prior to the assessment of an individual patient's VEP examination as normal or abnormal, the criteria upon which this assessment is based must be determined. It is also essential that normal values are established by each individual laboratory as variations in stimulus and recording parameters can markedly influence the VEP (e.g Halliday et al., 1973).

Over 100 volunteers formed the control group for the PVEP. These comprised healthy individuals (mostly medical, technical and nursing staff), patients with no evidence of neurological disease (mostly orthopaedic patients awaiting or following cold surgery - generally these were older

subjects) and neurological patients with no evidence of optic nerve or cerebral involvement (mostly peripheral neuropathies or compressive cord lesions).

Unfortunately the FVEP's were not recorded in many of these subjects and the normal control group for the FVEP therefore consists of a smaller group of subjects; some healthy individuals (medical, technical and nursing staff) and some neurological patients with no evidence of optic nerve or cerebral involvement.

The findings in these subjects will be documented in a subsequent section.

2.2 Examination Procedure

The technique for recording the visual evoked potentials was, as far as possible, identical for all subjects. The laboratory in which the examination was performed, the background illumination during the recording session, the stimuli and the recording equipment were unchanged throughout.

On arrival the patient was seated in an adjustable, mechanically operated dentist's chair with a neck rest to ensure optimum comfort and the investigation procedure explained. The scalp was then measured and silver-silver chloride stick-on electrodes applied according to Pampiglione (1966) but with two occipital electrodes, situated 2 cm anterior and 2 cm lateral to the inion replacing the single midline occipital electrode. This is commonly called the Modified Maudsley system of electrode placement and is standard practice in this department.

Bipolar occipital-sylvian and occipital-parietal recordings were taken, the choice of these particular electrodes being based on experience gained by this author at the Neuropsychology Unit, University of Aston in Birmingham (see Harding, 1974), these electrode positions conforming fairly closely with those of the International 10 - 20 system (Jasper, 1958) used in that unit. Electrodes were also placed above the right eye (left eye in patients with right ocular palsies) and at the outer canthus of the eye so that horizontal and vertical eye movements could be monitored throughout the recording session. Electrode resistances were less than 5 kilohms. The four channels used are illustrated in Fig. 2.2.1.

From the scalp the signals were fed into an 8 channel EEG machine (S.L.E, Croydon, England) with a frequency response flat from 0.5 to 50.0 Hz, and thence to a Datalab Biomac 1000 averaging computer sampling every 1.3 msec. The primary EEG trace, in addition to any eye movements or blinks, was therefore monitored throughout the recording session.

Pattern reversal stimulation was provided by a Digitimer moving

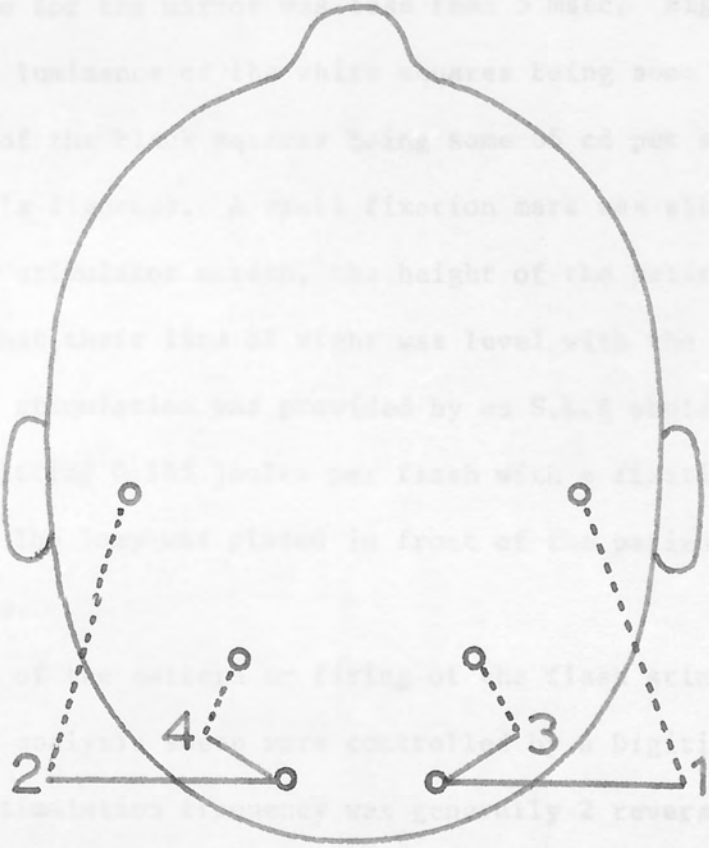


Fig. 2.2.1. Electrode montage

mirror stimulator routinely situated 80 cm from the patient and subtending a total field of 11^{o} with an individual check subtense of 26'. Additional stimulation was occasionally performed with 13' checks in an 8^{o} total field, with 48' checks in a 20^{o} total field, and with some other variations in field and check size which will be discussed where appropriate. Excursion time for the mirror was less than 5 msec. High contrast pattern was used, the luminance of the white squares being some 1085 cd per square metre; that of the black squares being some 85 cd per square metre (manufacturer's figures). A small fixation mark was situated in the centre of the stimulator screen, the height of the patient's chair being adjusted so that their line of sight was level with the fixation mark. Diffuse flash stimulation was provided by an S.L.E photostimulator (Xenon discharge) emitting 0.145 joules per flash with a fixation mark in the centre of the lamp. The lamp was placed in front of the patient, 30 cm from the patient's eyes.

Movement of the pattern or firing of the flash stimulus and initiation of the Biomac analysis sweep were controlled by a Digitimer 4030 pulse generator. Stimulation frequency was generally 2 reversals per second or 2 flashes per second with an analysis time of 320 msec. Responses were usually the average of 128 sweeps but on occasions 256 or even 512 stimulations were necessary to obtain a satisfactory trace. Pattern stimulation was always performed with the patient's vision corrected by spectacles where relevant. Flash stimulation was performed with vision uncorrected. Each eye was examined at least twice in all patients, the fellow eye being occluded. If excessive eye movements or blinks were present the run was discarded. Further repeats were performed whenever there was inconsistency of the waveform. The rhythmic after activity was elicited by binocular diffuse flash stimulation with the eyes closed using a cycle time of 720 msec and an analysis time of 640 msec.

Occasionally it was thought necessary to examine gross retinal function

using the electroretinogram (ERG). This was recorded from surface stick-on electrodes placed on the lower eyelids directly under the pupils in the primary position of gaze and at the outer canthi (see also Vaughan and Katzman, 1964; Jacobsen et al., 1968; Gilthrow-Tyler et al., 1978). An analysis time of 80 msec with a cycle time of 160 msec was used, the ERG's generally being the result of 16 or 32 stimulations.

The potentials displayed on the Biomac screen were written out by a Bryans 26000 A3 X-Y plotter to give a permanent record which was used for analysis.

CHAPTER THREE

RESULTS AND DISCUSSION

3.1 VEP Analysis

One of the main problems, though rarely discussed when dealing with multi-phasic potentials, is that of quantification. The features of interest are the latencies and amplitudes of each consistent deflection or component and although latency measurements are straightforward, amplitudes can be assessed either by peak-to-peak or baseline-to-peak measurements. Some authors have mixed both types of measurement (Goff et al., 1962) or have even required that a component must cross the baseline to be measured at all (Domino et al., 1964), thereby disregarding events which are consistent and possibly relevant.

Baseline-to-peak measures present the not inconsiderable problem of accurately establishing the baseline. Of course, once the 'baseline' has been established, amplitudes assessed in relation to this give rise to numerical data vastly different from peak-to-peak measures. There are also problems with polarity. If a positive-going peak begins negative to the baseline and fails to reach it then it will be considered as a negative value in measurement; if however it does cross the baseline it will then be considered as positive.

Peak-to-peak measurements however are purely descriptive of the multi-phasic curve and do not complicate matters with the above-mentioned, potentially serious inconveniences. In particular, the points of component onset and completion, determined partially by the immediately preceding activity, do not affect decisions on polarity. It is purely the polarity direction and the magnitude of the change which are taken into account.

In view of these considerations peak-to-peak amplitude measurements, along with latencies, were taken. In both the FVEP and the PVEP the major positive, P2 component (see Figs. 1.3.1 and 1.3.2 for details of component nomenclature) is clearly seen in the vast majority of subjects and this was taken as the reference for amplitude measurements, the N2-P2 and P2-N3 peak-to-peak amplitudes normally being considered. Detailed measurements

were taken from the occipito-sylvian traces (see Fig. 2.2.1) all measurements being the average of at least two trials for each eye. These findings were compared with those of the normal control groups (see section 3.2) and it should be noted that the findings in a given patient were only rated as abnormal if the abnormality found was reproducible. If no consistent abnormality was seen the findings were assessed as normal.

3.2 Normal Controls

i) Pattern visual evoked potential (PVEP).

One hundred and three subjects form the control groups for the PVEP. Analysis for clinical purposes centred on the major positive P2 component and, as peak-to-peak amplitude measurements were taken, negative components N2 and N3 (see Fig. 1.3.2 for nomenclature). In a significant proportion of subjects an earlier positive deflection, component P1, was also observed. Analysis of P1 latency but not amplitude is also included. These results are detailed in Figs. 3.2.1 and 3.2.2. These groups comprise both healthy volunteers and patients with no history of optic nerve or cerebral involvement. Some of the healthy individuals had amblyopic eyes. The findings from such eyes have been excluded from the analysis.

Of equal importance to the absolute latency and amplitude values in the magnitude of any possible interocular or interhemispheric asymmetry. These values are shown in Fig. 3.2.3. The ratios were calculated with the higher value as the numerator.

In addition six subjects above the age of sixty were seen. These values have not been detailed due to the high variability present in this group (interindividual not intraindividual) whose P2 latencies varied from 96 to 115 msec with a mean of 104 msec.

The PVEP values obtained, although different in absolute latency and thereby re-emphasising the need for each separate laboratory to establish its own control values, confirm earlier reports (e.g Halliday et al., 1972, 1973; Asselman et al., 1975 etc.) of the low variability and high consistency of the PVEP latency and the higher variability of the PVEP amplitude. For absolute latency values three standard deviations from the mean was set as the level of abnormality against which the findings in patients were assessed. None of the control subjects exceeded this value. Three standard deviations was used in an attempt to exclude any 'false positives'. The amplitude distributions may not follow a normal distribution and an arbitrary lower limit of normality was set

Age group		P1 (msec)	N2 (msec)	P2 (msec)	N3 (msec)	N2-P2 (μV)	P2-N3 (μV)
9 - 11	$\bar{x}$	55.10 (10)	72.56	105.39	137.67	18.09	13.49
N = 18	S.D.	1.20	2.57	3.53	7.32	5.56	6.66
NS = 9							
	$\bar{x}$+3S.D.	59	81	116	160		
14 - 19	$\bar{x}$	55.29 (24)	70.16 (31)	95.59	132.00 (30)	11.09	11.79
N = 32	S.D.	2.18	3.68	4.58	6.81	4.84	4.04
NS = 17							
	$\bar{x}$+3S.D.	62	82	110	153		
20 - 29	$\bar{x}$	54.69 (36)	69.34	94.09	127.66	7.05	8.82
N = 53	S.D.	2.42	3.08	2.96	7.19	3.62	3.58
NS = 27							
	$\bar{x}$+3S.D.	62	79	104	150		

N = No. of eyes

NS = No. of subjects

$\bar{x}$ = mean

S.D = standard deviation

The figures in brackets refer to the number of eyes displaying the given component when less than the total number of eyes.

Fig. 3.2.1. PVEP Normal Control Groups (9 - 29)

Age group		P1 (msec)	N2 (msec)	P2 (msec)	N3 (msec)	N2-P2 (μv)	P2-N3 (μv)
30 - 39	$\bar{x}$	55.88 (26)	71.63	94.70	128.05	6.55	9.49
N = 40	S.D	2.10	2.48	3.30	5.36	2.06	4.32
NS = 20							
	$\bar{x}$+3S.D.	63	80	105	145		
40 - 49	$\bar{x}$	55.25 (12)	69.70	94.00	126.41	7.96	11.62
N = 22	S.D	1.60	4.45	3.75	7.49	2.67	5.63
NS = 11							
	$\bar{x}$+3S.D.	61	84	106	149		
50 - 59	$\bar{x}$	57.20 (11)	73.46	97.88	135.73	8.07	12.08
N = 26	S.D	2.90	3.44	3.70	8.67	2.85	5.10
NS = 13							
	$\bar{x}$+3S.D.	66	84	109	162		

N = No. of eyes

NS = No. of subjects

$\bar{x}$ = mean

S.D = standard deviation

The figures in brackets refer to the number of eyes displaying the given component when less than the total number of eyes.

Fig. 3.2.2. PVEP Normal Control Groups (30 - 59)

Fig. 3.2.3. PVEP Normal Values

	mean	S.D.	mean + 3S.D.
Latency			
Interocular asymmetry P2 latency (msec)	1.07	0.92	3.84 (3)
Interhemispheric asymmetry P2 latency (msec)	1.12	1.04	4.24 (0)
Amplitude			
Interocular ratio N2-P2/N2-P2	1.14	0.16	1.63 (2)
Interocular ratio P2-N3/P2-N3	1.11	0.12	1.48 (3)
Interhemispheric ratio N2-P2/N2-P2	1.15	0.13	1.55 (1)
Interhemispheric ratio P2-N3/P2-N3	1.14	0.14	1.56 (4)

S.D. = standard deviation

The figures in brackets refer to the number of subjects who exceeded the mean + 3.S.D. value.

at 2.0μV, no control subject displaying either an N2-P2 or P2-N3 amplitude of less than this value. The upper limit of normal latency for those subjects over the age of sixty was set at 118 msec, some 10 msec above that for the group of subjects in the next youngest decade.

The interocular and interhemispheric latency values when the three standard deviation limits had been calculated, were exceeded by a very small number of subjects, never reaching more than 5 msec however, and 6 msec was therefore adopted as the criterion for an abnormally large interocular or interhemispheric latency asymmetry. The interocular and interhemispheric amplitude ratios were similarly exceeded by a few subjects, never reaching more than 1.8, and 2.0 was taken as abnormal i.e. a 50% asymmetry of amplitude, either interocular or interhemispheric, was taken as abnormal.

As previously noted the control groups consist of both healthy individuals, neurological patients with no evidence of optic nerve or cerebral involvement (mostly compressive cord lesions or peripheral neuropathies) and orthopaedic patients awaiting or following cold surgery. There are occasionally difficulties in establishing control groups due to the reluctance of people to volunteer for 'medical experiments', the unavailability of suitably aged subjects, etc. To examine the validity of mixing healthy individuals and patients a comparison was made of the means of the P2 component latencies in the 'normal patients' and the volunteer normals above and below the age of thirty-five but excluding the children and the over-sixties. The means of these groups did not differ significantly using the student t statistic (below 35: P2 at 94.92 msec, S.D. 3.73 for patients; 94.64 msec, S.D. 3.53 for normals, $t = 0.4$. Above 35: P2 at 95.18, S.D. 3.54 for patients; 95.14, S.D. 3.98 for normals, $t = 0.04$). The use of 'normal patients' as control subjects would therefore appear valid. Indeed it could be argued that the fact of hospitalisation may induce psychological differences in

patients from healthy individuals which may possibly affect the VEP. These findings do not support this argument.

Particularly noteworthy in these normal values are the changes in latency with age, and the importance of a control group covering a wide age spectrum, rather than for example a student population, is noted.

ii) Flash visual evoked potential (FVEP).

Thirty-five ophthalmologically normal subjects (other than possible refractive errors) aged 18 - 58 (mean 35.2) formed the control group for the FVEP. Some of these were healthy volunteers (medical, technical and nursing staff, mostly the younger subjects) and some were neurological patients with no evidence or history of optic nerve or cerebral involvement (mostly peripheral neuropathies or compressive spinal cord lesions). The latencies of components N1, P1, N2, P2 and N3 were measured where possible along with the N2-P2 and P2-N3 peak-to-peak amplitudes. The reader is referred back to Fig. 1.3.1 for description of the waveform. These findings are detailed in Fig. 3.2.4. The mean values for the interocular and interhemispheric amplitude and latency asymmetries are shown in Fig. 3.2.5. The ratios were computed with the larger value as the numerator.

Three standard deviations from the mean was adopted as the limit of normality for the latency measurements, a lower limit of 2.0 μV for the absolute amplitude. For the interhemispheric and interocular latency and amplitude values, 6 msec was adopted as representing a significant latency asymmetry, an amplitude ratio of 2.0 being adopted to represent abnormality (i.e the lower amplitude 50% of the higher). These values were not exceeded or reached by any of the normal control group, the closest being an interhemispheric amplitude ratio of 1.9 from one eye in one subject.

A comparison of these findings with those for the PVEP clearly shows the markedly less variable latency seen with pattern reversal stimulation, the main advantage of the PVEP in clinical usage. The FVEP amplitudes

	N1 (msec)	P1 (msec)	N2 (msec)	P2 (msec)	N3 (msec)	N2-P2 (μV)	P2-N3 (μV)
$\bar{x}$	58.16 (43)	72.31 (29)	83.15 (53)	112.59	147.13 (68)	7.22	7.82
S.D.	4.83	5.91	8.03	7.38	17.29	3.65	3.35
$\bar{x}$ + 3S.D.	72.64	90.04	107.25	134.71	199.01		

The figures in brackets indicate the number of eyes displaying the given component if less than the total number of eyes (70).

$\bar{x}$ = mean

S.D. = standard deviation

Fig. 3.2.4. FVEP values in 35 control subjects (mean age 35)

Fig. 3.2.5. FVEP Normal Values

	mean	S.D.	mean + 3S.D.
Latency			
Interocular asymmetry P2 latency (msec)	1.82	1.18	5.37 (0)
Interhemispheric asymmetry P2 latency (msec)	1.34	1.38	5.49 (0)
Amplitude			
Interocular ratio N2-P2/N2-P2	1.18	0.17	1.70 (0)
Interocular ratio P2-N3/P2-N3	1.17	0.20	1.77 (1)
Interhemispheric ratio N2-P2/N2-P2	1.30	0.17	1.82 (1)
Interhemispheric ratio P2-N3/P2-N3	1.25	0.17	1.76 (2)

S.D. = standard deviation

The figures in brackets refer to the number of subjects who exceeded the mean + 3S.D. value.

are however of very similar variability to the PVEP amplitudes in absolute terms but display a greater interocular and interhemispheric asymmetry.

3.3 Optic Nerve Demyelination

The patients in this group, having all been referred with a possible diagnosis of multiple sclerosis (?MS), were classified according to the criteria of McAlpine (McAlpine et al., 1972). Although recent criteria are more stringent (McDonald and Halliday, 1977) it was felt that a valid comparison with the results of other authors could only be attempted if the same diagnostic criteria were adopted. McAlpine's criteria are as follows:

Definite multiple sclerosis. 1) A history of an acute retrobulbar neuritis or of an episode of paraesthesiae, motor weakness, double vision, unsteadiness in walking or other symptom known to occur in multiple sclerosis which tended to improve or clear up, followed by one or more relapses during the course of years with, in addition, the presence of pyramidal and other signs indicative of multiple lesions in the central nervous system when the patient was first seen or subsequently. In mild cases these signs may remain minimal for many years.

2) A gradual onset of a paraplegia later followed by relapses and signs indicative of disease in brain-stem, cerebrum or optic nerve.

Probable multiple sclerosis. 1) During the original attack clinical evidence of multiple lesions which, at the time, suggested the probability or possibility of multiple sclerosis, followed by a good recovery. During a lengthy follow-up, relative or complete absence of fresh symptoms after the first year but with a tendency to variability in pyramidal and other signs originally present or the occasional late appearance of an extensor plantar response, nystagmus, tremor, or temporal pallor of a disc.

2) A history of one or more attacks of acute retrobulbar neuritis accompanied or followed by pyramidal or other signs, usually mild in degree. Subsequently no evidence of relapse.

Possible multiple sclerosis. 1) A history similar to that described under Probable (1) but with unusual features or a paucity of signs, or

insufficient follow-up information.

2) A history of a progressive paraplegia, usually in early middle-age without evidence of relapse or remission or of a lesion outside the spinal cord, appropriate investigations, including myelography, having excluded other causes of progressive paraplegia such as cervical spondylosis, spinal cord tumour and motor neurone disease.

Within this classification however no provision exists for the patient with a non-remitting/relapsing progressive paraplegia and signs suggestive of an additional lesion outside the spinal cord such as nystagmus, dysarthria or a pale disc. Patients with a history similar to this were classified as 'Probable' MS.

It should also be noted that as the role of PVEP in the diagnosis of MS was clearly established it is possible, as this examination was performed as a clinical service, that of these 100 patients, more patients with non-demyelinating spinal cord lesions will be included than in a centre without a clinical PVEP service. This is because PVEP examination would be requested in the hope of establishing a second lesion in the central nervous system and thus obviating the need for myelography even though a compressive cord lesion may have been suspected on clinical grounds. Similarly in some patients with abnormal PVEP's myelography was not performed but probably would have been had a clinical PVEP service not been available. Patients falling into this latter group have been incorporated into the classification criteria as if a normal myelogram, excluding compression as a cause of paraplegia, had been performed. Electrophysiological evidence per se of a lesion in the central nervous system has not been incorporated into the scheme of classification.

Of the 100 patients, 18 had Definite MS, 11 Probable MS and 17 Possible MS. There were 19 patients in whom a definite alternative diagnosis was established (see Fig. 3.3.1), the other 35 remaining undiagnosed. Of these 11 were suspected of having MS, 24 of not having MS

Fig. 3.3.1

Established alternative diagnoses in patients referred with suspected multiple sclerosis

Cerebrovascular disease	4
Disc lesion/cervical spondylosis	4
Intramedullary spinal cord tumour	2
Heredo-familial cerebellar degeneration	1
Peripheral neuropathy	1
Polyneuritis	1
Arachnoid cyst	1
Sarcoidosis	1
Motor Neurone Disease	1
Myasthenia Gravis	1
Uraemia	1
Functional	1
TOTAL	19

Fig. 3.3.2

Undiagnosed cases referred with suspected multiple sclerosis

Spinal cord lesion	13
Brain stem lesion	10
Cortical lesion	2
Vestibular neuronitis	2
Functional	2
Trigeminal neuralgia	1
Drug toxicity	1
Benign Intracranial Hypertension	1
Paroxysmal positional vertigo	1
Other	2
TOTAL	35

(see Fig. 3.3.2). None of the 100 patients had an acute retrobulbar or optic neuritis at the time of VEP examination.

The VEP findings in these patients can be seen in Fig. 3.3.3, abnormalities in the PVEP referring to the presence or absence of the major positive, P2, component compared with the normal control group. Flash VEP latencies were usually within normal limits, an abnormal FVEP often indicating the presence of an interocular latency asymmetry of abnormally large magnitude. 'Visual involvement' was determined by a) the presence on examination of disc pallor, an afferent pupillary defect or a central scotoma or b) the presence in the history of previous visual symptoms referrable to optic nerve dysfunction such as an episode of retrobulbar neuritis or uniocular blurring of vision or the presence of an uncorrectable visual acuity of 6/12 or below with no ophthalmological complications.

One potentially disastrous finding would be that of 'false positive' results, particularly in a patient with a compressive spinal cord lesion where the earliest surgical intervention possible is called for and where the presence of delayed PVEP may cause myelography not to be performed. In one patient with myasthenia gravis a significant interocular latency asymmetry acuity in the PVEP but there was considerably reduced visual acuity in the eye showing the longer latency which improved with pinhole correction. As the presence of reduced visual acuity produced by a 3 dioptre lens can increase the latency of the PVEP P2 component by some 20 msec (Duwaer and Spekreijse, 1978), this asymmetry has been discounted. In only one patient then without MS, and referred with ?MS was the PVEP abnormal. In this patient there was a significantly large interocular latency asymmetry, the absolute latency values from each eye falling within normal limits. The patient was found to be suffering from neurological sarcoid with unilateral optic nerve involvement.

There were 18 patients with Definite MS, 16 of whom had delayed PVEP's.

	Multiple Sclerosis			Undiagnosed		
	Definite	Probable	Possible	?MS	Not MS	Other diagnosis
No. of patients	18	11	17	11	24	19
Abnormal PVEP	16	10	8	2	0	1
Abnormal FVEP	9	5	2	0	1	1
Clinical optic nerve involvement	13	6	2	0	0	1
% abnormal (PVEP)	89	91	47			

Fig. 3.3.3 VEP abnormalities in 100 patients referred with suspected multiple sclerosis. See text for further details.

In 4 patients this delay was unilateral, in 12 bilateral. Only 9 of these patients had abnormal FVEP's. In one patient there was a bilateral delay, in one patient a unilateral delay, the remaining 7 patients displaying an interocular latency asymmetry of abnormally large magnitude.

Four of the 10 Probable MS patients had unilaterally delayed PVEP's, 5 bilaterally delayed PVEP's with the remaining patient showing a significant interocular latency asymmetry. Only 5 patients had abnormal FVEP's, this abnormality occurring bilaterally in 2 patients, the other 3 displaying abnormal interocular asymmetries.

Of the Possible MS patients 8 had delayed PVEP's, this delay occurring bilaterally in 4 patients and unilaterally in 2 patients. The other 2 patients had abnormal interocular latency asymmetries. Only 2 of this group had abnormal FVEP's, each representing an interocular latency asymmetry. A third patient displayed a unilaterally poorly formed FVEP compared with the fellow eye which was normal, but no definite latency asymmetry was seen.

In no patient with MS was the FVEP latency increased by more than 25 msec compared with normal or the fellow eye. The maximum PVEP delay was 97 msec.

It can also be seen that in the undiagnosed (not MS) group one patient had an abnormal FVEP. This was a 23 year old male with a one year history of both legs shaking uncontrollably when stretched, an 8 month history of stiffness in both legs and more recent weakness of the right hand. On examination there was a spastic paraplegia with a right sided emphasis and bilateral extensor plantar responses and a slight spastic weakness in the right arm. There was no sensory loss. Although originally thought to be suffering from multiple sclerosis he then developed wasting of the spinati and small muscles of the hand with fasciculation of the deltoids, spinati and triceps and the diagnosis of MS was considered unlikely. In his VEP's, the PVEP was normal but the left eye FVEP showed

an interhemispheric latency asymmetry of some 12 msec, the latency being longer in the right hemisphere traces. The significance of this finding is uncertain. The right eye FVEP was normal.

The mean PVEP latency values for the three groups of MS patients are shown in Fig. 3.3.4. The patients were also separated into two groups on the basis of there having been previous visual symptoms in the relevant eye (retrobulbar neuritis or blurring of vision). There is a highly significant difference between the mean P2 latency of those patients with and without visual symptoms ($p < 0.001$).

In contrast to the latency values, the amplitude of the PVEP was seldom abnormal, and abnormal amplitude values were usually seen in conjunction with reduced visual acuity. Unfortunately as only 4 eyes in the patients studied had a visual acuity of less than 6/12, a correlation between PVEP amplitude and visual acuity was impossible. The dissociation between amplitude and latency changes is illustrated by those MS patients with bilaterally normal visual acuity and unilateral PVEP abnormality. Although there is a highly significant difference between the normal and abnormal eyes for P2 latency, no such difference is seen in amplitude (see Fig. 3.3.5). FVEP amplitude values were non-informative.

Typical VEP findings are illustrated in Figs. 3.3.6 - 3.3.9; the case histories being as follows:

a) J.K Fig. 3.3.6. Five years prior to admission this 52 year old lady had suffered from an episode of diplopia which had resolved. Six weeks prior to admission she had experienced blurring of vision in the right eye of one week's duration. For four weeks prior to admission she had had nausea, vomiting, unsteadiness and some tingling in her fingertips. For two weeks she had suffered from drooping of the left eyelid with some blurring of vision. On examination there was bilateral ptosis, reduced adduction of both the right and left eyes, a partial left with a possible right 3rd nerve palsy, bilateral pyramidal signs in the limbs right

Fig. 3.3.4 Mean latency values of the P2 component in 52 eyes with abnormal PVEP in 46 patients with multiple sclerosis

	Definite MS	Possible MS	Probable MS
No visual symptoms	123.11 (18)	126.11 (9)	114.25 (8)
Previous visual symptoms	144.50 (10)	143.20 (5)	140.00 (2)

Combined values

	mean	S.D	N
No visual symptoms	121.86	14.87	35
Previous visual symptoms	143.59	25.33	17

The difference between the means of the patients with and without previous visual symptoms is significant at $p < 0.001$ ($t = 3.9$; $df = 50$).

Fig. 3.3.5 Dissociation of PVEP amplitude and component P2 latency changes in 8 patients with multiple sclerosis, normal visual acuity and unilateral PVEP abnormality.

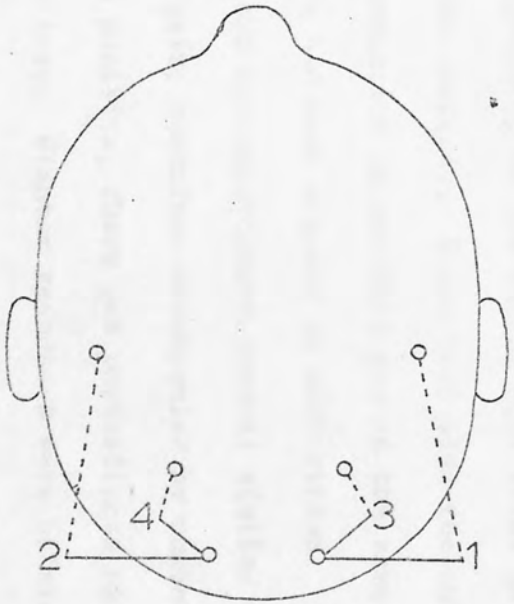
	Normal eye		Abnormal eye			
	Mean	S.D	Mean	S.D	t	
P2 latency (msec)	100.38	4.24	120.50	10.86	4.74	$p < 0.001$
N2 - P2 amp. (μV)	8.54	4.96	6.29	3.52	0.98	NS
P2 - N3 amp. (μV)	11.65	5.03	10.26	4.79	0.53	NS

NS - not significant

Fig. 3.3.6. VEP findings in a 52 year old lady with multiple sclerosis. (The broken vertical line indicates the upper limit of normal latency). See text for details.

J. K. aet 52

V.O.D. J2 V.O.S. J2



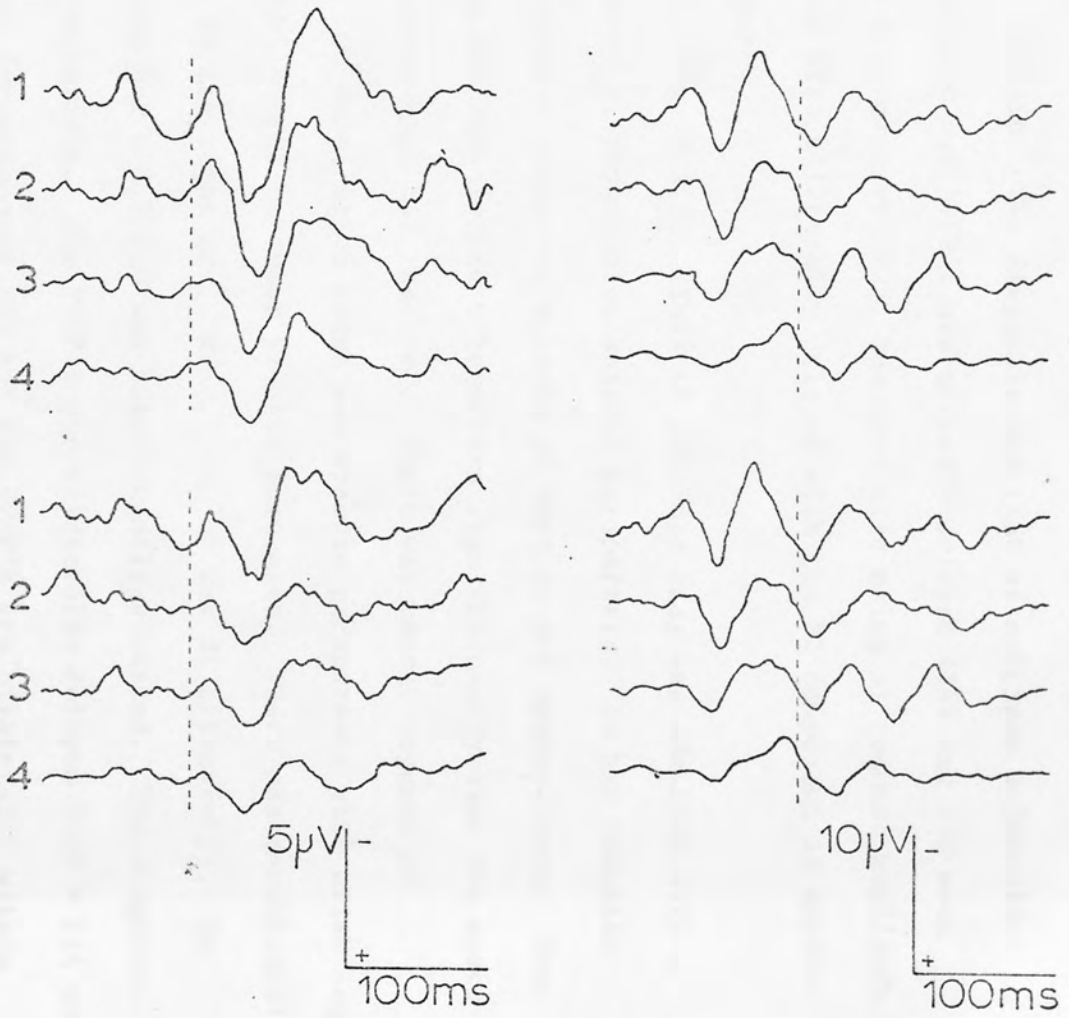


Fig. 3.3.6.

greater than left, with bilateral extensor plantar responses. Visual acuity was J2 bilaterally. In her C.S.F the IgG was greater than 25% of the total protein. The diagnosis was that of multiple sclerosis. The right and left eye PVEP's are markedly delayed (149 and 150 msec respectively for component P2), the left also being of reduced amplitude. The FVEP's are also bilaterally delayed with the P2 component at approximately 145 msec.

b) T.B Fig. 3.3.7. This 48 year old lady was admitted with a two year history of progressive spastic paraparesis. In her twenties she had experienced recurrent attacks of vertigo and unsteadiness. Some years ago she had experienced L'hermittes sign frequently over the space of several years which had resolved. There was recent urgency of micturition. On examination there was spastic paraparesis with brisk leg reflexes and bilateral extensor plantar responses. There was questionable sensory loss in the right arm. Visual acuity was J1 bilaterally. On lumbar puncture her C.S.F. IgG was significantly elevated. The diagnosis was multiple sclerosis. The PVEP's are bilaterally delayed (O.D = 114 msec; O.S = 121 msec for component P2) but the FVEP's are bilaterally within normal limits.

c) K.D Fig. 3.3.8. Three months prior to admission this 31 year old lady had unsteadiness of gait. It started with numbness in the lower part of both legs spreading to the thorax over three days. Her legs felt heavy and walking was unsteady. Since that time the numbness had gradually cleared. A heavy sensation in the left arm at the same time had resolved. For two months there had been urgency of micturition. In the previous five years the patient had experienced several similar episodes, usually of unsteadiness of gait, sometimes accompanied by numbness. On examination Rhomberg's sign was positive, there was unsteadiness of gait and a poorly performed heel-shin test. Plantar responses were bilaterally extensor. The right-sided abdominal reflexes were absent. There was bilateral loss

Fig. 3.3.7. VEP findings in a 48 year old lady with multiple sclerosis. (The broken vertical line indicates the upper limit of normal latency). See text for details.

T. B. aet 48
V.O.D. J1 V.O.S. J1

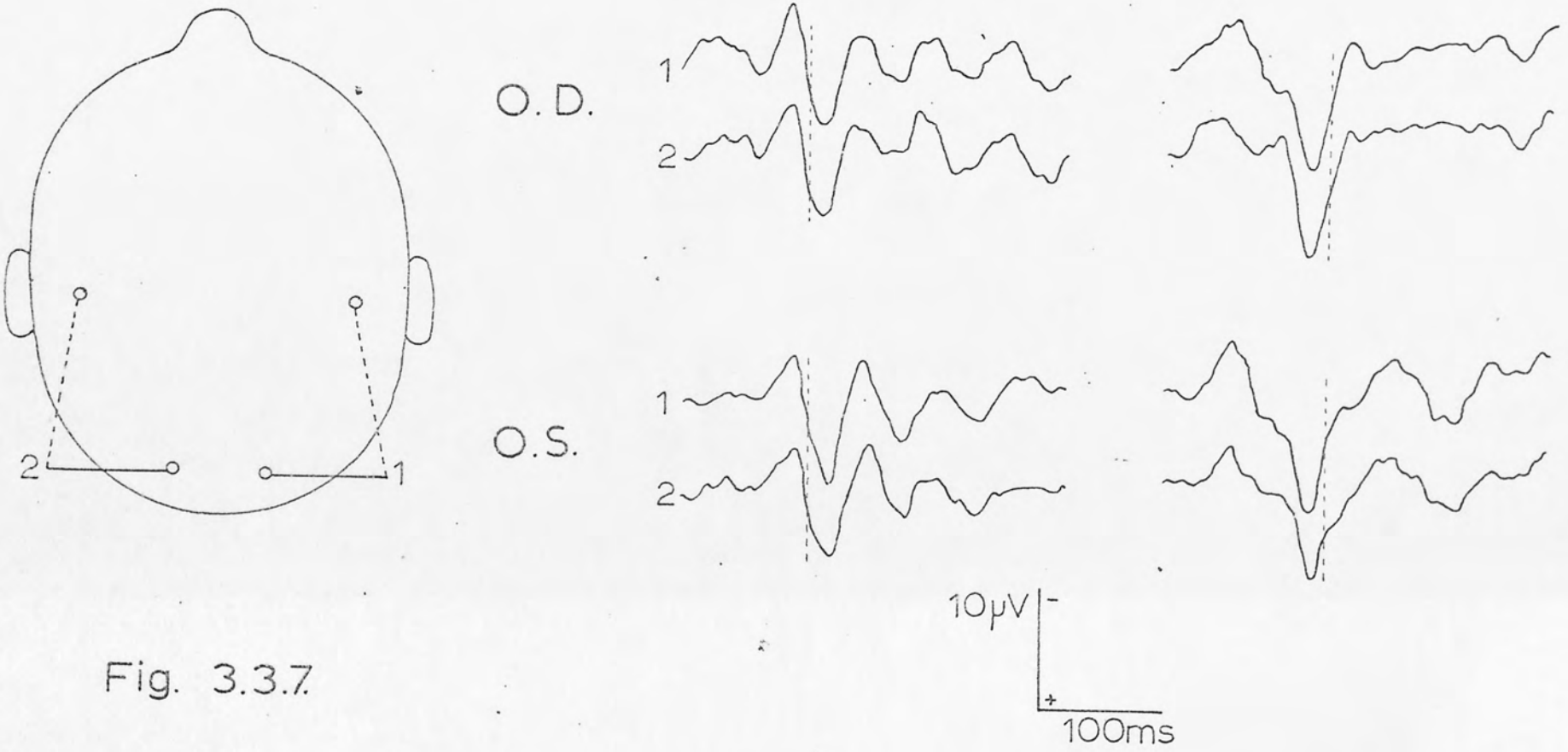


Fig. 3.3.7.

Fig. 3.3.8. VEP findings in a 31 year old lady with multiple sclerosis. (The broken vertical line indicates the upper limit of normal latency). See text for details.

K.D. aet 31

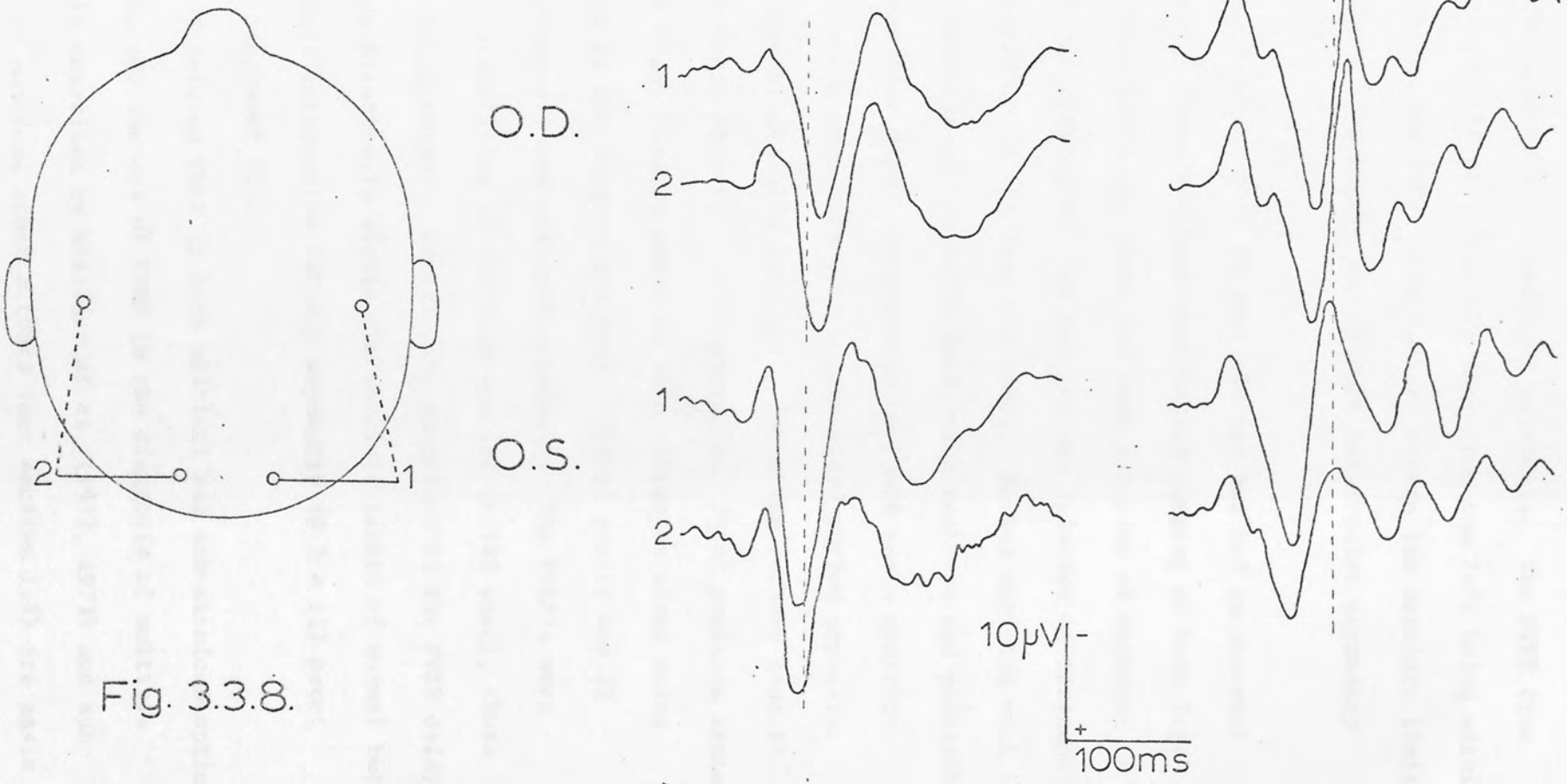


Fig. 3.3.8.

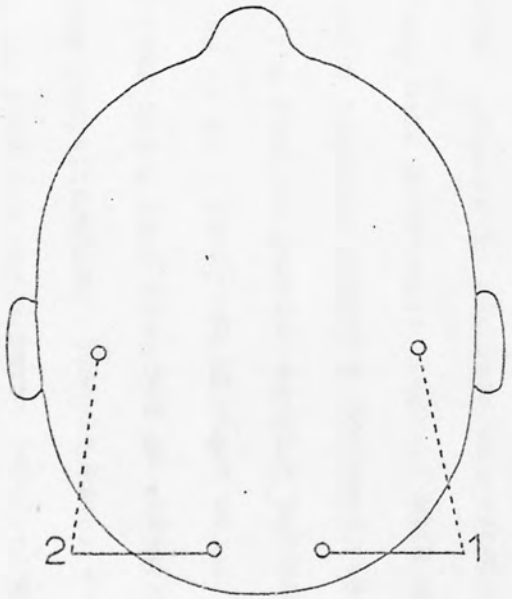
of sensation to pin prick from C4 - L1. Vibration sense was lost below the waist. The diagnosis was multiple sclerosis. The PVEP from the right eye is delayed (P2 at 118 msec), that from the left being within normal limits. Although the FVEP latencies are within the absolute limits of normal for age there is a highly significant interocular asymmetry of some 20 msec.

d) J.W. Fig. 3.3.9. This 59 year old man had had an abnormal gait for 8 - 10 years. There had been involuntary jumping of both legs for 5 - 6 years. Three years ago there had been a period of weakness in the right leg which had cleared up. He had had two episodes of frequency and urgency of micturition in the last two years. He was admitted with a six day history of weakness of the right hand, with weakness and paraesthesiae of all four limbs for four days. On examination there was a spastic quadriparesis right worse than left with a left-sided reflex emphasis. Plantar responses were bilaterally extensor. There was sensory loss to pin prick and light touch from C5 - C8 bilaterally. Joint position sense was impaired in the right fingers and toes with vibration sense being bilaterally impaired in the fingers and toes. Visual acuity was J2 bilaterally. The diagnosis was multiple sclerosis. The PVEP's were markedly delayed on stimulation of the left eye (P2 at 142 msec), those from the right eye being normal. Despite the magnitude of the PVEP delay, the flash VEP's were bilaterally within the absolute limits of normal but there is a significant interocular latency asymmetry (O.D = 117 msec; O.S = 125 msec for component P2).

The findings of delayed PVEP in both clinical and sub-clinical optic nerve demyelination, and the use of PVEP in the diagnosis of multiple sclerosis, initially described by Halliday et al. (1972, 1973) and subsequently reported by numerous other authors (see section 1.4) are again confirmed. Out of 46 patients with multiple sclerosis, 34 (74%) had delayed PVEP's only 21 of these having signs or symptoms suggestive of

Fig. 3.3.9. VEP findings in a 59 year old man with multiple sclerosis. (The broken vertical line indicates the upper limit of normal latency). See text for details.

J.W. aet 59
V.O.D. J1 V.O.S. J1



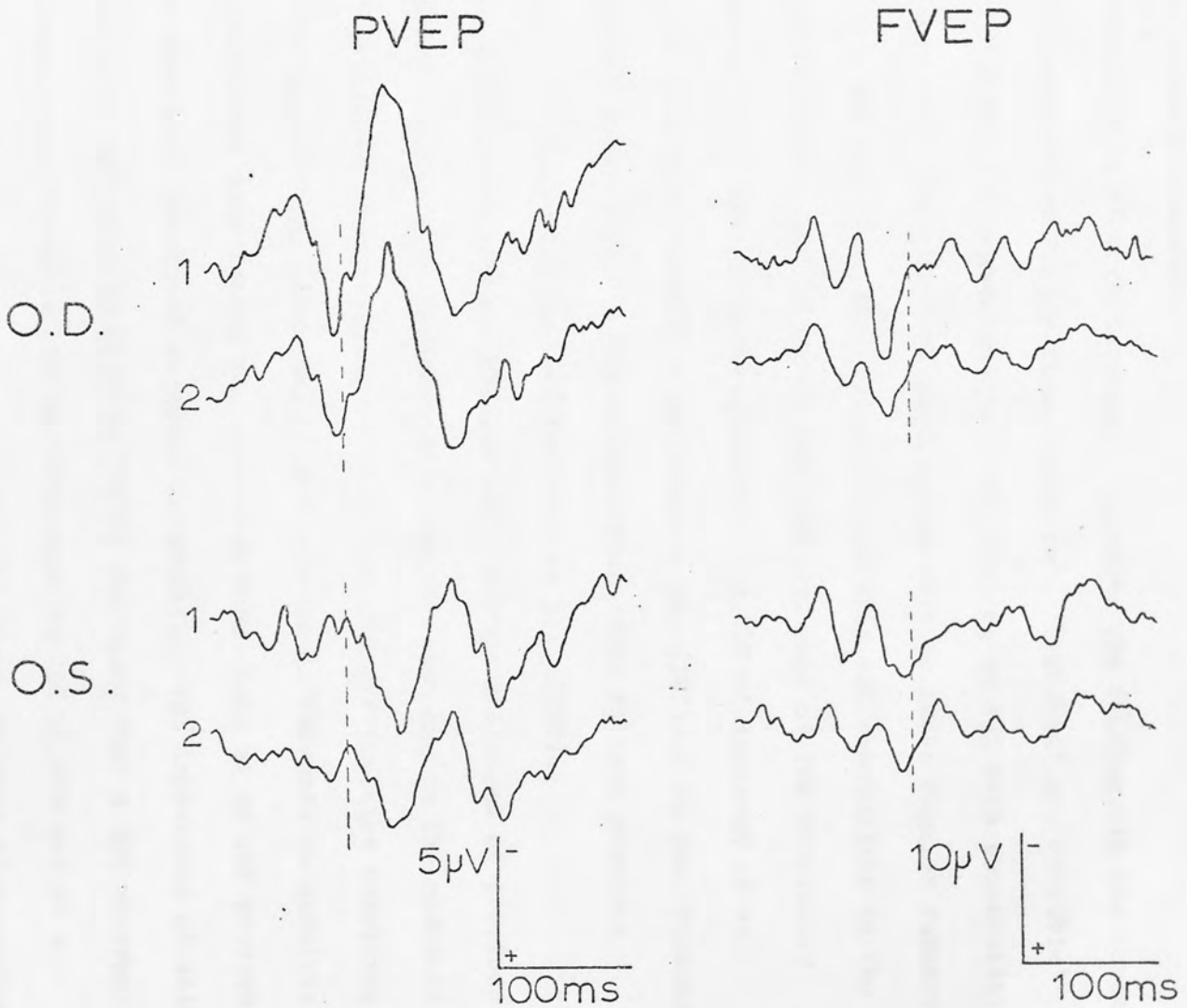


Fig. 3.3.9.

of optic nerve involvement.

However, it is of more interest to examine the findings in the three groups of patients suffering from 'Definite', 'Probable' or 'Possible' MS (89%, 91% and 47% respectively). The finding of 89% PVEP abnormality in patients with 'Definite' MS corresponds well to those figures reported by previous authors (see Fig. 1.4.1). Similarly 48% abnormality in the 'Possible' MS group is similar to the combined mean of the previously reported values although much higher than the 21% of Asselman et al. (1975) and less than the 92% of Halliday etal. (1973). In the 'Probable' MS group 91% abnormality is higher than that found by most previous authors but is less than that of Halliday et al. (1973).

The differences between the current findings and those of previous authors may represent differences in classification due to the possible lack of precision of McAlpine's criteria and the difficulties resulting from this imprecision. They may also represent differences in sensitivity due to different stimulating and recording parameters as no two previous authors have used identical stimulus parameters. The importance of stimulus parameters is indicated by Nilsson (1978) who found that a 30% abnormality in patients with 'Possible' MS was increased to 70% by the use of a pattern reversal stimulator based on the red light emitting diode design of Evans et al. (1974). Indeed it has been suggested that use of a red and white stimulus may have advantages compared with the more conventional black and white pattern reversal stimulus (McInnes, 1977).

The failure of the FVEP to provide similar percentage abnormalities to the PVEP (Halliday et al., 1972; Wildberger et al., 1976) is also seen in this study, the FVEP being less than 50% as effective as the PVEP in detecting optic nerve demyelination. Even in cases where there was some clinical suggestion of previous optic nerve involvement, normal FVEP's could be recorded. The extremely high incidence of FVEP abnormality reported by some authors (e.g Feinsod and Hoyt, 1975; Hennerici et al.,

1977) is not therefore supported by this work, but it is noted that marked differences in stimulation technique, and possibly even in analysis, may well be a contributory factor to this discrepancy.

On no occasion was a normal PVEP recorded where there was clincal suggestion of an optic nerve lesion. However, a normal PVEP following a definite attack of retrobulbar neuritis has been observed by this author in a patient not included in this series. Clearly it is very uncommon to find a normal PVEP in the presence of clinical optic nerve involvement, and particularly following an attack of optic or retrobulbar neuritis. This is to a certain extent supported by the findings documented in Fig. 3.3.4 where the mean latency delays in patients with and without visual symptoms are compared. The mean latency in those patients with previous visual symptoms is significantly longer than in those patients without previous visual symptoms.

Also in agreement with the initial findings of Halliday et al. (1972, 1973) is the value of PVEP latency compared to amplitude in the diagnosis of MS. This is partially due to the broad range of 'normality' possible with amplitude compared with the relatively small normal range for latency, but more to the fact that amplitude changes are often not seen even in the presence of marked latency abnormality. This dissociation between amplitude and latency (illustrated in Fig. 3.3.5) is in agreement with previous findings (Halliday et al., 1974c) but unfortunately the correlation between amplitude reduction and reduced visual acuity detailed in the same paper cannot be confirmed here due to insufficient data. It is however this author's impression based on PVEP examination in many other MS patients not included in this series, that one is indeed more likely to find a PVEP amplitude reduction where visual acuity is reduced but that amplitude reduction can also occur with normal visual acuity.

Despite the marked delays in PVEP, and to a much lesser extent FVEP latency, the mechanism of this delay remains problematical. Slowed

conduction through a demyelinated section of nerve has been demonstrated in both the central (e.g McDonald and Sears, 1970; Mayer, 1971) and peripheral (McDonald, 1963) nervous system and there has been estimated to be an approximately thirty fold (approximately 600 μsec compared with approximately 20 μsec) increase in internodal conduction time in demyelinated peripheral nerve fibres (Rasminsky and Sears, 1972). The mean length of a plaque of optic nerve demyelination is approximately 1 cm (McDonald, 1977). If therefore the slowing of conduction reported by Rasminsky and Sears (1972) is applicable to central nervous system fibres, then, if there are some 50 or so nodes in a 1 cm plaque (McDonald, 1977), the PVEP delay could possibly be explained if conduction was delayed in each of the internodal segments. However, computer simulation suggests it improbable that saltatory conduction of markedly reduced velocity could persist through many consecutive demyelinated internodes (Koles and Rasminsky, 1972).

It may also be relevant to consider the properties of the internodal axon membrane, normally sheathed in myelin but exposed by the process of demyelination. Ritchie and Rogart (1977), using measurements of tritiated saxitoxin binding to rabbit sciatic nerve, estimated the density of sodium channels in mammalian myelinated nerve fibres. They suggest a sodium channel density of some 10,000 per square micron at the nodes of Ranvier, but only some 25 channels per square micron in the internodal axon membrane. The specialised axons of the eel Sternarchus have been examined using the freeze fracture technique (Kristol et al., 1977), a higher density of outer leaflet membrane particles, thought to be related to the sodium channels (Rosenbluth, 1976), being found at the normally excitable nodes of Ranvier than at the non-excitable nodes. It should be noted that these specialised axons of Sternarchus have both excitable and non-excitable regions in the axon membrane.

Clearly then, there appear to be marked structural differences

between the nodal and internodal axolemma, but the specific effects of these differences on the conducting properties of the nodal and internodal axolemma are uncertain. Bostock and Sears (1976, 1978) examined conduction in small experimentally demyelinated rat ventral root fibres and found examples where the internodal membrane was excitable and supported continuous conduction along a demyelinated internode. Similar findings of continuous conduction have been reported by Rasminsky and Kearney (1976) who studied conduction in large diameter spinal root axons of dystrophic mice, which are either bare or sheathed with an abnormally thin covering of myelin. They found that adjacent portions of the axon membrane in dysmyelinated fibres were capable of sustaining both saltatory and continuous conduction.

Although extrapolation to the human visual system is fraught with dangers, if continuous conduction can be sustained over a series of internodes then this slow non-saltatory conduction may play a significant role in the increased VEP latency observed in demyelination.

3.4 Pre-chiasmal Lesions (Non-demyelinating)

Fifty-three patients form the subject matter in this section. The majority of these had optic nerve dysfunction but as VEP abnormality was seen in some patients with retinal or macular lesions these diagnostic categories have also been included. The breakdown of the fifty-three patients is shown in Fig. 3.4.1. Due to the wide variety of pathology each diagnostic category will be discussed individually. It should be noted that in some of these cases VEP findings were contributory to the final diagnosis, either by confirming the opinion of the referring consultant, or in suggesting an alternative diagnosis which was then confirmed by other investigations. In some patients however the final diagnosis was made on purely clinical criteria, no objective laboratory or investigative procedure findings being available. Many other cases of optic nerve dysfunction were seen but the diagnoses remained in some degree of doubt, and, for the most part, these patients have not been included.

Fig. 3.4.1 Patients with non-demyelinating optic nerve lesions

Ischaemic lesions	9
Toxic/Nutritional amblyopia	9
Retinal disease	5
Familial optic atrophy	5
Ocular trauma	4
Papilloedema	4
Central serous retinopathy	3
Amaurosis fugax	3
Optic nerve compression	3
Glaucoma	2
Macular degeneration	2
Congenital disc anomaly	2
Sarcoidosis	2

3.4.A Ischaemic Lesions

Nine patients are reported with presumed ischaemic lesions of the anterior visual pathways. Brief clinical details follow.

i) M.G. aet 43. Female. This patient presented with left optic atrophy and an inferior altitudinal field defect. The right eye was normal. Visual acuities were uncertain but were not thought to be severely reduced (the patient did not speak English). Presumed left ischaemic optic neuropathy.

ii) H.K. aet 49. Male. History of severe headache for two year period. During one of these vision was lost in both eyes for approximately fifteen minutes. Vision gradually returned in the right eye but not the left. Right visual acuity (V.O.D.) was 6/24 with no field loss. Left visual acuity (V.O.S.) was counting fingers in the peripheral field with a central scotoma. Ophthalmoscopic examination was thought to show ischaemic papillopathy.

iii) T.D. aet 50. Male. Recurrent headaches, blurring of vision. V.O.D. was 6/60 with a pale flat disc and vessel sheathing. There was gross field constriction with an inferior altitudinal defect. Fluorescein angiography showed ischaemic papillopathy.

iv) G.S. aet 54. Female. Blurred vision left eye with a history of transient ischaemic attacks, (T.I.A.). V.O.D. was 6/4, V.O.S. was 6/6 with an impaired temporal field. Fluorescein angiography was within normal limits but the lesion was assumed to be vascular in view of the previous history.

v) F.B. aet 59. Female. Left optic atrophy found on routine spectacle examination for blurred vision. V.O.D. was 6/9 with full visual field and a normal fundus. V.O.S. was 6/9 with an inferior altitudinal field defect and optic atrophy of the upper part of the disc. Left carotid angiography showed atheroma at the origin of the left internal carotid artery. The diagnosis was left ischaemic papillopathy.

vi) R.W. aet 59. Female. Loss of vision nasally in right eye. V.O.D. was 6/9 with inferior nasal field loss. V.O.S. was 6/5. The fundi were normal. There was a basal systolic bruit in the aortic area radiating up to the neck but with no definite cardiac source for emboli apparent on E.C.G. Presumed right ischaemic papillopathy/retinal vascular lesion.

vii) A.R. aet 71. Male. Past history of coronary thrombosis. Disturbance of vision right eye. V.O.D. was 6/18 with paracentral scotoma on Amsler charting and ischaemic damage at the macula. The left eye was normal.

The VEP findings in these patients are described in Fig. 3.4.2, sample tracings from patient (i) being shown in Fig. 3.4.3. A significant interhemispheric VEP asymmetry was not present in any of these patients.

The two additional patients both had ischaemic optic neuropathy associated with histologically proven giant cell arteritis. As the findings in these two patients differ somewhat from the other seven patients, they are treated separately.

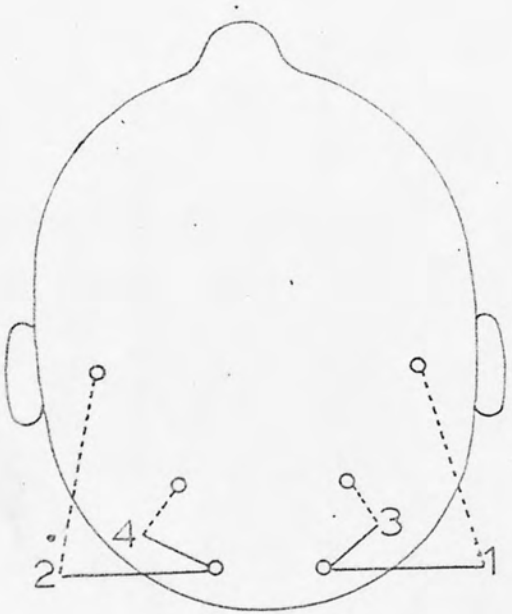
viii) A.S. aet 68. Female. Reduced vision (very poor historian). V.O.D. was 6/9, V.O.S. hand movements (H.M.). There was bilateral disc swelling with venous engorgement on the right, disc pallor and associated ischaemic changes on the left. Left temporal artery biopsy showed giant cell arteritis.

ix) L.M. aet 78. Female. Visual deterioration with headache and malaise. V.O.D. was J4, V.O.S. H.M with nasal field loss and disc swelling. Left temporal artery biopsy showed giant cell arteritis.

The VEP findings in these two patients were very similar. Both had an absent PVEP from the severely affected eye, that from the (relatively) normal eye being unremarkable. The FVEP in the bad eye was of severely reduced amplitude with a delay in the negative component N2 (compared

Fig. 3.4.3. VEP findings in a 43 year old lady with presumed left ischaemic optic neuropathy. See text for details.

M.G. aet 43



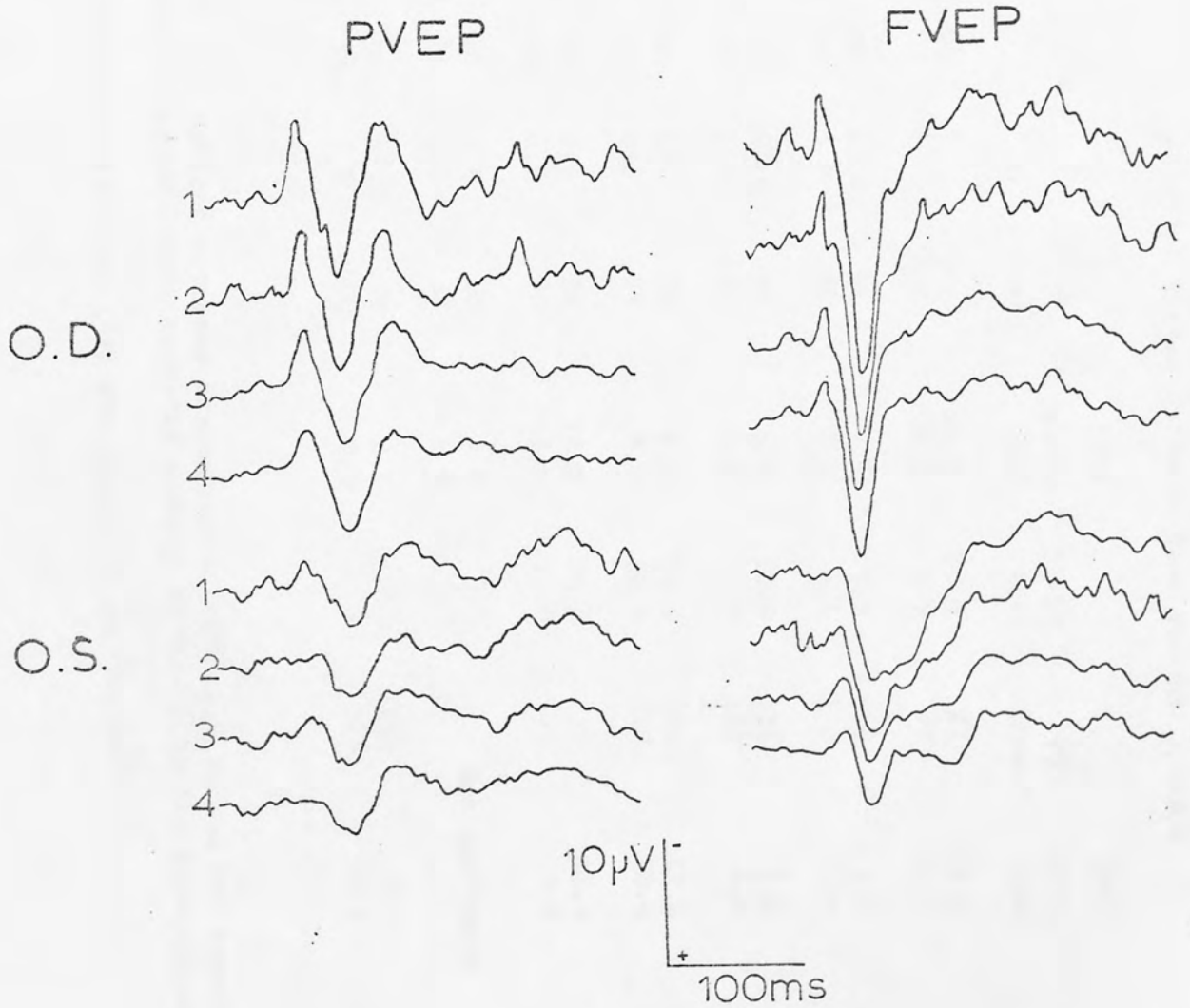


Fig. 3.4.3.

Fig. 3.4.2. VEP findings in patients with ischaemic lesions of the anterior visual pathways (see Section 3.4.A).

			PVEP			FVEP	
	V.A.	P2 (msec)	N2-P2 (μV)	P2-N3 (μV)	P2 (msec)	N2-P2 (μV)	P2-N3 (μV)
i) OD	?	101	10.8	11.5	87	18.6	*
OS	?	104	4.7	6.4	90	8.9	
ii) OD	6/24	96	7.6	9.1	116	3.6	4.0
OS	C.F.	98	3.4	4.6	116	3.6	4.4
iii) OD	6/18	96	6.0	10.0	116	8.8	6.8
OS	6/60	102	1.8	2.4	124	4.0	6.0
iv) OD	6/4	98	8.8	10.4	124	17.0	11.5
OS	6/6	99	8.8	10.6	118	18.4	11.7
v) OD	6/9	96	16.0	26.0	117	10.4	8.6
OS	6/9	98	7.6	10.8	121	9.8	5.6
vi) OD	6/6	90	3.6	4.4	Not performed		
OS	6/5	88	6.8	9.2			
vii) OD	6/18	99	2.3	5.3	122	9.5	5.9
OS	6/9	100	6.5	14.6	125	14.2	8.8

* In this patient accurate assessment of component N3 was not possible but P2-?N3 amplitude appeared reduced by 50-75% in the affected eye.

Patients (viii) and (ix) are discussed in the text.

with the good eye) of some 10-15 msec in patient (viii) and some 20-30 msec in patient (ix), the remainder of the waveform being somewhat distorted and precluding accurate assessment of the later components.

The PVEP was therefore abnormal in eight of the nine patients described with ischaemic lesions of the anterior visual pathways. In two patients the abnormality was that of an absent PVEP thus precluding latency measurements. In the other six patients with PVEP abnormalities, this abnormality always took the form of a significant interocular amplitude asymmetry in at least one of the two amplitude measures studied, the affected or worse affected eye showing the lower amplitude. In one patient (iii) the magnitude of the interocular latency asymmetry was marginally abnormal but an unequivocally abnormal latency was not seen in any of the patients studied.

The FVEP was abnormal in four of the eight patients in whom this investigation was performed. Again, these abnormalities generally took the form of a significant interocular asymmetry. Of the six patients without giant cell arteritis and with FVEP results, two had abnormal findings. In one of these (patient (i)) there was a significant interocular latency asymmetry in addition to an interocular amplitude asymmetry. It is noted that in these six patients the FVEP waveforms were essentially very similar in the two eyes.

In contrast to this, the two patients with giant cell arteritis both displayed marked interocular waveform asymmetries to the extent that accurate latency and amplitude measurements of particular components was not possible in the (worse) affected eye. There was however an overall amplitude reduction of some 80% from the bad eye in both of these patients.

In three patients (ii, v, vii) a PVEP abnormality was not accompanied by an abnormality in the FVEP. All patients with FVEP however also showed PVEP abnormality.

No correlation with visual acuity was noted. Indeed, in patient (ii)

a PVEP within the absolute limits of normal was rather surprisingly found in an eye with a visual acuity of counting fingers although there was a relative amplitude reduction compared with the good eye. Also, in patient (v), a markedly reduced amplitude PVEP was seen in the affected eye but there was no interocular visual acuity asymmetry.

The VEP is therefore a sensitive indicator of ischaemic lesions of the anterior visual pathways. The PVEP was abnormal in 89% of the patients studied, the FVEP in 50% of the eight patients in whom this investigation was performed. The findings of Wilson (1978) of amplitude rather than latency being the affected variable are confirmed, but this amplitude reduction was generally relative to the other eye and not, as additionally reported by Wilson (1978) in relation to the normal control group. Wilson also reports latency abnormalities for both flash and pattern reversal stimulation in 4/15 patients and it is of interest that the only patient in the present series with an abnormally asymmetrical PVEP latency also had an abnormally asymmetrical FVEP latency. Unfortunately Wilson (1978) does not discriminate between those patients with temporal arteritis and those without, and a direct comparison between the two studies for such patients is not therefore possible.

It may be of relevance that patient (iv) was the only patient not to show a PVEP abnormality, and indeed there was not even a suggestion of an interocular asymmetry. Fluorescein angiography failed to demonstrate a significant lesion and the vascular nature of the lesion was presumed because of the previous history of transient ischaemic attacks. As the temporal visual loss seen in this lady is not thought to be a feature of ischaemic optic neuropathy (Boghen and Glaser, 1975), perhaps this diagnosis should be reconsidered as neither the clinical nor neurophysiological findings appear totally compatible with such a diagnosis.

The reports of 'delayed' PVEP by Asselman et al. (1975) who describe three cases, and Hennerici et al., (1977, five cases) are not confirmed and although the findings of Ikeda et al. (1978, six cases) of reduced

amplitude are supported, the latency delay also described by these authors is not supported. Unfortunately these three previous reports do not supply clinical or VEP findings in any detail so the cause of this apparent discrepancy cannot be assessed. Differences in stimulation and recording techniques may be contributory as may the period of time elapsed between the onset of visual symptoms and VEP examination. The aetiology of the ischaemic lesion may also be relevant.

It is also noteworthy that patients (ii) and (vii) with central scotomata merely showed a reduced amplitude PVEP of normal waveform and not the 'scotomatous' waveform described by Halliday (1976) but in different clinical conditions.

There are potentially important clinical implications which follow from these findings. The sudden onset of visual deterioration frequently seen in ischaemic lesions also occurs in demyelinating optic nerve lesions and although other clinical features such as the presence or absence of pain, the age of the patient etc. often indicate the correct diagnosis, there also appears to be marked VEP differences between the two conditions which may supply objective evidence to assist the clinician in his decision. In demyelinating disease the findings are generally those of an increased latency of the P2 (major positive) component with or without an associated amplitude reduction. The clinically uninvolved eye can also show abnormalities, particularly in the PVEP (see sections 1.4 and 3.3 for further details of the VEP in optic nerve demyelination). In ischaemic optic neuropathy however, the characteristic VEP finding is that of normal latency but significantly reduced amplitude with any clinically uninvolved eye always having normal VEP.

It is also noted that differentiation between ischaemic optic neuropathy of the arteritic and non-arteritic types may be possible on the basis of the VEP findings as suggested by Crews and Harding (1978) and Harding et al. (1979). Although only two patients with proven giant

cell arteritis were examined, in both patients the PVEP was absent, but more importantly, the FVEP showed severely reduced amplitude with a delayed early negative component and distorted waveform. One of these two patients did not have a significantly raised erythrocyte sedimentation rate. This differentiation is clearly of importance as the involvement of the second eye which normally takes place in the arteritic form of ischaemic optic neuropathy (Francois, 1976) may be prevented by the early administration of corticosteroids (Cullen and Coleiro, 1976). However further research is needed before temporal artery biopsy is performed on patients with ischaemic optic neuropathy and relatively low E.S.R. purely on the basis of VEP findings.

3.4.B Amaurosis fugax.

In contrast to the previously described patients with permanent ischaemic damage, three patients with amaurosis fugax were examined. All were normal on ophthalmological assessment and all three patients had completely normal VEP's both in response to diffuse flash and pattern reversal stimulation.

3.4.C. Toxic or nutritional amblyopias.

Nine patients are included in this category. Five had presumed tobacco or tobacco/alcohol amblyopia. In three of these a marked improvement in vision occurred following a reduction in alcohol and/or tobacco intake and the administration of hydroxycobalamin. The fourth patient, with an extremely high intake of both alcohol and tobacco, persistently failed to attend for medication and did not reduce his alcohol or tobacco intake. In the fifth patient the diagnosis was presumed but uncertain. These five patients are detailed below:

i) H.P. aet 56. Male. The patient complained of sudden visual deterioration. There were bilateral central scotomata with visual acuities of 6/60. The optic discs were thought to be pale. His daily intake of tobacco and alcohol was ½ oz of heavy pipe tobacco and eight pints of beer. Following a marked reduction in tobacco and alcohol intake and treatment with hydroxycobalamin, vision improved to 6/5 bilaterally.

ii) J.T. aet 68. Male. This patient had three to four months difficulty in reading and smoked 2½ oz of heavy pipe tobacco per week. There was a past history of heavy alcohol consumption. V.O.D. was 6/60, V.O.S. 6/24 with bilateral central field defects to a red object. Hydroxycobalamin produced a marked improvement in vision.

iii) G.P. aet 69. Male. Eighteen month history of failing eyesight. He was a lifelong heavy smoker of pipe tobacco which he inhaled. V.O.D. was 6/24, V.O.S. 6/36 with bilateral centro-caecal scotomata and bitemporal disc pallor. The scotomata resolved and the acuities improved substantially following hydroxycobalamin therapy.

iv) W.W. aet 38. Male. Sudden blurring of vision two months prior to examination. Visual acuity was 6/36 bilaterally with probable central field defects to a red object (poor witness). He smoked sixty cigarettes and drank eight pints of beer per day. The diagnosis was that of tobacco/alcohol amblyopia but he failed to attend for hydroxycobalamin therapy.

v) E.E. aet 51. Female. She suddenly found that she could not read small print. Visual acuities were less than 3/60 with bitemporal disc pallor. There was bilateral central field loss. She smoked forty untipped cigarettes a day, was a heavy drinker, and worked in a dry cleaners. There was only a slight improvement following hydroxycobalamin.

The VEP findings from these five patients are summarised in Fig. 3.4.4. Patients (i) and (v) were re-examined following hydroxycobalamin. In patient (i) the visual æuities had recovered to 6/5 bilaterally. PVEP examination showed bilaterally delayed P2 components (O.D 120 msec; O.S 119 msec) of normal amplitude. FVEP examination showed markedly improved latencies (O.D 142 msec; O.S 148 msec) with marginally improved amplitudes. Patient (v), although visual acuity did not improve significantly, showed a 100% amplitude increase in the FVEP's with no latency change. PVEP's remained absent.

None of these five patients showed a significant interhemispheric VEP asymmetry.

The PVEP findings in patient (iv) can be seen in Fig. 3.4.5.

Two patients had quinine retinopathy/amblyopia following an overdose. Both went totally blind initially but had some recovery of vision following stellate ganglion block. Both were left with severely constricted visual fields and bilateral disc pallor.

vi) R.C. aet 30. Male. This patient was seen some fifteen months following overdose when V.O.D. was 6/18, V.O.S. perception of light with accurate projection. The patient was also an alcoholic.

No definite PVEP was seen from either eye with a 26' check pattern, but rather curiously a delayed P2 at 122 msec was seen from the right eye with a 13' check pattern. FVEP's were very poorly formed, of very low amplitude and displayed high variability.

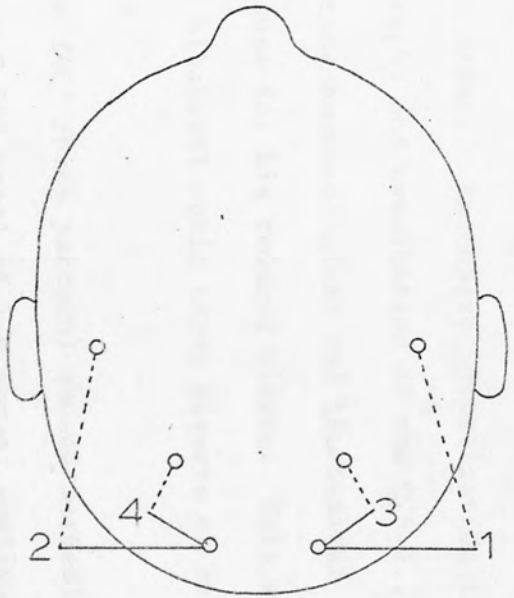
vii) J.R. aet 37. Male. Serial VEP recordings were taken in this patient at 5, 19, 31 and 45 days following overdose. The highly abnormal findings, with marked delay in the PVEP and FVEP, obtained at the initial

Fig. 3.4.4 VEP findings in patients with tobacco or tobacco/alcohol amblyopia (see text for details).

i)	Bilaterally absent	Bilaterally delayed (O.D 170 msec; O.S 165 msec)
ii)	Bilaterally absent	Bilaterally low amplitude. P2 lat. ↑ 10-20 msec O.D. compared with O.S.
iii)	Absent on left. Unusual W-shape (100,125, 140 msec) from right eye.	Normal, symmetrical.
iv)	Bilaterally delayed (O.D 136; O.S 140 msec). Low amplitude.	Bilaterally low amplitude O.D > O.S.
v)	Bilaterally absent	Bilaterally low amplitude.

Fig. 3.4.5. PVEP findings in a 38 year old man with presumed tobacco/alcohol amblyopia. (The broken vertical line indicates the upper limit of normal latency). See text for details.

W.W. aet 38
V.O.D., V.O.S. 6/36



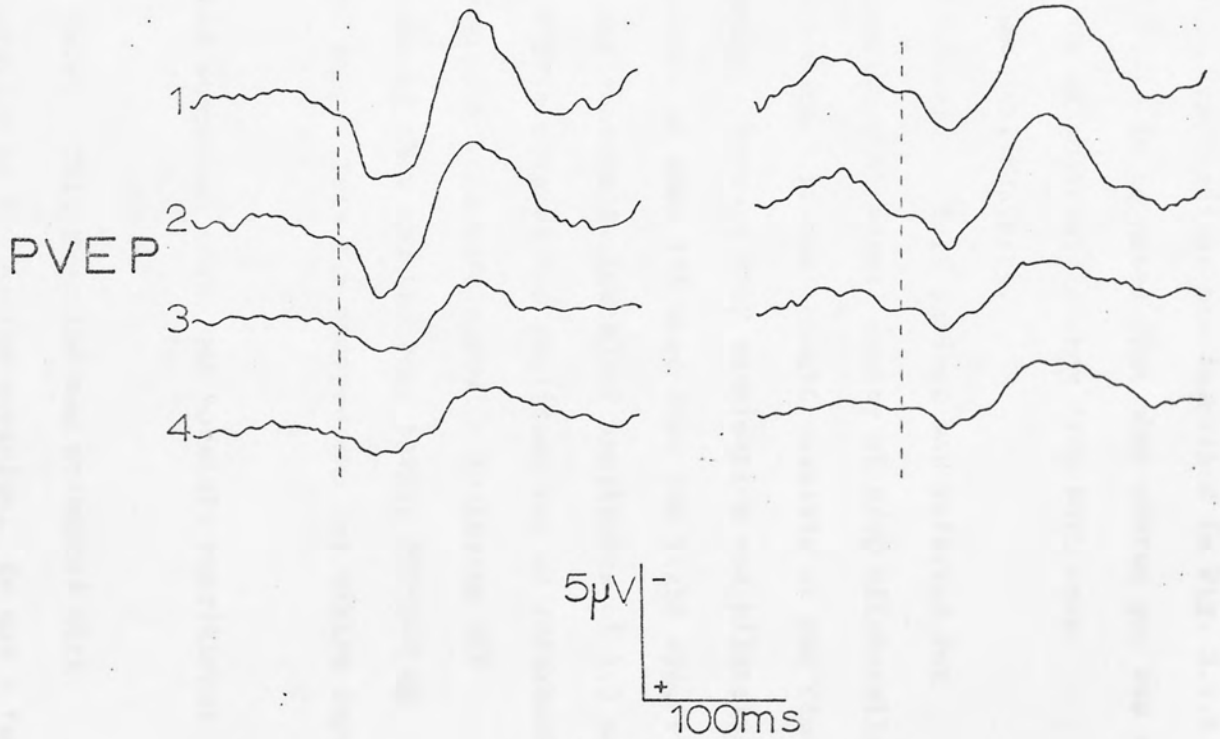


Fig. 3.4.5.

examination rapidly improved, but by the fourth examination no further improvement was apparent. The findings are described in Fig. 3.4.6 and are shown in Fig. 3.4.7. It is noted that when status quo was reached the PVEP continued to show an abnormal latency from both eyes.

One patient had ethambutol toxicity.

viii) M.S. aet 74. Female. This patient was referred for electrodiagnostic examination with visual acuity of 6/60 bilaterally and questionable central scotomata. It was thought possible at the time that there was no organic lesion. However PVEP examination was bilaterally abnormal with the P2 component at some 135 msec from the right eye, 140 msec from the left eye and abnormally low N2-P2 amplitudes of 1.3 and 0.75 μV respectively. FVEP's were of low amplitude but no interhemispheric asymmetry was seen. Latency values were normal. Following VEP examination it was discovered that she had been taking 800-900 mg ethambutol daily for one year. This was stopped and her vision improved to 6/18 bilaterally.

The last patient had suspected toxic but possibly nutritional amblyopia.

ix) A.W. aet 61. Male. This Nigerian man presented with bilateral visual deterioration of 4-5 months duration. He was a heavy smoker. Visual acuity was 6/24 bilaterally with normal fundi and no definite visual field defect. Extensive investigation including E.M.I scan, air encephalography and examination of the C.S.F., fluorescein angiography, and routine haematological and biochemical investigation failed to reveal a cause for his reduced vision. This was eventually thought to represent bilateral optic nerve disease of suspected toxic (? tobacco) aetiology.

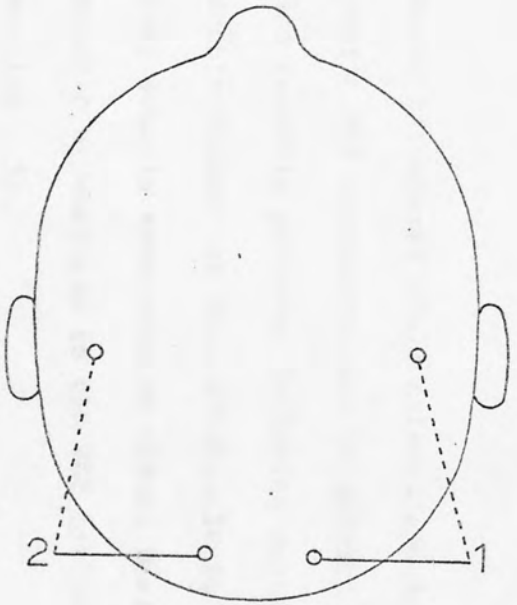
PVEP examination (40' check pattern) showed markedly delayed P2 components (O.D 155; O.S 147 msec) of low normal amplitude. FVEP's were of low amplitude with no definite latency delay. No significant inter-

		PVEP					FVEP				
		msec			μV		msec			μV	
		N2	P2	N3	N2-P2	P2-N3	N2	P2	N3	N2-P2	P2-N3
5.5.1977	O.D	100	136	172	3.4	5.6	?160	?190	?230	?1.5	?2.5
	O.S	96	144	176	3.4	5.8	?160	?185	?230	?1.0	?1.5
19.5.1977	O.D	86	125	173	5.6	8.3	?140	?175	?230	?1.0	?4.0
	O.S	90	123	170	4.8	7.7	?140	?175	?230	?1.0	?4.0
31.5.1977	O.D	84	120	160	5.7	8.4	120	167	220	3.8	5.0
	O.S	82	120	162	5.4	7.8	123	170	220	4.4	6.2
16.6.1977	O.D	80	121	168	4.7	6.6	120	170	228	4.3	5.2
	O.S	82	120	165	5.8	7.6	120	165	220	3.0	4.5

Fig. 3.4.6. Results of serial VEP recording in a 37 year old man following quinine overdose. V.O.D., V.O.S. 6/5. See also Fig. 3.4.7.

Fig. 3.4.7. Serial VEP recordings in a 38 year old man with quinine amblyopia following an overdose. (The broken vertical line indicates the upper limit of normal latency). See text for details.

J.R. aet 38



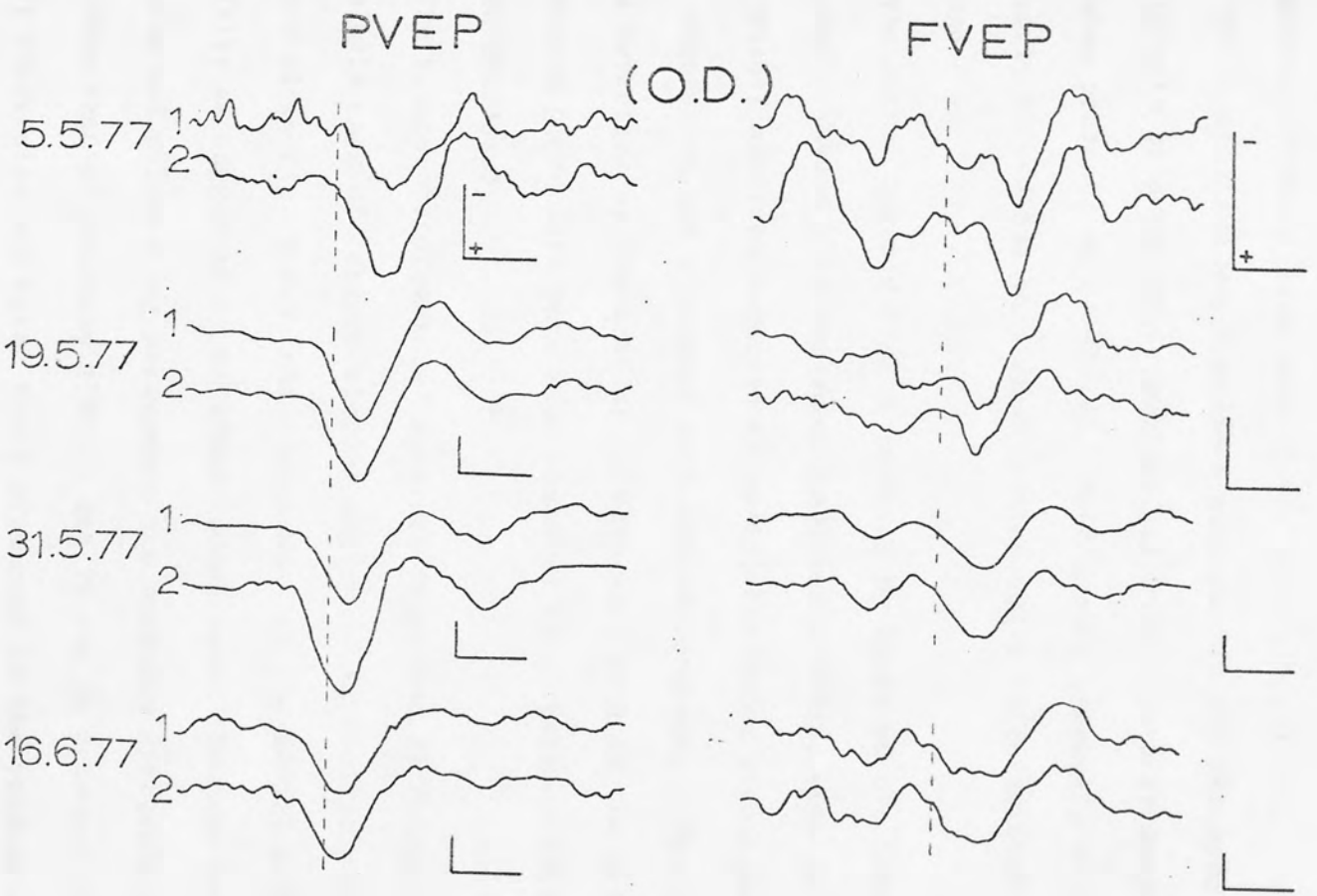


Fig. 3.4.7.

Calibration 2.5μV, 50msec

hemispheric asymmetry was seen.

VEP examination was therefore abnormal in all the nine patients studied with presumed toxic amblyopia. PVEP's were frequently absent but, when present, were delayed. FVEP's were generally of low amplitude and poorly formed but only on occasions was a definite FVEP delay observed.

The normal latency PVEP's reported by Ikeda et al. (1978) are not confirmed. When a PVEP was seen there was a delay, even in the patient whose visual acuities returned to normal following withdrawal of the toxic substances and treatment with hydroxycobalamin. The low amplitude FVEP's described by Ikeda et al. (1978) were seen in the present series but delayed potentials were also observed (e.g. patient (vii) following quinine overdose).

The typical 'scotomatous' waveform described by Halliday (1976) in a single case of tobacco/alcohol amblyopia is similarly not confirmed. Illustrated in Fig. 3.4.5, the replacement of the normal positivity by negativity as suggested by Halliday is not seen. However both the recording and stimulating parameters are markedly different in this study from that of Halliday (1976), and it can be presumed that the much smaller check size and total field size used in the present study would be expected to produce different findings in patients with central field loss.

No patient showed bitemporal field defects and in addition there was no interhemispheric VEP asymmetry seen to support the possible chiasmal dysfunction found in primates following experimental ethambutol toxic amblyopia (Brontë-Stewart et al., 1976). It is known that chiasmal dysfunction, even in eyes with no visual field defect can produce interhemispheric asymmetries in the VEP following monocular stimulation (see section 3.5).

The findings presented in the immediately preceding section and

reviewed in section 1.4 show that delayed VEP's are characteristically seen in the optic nerve demyelination of multiple sclerosis or retrobulbar neuritis. Both ethambutol (Schmidt, 1966) and tobacco (Foulds et al., 1974) seem capable of producing demyelination of the optic nerve fibres. It is not then particularly surprising that delayed VEP's may be seen in patients with tobacco or ethambutol amblypia. The mechanism of visual improvement following withdrawal of the toxic substance has been suggested to be due to remyelination (Foulds et al., 1974) but the evidence for functionally complete remyelination in the central nervous system is scanty (see McDonald, 1974 for review). The suggestion by Ikeda et al. (1978) that the toxic substances could have a major effect upon the enzymic and transport processes of the relay cells and axons would be compatible with improvement following withdrawal of the toxic substance. However, as the patients described in the present series continued to show PVEP delay when re-examined following clinical recovery, it is possible that a combination of the two effects of demyelination and metabolic disturbance should be considered.

In quinine toxicity there is ascending optic atrophy following retinal ischaemia from constriction of the retinal arteries (Walsh and Hoyt, 1969). The conduction delay in quinine amblyopia is then still more difficult to explain. It is of interest that although both cases described of quinine toxicity showed unequivocal delay in the presence, in one case, of normal visual acuities, a single case is mentioned by Ikeda et al. (1978) as showing a reduced amplitude VEP of normal latency. Unfortunately no further details are supplied but her findings are similar to those described in ischaemic optic neuropathy of the non-arteritic type (see section 3.4.A).

3.4.D. Heredo-familial optic atrophy

Five patients are included in this grouping. Three had definite heredo-familial optic atrophy. A 24 year old girl with bilateral visual acuity of 6/60 in whom optic atrophy was noted at the age of three whose brother, sister and probably father were similarly affected; and two sisters, one severely affected with visual acuities of 4/60 on the right, 3/60 on the left, and one mildly affected with acuities of 6/9 and 6/12. The fourth patient, a 27 year old male, presented with counting fingers bilaterally and a history thought by the referring ophthalmologist to be classical of Leber's optic atrophy. The fifth patient, a 25 year old male, presented with bilateral optic atrophy and visual acuities of 6/18 bilaterally for which no cause could be found and a diagnosis of Leber's optic atrophy or some variant of this was made. However, he was then seen elsewhere and it was noted that the striking feature was the small size of the optic discs and relatively large area of peripapillary degeneration. The possibility of congenitally hypoplastic discs with a visual defect present since birth was raised.

Of the three patients in whom familial optic atrophy was established, the patient with the relatively normal vision, despite early clinical changes, had completely normal PVEP and FVEP examination. The sister of this lady showed, on pattern reversal stimulation, a distinctive triphasic complex in place of the normal major positivity, somewhat akin to a W but with an emphasis on the inner limb. This may be regarded either as a replacement of the normal positivity by a negativity or as a delayed P1-N2-P2 complex. No consistent interocular or interhemispheric asymmetry was present and FVEP examination was normal. The third patient showed extremely variable PVEP's, occasionally seeming to show the W shaped complex, occasionally the latter limb of the W being enhanced at the expense of the anterior limb giving the appearance of a P2 component of normal morphology but with a marked latency delay. FVEP examination in this lady was normal. An example of this PVEP W shaped triphasic wave-

form can be seen in Fig. 3.4.8.

The fourth patient with the suspected Leber's optic atrophy had absent PVEP's and reduced amplitude FVEP's with a possible contralateral predominance in amplitude. No interhemispheric latency asymmetry was seen.

The final patient, with a possible Leber's variant in whom the possibility of congenital optic disc hypoplasia had been raised had a normal latency, fairly low amplitude PVEP with a completely normal FVEP.

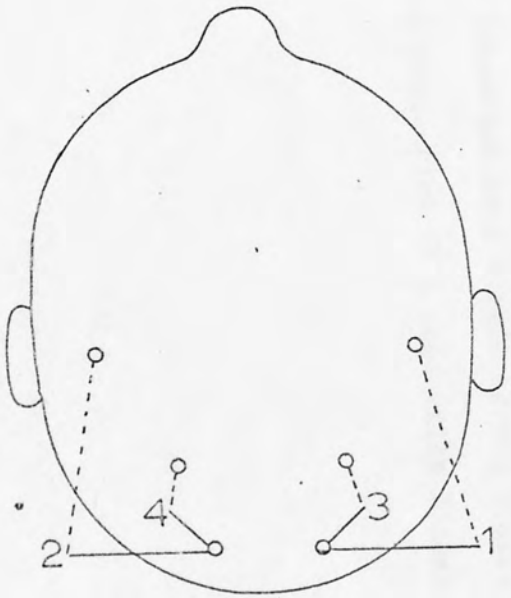
The W-shaped triphasic configuration seen in two of the three definite heredo-familial optic atrophy patients is similar to that previously described by Harding et al. (1979) in dominant hereditary optic atrophy and Leber's optic atrophy, and also by Halliday (1976) in Leber's optic atrophy and tobacco amblyopia. Although this PVEP waveform is suggested by the latter author to be typical of a central scotoma in the visual field, reference to section 3.4.C shows that the present study cannot confirm the 'scotomatous' nature of this PVEP configuration, nor its presence in tobacco amblypia. However it does appear to be a relatively consistent finding in heredo-familial optic atrophy and is similar to the 'bifid positivities' described by Carroll and Mastaglia (1978) and the double positive peak described by Dorfman et al. (1977) in one of their two cases.

The FVEP, completely normal in four patients, but of low amplitude and relatively poorly formed in the patient with a bilateral visual acuity of counting fingers, has not been previously reported in heredo-familial optic atrophy.

As the previous authors all describe a delayed, absent, or triphasic major positivity in the PVEP, the visual dysfunction in the fifth patient described with a normal PVEP seems more likely to be due to the possible disc anomalies than to a variant of Leber's optic atrophy.

Fig. 3.4.8. VEP findings in a 30 year old lady with heredo-familial optic atrophy. (The broken vertical line indicates the upper limit of normal latency). See text for details.

I.P. aet 30
V.O.D., V.O.S. C.F.



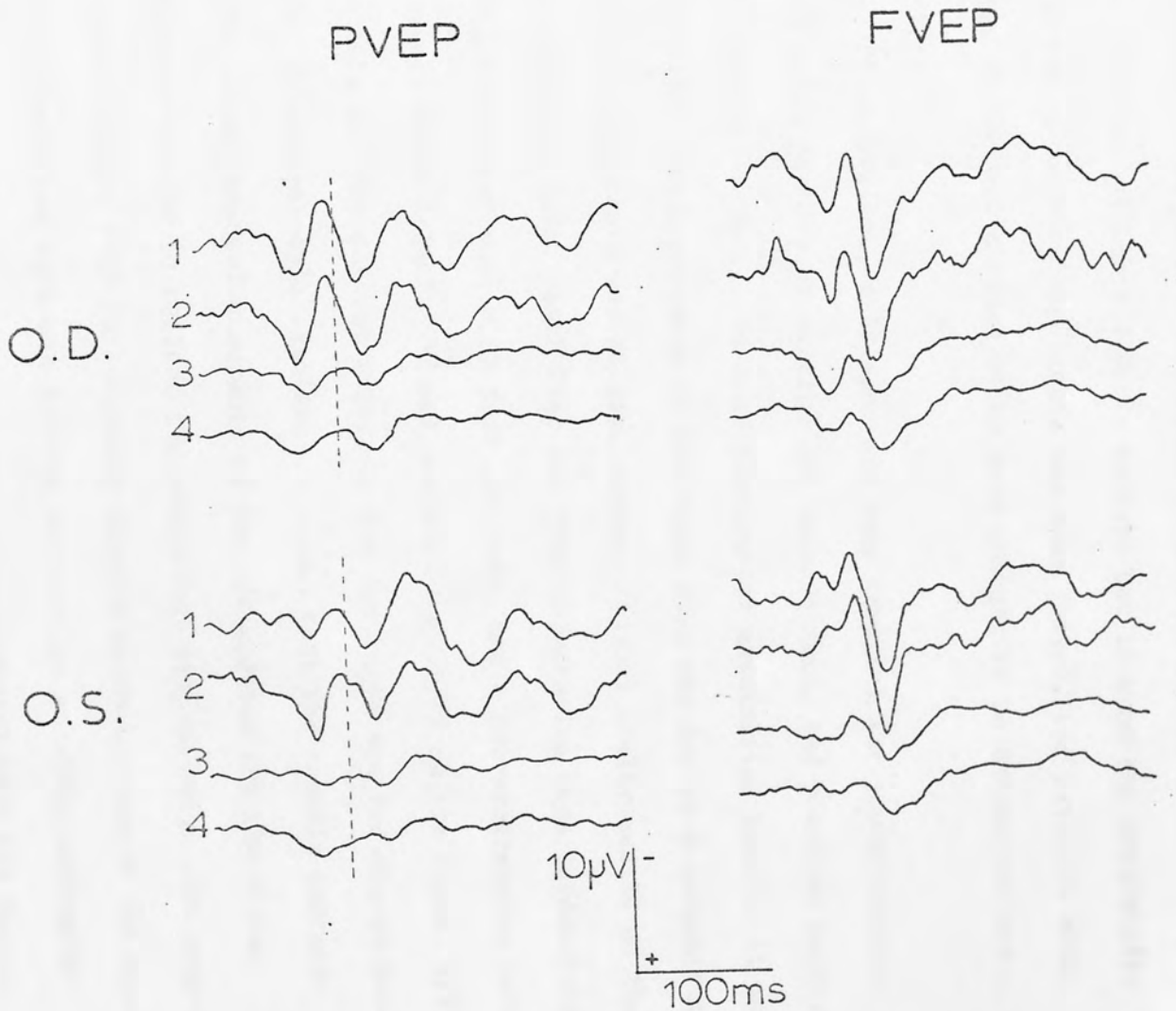


Fig. 3.4.8.

3.4.E. Congenital disc anomalies

Further to the patient described in section 3.4.D, thought originally to have a variant of Leber's optic atrophy but in whom the possibility of bilateral optic disc hypoplasia had been raised, two patients with anomalies of the optic discs which were thought to be congenital are described.

The first patient, a 59 year old lady admitted for investigation of a six month history of vertigo and unsteadiness, had possible swelling of the right optic disc. On ophthalmological examination however it was felt sure that the appearance of the right disc was due to a congenital anomaly and that there was no disc oedema. Visual acuity was J4 on the right, J1 on the left. Both PVEP and FVEP examination were unremarkable.

The second patient, a 39 year old lady, had a non-progressive inferior altitudinal field defect. Visual acuities were 6/12 on the right, 6/9 on the left but the patient reported that her right eye had always been 'weak'. Ophthalmoscopic examination showed that the vessels emerged from the upper temporal quadrants of the optic discs and the visual fields were thought to reflect the congenital disc anomaly. The magnitude of the interocular PVEP P2 component latency asymmetry was at the upper limit of normal but this was felt to reflect the possible amblyopia as stimulation of the right eye evoked the potential with the longer latency. Absolute latencies were within normal limits, as were the FVEP's, and were not suggestive of a conduction defect.

3.4.F. Optic nerve compression

Three patients with optic nerve compression are described. In two the compression resulted from a sphenoidal wing meningioma, in the third from a nasopharyngeal lymphoepithelioma.

Brief clinical details follow, the VEP findings being detailed in Fig. 3.4.9.

i) P.T. aet 46. This lady presented with a nine month history of visual deterioration in the right eye. On examination there was right anosmia; visual acuities were hand movements on the right, J2 on the left. E.M.I scan showed a well-defined mass lying just above the right anterior clinoid process which at operation was found to be a meningioma arising from the sphenoid wing. VEP examination was repeated 24 days after surgery at which time the right visual acuity had improved to J12. Sample tracings pre- and post-operation are shown in Fig. 3.4.10.

ii) E.N. aet 61. This lady was re-admitted for investigation of probable recurrence of a left sphenoid wing meningioma which had been removed three years previously. On examination there was bilateral papilloedema, worse on the left with left proptosis and a left visual acuity of perception of light. Right visual acuity was 6/6. Angiography suggested marked extension down the clivus and through the tentorium. It was felt that there was no place for further surgery.

iii) H.D. aet 59. This man was admitted with pains on the left side of his head and left ptosis. On examination there was involvement of the second to the tenth cranial nerves on the left with a left visual acuity of 6/24. Right visual acuity was 6/6. There was bilateral papilloedema. Skull X-ray showed erosion of the base of the skull with a mass in the left nasopharynx which at biopsy was found to be an anaplastic carcinoma with extensive lymphocytic infiltration.

The VEP findings in these patients are detailed in Fig. 3.4.9, and were highly abnormal in all three cases of optic nerve compression.

			PVEP					FVEP				
			msec				μV	msec				μV
			N2	P2	N3	N2-P2	P2-N3	N2	P2	N3	N2-P2	P2-N3
i)	VOD	HM			Absent			120	?140	?175	2.0	2.0
	VOS	J2	75	95	122	7.7	17.7	68	118	150	10.8	8.0
after surgery (24 days)												
	VOD	J12	100	140	190	2.8	6.5	?70	130	175	6.0	6.5
	VOS	J2	74	98	130	9.4	16.7	66	120	152	13.0	8.0
ii)	VOD	6/6	74	104	136	8.1	8.4	68	106	136	7.0	6.2
	VOS	PL			Absent				Distorted waveform*			
iii)	VOD	6/6	72	100	135	6.6	11.7	?80	120	170	6.5	6.5
	VOS	6/24	96	130	180-90	1.9	2.8	?80**	128	180	6.5	6.5

* Accurate assessment impossible. Early negative component delayed by approx. 25 msec. Amplitude reduced by approx. 50%.

** Early components reduced in amplitude on the left.

Fig. 3.4.9. VEP findings in patients with optic nerve compression (section 3.4.F).

Fig. 3.4.10. Pre- and post-operative VEP findings in a 46 year old lady with a right sphenoid wing meningioma. See text for details.

P. T. aet 46

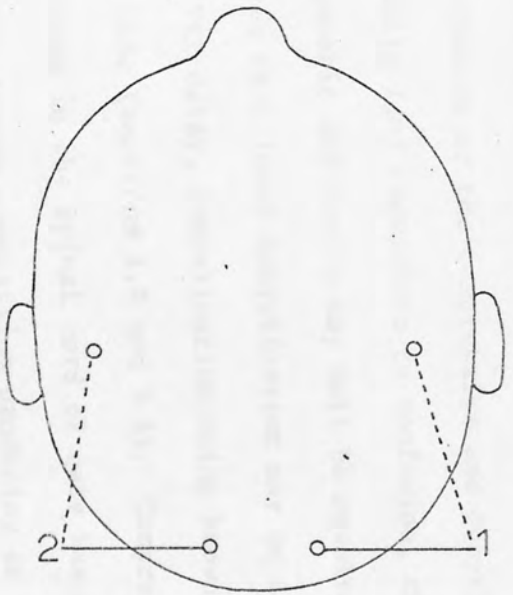
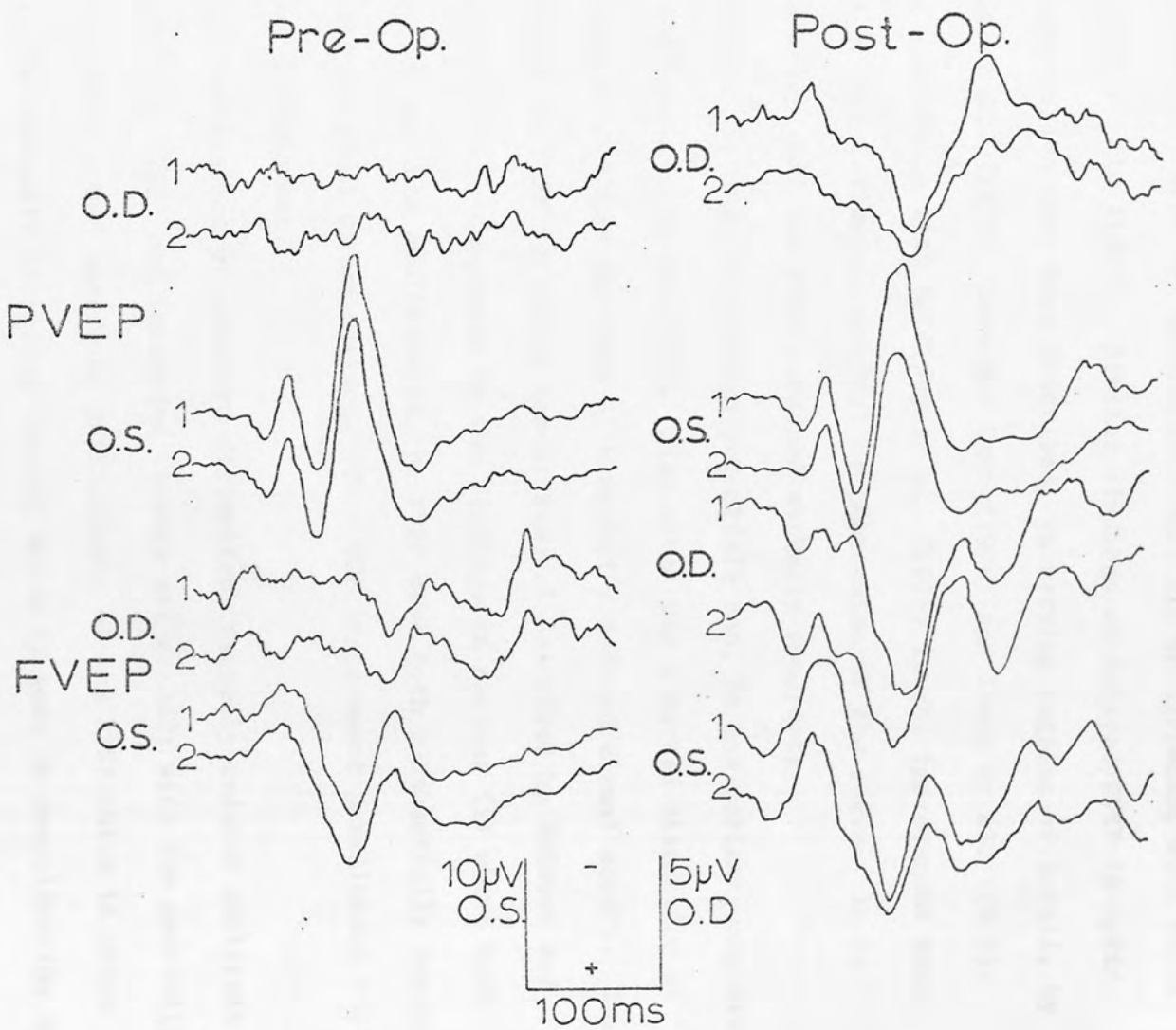


Fig. 3.4.10.



The salient findings in the PVEP of markedly reduced amplitude (absent in two cases) and extended latency are in agreement with those of Halliday et al. (1976). Similar findings of delayed PVEP in optic nerve compression have been described, in varying degrees of detail, by Asselman et al. (1975), Hume and Cant (1976) and Ikeda et al. (1978). Also in accordance with Halliday et al. (1976) is the improvement seen in patient (i) following surgical decompression of the nerve. It is noted however that the PVEP remained markedly abnormal.

Similar findings of delayed potentials and, in one patient, amplitude reduction are seen in the FVEP. Also noted was a marked distortion of the waveform in those patients with markedly reduced visual acuity. The improvement in FVEP following tumour removal described by Feinsod and Auerbach (1971) is supported by the findings in patient (i) where both the latency and the amplitude of the FVEP were both substantially improved following surgical decompression. This VEP improvement parallelled the clinical improvement.

The combination of waveform distortion, markedly reduced amplitude (particularly PVEP) and increased latency are at odds with the generally intact amplitude and waveform, particularly of the FVEP which is often normal, but markedly increased latency which is seen in demyelinating optic nerve lesions. (See sections 1.4 and 3.3). Although the clinical course and mode of presentation of the compressive and demyelinating optic nerve lesion do not usually lend themselves to confusion, the occasional differential diagnostic difficulty may well be resolved by VEP examination.

It is possible that local demyelination may be a contributory mechanism to the VEP delay, demyelination being known to increase optic nerve conduction time (sections 1.4 and 3.3). Compression of central nervous system fibres in the spinal cord of cats has been shown to produce local demyelination, severe compression producing an increased amount of Wallerian degeneration (Harrison and McDonald, 1977). Following decompression there is rapid partial recovery, possibly due to resolving oedema, following

which remyelination takes place. However the internodal length remains inappropriately short for some six months following decompression (Gledhill and McDonald, 1977). The contribution of remyelination to clinical recovery is unclear, but it may be that remyelination is responsible for some of the improvement in VEP latency following decompression. An ischaemic component of the neurophysiological dysfunction due to vessel constriction through compression is also possible, but the extent, if any of the contribution of this component is uncertain. Long-term serial VEP recordings following tumour removal in optic nerve compression may help to expand our knowledge in this field.

3.4.G. Sarcoidosis

Sarcoidosis is a granulomatous inflammatory disease in which central nervous system or ophthalmic involvement is not uncommon. The optic nerve can be involved producing papilloedema (e.g Obenauf et al., 1978), papillitis or optic neuritis (e.g Statton et al., 1965). Retinal periphlebitis is also a feature (e.g Gould and Kaufman, 1961).

Two patients with probable, but not histologically proven, sarcoidosis are described. The first patient, a 19 year old girl, was admitted for investigation of a six month history of numbness and weakness of both legs with more recent blurring of vision. Ophthalmic examination showed visual acuities of 6/5 on the right, 6/6 on the left with a mild right afferent pupillary defect. Visual fields were full. There were some focal areas of pallor on the retinae with vitreous cells in both eyes and localised foci in the inferior vitreous. The appearances were thought to be those of ocular sarcoidosis. PVEP's from both eyes were of normal and symmetrical amplitude and although the absolute P2 (major positive) component latencies from both eyes were within normal limits, there was a significant 9 msec interocular P2 latency asymmetry, the right eye showing the longer latency. Diffuse flash stimulation showed a 4-8 msec increased latency of the right eye P2 relative to the left but was otherwise unremarkable. Lumbar puncture showed 70 lymphocytes with a protein of 44 mg/100 ml and normal sugar and was thought to confirm the presence of inflammatory disease.

The second patient was a 51 year old lady with a seven year history of ophthalmic disease. When admitted to the Brook Hospital ophthalmic examination showed bilateral disc swelling with increased blind spots and visual acuities of 6/9 bilaterally. There was evidence of intra-ocular inflammatory disease with a few keratic precipitates, vitreous cells and evidence of retinal phlebitis. Fluorescein angiography confirmed disc oedema and showed focal areas of leakage with some peripheral areas of retinitis. The appearances were thought to be consistent with

sarcoidosis. PVEP's from both eyes were markedly delayed with the P2 components at 145 and 135 msec for the right and left eyes respectively. Flash stimulation unfortunately could not be performed.

In both of these patients there was PVEP delay. In the second patient, although this delay was substantial, visual acuity was hardly impaired at 6/9 bilaterally. The patient had other signs of central nervous system involvement and without accurate interpretation of the ophthalmoscopic findings may then have been provisionally diagnosed as suffering from demyelinating disease, which would of course have been supported by the delayed PVEP's. The other patient also showed relative delay from an eye with normal visual acuity and again ophthalmoscopic examination coupled with the PVEP findings appeared to establish the probable nature of this patient's optic nerve and central nervous system disease.

The necessity for at least the results of competent ophthalmoscopic examination to be available to the neurophysiologist when diagnostic PVEP's (and VEP's generally) are reported is emphasised by the findings in these two patients.

No previous reports of either PVEP or FVEP in sarcoidosis have been traced by this author, but the presence of a delay in the PVEP is not particularly surprising. A compressive effect on the optic nerve or chiasm resulting from a leptomeningitis involving the basal areas has been described (Meyer et al., 1953) and indeed Gass and Olsen (1976) describe infiltration of the optic nerves in sarcoidosis by non-caseating tubercles. They also report perivascular lymphocytic and neutrophilic infiltration of the blood vessels of the optic nerve.

3.4.H. Papilloedema

Four patients with papilloedema but no localising signs are described. There was a 45 year old lady with benign intracranial hypertension; a 13 year old girl with hydrocephalus from aqueduct stenosis; a 28 year old man with intracranial hypertension subsequent to viral meningitis and a 25 year old lady who developed severe papilloedema during her first pregnancy two years prior to VEP examination which had only partially subsided. The first three patients had enlarged blind spots, but all four had normal visual acuity with no evidence of secondary optic atrophy. PVEP and FVEP examination were completely normal in all four patients.

These normal findings are in agreement with those of Asselman et al. (1975) using pattern reversal stimulation. Indeed reference to other sections, particularly section 3.6 where many patients had papilloedema as a result of space-occupying lesions, shows that VEP abnormality related to the papilloedema per se rather than to the causative lesion was never seen.

3.4.I. Macular degeneration

Two patients are described with bilateral macular degeneration. One was a 73 year old man with a one year history of deteriorating vision. Ophthalmic examination showed pigment epithelial changes at both maculae with bilateral central scotomata and visual acuity of counting fingers bilaterally. PVEP's were absent; FVEP's showed delayed early components with an absence of major positive component P2.

The second patient was a 78 year old lady with a one year history of failing vision. Ophthalmic examination showed pigmentary changes at both maculae with right visual acuity of 6/60, left of 6/36. Testing on the Friedmann analyser showed very high macular thresholds to light with central scotomata extending out to 5^{o} around fixation. PVEP's were bilaterally delayed (P2 at 154 msec on the right, 141 msec on the left) but of normal amplitude. FVEP's showed questionably delayed early components with a virtual absence of component P2. These findings are illustrated in Fig. 3.4.11.

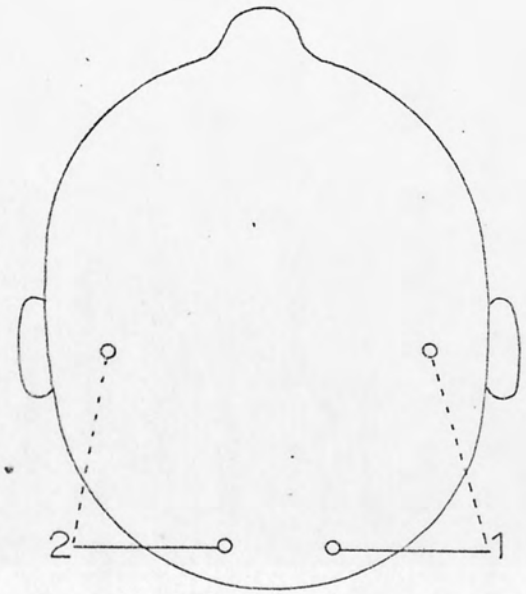
The FVEP findings of reduced P2 component are compatible with those of previous authors (Fishman and Copenhaver, 1968; Roper-Hall et al., 1971).

The PVEP was absent in one patient and markedly delayed in the second. This delay is apparently discrepant with the normal latency, reduced amplitude PVEP described by Sanders (1976) in a 22 year old patient thought to have suffered an acute maculpathy of possible inflammatory nature but a patient has previously been described (patient 3.4.A. vii) with an ischaemic maculopathy who showed similar findings to those in Sanders' patient.

The findings of an absent or relatively absent P2 component with an intact but possibly delayed P1 component in the FVEP seem pathognomic of macular degeneration, no similar waveform having been reported in other conditions. Further conformation with a more extensive series may however

Fig. 3.4.11. VEP findings in a 78 year old lady with bilateral macular degeneration. (The broken vertical line indicates the upper limit of normal latency). See text for details.

E.C. aet 78
V.O.D. 6/60 V.O.S. 6/36



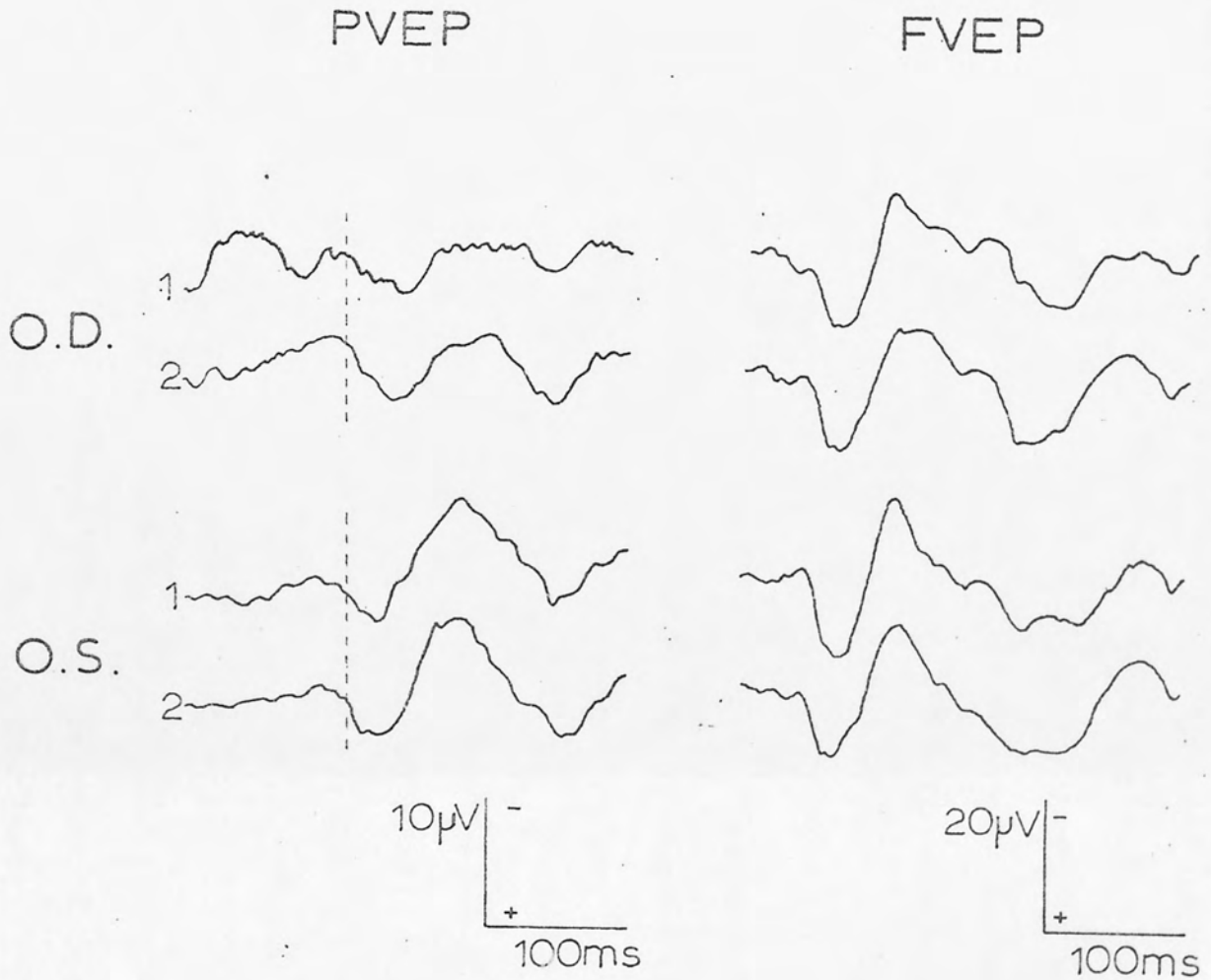


Fig. 3.4.11.

be required before the pathognomic nature of these findings can be unequivocally accepted.

3.4.J. Central serous retinopathy (C.S.R)

This is a form of macular detachment characterised by fairly rapid loss of central vision in the affected eye. Micropsia, teleopsia and difficulty in dark adaptation are also described (see Cogan, 1966a). It has been associated with congenital pits of the optic disc (e.g Ferry, 1963) and indeed Sugar (1964) actually suggested that the detachment is explained by direct leakage of fluid from the vitreous space through the hole and thence beneath the retina.

Three patients with C.S.R are described. In the first, a 39 year old man with visual acuity mildly reduced to 6/9 in the affected eye with a probable central scotoma, both PVEP and FVEP examination were completely normal.

The second patient, a 47 year old man with a visual acuity of 6/18 in the affected eye, displayed a 5 msec interocular P2 latency asymmetry in the PVEP (marginally within normal limits), the FVEP showing a simplified waveform in the affected compared with the non-affected eye. No amplitude asymmetry was present.

The third patient, a 46 year old man, also had visual acuity reduced to 6/18 in the affected eye. Although there was distortion of the Amsler chart, there was no definite scotoma. The PVEP from the affected eye showed a mildly abnormal P2 latency of 110 msec (103 msec in the unaffected eye), the FVEP showing a P2 component delayed by some 10 msec compared with the fellow eye. No interocular amplitude asymmetries were seen but again the FVEP from the affected eye was thought to be of rather simplified waveform compared with the normal eye.

This author has been unable to trace a previous report of the VEP in central serous retinopathy with which to compare these findings.

Cogan (1966, b) suggests that C.S.R is the condition most likely to be mistaken for a demyelinating retrobulbar neuritis. The VEP differences however appear on the basis of these three patients to be relatively marked. In C.S.R PVEP examination was either normal or there was a mild

latency delay, the FVEP also being involved to some extent. The marked dealy in the PVEP accompanied by the less abnormal, often normal, FVEP which is seen in optic nerve demyelination has been described in section 3.3 and reviewed in section 1.4. The VEP interpreter should then be alert for the possibilities of C.S.R when a mildly delayed or normal PVEP, possibly accompanied by waveform simplification or mild relative delay in the FVEP, is found in a patient referred with suspected optic nerve demyelination in whom ophthalmoscopic examination of the fundus is said to be normal. C.S.R can easily be missed ophthalmoscopically if the examiner's attention is focussed on the optic disc and not on the macula.

3.4.K. Retinal lesions

Five patients are described in this classification. One with a retinal/choroidal dystrophy (? choroideraemia), one with a cone/rod dystrophy, one with a cone dystrophy and bulls eye maculopathy and two with retinitis pigmentosa which in one of the patients was unilateral. The VEP findings are summarised in Fig. 3.4.12.

VEP examination was unequivocally abnormal in four of the five patients studied with retinal disease. The exception was the patient (iv) with early retinitis pigmentosa. In the patient (v) with unilateral retinitis pigmentosa the PVEP was completely normal but in the other three patients (i, ii, iii), with more generalised dystrophy, the PVEP was severely affected. Visual acuity reductions were however present in those patients. The FVEP was generally of reduced amplitude.

These findings of reduced amplitude and high variability seen in these patients are similar to those in the patients with retinitis pigmentosa described by Jacobsen et al. (1968) but it is recognised that the small number of patients in the present series is too small for an accurate comparison to be made.

The findings in patient (v) are shown in Fig. 3.4.13. The clinical details are as follows:

v) M.S. aet 27. This lady, who was a strict vegan vegetarian, was referred with a six month history of reduced vision in the right eye. She had consulted her optician who referred her to an ophthalmologist whence she was referred for neurological assessment of a suspected retrobulbar neuritis. She had a brother with confirmed multiple sclerosis and visual involvement, and a sister who had attended an Ophthalmic Hospital complaining of reduced vision where steroids were prescribed. On examination right visual acuity was 6/9 with relative pallor of the optic disc. Fundus examination was otherwise normal. There was a mild generalised visual field constriction. Left visual acuity was 6/5 with

	Pt	aet	diagnosis/V.A/ fields	PVEP	FVEP
i)	S.R.	14	Choroideraemia VOD 6/9; VOS < 6/60 OS central scotoma	OD : normal OS : ?P2 delayed at 160 msec. Amp ↓ 50%	OS amp. ↓ 60% relative to OD. P2 lat. ↑ 4-10 msec. ERG bilat. abnormal.
ii)	A.K.	32	Cone/rod dystrophy V. acuity ? (no English)	Bilaterally absent.	Delayed. Poorly formed. Amplitude 1.0-2.0 μV. ERG absent.
iii)	M.P.	19	Cone dystrophy VOD, VOS 6/24 Bulls eye maculae	OD : questionable P2 at 120-140 msec. OS : absent	Bilat. subnormal amplitude of approx 1.0 μV. ERG absent.
iv)	D.F.	19	Retinitis pigmentosa (R.P) VOD, VOS 6/5 30% field constriction.	Bilaterally normal	Poorly formed early components. Otherwise normal but amp. low. ERG ↓ with no dark adaptation
v)	M.S.	27	Unilateral R.P. sine pigmento. VOD 6/9 some field constriction. VOS 6/5	Bilaterally normal	OD amp ↓ 50-75% relative to OS. OS ERG normal, OD absent.

Fig. 3.4.12. Patients with retinal dysfunction.

amp : amplitude
lat : latency

Fig. 3.4.13. VEP and ERG findings in a 27 year old lady with right retinitis pigmentosa sine pigmento. See text for details.

M. S. aet 27
V.O.D. 6/9 V.O.S. 6/5

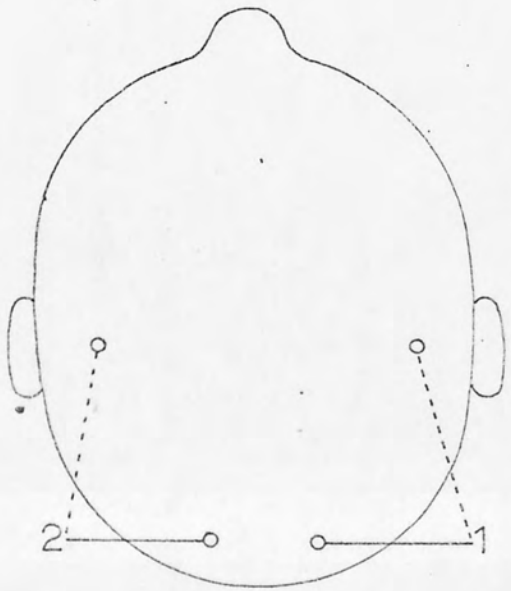
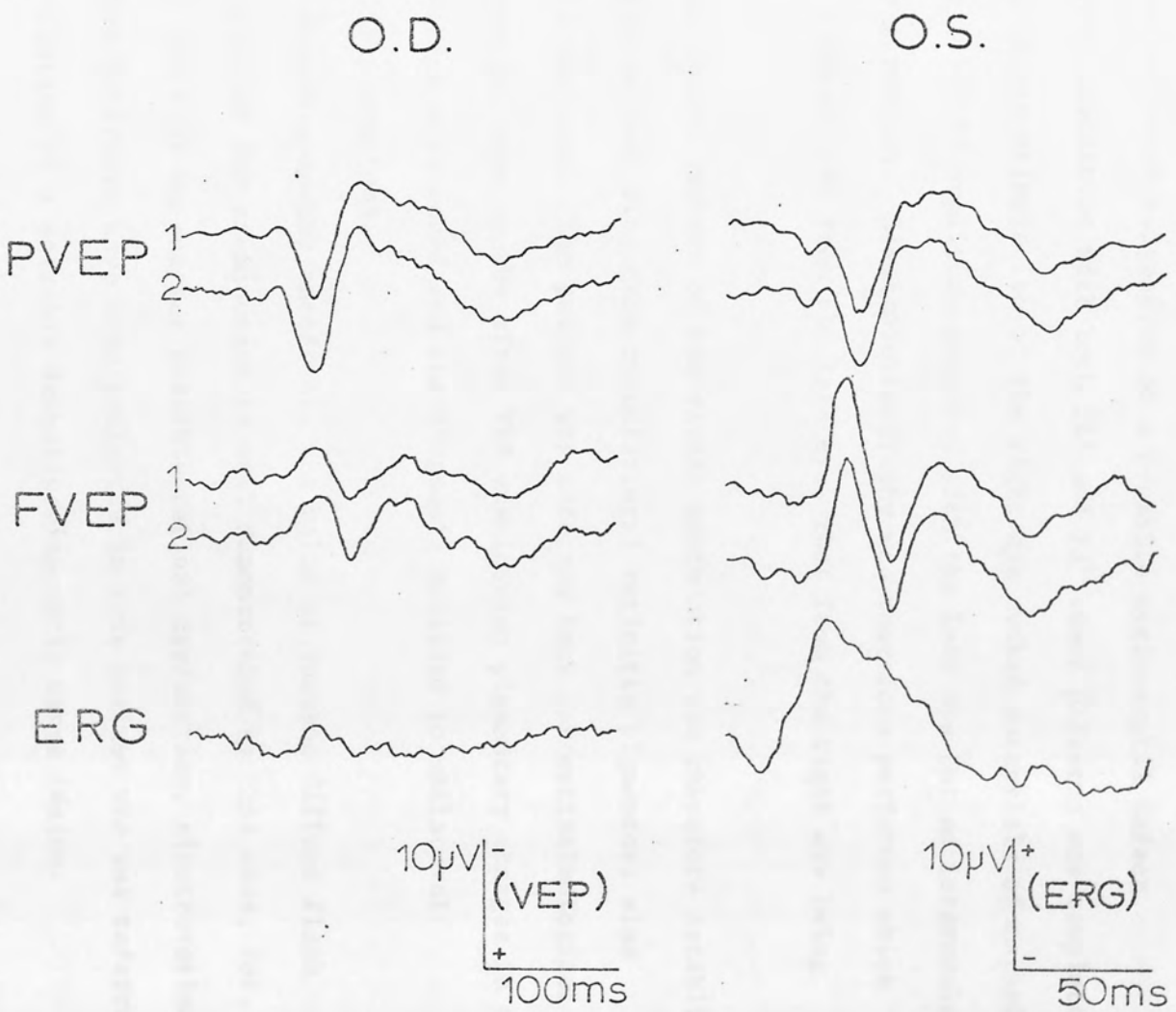


Fig. 3.4.13.



a normal fundus and full visual field. In the cardiovascular system there was a mid-systolic murmur at the left sternal edge with a widely split second sound suggestive of a possible atrio-septal defect.

PVEP examination with both 26' and 13' check patterns was completely normal. Flash stimulation of the right eye evoked potentials of markedly reduced (55-75%) amplitude compared with the left eye but no interocular latency asymmetry. Electroretinography was therefore performed which showed a normal ERG from the left eye, that from the right eye being absent.

The retinal nature of the visual dysfunction was therefore established and a provisional diagnosis of unilateral retinitis pigmentosa sine pigmento was made. The patient was referred back for ophthalmological follow-up and nine months after VEP examination pigmentary changes in the right retina were found and the diagnosis modified to unilateral retinitis pigmentosa.

Although somewhat anecdotal, the value of routine diffuse flash stimulation at VEP examination is well demonstrated by this case, for, without the FVEP to suggest possible retinal dysfunction, electroretinography would not otherwise have been indicated in this patient who was referred for evaluation of a possible demyelinating optic nerve lesion.

3.4.L. Glaucoma

Two patients are described with chronic glaucoma. One was a 15 year old girl who was admitted for investigation of curious binasal field defects involving the inferior quadrants of both eyes. Visual acuities were 6/5 on the right, 6/6 on the left with cupped discs. Intraocular pressures were at the upper limits of normal. FVEP examination was normal. In the PVEP's however, there was a consistent 8-15 msec P2 delay in the right hemisphere traces on stimulation of the right eye, thought to be compatible with a nasal field defect (see also sections 3.5 and 3.6 for VEP findings in patients with hemianopic field defects). Left eye PVEP examination was essentially normal though there were hints of a latency delay in the left hemisphere traces, suggesting a similar process to that affecting the right eye.

The second patient was a 67 year old man referred for investigation of progressive visual loss in the right eye, the nasal field being the worse affected. Visual acuity on the right was counting fingers in the temporal field only. There was optic atrophy and an afferent pupillary defect. Left eye examination was normal. In the VEP's, no potentials were evoked by pattern reversal stimulation of the right eye, that from the left being normal. Flash stimulation evoked no consistent significant interocular or interhemispheric asymmetry of amplitude or latency. The findings were not thought to be compatible with the suspected right optic nerve compression for which the patient was referred. Subsequent ophthalmic assessment showed chronic simple glaucoma in the right eye.

Delayed (phase shift) steady state PVEP's have previously been described in glaucoma (Cappin and Nissim, 1975; Bartl, 1978) and these findings are partially supported by the ipsilateral PVEP seen on right eye stimulation in the first patient described.

A delay in the FVEP evoked by a light emitting diode stimulus has recently been reported (Mierdel and Marre, 1978). No similar delay was

seen in the FVEP's of the two patients in the present series. Other than possible patient differences, the differences in stimulus parameters are extensive and this may be contributory to the apparent discrepancy.

3.4.M. Ocular trauma

The main objective in electrodiagnostic assessment of the visual system following trauma is the determination of the functional state of the retina and optic nerve. This is often extremely difficult by conventional ophthalmoscopic techniques due to the presence of hyphaema and/or traumatic cataract.

Three patients with traumatic injuries to the eye are described. One had a non-perforating injury. Vision was mildly reduced to 6/12 in the affected eye. PVEP, FVEP and ERG examination were all normal.

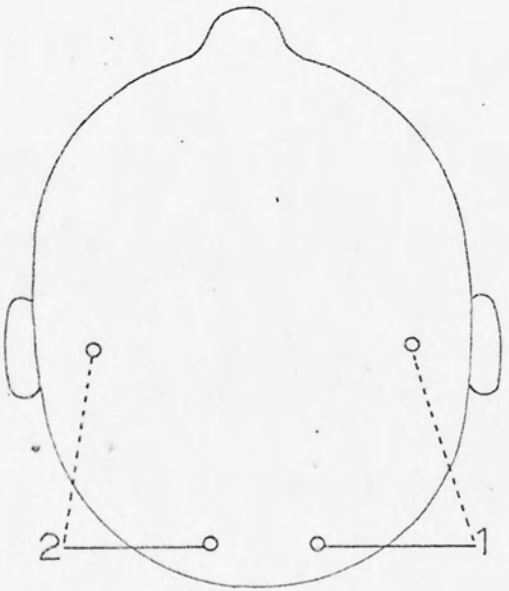
The second patient had received a perforating injury to the left eye some three years prior to VEP examination. Visual acuity was hand movements and there was vascularised corneal scarring with dense cataract. Diffuse flash stimulation evoked potentials which were of slightly higher amplitude from the affected eye. Left eye ERG's were also slightly larger than those from the right. These findings suggested that there was preserved retinal and optic nerve function. Six months following an extracapsular cataract extraction, the left visual acuity was 6/9 with suitable correction confirming the good prognosis for visual recovery following cataract removal suggested by the VEP findings.

The third patient was referred for acute retinal and optic nerve assessment following a glass bottle explosion six days earlier from which he had received lacerations of the cornea, sclera, iris and lens of the right eye. On examination there was dense traumatic cataract with a visual acuity of perception of light with accurate projection in three directions. The left eye was normal. The FVEP amplitude from the right eye was not significantly reduced compared with the left though there was some simplification of the waveform. The right ERG was of slightly higher amplitude than the left. These findings are shown in Fig. 3.4.14.

The clinical problem in this type of patient is to balance the potential visual recovery of the damaged eye against the possible dangers of

Fig. 3.4.14. VEP and ERG findings in a 30 year old man following major trauma to the right eye. See text for details.

C. A. aet 30
V.O.D. P.L. V.O.S. 6/5



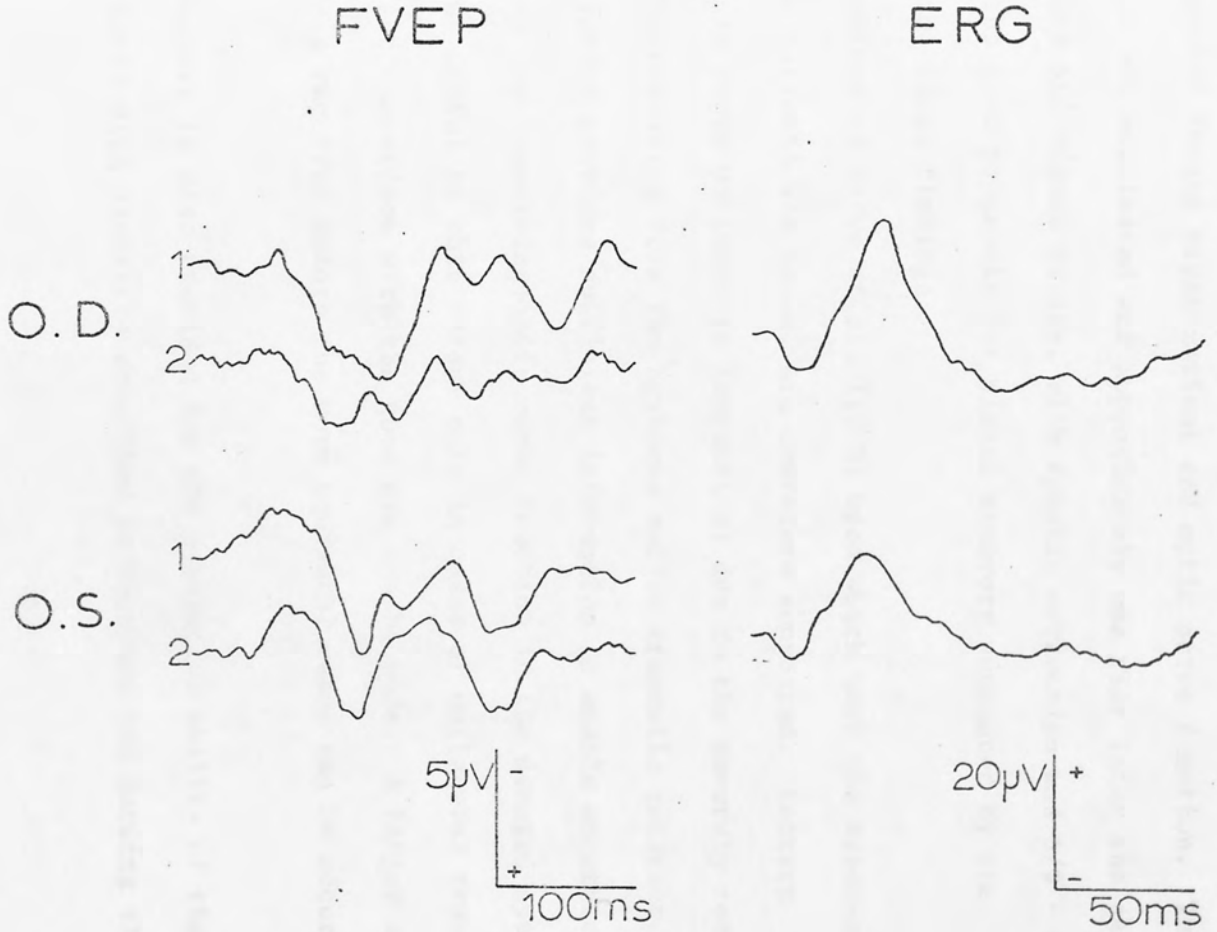


Fig. 3.4.14.

sympathetic ophthalmitis and an early decision to enucleate or retain the eye has to be taken. The electrophysiological findings in this patient suggested intact right retinal and optic nerve function. The right eye was not enucleated and approximately one year later the cataract had reabsorbed and visual acuity, with aphakic correction was 6/9 - 6/12 confirming the good prognosis for visual recovery suggested by the electrophysiological findings.

The findings of Crews et al. (1975) upon which work the assessment in these two patients was based, are therefore supported. Pattern stimulation in these patients is impractical due to the severely reduced visual acuity resulting from the hyphaema and/or traumatic cataract, and flash stimulation provides sufficient information to enable accurate assessment of the (remaining)optic nerve function in the damaged eye. It is however useful to this extent only in cases of unilateral trauma where a direct comparison with the good eye can be made. A larger series of patients is required before the more equivocal cases can be accurately assessed.

Some support is also provided for the predictive ability of the FVEP in patients with cataracts described by Thompson and Harding (1978).

3.5 Lesions of the Optic Chiasm

Fourteen patients with compressive chiasmal dysfunction are included in this series. Ten had pituitary tumours, two had aneurysms, one a craniopharyngioma and one an empty sella syndrome at the time of examination. A further patient with a parapituitary epidermoid cyst was also examined but as this patient had an homonymous scotomatous visual field defect, he will be included in the following section which deals with post-chiasmal lesions. The diagnoses were established by E.M.I scan, air encephalography or at operation. Some of the patients have been discussed in previous presentations by this author (Holder, 1977, 1978a - see appendix). All patients had visual field defects and these are documented with the diagnoses in Fig. 3.5.1. Patients 7 and 8 were both found to have visual field defects on routine spectacle examination, and patient 9, with a large suprasellar extension of a pituitary adenoma, presented with temporal lobe epilepsy. Visual failure was the presenting symptom in all other patients.

The VEP findings are documented in Figs. 3.5.2 and 3.5.3. Initially the PVEP findings will be considered, the examination being abnormal in all patients studied.

As many of the patients presented with impaired vision it may be suspected that there would be a relationship between the PVEP findings and visual acuity. No such relationship is apparent. A pathologically delayed major positive, P2, component was seen in the right eye of patient 10 although the visual acuity at the time of VEP examination was normal at 6/6. In contrast, a normal latency P2 was seen on stimulation of the right eye of patient 1 when the visual acuity was 6/36. In patient 4, although the left eye visual acuity was only marginally reduced at Jaeger 6 (J6) compared with the right eye at J4, the major positive component showed a marked delay with an amplitude reduction of some 60 - 70%. Absent PVEP's were found in patients 9, 11 and 14, the visual acuities

Fig. 3.5.1 Patients with chiasmal dysfunction

Females

		aet	pathology	visual fields
1	M.F.	35	Pituitary adenoma	Temporal loss, O.D.
2	L.C.	49	Craniopharyngioma	B.T.H., O.S.> O.D.
3	P.G.	54	Pituitary adenoma	Paracentral scotomata extending to upper temporal fields
4	J.A.	56	Pituitary adenoma	Temporal loss, O.D.
5	M.P.	59	Pituitary adenoma	B.T.H., O.S.> O.D.
6	J.D.	60	Pituitary tumour ?adenoma	B.T.H., O.S. > O.D.
7	R.G.	63	Aneurysm (?basilar)	B.T.H., O.S.>> O.D.
8	M.A.	71	Pituitary adenoma	Temporal loss, O.D.

Males

9	K.A.	30	Pituitary adenoma	Severe temporal and nasal loss, O.D.; temporal loss, O.S.
10	B.S.	39	Pituitary adenoma	Slight loss both upper temporal fields
11	W.R.	56	Aneurysm (a.c.a.)	Temporal loss, O.D.; N.P.L, O.S.
12	R.D.	60	Empty sella syndrome	B.T.H
13	G.N.	63	Pituitary adenoma	B.T.H. O.S. >> O.D.
14	H.F.	74	Pituitary adenoma	B.T.H. O.D. > O.S.

B.T.H Bitemporal hemianopia
a.c.a Anterior communicating artery
N.P.L No perception of light
O.D. Right eye
O.S. Left eye

Fig. 3.5.2 PVEP findings in patients with chiasmal dysfunction

Pt	Eye	V.A.	P2 (msec)	N2-P2 (μV)	P2-N3 (μV)	Contralateral potential (P2 unless specified)
1	OD	6/36	96.N	2.0	3.0	Absent
	OS	6/9	96.N	4.0	5.5	P2 lat↑6 msec; N3 lat↑20 msec
2	OD	6/9	104.N	5.0	5.6	Amp↓50%; lat↑5-8 msec
	OS	6/9	108.N	3.4	3.4	Absent
3	OD	6/18	104.N	4.8	5.0	As ipsilateral
	OS	6/24	100.N	9.8	7.6	Amp↓70%; lat↑4-6 msec
4	OD	J4	102.N	16.0	18.0	As ipsilateral
	OS	J6	117.A	4.4	6.8	As ipsilateral
5	OD	6/5	96.N	6.0	13.2	Amp↓50 - 60%
	OS	6/9	106.N*	3.6	4.8	Amp↓40-50%; lat↑4-8 msec
6	OD	6/9	104.N	6.4	6.8	Amp↓70%
	OS	6/60	120-30.A	2.0	5.6	Absent
7	OD	6/9	120.A	0.8	1.9	Variable. Often lat↑, amp↓
	OS	6/18	140.A	1.3	1.5	Absent
8	OD	6/9	101.N	4.7	8.4	Amp↓40%; N3 lat↑10 msec
	OS	6/24	130.A	1.0	1.0	Absent
9	OD	6/36	Absent	-	-	-
	OS	6/5	100.N	2.0	4.5	As ipsilateral
10	OD	6/6	116.A	7.0	10.8	As ipsilateral
	OS	6/5	104.N	9.4	14.6	As ipsilateral
11	OD	CF	Absent	-	-	-
	OS	NPL	Absent	-	-	-
12	OD	6/36	148.A	4.4	3.0	When seen, P2 lat↑10-15 msec
	OS	6/36	150.A	2.0	2.2	When seen, P2 lat↑10-15 msec
13	OD	6/12	118.A	4.4	6.4	P2 lat↑4 msec; N3 lat↑20 msec
	OS	6/60	140.A	2.4	4.2	Absent
14	OD	6/24	145.A	2.1	1.2	Absent
	OS	6/24	Absent	-	-	-

* In this patient, although the absolute latencies from both eyes are within normal limits, the magnitude of the interocular latency asymmetry is abnormally large.

A Abnormal

N Normal

Fig. 3.5.3 FVEP findings in patients with chiasmal dysfunction

Pt	Eye	P2 (msec)	N2-P2 (μV)	P2-N3 (μV)	Contralateral potential (P2 unless specified)
2	OD	116.N	5.0	7.0	N3 lat ↑ 8-12 msec
	OS	120.N	2.6	4.2	P2 lat ↑ 5-10 msec
3	OD		Unusual waveform. No significant		
	OS		interocular or interhemispheric asymmetry		
4	OD	108.N	4.8	5.6	As ipsilateral
	OS	92-128.N	2.1	4.0	WFD
5	OD	120.N	9.6	8.8	Amp ↓ 50%
	OS	120.N	8.0	7.2	As ipsilateral
6	OD	138.N	6.4	3.8	As ipsilateral
	OS	130.N*	11.0	9.6	As ipsilateral
7	OD	132.N	3.6	3.4	As ipsilateral
	OS	148.A	3.0	2.8	As ipsilateral
8	OD	115.N	3.0	6.4	As ipsilateral
	OS	110.N	2.8	5.4	Amp ↓ 75%
9	OD	124.N	1.0	2.0	As ipsilateral
	OS	116.N*	4.6	7.2	As ipsilateral
10	OD	126.N	2.0	5.8	As ipsilateral
	OS	120.N	5.2	10.4	As ipsilateral
11	OD	140-50.A	1.0	1.0	Absent
	OS	Absent	-	-	-
12	OD	121.N	6.1	6.7	As ipsilateral
	OS	119.N	6.6	6.4	As ipsilateral
13	OD	136.N	6.0	5.6	As ipsilateral
	OS	152.A	3.0	2.2	As ipsilateral
14	OD	153.A	3.3	4.8	Amp ↓ 60-70%
	OS	150.A	2.8	4.2	As ipsilateral

* significant interocular asymmetry

WFD waveform distortion

ranging from 6/24 to no perception of light. Clearly then no immediately apparent correlation exists between visual acuity and PVEP findings in patients with chiasmal compression.

Reduced amplitude potentials were seen in eight patients (1, 3-8 and 12), generally the potential evoked by stimulation of one eye being significantly reduced compared with the fellow eye. Absent responses are not classed as amplitude reductions per se.

Delayed latencies of the P2 (major positive) component occurred in nine patients (2, 4, 6, 7, 8, 10, 12, 13 and 14). In patient 5, although the absolute latencies from both eyes were within normal limits for age, the interocular latency asymmetry of 10 msec is highly significant. The maximum latency delays seen were some 35 - 40 msec above the upper limit of normal (patient 12).

It can be seen (Fig. 3.5.2) that considering amplitude and latency measures only, together with the presence or absence of the PVEP, that PVEP examination was abnormal in all patients studied with compressive chiasmal dysfunction.

However, most of these patients had bitemporal visual field defects, due to pressure on the decussating fibres in the optic chiasm. That is, fibres from the optic nerve on one side to the contralateral hemisphere are involved in the production of the field defect. Similarly one of the striking features in these patients was an asymmetrical distribution of the PVEP over the two hemispheres, the contralateral potential always being affected relative to the ipsilateral where an interhemispheric asymmetry was present. Indeed, in only four patients (4, 9, 10, 11) was there no interhemispheric asymmetry. Of the remaining twenty eyes, only four failed to show an unequivocal interhemispheric asymmetry (the right eye of patients 3, 7 and 8; the left eye of patient 14). In six patients therefore, in addition to any ipsilateral abnormalities which may be present, stimulation of either eye evoked potentials in which

further abnormality was localised contralaterally to the stimulated eye. This corresponds with the findings that would have been predicted on a purely neuroanatomical basis. There was no specificity to this contralateral abnormality which could take the form of a latency delay (e.g patient 12), an amplitude reduction (e.g patient 5), a combination of amplitude and latency changes (patient 2) or the absence of a contralateral potential (e.g patient 1).

It is of interest here that in the left eyes of patients 1 and 8, a contralateral abnormality localisation was apparent in the absence of visual field defect. In other patients however no significant interhemispheric asymmetry was seen despite the presence of a visual field defect (the left eyes of patients 3 and 9; the right eye of patient 4; both eyes of patient 10). Eyes from which no PVEP could be elicited have not been included as failing to show an interhemispheric asymmetry.

Additional recordings with the 13' check pattern in an 8^{o} total field were taken in patients 3-7, 9, 10 and 13. In patients 4 and 13 the findings were essentially unchanged from those with the standard stimulus (26' checks, 11^{o} total field). In all other patients the magnitude of the interhemispheric asymmetry seen with the 26' check stimulus was enhanced, and indeed, in patient 10 a significant interhemispheric latency asymmetry (contralateral potential delayed with respect to the ipsilateral potential) was observed in the major positive component which had not been present using the 26' check stimulus.

The findings obtained with diffuse flash stimulation are detailed in Fig. 3.5.3. Monocular diffuse flash stimulation was not performed in patient 1. Potentials of abnormal amplitude, usually reduced compared with the fellow eye were seen in six patients (4, 6, 9, 10, 11, 13), while potentials displaying latency abnormalities were seen in seven patients (6, 7, 9, 10, 11, 12, 14). The latency changes represented absolute abnormalities in five eyes of four patients (7, 11, 13, 14),

the remaining three patients (6, 9, 10) showing an interocular latency asymmetry of abnormally large magnitude. No potential was recorded following left eye stimulation in patient 11, this being the only absent potential being noted in the FVEP's.

An interhemispheric potential asymmetry occurred in seven eyes of six patients (2, 4, 5, 8, 11, 14). In patient 2 there was an interhemispheric latency asymmetry, in patients 5, 8 and 14 there was an interhemispheric amplitude asymmetry, and no potential was seen in the left hemisphere traces following stimulation of the right eye in patient 11. A marked distortion of the waveform in which no components could be accurately identified was seen in the right hemisphere traces of patient 4 when the left eye was stimulated, and even in the left hemisphere traces the major positive component was rather extended and modified compared with the fellow eye.

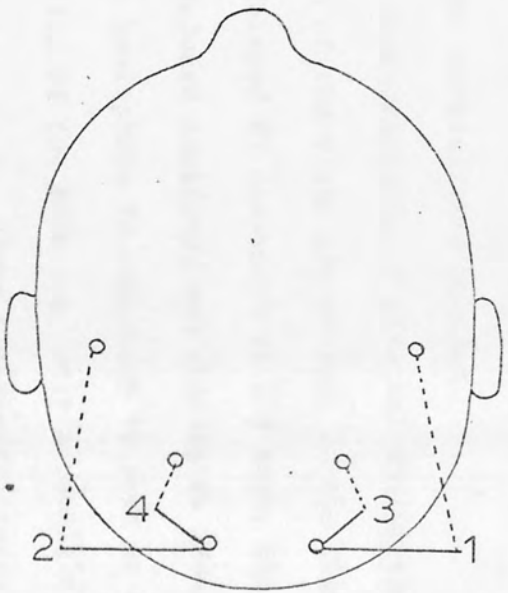
A completely normal FVEP examination occurred in two patients (3, 12).

Typical VEP findings are illustrated in Figs. 3.5.4 - 3.5.7; the case histories are as follows:

i) Fig. 3.5.4 L.C. (patient 2). One year prior to admission this 49 year old lady had experienced a two month period of headaches and lethargy which had cleared up spontaneously. Immediately prior to admission this had returned associated with reduced vision in the temporal field of the left eye. On examination visual acuity was 6/9 bilaterally. There was bitemporal hemianopia, marked in the left eye with probable macular involvement, the right eye showing superior temporal field loss only. There was thought to be mild left proptosis. Skull X-ray showed an area of calcification thought to be suggestive of a craniopharyngioma; an air encephalogram showed a suprasellar mass which was found at operation to be a craniopharyngioma. In the PVEP's stimulation of the right eye evokes a potential of reduced amplitude and increased latency in the left hemisphere traces compared with the right; stimulation

Fig. 3.5.4. VEP findings in a 49 year old lady with a craniopharyngioma. See text for details.

L.C. aet 49
VOD 6/9 VOS 6/9



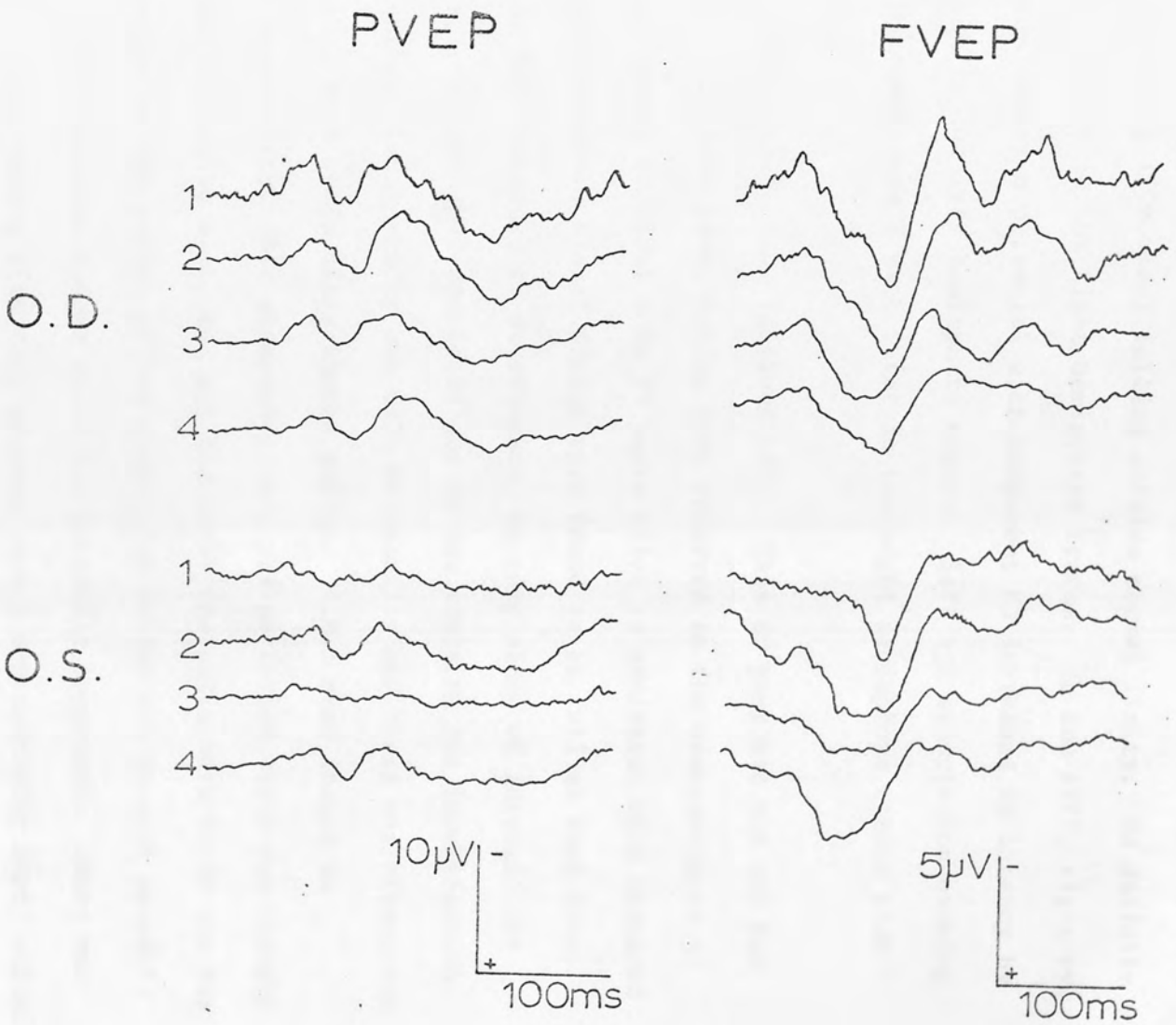


Fig. 3.5.4.

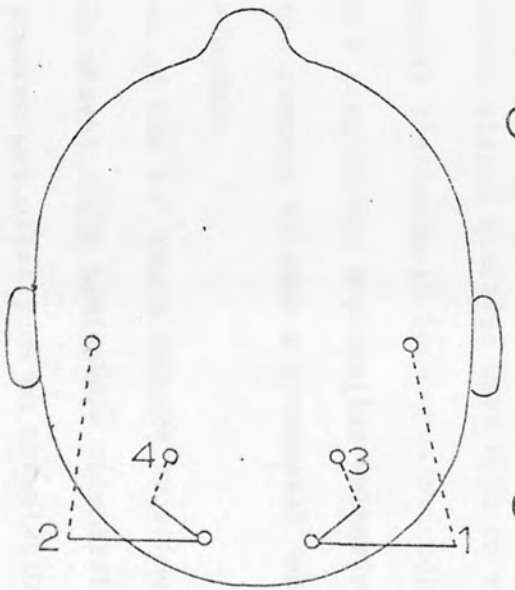
of the left eye evokes a left hemisphere potential with the major positive component latency (108 msec) falling outside normal limits. No definite potential is seen in the right hemisphere traces. In the FVEP, right eye stimulation evokes a potential with component N3 increased in latency by 8 - 12 msec in the left hemisphere traces; left eye stimulation evoking the P2 component some 8 msec later in the right hemisphere traces than the left.

ii) Fig. 3.5.5 R.D. (patient 12). This 60 year old man had had poor vision for some time, having been referred to the neurosurgeons at the Brook General Hospital some 25 years prior to admission with impaired vision and headache. Visual fields were found to be full at that time. His vision had continued to deteriorate, he complained of intermittent giddiness, the headaches continued and he was admitted for investigation. On examination visual acuity was 6/36 bilaterally and there was bitemporal hemianopia. Both optic discs showed pallor. E.M.I scan showed no definite abnormality. Air encephalography was performed which was thought not to show an active mass, but air did enter the sella anteriorly and the configuration of the region of the tuberculum sellae was thought possibly to represent a previous tumour which had partially regressed. There was presumed to have been a pituitary adenoma with a now partially empty sella. It was felt that there was no evidence of an active chiasmal lesion and therefore no place for surgical exploration.

The PVEP's are characteristic of chiasmal dysfunction. Pattern reversal stimulation of the right eye evoked, in the right hemisphere traces, a markedly delayed P2 component at 148 msec, the left hemisphere potential being of reduced amplitude and showing an additional 10 - 15 msec delay. A clear left hemisphere P2 component is seen at approximately 150 msec on stimulation of the left eye, only a possible P2 being seen at approximately 160 msec in the right hemisphere traces. In contrast, no consistent significant interocular or interhemispheric asymmetry of amplitude or latency is seen in response to diffuse flash stimulation,

Fig. 3.5.5. VEP findings in a 60 year old man with an empty sella syndrome. See text for details.

R.D. aet 60
V.O.D. 6/36 V.O.S. 6/36



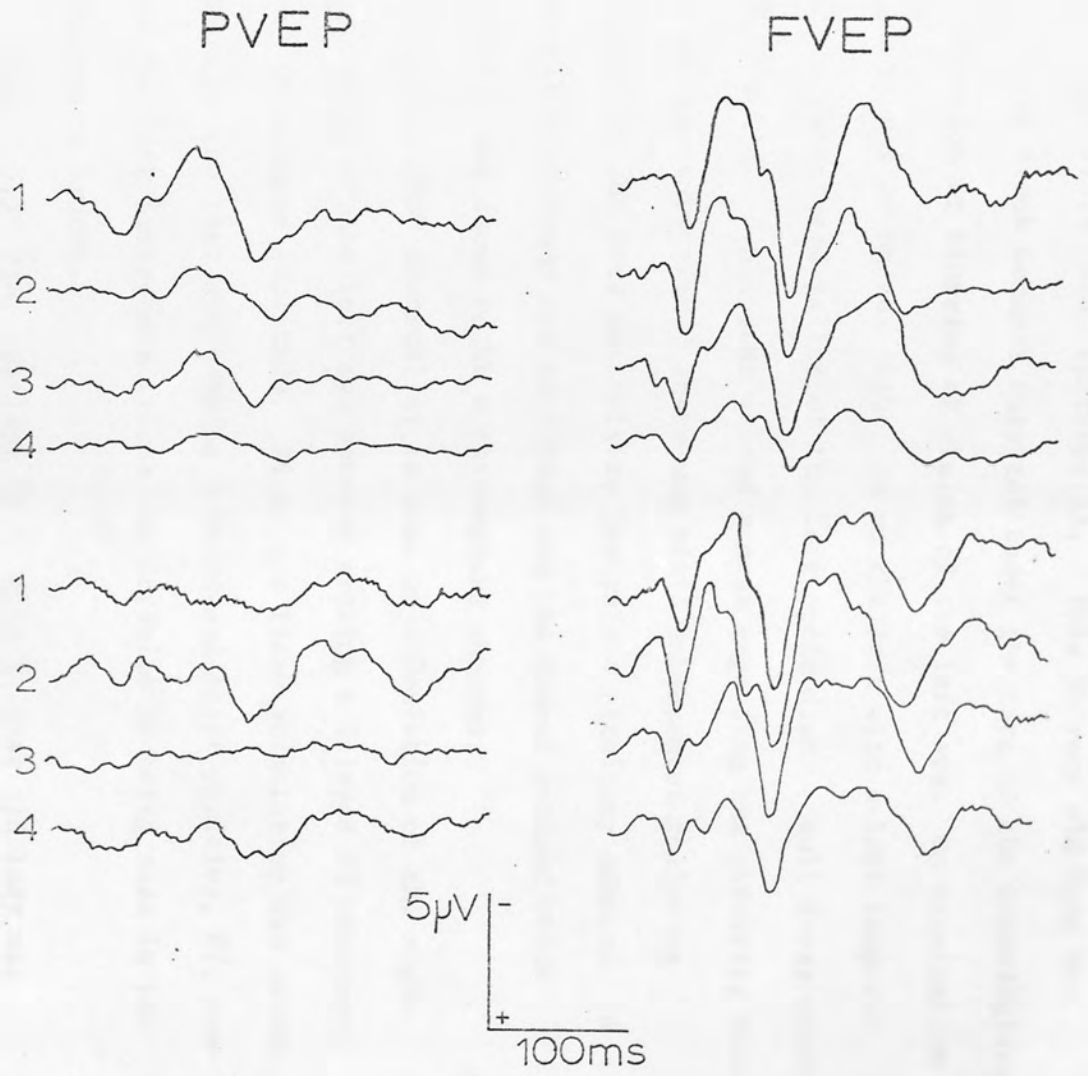


Fig. 3.5.5.

the FVEP's being within normal limits.

iii) Fig. 3.5.6 J.A. (patient 4). This 56 year old lady was admitted to the Brook General Hospital under the care of the neurologists for investigation of blurring of vision of the left eye. On examination visual acuity was J4 on the right, J6 on the left with a left temporal visual field defect and pallor of the left optic disc. Skull X-ray showed an enlarged sella. E.M.I scan showed a mass expanding the pituitary fossa with suprasellar extension. There was vivid enhancement following Conray injection and this was felt to indicate a pituitary adenoma. A right frontal craniotomy was performed and the tumour excised which histologically was shown to be a chromophobe adenoma.

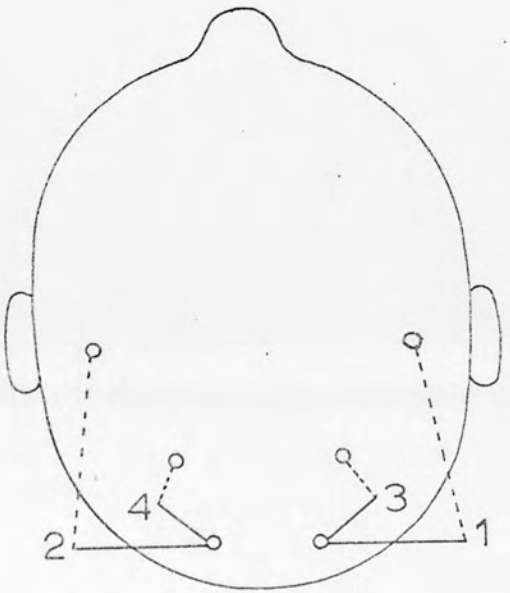
No definite PVEP abnormality is seen on stimulation of the right eye, stimulation of the left eye however evoking a delayed P2 component (120 msec) of reduced amplitude. Right eye flash stimulation was normal, stimulation of the left eye evoking a broadened major positive, P2, component in the left hemisphere traces, no definite P2 being seen in the right hemisphere traces.

iv) Fig. 3.5.7 P.G. (patient 3). This 54 year old lady was admitted to the Regional Neurological Unit at the Brook General Hospital for investigation of mild visual disturbance of approximately one year's duration. On examination visual acuities were 6/18 on the right, 6/24 on the left with paracentral scotomata in both eyes extending into the upper temporal fields. E.M.I scan showed suprasellar extension of a pituitary tumour. The tumour was removed through a transnasal approach and found to be a chromophobe adenoma.

In the PVEP's use of the 13' check pattern to stimulate the left eye results in a virtually absent right hemisphere potential compared with the reduced but clearly present potential seen on stimulation with the 26' check pattern. An increased P2 component latency can also be seen in the right hemisphere traces with the larger check pattern.

Fig. 3.5.6. VEP findings in a 56 year old lady with a chromophobe adenoma of the pituitary. See text for details.

J.A. aet 56
VOD J4 VOS J6



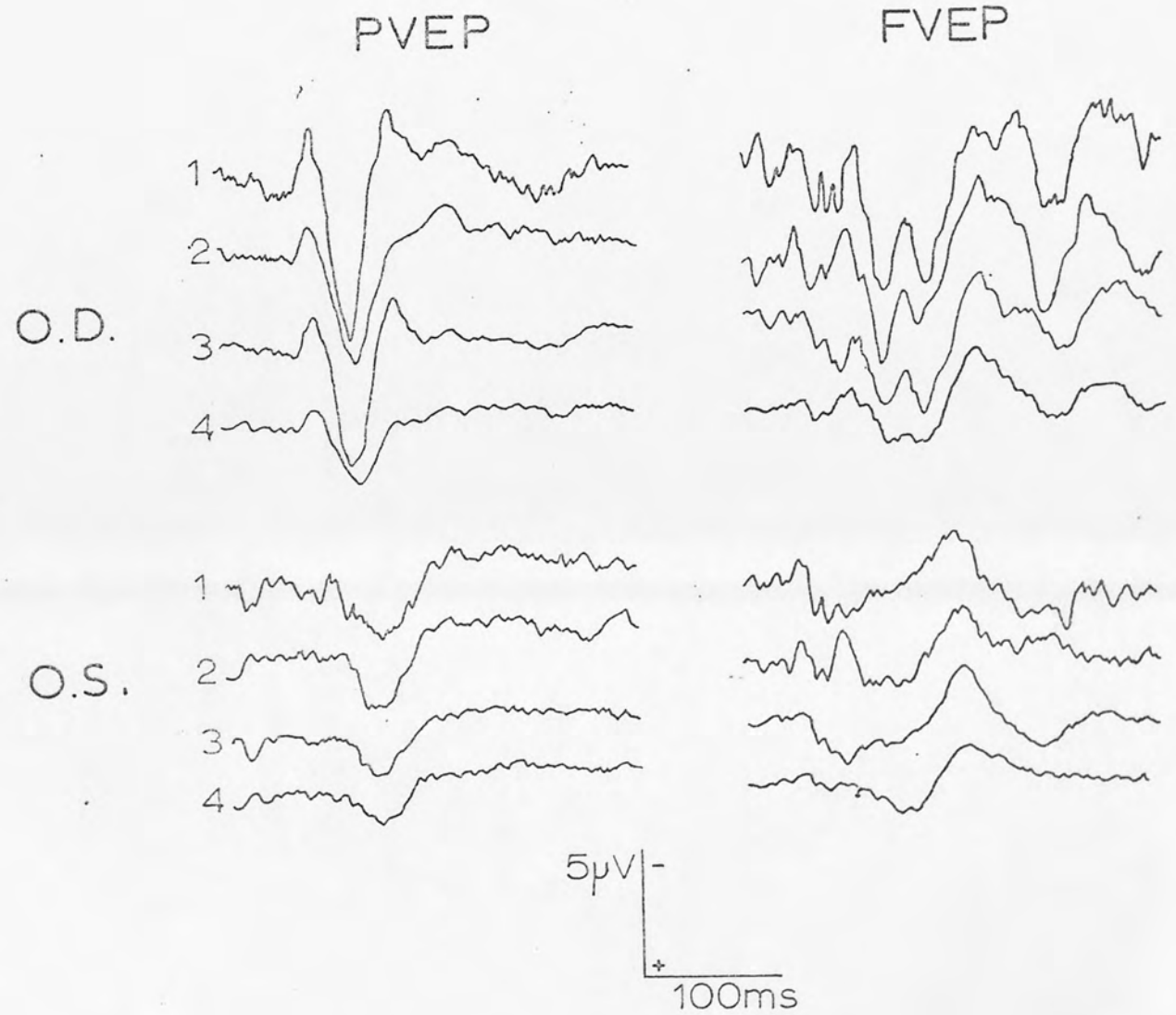


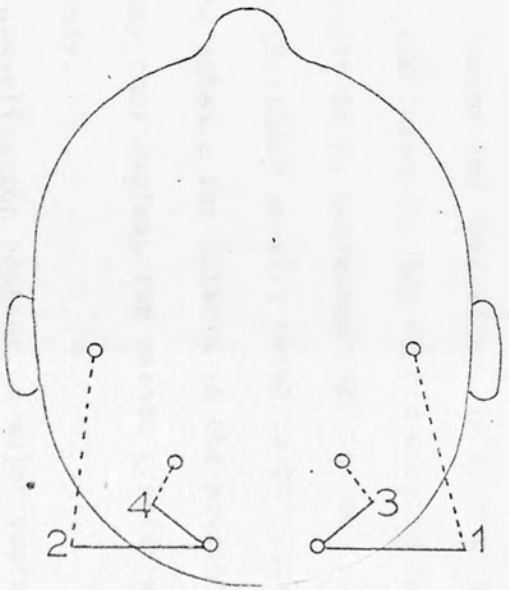
Fig. 3.5.6.

Fig. 3.5.7. The effects of changes in stimulus parameters in a 54 year old lady with a chromophobe adenoma of the pituitary. See text for details.

P.G. aet 54
VOS 6/24

PVEP
26'/11°

PVEP
13'/8°



O.S.

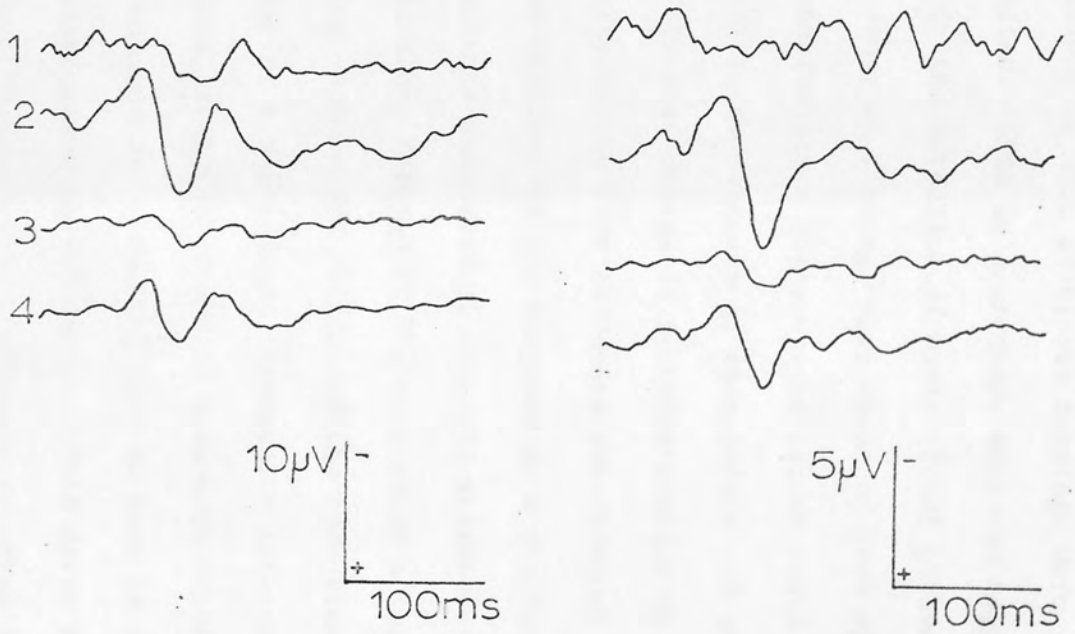


Fig. 3.5.7.

The value of the PVEP in chiasmal compression is confirmed, for, as in a previous report (Halliday et al., 1976) the findings were abnormal in all patients studied. Also in accordance with that report, the sensitivity of the PVEP in the detection of early visual pathway involvement is confirmed as abnormal findings were obtained from eyes which clinically showed no abnormality - there was no visual field defect, no loss of visual acuity, no evidence of disc pallor and yet the PVEP could be abnormal. This of course is somewhat similar to demyelination where the ability of the PVEP to detect sub-clinical optic nerve demyelination has resulted in its adoption as a standard clinical investigation in patients suspected of multiple sclerosis.

Again similar to demyelination, delayed PVEP's were often a feature in chiasmal compression, being seen in 39% (11/28) of the eyes studied, with a further patient displaying a significant interocular latency asymmetry although the absolute latencies from both eyes were within normal limits. Indeed, the maximum delay seen of 35 - 40 msec is akin to those regularly seen in optic nerve demyelination. This delay is rather greater than the maximum 20 msec delay previously reported in compressive lesions (Halliday et al., 1976), and it is possible that this reflects the differences in stimulus parameters, particularly as the maximum delays were found in patients with reduced visual acuity. It has been suggested (Duwaer and Spekreijse, 1978) that reduced visual acuity simulated by the interpolation of a 3 dioptre lens between patient and stimulus may result in an increased PVEP latency. A reduction in check size from 50' (Halliday et al., 1976) to 26' (used in the present study) may therefore enhance the effects in the presence of reduced visual acuity and may thus explain the rather greater maximum delay observed in this study.

In contrast to demyelination however, a major feature of the PVEP in chiasmal compression is the presence of an interhemispheric asymmetry

seen in 70% (10/14) of the patients studied. Invariably this additional abnormality was localised contralaterally to the stimulated eye, and therefore contralaterally to any visual field defect which may be present. It is emphasised that this interhemispheric asymmetry is a strong pointer towards a compressive lesion, particularly if seen with both eyes (forming the 'crossed' asymmetry to use the term originally coined by Halliday et al., 1976), and the importance of multichannel recording using electrodes situated away from the mid-line is stressed. The differentiation between optic nerve demyelination and a compressive chiasmal lesion is clearly important as early surgical intervention in a compressive lesion may well result in complete recovery. The use of a single recording channel by Wildberger et al. (1977) may possibly explain their failure to correctly diagnose compression in their two reported cases.

The finding of abnormality contralateral to the visual field defect is in agreement with the findings of Wildberger et al. (1976) who used 8/sec stimulation, and is also in agreement with the findings that would have been predicted on a purely neuroanatomical basis. It is however in disagreement with the invariably ipsilateral abnormality localisation reported by Halliday et al. (1976) and also by Hume and Cant (1976) though the latter authors only cite one case. This apparent discrepancy may well be due to differences in stimulus and recording parameters. The possible importance of stimulus parameters is illustrated by the finding that changing the stimulus parameters when examining the PVEP in a single patient with a pituitary tumour could cause the abnormality to change sides (Harding, G.F.A. Personal communication: Discussion EEG Society meeting, London, January 1977). The possible influence of stimulus parameters is also supported by the increased contralateral abnormality localisation seen with the 13' checks in an 8^{o} field.

The problem of abnormality lateralisation in relation to visual field defects is also of particular relevance to patients with homonymous field defects and will be discussed in detail in the following section which deals with more posteriorly situated lesions.

A further possible distinguishing feature between the delay of demyelination and the delay of compression is the amplitude and waveform associated with this delay (see also section 3.4.F dealing with optic nerve compression). Amplitude reductions can be observed in demyelination but tend to be associated with markedly reduced visual acuity and/or a markedly delayed major positivity. Similarly, disturbances of waveform are possible but uncommon in demyelination. However it can easily be seen from Fig. 3.5.2 that marked amplitude reductions in the presence of relatively mild latency delays are not uncommon in compressive chiasmal lesions, and this combination may again alert the interpreter to the possibility of a compressive rather than a demyelinating lesion. To reiterate, however, it is the interhemispheric asymmetry with the abnormality contralateral to the stimulated eye (but possibly ipsilateral in other laboratories dependent on stimulus and recording parameters) that convincingly points towards a compressive lesion.

The high incidence (100%) of PVEP abnormality seen in compressive chiasmal lesions is not however seen with diffuse flash stimulation. Completely normal FVEP's were recorded in two patients, three further patients only displaying a significant interhemispheric asymmetry. In two of these the interhemispheric asymmetry was only seen on stimulation of one eye, in the third an equivocal interhemispheric asymmetry was also seen in the second eye. Only three (23%) displayed absolute abnormalities, the remaining four patients showing a significant interocular asymmetry. 27% (7/26) of the eyes examined showed an interhemispheric asymmetry compared with 57% (16/28) for the PVEP. This abnormality, as with the PVEP, always occurred contralaterally to the stimulated eye, and therefore contralaterally to the field defect. The changes were not

confined to either amplitude or latency, no clear pattern of abnormality being evident. This contralateral abnormality localisation is in agreement with those few cases previously reported (Vaughan and Katzman, 1964 (5 cases); Jacobsen et al., 1968 (1 case); Fisher et al., 1968 (1 case); Kooi et al., 1973 (1 case), but the maximum effect on the early components of the FVEP (Kooi et al., 1973) cannot be confirmed.

None of the patients with abnormal FVEP had a normal PVEP but in one patient the PVEP was absent but the FVEP, although of low amplitude, displayed a significant contralateral abnormality (no contralateral potential was seen), suggestive of dysfunction of the decussating fibres. Flash stimulation may then be most useful where the pattern response is absent, the FVEP per se being much less sensitive in chiasmal compression than the PVEP.

3.6 Post-Chiasmal Lesions

Forty-five patients form the subject matter for this group, thirty-seven of whom had visual field defects. In twenty-one patients there was a space-occupying lesion (S.O.L), sixteen of these having visual field defects. These patients are detailed in Fig. 3.6.1. Twenty-three patients had lesions which were not space-occupying (non-S.O.L), twenty-one of whom had visual field defects. The forty-fifth patient had both space-occupying and non-space-occupying lesions. These patients are detailed in Fig. 3.6.2. In all cases the diagnosis was established by E.M.I scan, angiography or at operation. Patient 7 with a parapituitary epidermoid cyst had an homonymous scotomatous hemianopic field defect and it was therefore felt more appropriate to classify him as post-chiasmal rather than chiasmal. Patient 16 was examined following occipital lobectomy for adenocarcinoma. Some of these patients have been partially described in a previous report by this author (Holder, 1978b, see appendix).

The VEP findings will initially be discussed with reference to the presence of S.O.L or non-S.O.L. In all but two patients (17 and 45) there was no significant interocular asymmetry, the abnormality generally being of an interhemispheric nature. In this section therefore the terms unilateral and bilateral will refer to hemispheric values and not ocular values.

Patient 17 had a very large tumour arising from his right temporal lobe which clinically had extended anteriorly to the medial aspect of the sphenoid giving rise to a Foster-Kennedy syndrome of right optic atrophy and left papilloedema. The VEP's were highly abnormal and because of the additional involvement of the anterior visual pathways this patient will be discussed individually and is therefore excluded from the immediately following results summaries.

i) Patients with space-occupying lesions.

An abnormal PVEP was seen in fifteen patients, fourteen of whom had visual field defects. The patient with abnormal PVEP but no visual field

Fig. 3.6.1 Patients with space-occupying post-chiasmal lesions

	Pt	aet	diagnosis	Visual Fields
Females				
1	S.D.	34	L. temp.-par. astrocytoma	RHSQ
2	I.C.	48	L. thalamic astrocytoma	Full
3	R.P.	54	L. temp.-occ. glioma	RHSQ
4	G.K.	55	L. occipital glioma	RHH
5	O.W.	55	L. parietal glioma	RHH
6	J.B.	61	L. temp,-par.-occ. glioma	RHH
Males				
7	D.L.	23	Parapituitary epidermoid cyst	RH scot.
8	D.W.	38	R. temporal astrocytoma	LHH
9	R.W.	39	R. parietal glioma	Full
10	W.B.	42	L. occ.-par. I.C.H	RHH
11	R.C.	43	R. parietal secondary	Full
12	K.S.	52	R. par.-occ. melanoma	LHH
13	L.M.	54	L. temp.-par. secondary	Full
14	E.P.	54	R. parietal astrocytoma	LHIQ
15	C.W.	55	L. par.-occ. glioma	RHH
16	A.B.	58	R. occipital adenocarcinoma	LHH
17	V.C.	58	R. temporal glioma	LHH
18	H.W.	62	L. temporal glioma	Full
19	W.T.	63	L. temporal glioma	RHH
20	H.W.	63	R. par.-occ. I.C.H	LHH
21	J.S.	67	L. temp.-par. astrocytoma	RHH

temp. - temporal; par. - parietal; occ. - occipital
I.C.H. - intracerebral haematoma
(R)HH - (right) homonymous hemianopia
(L)HSQ - (left) homonymous superior quadrantanopia
HIQ - homonymous inferior quadrantanopia
H.scot. - homonymous scotomatous field defect

Fig. 3.6.2 Patients with non space-occupying post-chiasmal lesions

	Pt	aet	diagnosis	visual fields
Females				
22	V.M.	68	L. post. cer. art thrombosis	RHH
23	E.L.	69	Bilat. occipital infarction	RHH, LHIQ
Males				
24	A.R.	21	R. parietal infarct (P.N.)	LHH
25	J.M.	22	R. occipital infarct	LHH
26	C.S.	23	L. post. cer. art. stenosis	RHH
27	P.R.	46	L. occipital infarct	RHH
28	S.M.	49	R. embolic C-V episodes	LHH
29	C.C.	52	Bilat. occipital infarction	LHSQ
30	J.T.	56	R. occipital infarct	LHH
31	I.T.	56	R. par.-occ. infarct	LHH
32	W.S.	57	L. par.-occ. infarct	RHIQ
33	J.H.	58	R. Int. carotid occlusion	Full
34	J.N.	58	R. post. cer. art. thrombosis	LHH
35	R.H.	59	Bilat. occipital infarction	LHH, RHSQ
36	C.K.	62	Bilat. occipital infarction	NPL
37	J.M.	63	Bilat. occipital infarction	RHH, LHIQ
38	W.S.	64	L. Int. carotid occlusion	Full
39	J.H.	65	R. occipital infarct	LHSQ
40	T.N.	67	Bilat. occipital infarction	see below
41	F.B.	70	L. occipital infarct	RHH
42	A.B.	70	R. occipital infarct	LHIQ
43	G.S.	71	Bilat. occipital infarction	see below
44	H.F.	74	L. occipital infarct	RHSQ

Contd./...

Fig. 3.6.2 continued

Female miscellaneous

45	J.H.	27	Agenesis of corpus callosum	Full

par.	-	parietal; occ. - occipital
post. cer. art.	-	posterior cerebral artery
C-V.	-	cerebro-vascular
P.N.	-	polyarteritis nodosa
(R)HH	-	(right) homonymous hemianopia
(L)HSQ	-	(left) homonymous superior quadrantanopia
HIQ	-	homonymous inferior quadrantanopia
NPL	-	no perception of light.

Patient 40 had a partial altitudinal field defect involving the temporal and nasal fields of both eyes.

Patient 43 had, to a 5 mm pin, small preserved areas of vision in both eyes, just below and internal to the fixation point.

Patient 45, with agenesis of the corpus callosum, also had a lipid filled cyst at the anterior end of the third ventricle.

defect (patient 2) was a lady with a left thalamic astrocytoma. PVEP's of normal latency but abnormally large amplitude were recorded bilaterally in this patient with no interhemispheric asymmetry. This patient is also unique in having a lesion confined to one hemisphere but bilaterally abnormal PVEP's. Of the five patients with normal PVEP examination, four had full visual fields.

The remaining fourteen patients with abnormal PVEP's all had visual field defects. Unfortunately formal perimetry was not performed in all these patients and the presence or absence of macular involvement on visual field examination is therefore uncertain in some of these cases. Although various types of abnormality were seen, in all cases the abnormality, represented by a significant interhemispheric asymmetry, was recorded over the involved hemisphere and therefore contralaterally to the visual field defect. This is, of course, what would have been predicted on a purely neuroanatomical basis.

An increased latency of component P2 (major positive) was seen over the involved hemisphere in seven patients (1, 5, 14, 16, 19, 20, 21). The maximum increase, compared with the non-involved hemisphere was 20 msec (patient 16), but the more usual latency delay was of the order of 10 msec. An increased latency of 10 - 15 msec confined to component N3 was seen in patient 10.

The amplitude of component P2 was significantly reduced in six patients (4, 6, 12, 15, 20, 21) with an absent P2 occurring in two patients (7, 8). A fairly marked distortion of the waveform (WFD) was seen over the involved hemisphere in seven patients (4, 6, 8, 15, 16, 20, 21) but this was frequently not a consistent observation. The findings, despite many repeated trials, were sometimes highly variable, gross distortions in waveform being seen in some trials and not in others. In no case however was a marked waveform distortion recorded on one trial and normal potentials on another; the potentials always remained abnormal.

In patient 8 the waveform over the non-involved hemisphere was also of somewhat unusual appearance, but no definite abnormality could be said to be present. In only one patient then (12) was an amplitude reduction the only abnormality, most patients displaying a combination of abnormalities.

An abnormal FVEP was recorded in fourteen of the twenty patients remaining following the exclusion of patient 17. Eleven of these patients had visual field defects. The three patients with abnormal FVEP but no field defect were 9, 13 and 18. Of the four patients with normal FVEP (2, 7, 11, 14) two (7, 14) had visual field defects. In two patients (3, 10) the only abnormality was an absence of the early components (N1, P1, N2) on the side of the lesion and as early component asymmetry can occur in normals, this was regarded as equivocal.

There was a significant increase in the latency of component P2 on the side of the lesion in four patients (5, 9, 18, 21), this latency asymmetry never exceeding 15 msec. Although an increased latency confined to component N3 was not observed, in two patients (12, 20) component N3 and later components were of severely reduced amplitude.

Although these latter two patients, by virtue of their severely reduced N3 components, had a reduced P2 - N3 peak-to-peak amplitude, an overall reduced amplitude FVEP was seen over the involved hemisphere in two patients (5, 6). A significant interhemispheric amplitude asymmetry was also observed in patient 8, but here the amplitude was significantly larger over the involved hemisphere. A non-significant amplitude increase on the side of the lesion was also seen in patient 12, but, as stated above, component N3 and later components were of severely reduced amplitude. Seven patients showed a reduction in the rhythmic after activity (1, 4, 13, 15, 16, 19, 21) and in five of these (1, 13, 15, 16, 19) this was the only significant interhemispheric asymmetry seen.

Combining the FVEP and the PVEP findings (patient 17 excluded) only two patients (11,3) had both a normal FVEP and PVEP. Patient 11 had a

superiorly placed right parietal secondary from a bronchial carcinoma and did not have a visual field defect. A normal PVEP with an abnormal FVEP was seen in three patients (9, 13, 18), none of whom had a field defect. An abnormal PVEP with a normal FVEP occurred in four patients (2,7, 10,14), the patient without a field defect being the lady (patient 2) with a thalamic astrocytoma and bilaterally abnormal PVEP. The remaining eleven patients had both abnormal PVEP and abnormal FVEP. All of these had visual field defects.

In all, fifteen patients with space-occupying lesions had visual field defects. The single patient of these who had a normal PVEP (patient 3) had an homonymous superior quadrantanopia from her tempero-occipital glioma. Two patients had normal FVEP; one (7) had an homonymous scotomatous field defect from a parapituitary epidermoid cyst, the other (14) had an inferior quadrantic defect from his parietal astrocytoma. The FVEP findings in patients 3 and 10 were equivocal.

Patient 17 displayed both anterior and posterior abnormalities in the VEP. He had a massive malignant glioma in his right hemisphere. In the right eye there was pallor of the optic disc with visual acuity reduced to 6/60. In the left eye there was gross papilloedema with haemorrhage and exudate and a visual acuity of 6/9. There was complete left homonymous hemianopia. In the PVEP's, stimulation of the left eye evoked potentials of bilaterally normal latency which were of significantly reduced amplitude in the right hemisphere traces. No consistent potential was seen on stimulation of the right eye. Flash stimulation of the left eye resulted in a reduced amplitude potential in the right hemisphere traces, no significant interhemispheric latency asymmetry being apparent. Right eye flash stimulation evoked potentials which were bilaterally delayed and of reduced amplitude compared with those of the left eye (8 - 14 msec increase in latency) but which were best seen in the right hemisphere traces. An additional delay of some 10 msec was

occasionally present in the left hemisphere traces. Bilateral flash stimulation with the eyes closed showed reduced rhythmic after activity in the right hemisphere traces. The VEP's therefore appear to indicate involvement of the right optic nerve, the optic chiasm and the right post-chiasmal pathways. It is significant that at operation the right optic nerve was found to be grey and thin due to intrinsic tumour infiltration from below which was arising from the right temporal lobe.

ii) Non space-occupying lesions

There were twenty - three patients with non space-occupying lesions, only two patients (33, 38), both with internal carotid artery occlusion, not having visual field defects. A further patient (45), in addition to agenesis of the corpus callosum, also had a lipid filled cyst at the anterior end of the third ventricle. This patient will be discussed individually later in this section, and her results are not therefore included in the immediately following text.

The PVEP was normal in eight patients (24, 25, 28, 29, 39, 40, 42, 44), all of whom had visual field defects. In seven of these patients the macula was thought not to be involved in the field defects which were partial. In the eighth, (28), although left homonymous hemianopia was recorded, the macula was not referred to. The patient spoke poor English and was not thought to be a totally reliable witness.

Reduced amplitude potentials were seen in nine patients (22, 27, 30, 31, 34, 35, 37, 41, 43). Two of these patients, both with bilateral occipital infarction, displayed potentials that were bilaterally of subnormal amplitude. In the other seven patients, six showed a unilateral amplitude reduction over the involved hemisphere. In the seventh (patient 35), although there was clinical evidence of bilateral occipital infarction, it was only the right hemisphere changes which were of reduced amplitude. It is of interest that the island of preserved vision in this patient was situated in the right inferior quadrant, the normal PVEP

occurring contralaterally to this over the left hemisphere. Patient 23, with bilateral occipital infarction showed bilaterally absent PVEP's, and in patient 36, also with bilateral occipital infarction, a PVEP was only occasionally seen, confined to the right hemisphere traces. The E.M.I scan suggested that this was the more normal hemisphere.

Interhemispheric latency asymmetries occurred in eight patients (22, 26, 32, 33, 37, 38, 41, 43), the maximum latency increase being some 15 msec (37). In only four of these patients (26, 32, 33, 38) were no associated amplitude changes present and it may be relevant that two of these patients, both of whom showed latency increases of 6 - 8 msec, were the patients with internal carotid artery occlusion and full visual fields. A marked distortion of waveform, other than where the PVEP was absent, was really only seen in one patient (22) with a posterior cerebral artery thrombosis.

In five patients then the only abnormality seen was confined to an amplitude reduction over the involved or more involved hemisphere. Indeed, in all the patients the maximum abnormality was invariably recorded over the involved or more involved hemisphere and therefore contralaterally to the maximum visual field defect.

A normal FVEP was seen in six patients (26, 33, 35, 39, 42, 44) and an equivocal FVEP in five patients (29, 30, 34, 40, 43). In four of these there was early component absence, in the fifth (29) an intermittent latency delay of 4 - 8 msec was seen in the P2 component over the involved right hemisphere.

Twelve patients then had abnormal FVEP. A P2 amplitude reduction was seen in seven patients. In five of these (22, 27, 36, 37, 41) there was a clear amplitude reduction over the involved or worse affected hemisphere. In patient 24 there was an amplitude reduction maximal in the P2 - N3 value, the N2 - P2 value not being significantly reduced. Patient 31 had FVEP's of low amplitude and high variability, but these

were better seen over the uninvolved left hemisphere.

Latency asymmetries occurred in six patients (22, 23, 25, 32, 36, 38), the maximum asymmetry being some 10 msec. In patient 23 there were bilaterally abnormal latencies of 140 - 160 msec with the left hemisphere traces showing a further (4 - 6 msec) increase in latency. A reduction in rhythmic after activity was unilaterally seen in three patients (22, 27, 28). There was only one patient in whom waveform distortion was seen, and this was not a consistent finding.

Five patients then had normal PVEP and normal or equivocal FVEP (29, 39, 40, 42, 44). All of these patients had visual field defects but of a quadrantic or altitudinal nature. Six patients (26, 30, 33, 34, 35, 43) had an abnormal PVEP with a normal FVEP. All except one (33) of these patients had field defects. Three patients had a normal PVEP with an abnormal FVEP (24, 25, 28). All these had visual field defects. The remaining nine patients displayed abnormalities in both the PVEP and the FVEP. Only one of these patients (38) had full visual fields.

Patient 45 was unique in that there was evidence of both space-occupying and non space-occupying lesions. She had agenesis of the corpus callosum, established by air encephalography many years prior to the admission during which her VEP's were recorded, and in addition had what was thought to be a lipid containing cyst. The E.M.I scan showed abnormal ventricular anatomy, compatible with partial agenesis of the corpus callosum, with a spherical, clearly defined low density lesion (density values compatible with fat) in the midline at the anterior end of the third ventricle. In the PVEP's the P2 (major positive component) was delayed from both eyes (117 msec in the right eye; 127 msec on the left but with reduced acuity at 6/36 on the left thought to be due to amblyopia ex anopsia) with no interhemispheric asymmetry. The potentials evoked by pattern stimulation of the left eye were reduced in amplitude by some 60 - 70% compared with the right. The potentials evoked by flash

stimulation were also delayed (right eye P2 at 150 msec; left eye P2 at 158 msec) with no interhemispheric asymmetry.

The VEP findings are summarised in Figs. 3.6.3 and 3.6.4. A table of the overall findings in patients with post-chiasmal lesions is shown in Fig. 3.6.5.

Illustrative findings can be seen in Figs. 3.6.6 - 3.6.10. The case histories are as follows:

i) Fig. 3.6.6. C.W (patient 15). This 55 year old man was admitted with a five month history of impaired vision in his right visual field, increasing headache and more recently a 'strange sensation' in his right leg. On examination he was dysphasic with a tendency to perseverate; there was right homonymous hemianopia, a mild right pyramidal deficit and early papilloedema in the left eye. E.M.I scan showed a left parieto-occipital lesion thought probably to be a glioma. A biopsy was taken which only showed necrotic tissue but the appearances at operation were thought by the surgeon to be those of a malignant glioma. In the pattern VEP's the left hemisphere potentials are of significantly reduced amplitude and although monocular flash stimulation with the eyes open was normal, flash stimulation with the eyes closed shows a virtual loss of rhythmic after activity over the involved left hemisphere.

ii) Fig. 3.6.7. J.B (patient 6). This 61 year old lady was admitted for investigation of memory loss and right homonymous hemianopia. On examination there was bilateral papilloedema, right homonymous hemianopia, dyslexia, agraphia and dyscalculia. E.M.I scan showed a large tempero-parieto-occipital lesion thought to be a glioma. It was felt, in view of the position and extent of the tumour that there was no place for surgery. In the VEP's, pattern stimulation evoked potentials of reduced amplitude and distorted waveform in the left hemisphere traces. Flash stimulation also evoked potentials of altered waveform and reduced amplitude on the left, most marked in the parieto-occipital trace.

Fig. 3.6.3 VEP findings in patients with post-chiasmal lesions

Space-occupying lesions*

	No.	V.F.D.
Normal PVEP, normal FVEP	2	1
Normal PVEP, abnormal FVEP	3	0
Abnormal PVEP, normal FVEP	4	3
Abnormal PVEP, abnormal FVEP	11	11
TOTAL	20	15

Non space-occupying lesions**

Normal PVEP, normal FVEP	5	5
Normal PVEP, abnormal FVEP	3	3
Abnormal PVEP, normal FVEP	6	5
Abnormal PVEP, abnormal FVEP	9	8
TOTAL	23	21

V.F.D. - visual field defect

* Patient 17 had evidence of both anterior and posterior dysfunction and has been excluded from this tabulation. See text for details.

** Patient 45 has also been excluded due to the unique nature of the case. See text for details.

Fig. 3.6.4 Types of abnormality in patients with post-chiasmal lesions (the bracketed figures refer to patients with visual field defects)

Space-occupying lesions*

	PVEP	FVEP
Amplitude only**	1 (1)	2 (2)
Latency only	3 (3)	2 (2)
Combination of abnormalities	10 (10)	10 (9)
RAA reduction	-	7 (6)

Non space-occupying lesions***

Amplitude only	5 (5)	2 (2)
Latency only	4 (2)	4 (3)
Combination of abnormalities	6 (6)	6 (6)
RAA reduction	-	3 (3)

* Patients 17 and 2 have been excluded. Patient 17 had both anterior and posterior dysfunction. Patient 2 had bilaterally supernormal PVEP's. See text for further details.

** In one patient the FVEP amplitude was significantly lower over the non-involved hemisphere.

*** Patient 45 is excluded. See text for details.

RAA - rhythmic after activity.

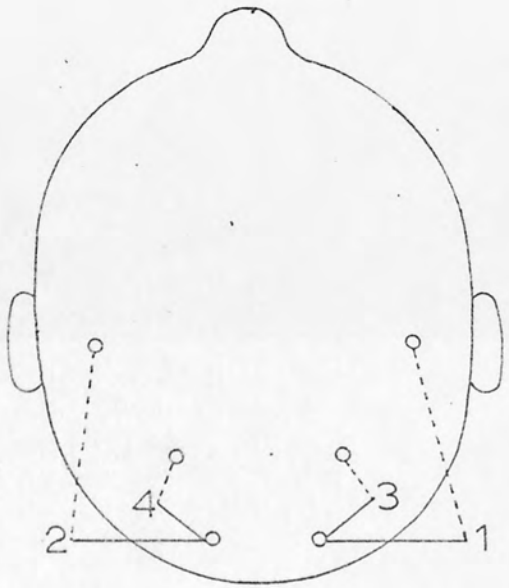
Fig. 3.6.5 Overall findings in patients with post-chiasmal lesions

	% abnormal PVEP	% abnormal FVEP	Total % abnormal
All patients (N = 45)	71	62	84
Patients with V.F.D. (N = 37)	76	62	84
Patients without V.F.D. (N = 8)	50	63	88

V.F.D. - visual field defect

Fig. 3.6.6. VEP findings in a 55 year old man with a left parieto-occipital glioma. See text for details.

C.W. aet 55



PVEP

FVEP
(Eyes closed)

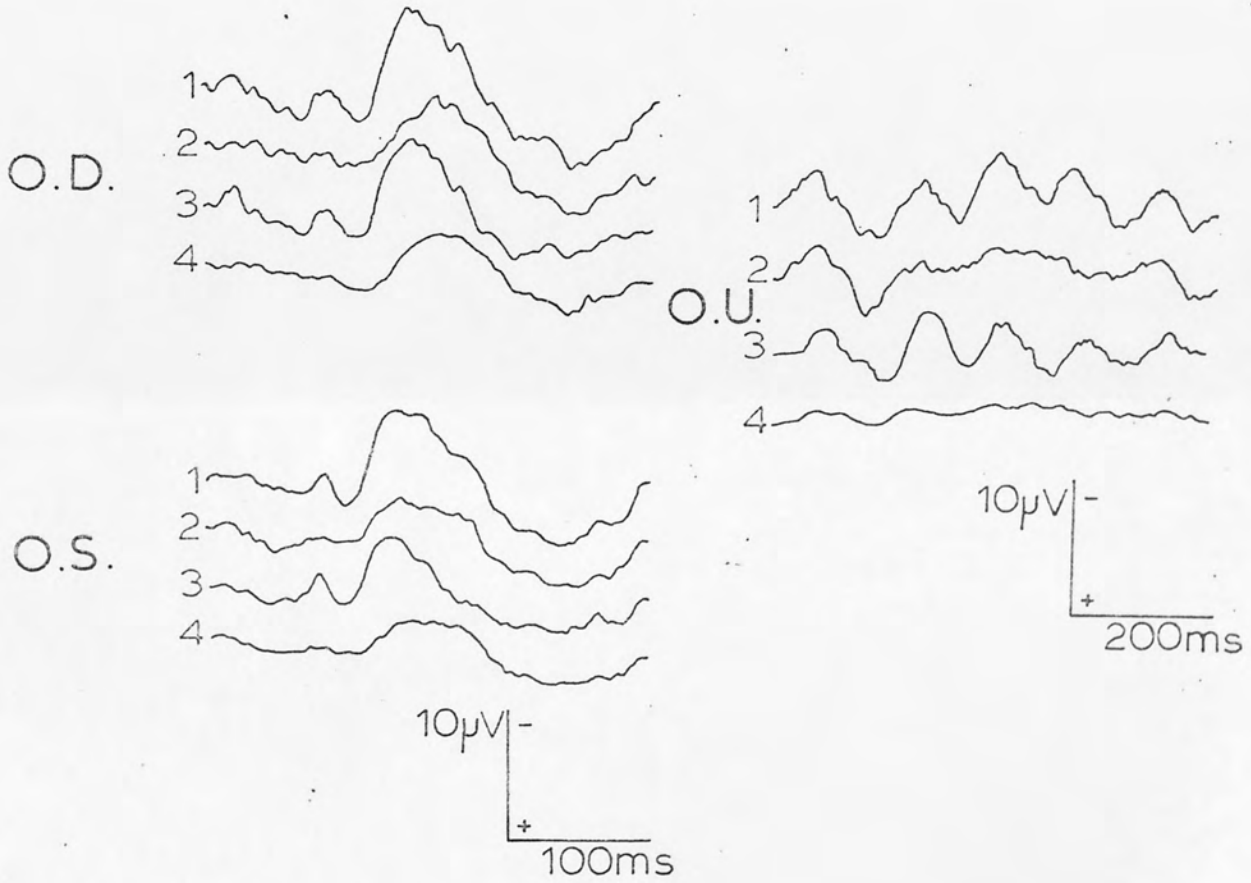


Fig. 3.6.6.

Fig. 3.6.7. VEP findings in a 61 year old lady with a large left tempero-parieto-occipital glioma. See text for further details.

J.B. aet 61

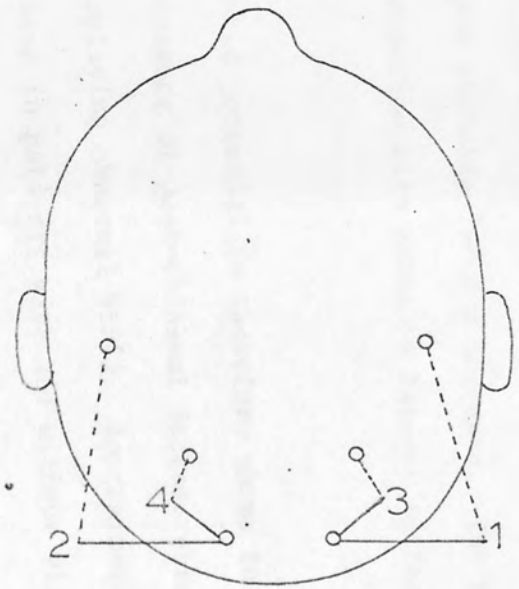
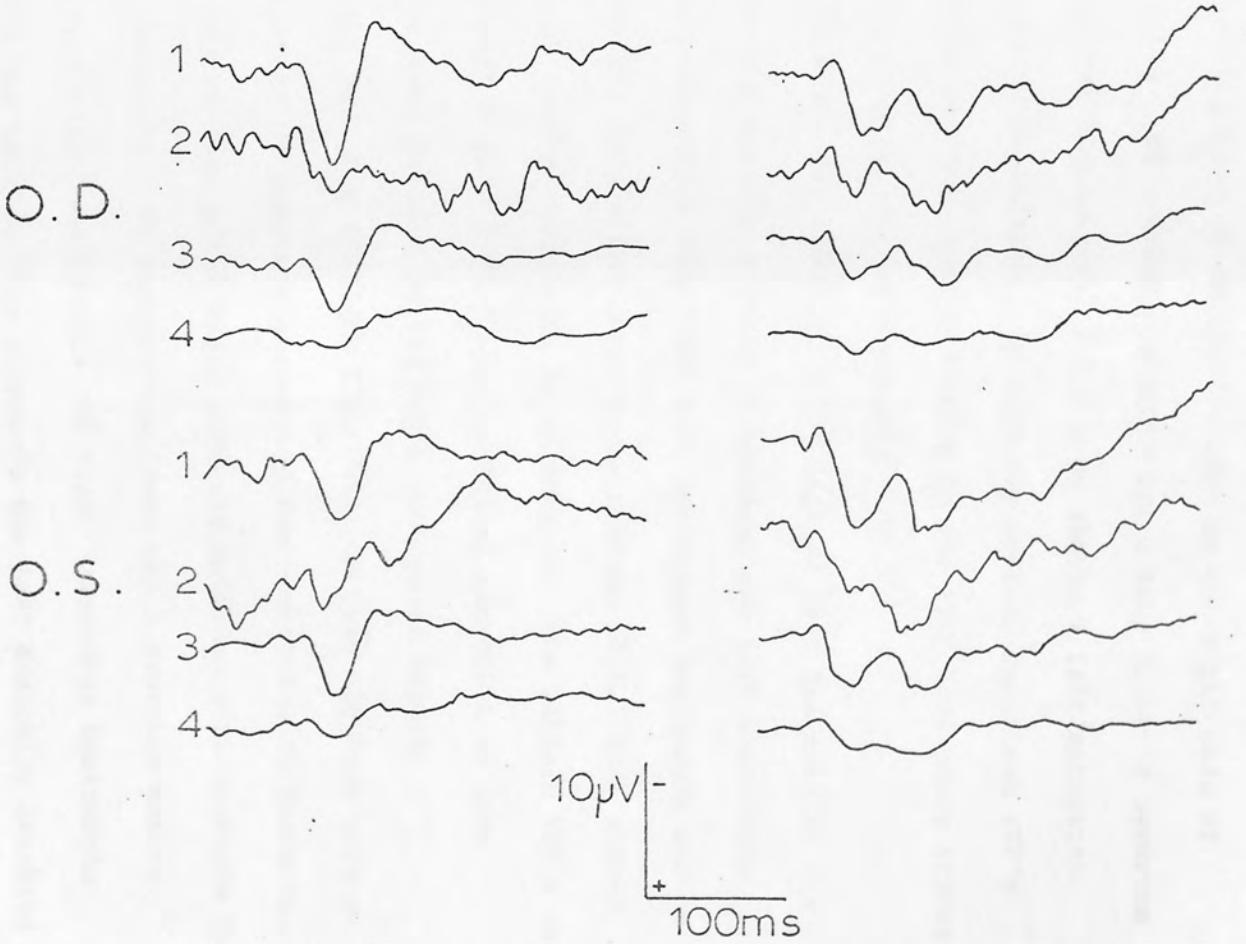


Fig. 3.6.7.



iii) Fig. 3.6.8. P.R (patient 27). This 46 year old man was admitted for investigation of impaired vision on the right side of six weeks' duration. On examination there was a left Horner's syndrome and right homonymous hemianopia. E.M.I scan showed a left occipital lesion thought to be an infarct. In both the pattern and flash VEP's there is a significant amplitude reduction in the left hemisphere traces with no interhemispheric latency asymmetry.

iv) Fig. 3.6.9. J.M (patient 25). This 22 year old soldier was investigated for one month's history of headache and left homonymous hemianopia. On examination there was left homonymous hemianopia and on formal perimetry the macula was shown to he spared. E.M.I scan showed a right occipital lesion thought to be an infarct. The pattern VEP's are normal but the FVEP's show a P2 (major positive) component of some 6 - 10 msec increased latency in the right hemisphere traces.

v) Fig. 3.6.10. V.M (patient 22). This 68 year old lady with a past medical history of coronary thrombosis was admitted with headache, confusion and memory loss after being suddenly awakened with headache in the middle of the night. On examination there was a profound memory deficit, alexia, a right hemiparesis and right homonymous hemianopia thought to split the macula. The diagnosis was left posterior cerebral artery thrombosis. The left hemisphere PVEP's are virtually absent with reduced amplitude and probable latency increase. The FVEP's also show marked amplitude reduction with probable latency increase and distortion of the waveform.

The visual evoked potential is therefore shown to be a sensitive indicator of the presence of post-chiasmal intracerebral lesions, some 85% of patients displaying abnormal VEP's. Approximately equal percentage abnormalities are seen in patients with and without visual field defects and the involvement of the posterior visual pathways, be it direct or

Fig. 3.6.8. VEP findings in a 46 year old man following left occipital infarction. See text for details.

P.R. aet 46

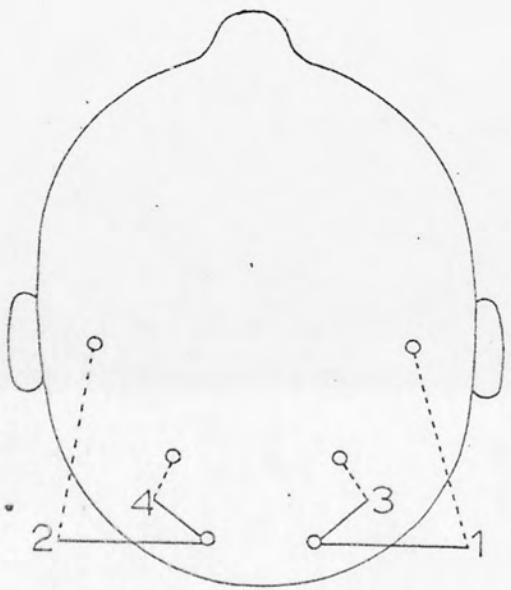


Fig. 3.6.8.

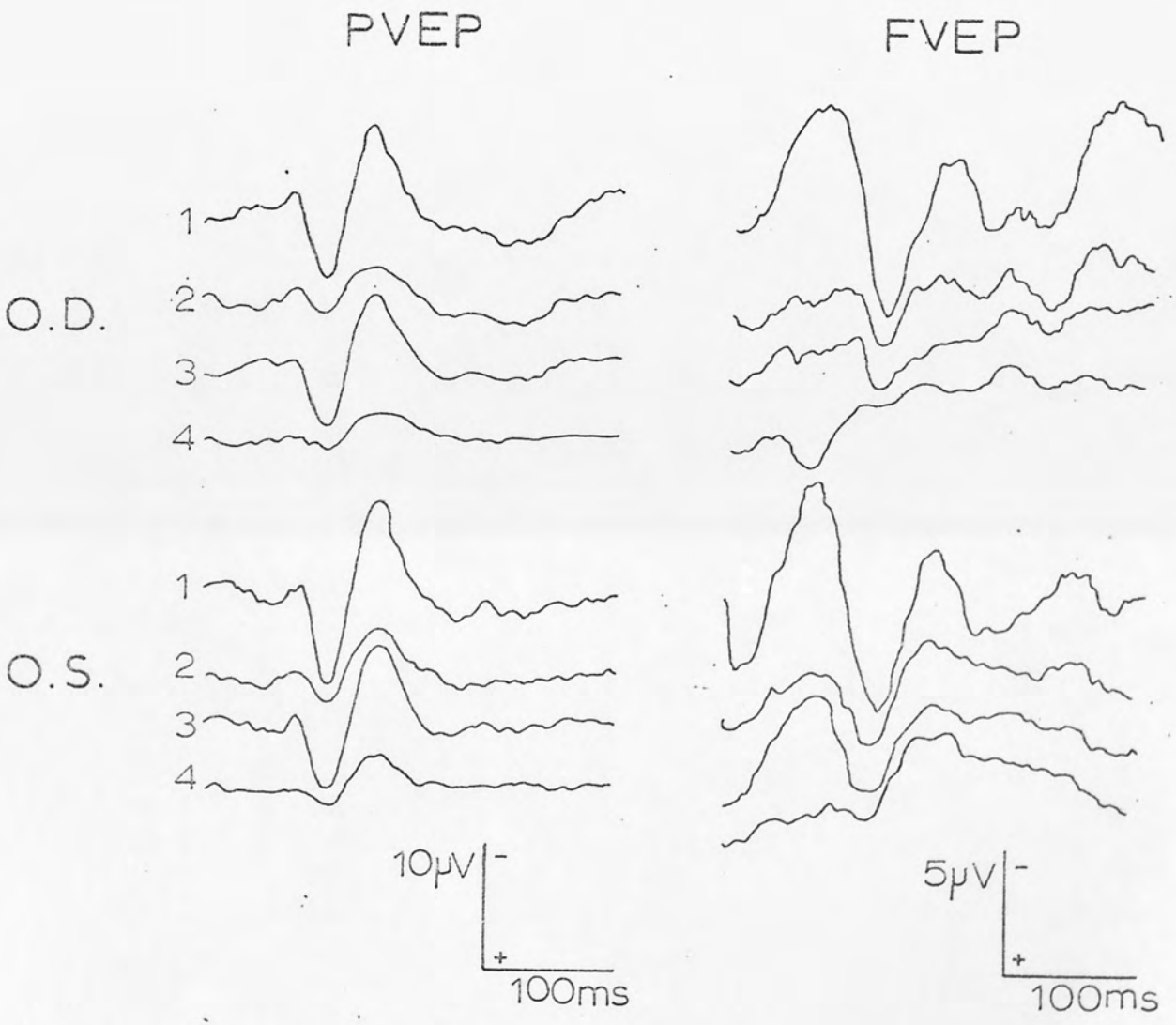
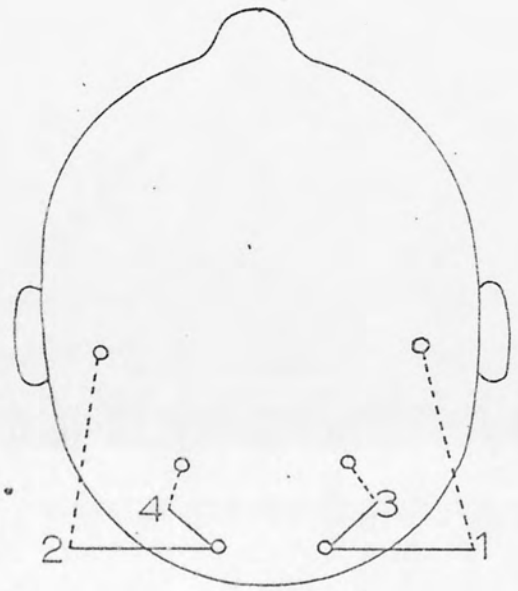


Fig. 3.6.9. VEP findings in a 22 year old man with a macular sparing left homonymous hemianopia following right occipital infarction. See text for details.

J.M. aet 22



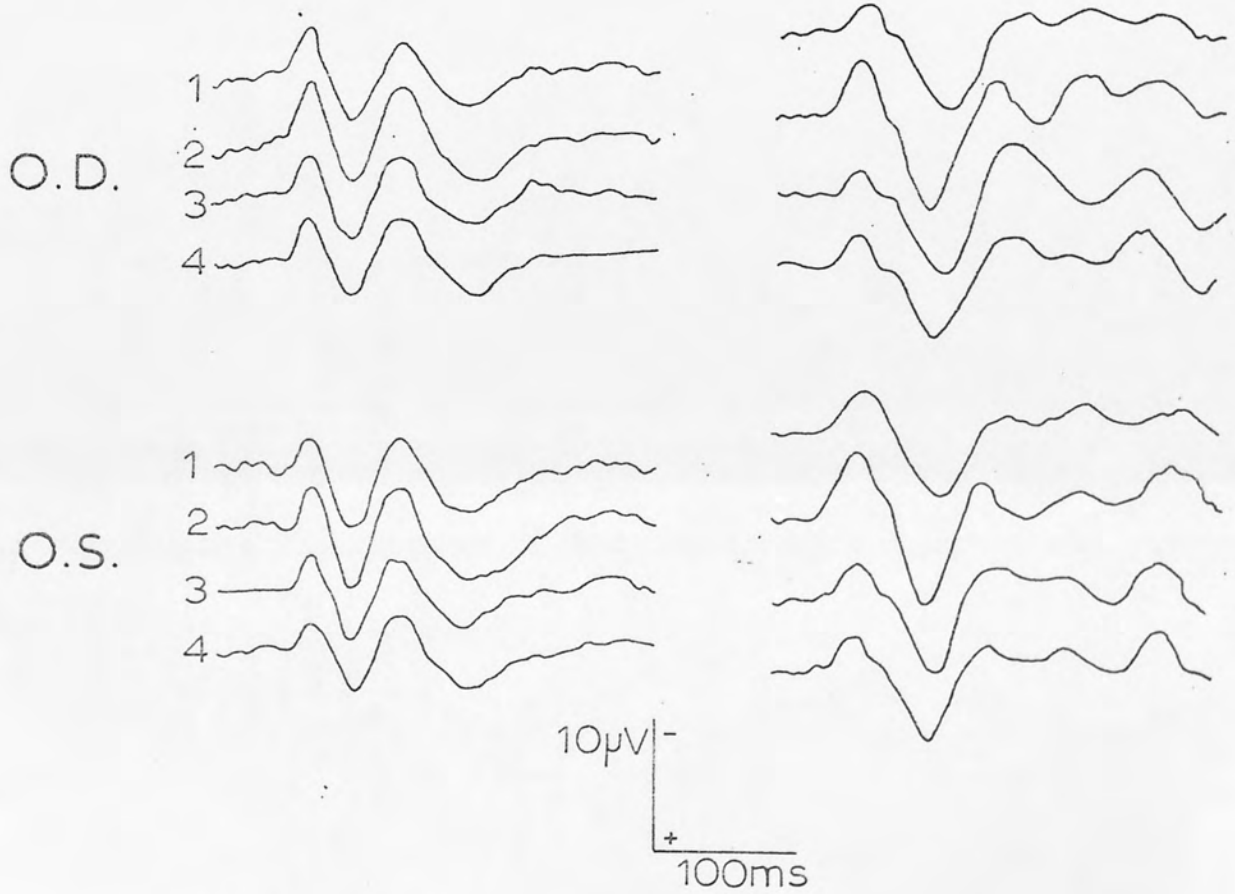


Fig. 3.6.9.

Fig. 3.6.10. VEP findings in a 68 year old lady with a macular splitting right homonymous hemianopia following left posterior cerebral artery thrombosis. See text for details.

V.M. aet 68

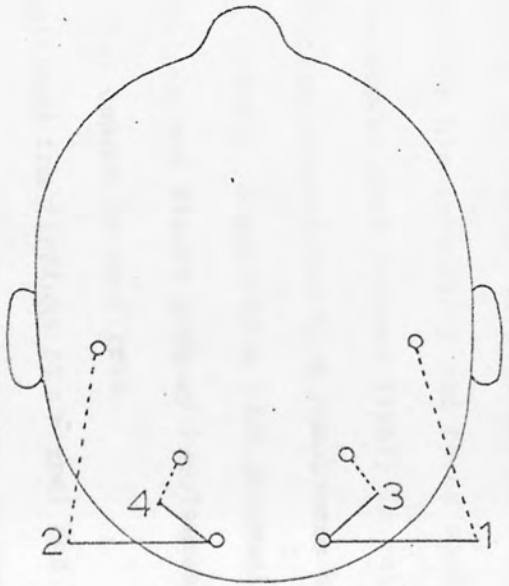
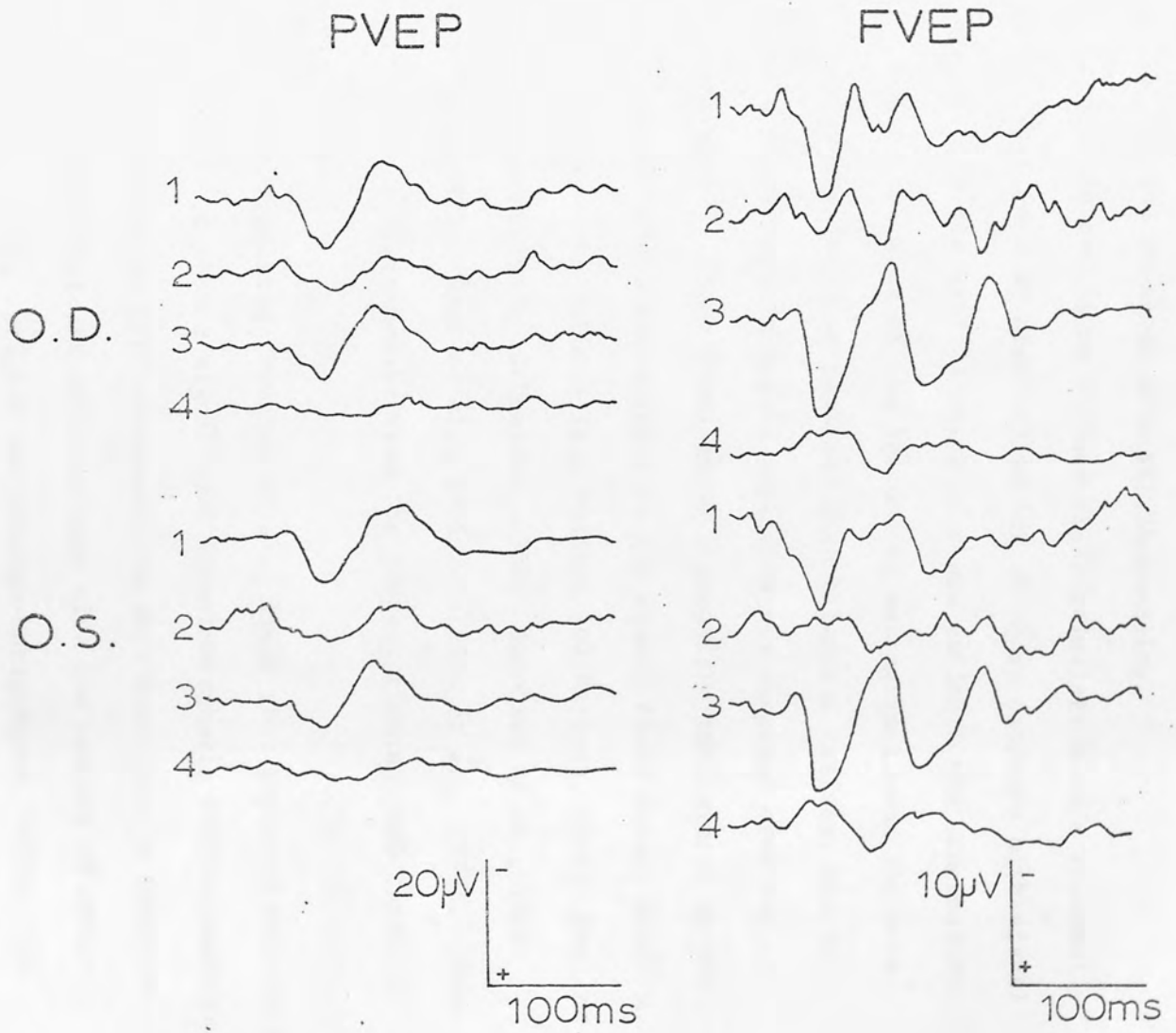


Fig. 3.6.10.



indirect from a more superiorly placed lesion, is therefore not a prerequisite for the presence of a VEP abnormality.

The potentials evoked by diffuse flash stimulation were abnormal in 62% of all patients studied and in 68% of those patients with visual field defects. In the vast majority of these patients the abnormality was localised to the side of the lesion, or was maximal over the more affected hemisphere in those patients with bilateral lesions, but in one patient a significantly higher amplitude was recorded over the involved hemisphere. These findings of abnormality ipsilateral to the lesion and therefore contralaterally to any visual field defect confirm the reports of previous authors (e.g Vaughan and Katzman, 1964; Kooi et al., 1965; Jonkman, 1967; Schneider, 1968; Jacobsen et al., 1968; Feinsod et al., 1975; Kooi et al., 1975; Galkina et al., 1975). There are however some differences between the present findings and those of previous authors.

It has been suggested (Vaughan et al., 1963) that patients with full visual fields do not show a significant interhemispheric FVEP asymmetry. This is not confirmed as FVEP abnormalities were seen here in patients without visual field defects in accordance with the results of other authors (Jonkman, 1967; Crighel and Sterman-Marinchescu, 1971). It is however noted that there are marked differences in the methods of analysis used by Vaughan and his co-workers and those used in this study. This study is also in agreement with Jonkman (1967) in failing to find the consistent abnormalities in patients with homonymous hemianopia reported by Kooi et al. (1965). Similarly a 100% abnormality in patients with space-occupying lesions and visual pathway involvement (Bergamini and Bergamasco, 1967) also cannot be confirmed.

Jonkman (1967) confirmed the findings of Crighel and Botez (1966) in occasionally finding an increased FVEP amplitude on the side of the lesion, suggesting that this occurred in patients with frontal or fronto-

temporal tumours. This was further reported by Galkina et al. (1975) who suggested that this ipsilateral amplitude increase was confined to patients with lesions predominantly affecting the medio-basal areas of the temporal lobe. Some support for these findings is given by the present study, the only patient showing an unequivocal amplitude increase ipsilaterally to the side of the lesion having an astrocytoma arising in the right temporal lobe.

The absence of component N3 and later components was seen here in two patients, both with superiorly situated parieto-occipital lesions, and confirms the findings of Feinsod et al. (1974, 1975) in 'suprastriate hemianopia'. It is therefore suggested that when N3 and later components are (virtually) absent, direct involvement of the geniculo-calcarine pathways is unlikely, a more superiorly placed lesion being indicated. It is noted, however, including the example of Feinsod, that this suggestion is put forward on the basis of only three patients. Considering the differences in opinion amongst earlier authors as to whether component P2 should be included in the primary or secondary response, these findings in suprastriate hemianopia appear to suggest that the positive going deflection of this component may best be regarded as part of the primary response, the succeeding negative going component being part of the secondary response. This is partially in agreement with the suggestion of Jonkman (1967) but not with Ciganek (1961).

The reduction in rhythmic after activity found in the FVEP of 25% of all patients studied with post-chiasmal lesions supports similar findings of such reduction reported by Jonkman (1967); Schneider (1968); Oosterhuis et al. (1969) and Bergstrom and Nystrom (1970).

The potentials evoked by pattern reversal stimulation were abnormal in 71% of all the patients studied with post-chiasmal lesions and in 76% of those patients with visual field defects. Thus, patients without field defects may have an abnormal PVEP and patients with field defects may have

a normal PVEP. It is thought though that the PVEP was abnormal in all patients where there was definite macular involvement in the field defect.

Apart from one patient with a unilateral thalamic astrocytoma in whom the PVEP's were of bilaterally supernormal amplitude, no interhemispheric asymmetry being seen, and the patient with agenesis of the corpus callosum, the abnormality was always localised to the side of the lesion or was maximal over the more affected hemisphere in those patients with bilateral lesions. In patients with visual field defects then, the abnormality is consistently located contralaterally to the field defect. This is of course what would have been predicted on a purely neuroanatomical basis, and is in agreement with the contralateral (to the field defect) lateralisation reported by Wildberger et al. (1976) though these authors used 8/sec stimulation. The abnormality localisation contralateral to the visual field defect invariably seen in the present series is however in disagreement with Blumhardt et al. (1977) who suggest a paradoxical ipsilateral lateralisation. In a more recent paper (Harmony et al., 1978), using flashed pattern stimulation, no consistent abnormality lateralisation was found. The problem of PVEP abnormality localisation in patients with visual field defects is discussed in detail below.

In a further recent report (Ashworth et al., 1978) bilaterally delayed PVEP's in a patient with a corpus callosal tumour are described. However, no normal values are given, the authors quoting values obtained elsewhere "with a very similar apparatus". Despite this "very similar apparatus", the total field size, the individual check size and the positioning of the recording electrodes are all different from the other laboratory whose values are quoted, and the 'delay' described in this paper must clearly be treated with some suspicion. No similar patient is described in the present series to enable direct comparison to be made, but it is noted that the patient described with agenesis of the corpus callosum and a lipid filled cyst at the anterior end of the third ventricle

did show bilaterally delayed PVEP's in the true statistical sense.

Combining the PVEP and FVEP findings the incidence of abnormality is increased to 84% both for the total group of patients and for those patients with visual field defects. The type of abnormality seems as if it may be partially related to the type, but not the site, of the lesion. In patients with space-occupying lesions the PVEP abnormality was confined to an amplitude reduction in only one patient. In non space-occupying lesions five patients showed purely amplitude reductions in the PVEP. It appears then that one is much more likely to find an amplitude reduction in infarction than in tumour or intracerebral haematoma. In an ischaemic lesion it can be presumed that fewer cells are capable of firing which would give rise to the amplitude reduction. With a space-occupying process however, although the number of cells capable of firing may be reduced by direct tumour invasion, there will also be associated oedema in neighbouring areas, representing a greater physiological disturbance. This is supported by the well-recognised observation that the symptoms of patients with cerebral tumours frequently improve following the introduction of corticosteroid therapy (e.g Long et al., 1966a), corticosteroids acting to reduce oedema (e.g Long et al., 1966b). It is of interest here that although waveform distortion was relatively common in those patients with space-occupying lesions, only one patient (4%) in the non-S.O.L group displayed WFD. This particular patient was examined within one week of acute posterior cerebral artery thrombosis and the possibility of oedema following acute infarction is well-recognised (e.g Berry and Alpers, 1957). It is also possible that the more extensive physiological disturbance seen with a space-occupying process may account for the greater proportion of patients with S.O.L (38%) than non-S.O.L (13%) who showed reduced rhythmic after activity in the FVEP, this activity presumably reflecting the activity of secondary non-specific pathways.

The extent of a visual field defect may also, in some patients, be predicted by a combination of PVEP and FVEP. In patients with field

defects confined to the macular region a PVEP abnormality may be associated with a normal FVEP (e.g patient 7); a patient with macular and peripheral field loss may give an abnormal PVEP and an abnormal FVEP (e.g patient 22) and a defect with macular sparing may give an abnormal FVEP with a normal PVEP (e.g patient 25). Unfortunately formal assessment of the visual fields by perimetry is available in too few patients to enable accurate assessments to be made, but it is noted that at least seven of the nine patients with visual field defects and normal PVEP had macular sparing and eight of the fourteen patients with visual field defects and normal FVEP had quadrantic, altitudinous or scotomatous defects.

However one of the most important problems to emerge from this work is that of PVEP abnormality lateralisation in patients with hemianopic visual field defects (the reader is also referred back to the section dealing with chiasmal lesions at this point).

On a purely neuroanatomical basis it would be predicted, both in patients with bitemporal hemianopic field defects resulting from chiasmal compression and in patients with homonymous hemianopic defects resulting from more posteriorly placed lesions, that the PVEP abnormality would be localised contralaterally to the visual field defect as is found with the FVEP. Indeed, this localisation of the abnormality contralaterally to the visual field defect is seen in all the patients with hemianopic field defects studied by this author either with chiasmal or post-chiasmal lesions. However there is a marked discrepancy between these findings and those of Halliday and his co-workers (Barrett et al., 1976a, b; Blumhardt et al., 1977, 1978; Halliday et al., 1976). Halliday et al. (1976) found a PVEP abnormality invariably ipsilateral to the visual field defect in patients with bitemporal hemianopia from chiasmal compression. Results on half-field stimulation in normals (Barrett et al., 1976a, b; Blumhardt et al., 1977, 1978) also show the normal response ipsilateral

to the stimulated field, the predicted abnormality ipsilateral to the field defect in homonymous visual field loss being confirmed in a single patient following occipital lobectomy (Blumhardt et al., 1977). Although half-field stimulation in normals is the best experimental model we have for the study of half-field defects, it is felt that the results must be treated with caution when extrapolating to patients since half-field stimulation in normals can only ever approximate to whole field stimulation in patients with hemianopic defects, particularly in the case of space-occupying lesions where we are dealing with the properties of normal brain tissue mingled with tumour cells, oedema, etc.

The question which remains is why are these sets of results so apparently discrepant. Clearly, in a patient following occipital lobectomy, potentials can only arise from the remaining occipital lobe and for one laboratory to obtain contralateral abnormality in such a patient, and another to obtain ipsilateral abnormality, factors other than the patients themselves must be dominant. Initially the recording parameters are markedly different. Halliday and his co-workers (op. cit.) use active electrodes situated 5 cm anterior and 5 cm lateral to the inion referred to a mid-frontal electrode. In this study the occipital electrodes are 2 cm anterior and 2 cm lateral to the inion referred to an ipsilateral sylvian electrode. It has been suggested (Barrett et al., 1976a) that bipolar recording methods may artificially induce a contralateral abnormality localisation due to the effects of potential gradients, when the abnormality should really be localised ipsilaterally. This is also described by Shagass et al. (1976) and whilst this is undoubtedly true when recording with a transverse chain of closely spaced electrodes, the argument does not appear relevant to widely spaced electrodes in an anterior-posterior plane. This is illustrated by the PVEP findings in patient 8 (Fig. 3.6.11), where the relevant abnormality is an absent P2 component ipsilaterally to the lesion, all other parameters showing no

Fig. 3.6.11. PVEP findings in a 38 year old man with a right temporal astrocytoma. See text for details.

D. W. aet 38

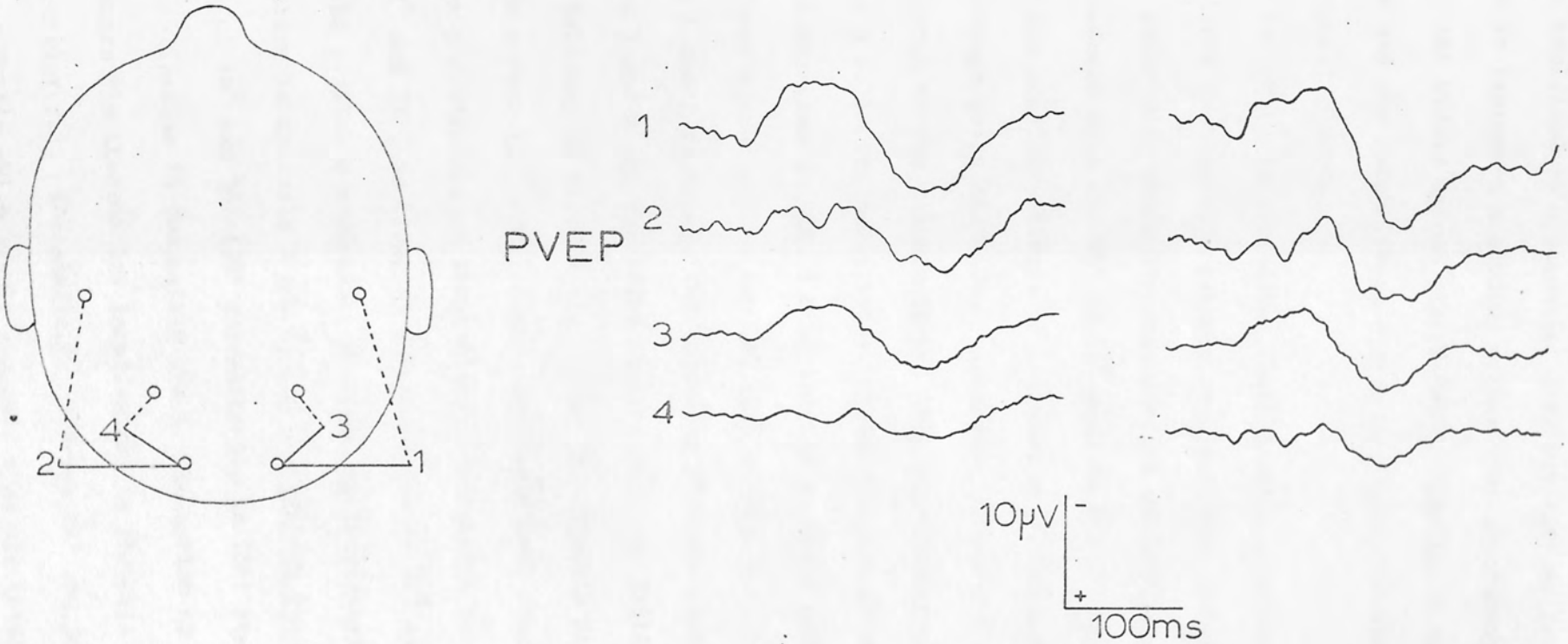


Fig. 3.6.11.

significant interhemispheric asymmetry. It is felt that this type of abnormality cannot be explained on a potential gradient/bipolar recording model and is presumed to represent a genuine rather than artefactual abnormality. Equally the widely spaced electrodes of Harding et al. (1978) confirm these results and the lateralisation seen even with reference recording to a mid-frontal electrode.

The other main factor to be considered, both laboratories using high contrast stimuli are the stimulus parameters. Halliday and co-workers (op. cit.) use a 50' individual check subtense pattern subtending a total field of 32^{o} compared with the 26' in 11^{o} used in the present study.

To investigate the possible effects of stimulus and recording parameters, further recordings using additional electrodes situated 5 cm anterior and 5 cm lateral to the inion referred to a mid-frontal electrode were taken in patient 4 following occipital lobectomy for her glioma. These findings are illustrated in Fig. 3.6.12 and due to their relatively complex nature have been summarised in tabular form in Fig. 3.6.13. In Fig. 3.6.12 channels 1 and 2 represent the recording channels used by this author, channels 3 and 4 the recording channels used by Halliday and his colleagues (e.g Halliday et al., 1976). Using the stimulus parameters normally used by this author (11^{o} total field, 26' individual check) channels 3 and 4 show a contralateral abnormality. Increasing the field and check size to 22^{o} and 57', as close an approximation to 32^{o} and 57' as was possible using the available equipment, produces an ipsilateral abnormality localisation in channels 3 and 4, the abnormality thus changing sides! Use of 16^{o} and 30' (30' approximating to 26') probably gives ipsilateral localisation in channels 3 and 4. Reduction to 8^{o} and 13' then further changes the abnormality localisation in channels 3 and 4 which reverts to contralateral. The similarity between 26' and 30' and the markedly different PVEP's which result suggests that the total size of the stimulating field, rather than the individual check size, is

Fig. 3.6.12. (see also Fig. 3.6.13. and text) The effects of variations in the total field and individual check subtense on the potentials recorded by electrodes 2 cm anterior and lateral to the inion (channels 1 and 2) and 5 cm anterior and lateral to the inion (channels 3 and 4) in a 55 year old lady following left occipital lobectomy for glioma. Note particularly the marked changes in channels 3 and 4 in response to variations in stimulus parameters compared with the relative stability of channels 1 and 2.

G.K. aet 55

L occipital lobectomy
V.O.D. J6

Pattern VEP

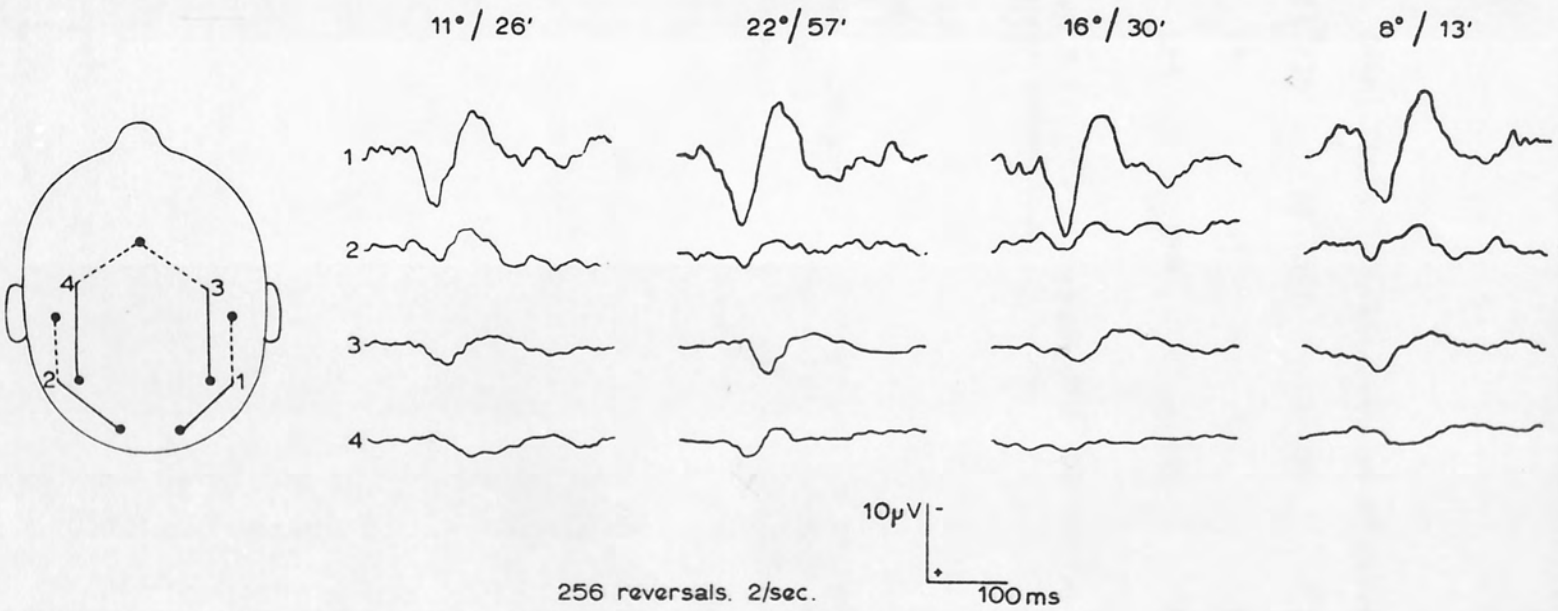


FIG. 3.6.12.

Fig. 3.6.13 The effects of variations in stimulus and recording parameters on PVEP abnormality localisation (patient 4, see Fig. 3.6.12)

	Total field/Individual check subtense			
	$11^{o}/26'$	$22^{o}/57'$	$16^{o}/30'$	$8^{o}/13'$
Channels 1 and 2	L*	L*	L*	L*
Channels 3 and 4	L**	R**	(R)***	L**

L (left) and R (right) represent the hemisphere over which the abnormality is seen.

* amplitude reduced
** latency extended
*** Here, although the left hemisphere potential is of reduced amplitude, the right hemisphere potential is delayed and it is felt that this delay is probably more significant.

the relevant factor. Electrodes 2 cm anterior and 2 cm lateral to the inion, referred to the ipsilateral sylvian electrodes (channels 1 and 2), are relatively unaffected by the changes in stimulus parameters and correctly localise the abnormality to the affected hemisphere throughout.

Similar additional recordings were taken in patient 16 following occipital lobectomy for adenocarcinoma and in a patient not described here with demyelinating disease and homonymous hemianopia. In these two patients, although abnormality localisation in recordings from electrodes 5 cm anterior and lateral to the inion could be markedly affected by variations in stimulus parameters, the changes occurred at different parameters suggesting an interindividual difference factor. Indeed, individual differences in the underlying anatomy of the occipital lobe have been described (Polyak, 1957). Traces from electrodes 2 cm anterior and lateral to the inion however were relatively unaffected by changes in stimulus parameters and localised the abnormality to the affected hemisphere throughout, i.e contralaterally to the visual field defect.

The mechanisms of this abnormality lateralisation reversal described here in response to change in stimulus parameters are uncertain, but may be related to the cortical representation of the macula at the occipital pole where the generator neurones are posteriorly orientated and of the peripheral retina on the medial surface of the hemisphere. It is possible then that potentials evoked by largely macular hemifield stimulation may best be seen over the scalp ipsilateral to the stimulated hemisphere whereas, due to the orientation of the generator neurones, potentials evoked by more peripheral retinal stimulation may be seen over the scalp contralateral to the stimulated hemisphere. This was suggested by Halliday and his co-workers (Barrett et al., 1976b) who, using half-field stimulation in normals and with recording electrodes 5 cm anterior and lateral to the inion, found that their normally ipsilateral (to the stimulated half field) response could in fact have a contralateral predominance if stimulation were confined to

the macular area. Whilst this may be applicable to recording electrodes situated 5 cm anterior and lateral to the inion, no support for this hypothesis is provided by the results of the present study as the invariably contralateral abnormality localisation in patients with hemianopic defects was not affected by changes in stimulus parameters using recording electrodes situated 2 cm anterior and lateral to the inion.

Recently, Halliday (1978, in discussion of Holder, 1978b) has confirmed, using stimulation confined to the macular area in patients with homonymous hemianopia, that the abnormality, even using recording electrodes situated 5 cm anterior and lateral to the inion referred to a mid-frontal electrode, can be located contralaterally to the visual field defect. Half-field pattern appearance stimulation to the foveal region in normals has also been shown to have a contralateral localisation (Drasdo, 1978) and, in a further paper presented at the same symposium, Harding et al. (1978) demonstrated, starting with a 28^{o} total field and 56' checks, that the lateralisation of the ipsilateral response to half-field stimulation in normals was unaffected by reducing the individual check size, but that following a reduction in the size of the stimulating field, the response was localised contralaterally.

Clearly it is vital when writing diagnostic reports to be as certain as possible that misinterpretation is not occurring, particularly where localisation of the responsible lesion to one hemisphere of the brain or the other is concerned. It is therefore suggested, as a marked PVEP susceptibility to change in stimulus parameters is extremely unsatisfactory from a clinical point of view, that laboratories using electrodes 5 cm anterior and 5 cm lateral to the inion pay very close attention to their stimuli so as to avoid the false or equivocal abnormality localisation which may possibly be obtained with such recording parameters. This seems particularly relevant for stimulus parameters similar to those readily obtained from the commercial stimulator used in this study and

standardisation with 'normal hemianopic' controls is therefore considered advisable.

3.7 Non-organic visual loss

This group consists of twenty-one patients all of whom were eventually diagnosed as having at least a substantial degree of non-organic visual loss. As each patient is to a certain extent unique, the clinical history and VEP findings will be individually discussed. Some degree of categorisation has been attempted as age related and other groupings became apparent. It should be noted that the objective assessment of the intracranial visual pathways provided by VEP examination was instrumental in the final diagnosis of many of these patients.

a) Communication difficulties. i) G.K. This 27 year old Indian lady, who spoke extremely poor English, presented with a gradual reduction in left visual acuity over a two year period. She was referred for electrodiagnosis with probable pallor of the left optic disc and a left visual acuity of 6/36 with a -5.5 sphere correction. The VEP's to a 40' check pattern, the FVEP's and the ERG's were all completely normal with no interocular asymmetry. Left eye pattern responses to a 26' check pattern showed a relative amplitude reduction, but the symmetrical findings obtained with the larger check size were not felt compatible with a significant degree of organic disease. She was carefully re-examined by the referring ophthalmologist who found that she corrected to 6/9 with an -8.0 sphere, -3.0 cylinder. The probable disc pallor was thought to be related to the myopia.

b) Litigation cases. i) E.L. This 20 year old soldier was referred for electrodiagnosis after presenting with left visual loss of sudden onset. Ophthalmic examination showed a left visual acuity of perception of light with accurate projection and small foci of choroiditis along the superior nasal vesses which was not thought to be significant. Despite the fact that the checks and pattern were 'not seen' with the left eye, no interocular asymmetry was seen in the PVEP or the FVEP strongly suggesting psychogenic visual loss. There was clinical evidence of organic disease

(the choroiditis) but there was marked overlay. The desire for a medical discharge from the army was felt to be the relevant factor.

ii) F.S. This 54 year old man was involved in an accident in which liability was admitted and for which a compensation claim was pending. He complained of impaired vision in the left eye since the accident. The only finding on ophthalmic examination was a left visual acuity reduced to 6/36. The right eye was normal. Stimulation with a 13' check pattern evoked higher amplitude potentials (not significant) when the left eye was stimulated than the right but subjectively the patient claimed to see the pattern 'very much clearer' with the right eye than the left. The discrepancy between the subjective and objective findings, and the failure to find PVEP changes to a 13' pattern in an eye with a claimed visual acuity of 6/36, were not thought to be compatible with organic disease. The patient was felt by the ophthalmologist to be malingering.

c) Psychogenic or hysterical visual loss; children. i) A.C. This $4\frac{1}{2}$ year old boy was referred for VEP studies to investigate severely reduced vision in the right eye from a right convergent squint which had not responded to glasses, occlusion or surgery. Right eye visual acuity was less than 1/60. No significant interocular latency asymmetry was seen in the PVEP's, but P2-N3 amplitude was reduced by approx. 55% in the right eye traces compared with the left. FVEP's were of marginally higher amplitude from the right eye and electroretinography was normal. It was not felt that an amplitude reduction confined to component N3, with no latency changes, was compatible with the severely reduced visual acuity claimed by the patient, but would be compatible with a mild strabismic amblyopia. The final diagnosis was one of probable strabismic amblyopia with marked functional overlay.

ii) S.P. This 11 year old girl, whose mother has multiple sclerosis, was referred for investigation of blurring of vision in the left eye.

Some weeks prior to this she reported that her left leg had given way while at school. On examination there were no physical signs but there was an arcuate type of scotoma on Amsler charting. However, as the chart was rotated, the scotoma rotated! Both the PVEP and FVEP were normal and the diagnosis was one of non-organic visual loss.

d) Psychogenic or hysterical visual loss; 18-30. i) D.B. This 18 year old girl was admitted with a sudden onset of bilateral blindness for the third time. Examination on admission showed no perception of light bilaterally but the pupils reacted equally and briskly to light. VEP examination was performed the day following admission when she confessed to a bilateral visual acuity of counting fingers at one metre. VEP's to pattern reversal and diffuse flash stimulation were completely normal despite the severe loss of acuity. A diagnosis of hysterical blindness was made. The patient was seen by the psychiatrists who elicited a fraught family situation with additional boyfriend trouble.

ii) M.W. This 24 year old unmarried female teacher was admitted when marked visual field constriction was found after she presented with impaired vision. On examination she was placid and not at all concerned or anxious about her symptoms. Corrected visual acuities were J8 on the right, J18 on the left. There was marked field constriction bilaterally. Formal perimetry showed gross tunnel vision, particularly in the left eye. All investigations including skull X-ray, E.M.I scan and examination of the cerebrospinal fluid were completely normal. The FVEP and ERG were normal, as was the PVEP, even when a 13' pattern was used. There were occasionally marked discrepancies between the subjective perception of the stimulus ("I could hardly see the pattern") and the intact PVEP. It is of interest that when the visual acuities were being measured, the patient reported monocular diplopia with the right eye at the 6/18 line. It was felt fairly certain that there was no underlying pathology. In addition to VEP incompatibility she was able to find her way round the ward with no difficulty and without

bumping into things despite the reduced visual acuity and gross tunnel vision. No history of work or social problems could be obtained.

iii) C.M. This 24 year old unmarried female shop assistant was admitted complaining of headache, blurred vision, weakness in both lower limbs, unsteadiness and drowsiness following an upper respiratory tract infection. In the past she had been raped at the age of 14 by a friend of her father who was subsequently jailed, she had left home because of family problems and had taken an overdose when aged 21. On examination there was hemianaesthesiae to pin-prick on the right and a claimed left visual acuity of 6/24. No objective abnormality was found. EEG and other investigations were normal. VEP examination was completely normal and symmetrical, even with a 13' check pattern, despite the claimed acuity asymmetry. At times part of the pattern stimulus was reported as totally blank. The diagnosis was one of hysteria.

iv) S.M. This 26 year old male post office worker consulted his optician with failing vision in August 1975. Severely reduced visual acuity and markedly constricted visual fields were found and he was referred to his G.P. and thence to the ophthalmologists. Ophthalmic examination revealed normal fundi but gross visual field constriction and visual acuities of counting fingers on the right, 6/36 on the left. Electrodiagnostic studies at another centre were reported as indicating mildly reduced photopic function. On the basis of this single objective finding he was registered blind in March 1976 when his visual acuities were counting fingers in the right eye and 3/60 in the left. However it was noted that the patient did not behave as if his fields were constricted and dark adaptation in May 1976 produced findings strongly suggestive of an hysterical state. On examination at this time there were grossly constricted fields to within 5^{o} of fixation bilaterally with visual acuities of C.F. on the right, 2/60 on the left. The fundi were thought to be normal though there was possibly some narrowing of the inferior

retinal artery in the right eye. Electrodiagnosis was performed in July 1976. FVEP and ERG examination were totally normal. In the PVEP's the left eye findings were normal, the right eye showing a mild relative delay. There was a marked discrepancy between the subjective and objective findings: clear right eye PVEP's were seen but all perception of the stimulus was denied by the patient; clear left eye PVEP's were seen and although perception of the stimulus was reported, all perception of movement of the stimulus was denied. When his low visual aid correction was used with the left eye a greater clarity of the stimulus was reported, but the PVEP showed a mild latency delay, most marked in component N3, and amplitude reduction compared with the uncorrected findings. In October 1976 a spontaneous improvement was reported and it was felt at the time that the right eye was probably amblyopic but that there was no organic disease and nothing wrong with the left eye. The findings in this patient are illustrated in Fig. 3.7.1.

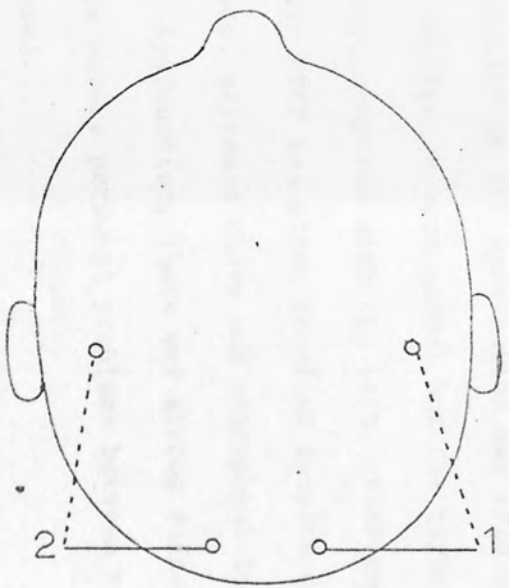
v) K.D. This 30 year old unmarried lady was initially seen following painful blurring of vision in the left eye. On examination she was obese with a left visual acuity of 6/36 - 6/60 and marked field constriction. The fundi were normal. The FVEP and PVEP, even with a 13' check pattern, were completely normal and symmetrical despite the visual acuity asymmetry. The patient was re-examined three months later when the left visual acuity had further deteriorated to 3/60. The patient reported that on this occasion the pattern stimulus was very poorly seen and the flash "in a mist" with the left eye. The VEP's were unchanged from the previous recordings despite the progressive loss of left visual acuity reported by the patient. All other investigations including E.M.I scan were normal and the diagnosis of hysterical visual loss was made.

e) Psychogenic or hysterical visual loss; 47+. All except one of these patients were female and post-menopausal. The only exception was a 56 year old man whose wife had disabling multiple sclerosis. The reader is now familiar with the type of case and details will be shortened in the following patients.

Fig. 3.7.1. PVEP findings in a 26 year old man with non-organic visual loss. See text for details.

S.M. aet 26

V.O.D. C.F., V.O.S. 2/60



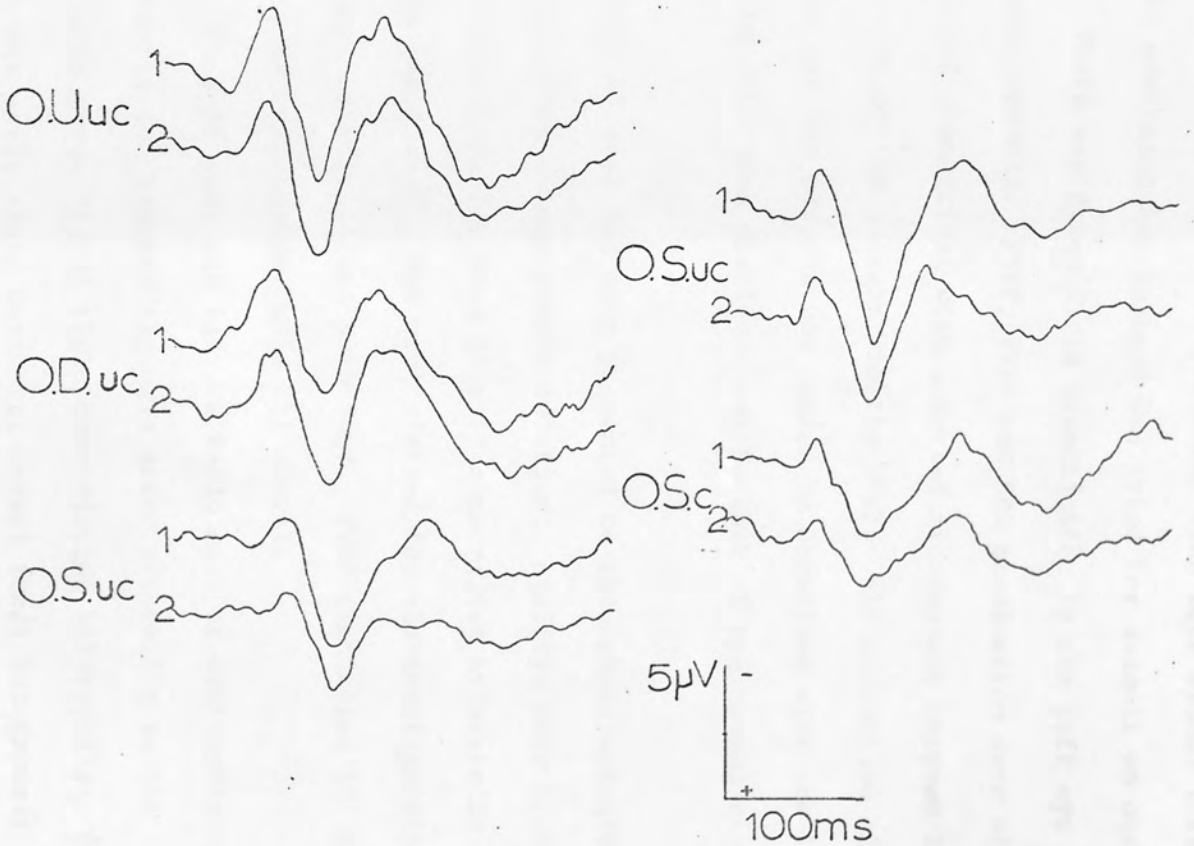


Fig. 3.7.1.

i) M.H. A 47 year old lady described by her daughter as excessively nervous and anxious. She presented with left visual loss. Two years prior to admission her husband was tried for assault on one of their daughters. There was gross field constriction in the left eye and mild iron deficiency anaemia. PVEP, FVEP and ERG examination were all completely normal and symmetrical with a marked discrepancy between the subjective perception of the pattern and the PVEP; all perception of pattern or movement of the pattern was denied on occasions with the left eye even though the PVEP seen was identical to that of the normal right eye.

ii) K.M. This 47 year old lady presented to the ophthalmologists with visual deterioration of one year's duration. Acuities were 6/18 bilaterally. The visual fields were grossly constricted bilaterally and were thought to be functional. She was referred for electrodiagnosis to exclude the presence of significant pathology. PVEP (including 13' check pattern), FVEP and ERG examination were all normal.

iii) V.B. This 56 year old lady, a known case of dystrophia myotonica, was referred for electrodiagnosis after presenting to the ophthalmologists with gross visual field constriction bilaterally. On examination there was early right cataract, normal fundi but grossly constricted fields which were not thought to represent organic disease. Her claimed visual acuity at VEP examination was 1/24 on the right, 1/18 on the left. PVEP amplitudes were normal but the right eye P2 component was delayed by 11 msec compared with the left. FVEP and electroretinography were normal. A clear PVEP was often obtained despite denial of perception of the pattern. Thus, although there was neurophysiological evidence of mild right anterior dysfunction, there was strong suggestion of marked overlay. There were severe personal problems between the patient and her non-supportive husband.

iv) V.G. This 56 year old lady presented with headaches and loss

of vision on the right. In the past there was a history of two nervous breakdowns, an overdose and a chronic anxiety state. VEP and ERG examination were normal. When seen again by the referring physician it was not felt that the loss of vision was neurological. Colour vision, visual acuity and peripheral fields were all normal, the latter despite the patient's claim that she had to turn her head a full 90^{o} when about to cross a road.

v) A.L. This 56 year old man, whose wife had multiple sclerosis, presented with a one year history of binocular lower altitudinal field defect in the evening associated with 'heavy' eyelids. Although formal testing showed a visual acuity of 6/6 bilaterally the 13' check pattern was reported as "much clearer with the right eye than the left". There was a slight amplitude reduction (relative) in the right eye potentials. Bizarre symptoms occurred during PVEP recording. With a 26' check pattern the lower field appeared light blue, the upper field dark blue; with the 13' check pattern the lower field appeared orange and the upper field black. Normal PVEP's were recorded throughout. Mild cerebellar and cortical atrophy on E.M.I scan was the only abnormal finding and a functional disturbance was diagnosed.

vi) E.L. A 56 year old lady with an eighteen month history of deteriorating vision and headache. On examination there was a variable visual field defect with visual acuities of 6/36 on the right, 3/60 on the left. Despite the marked visual acuity asymmetry the VEP's (flash and pattern) were completely normal and symmetrical. E.M.I scan showed mild cerebral atrophy, all other investigations were normal. On being informed that there was nothing seriously wrong with her, she broke down and confessed numerous personal problems.

vii) S.M. This 57 year old nurse presented with an eighteen month history of progressive visual loss, worse in the last six months. After testing by an ophthalmologist she noticed bilaterally constricted visual

fields. The only findings of note on ophthalmic examination were bilateral visual acuities of 6/36 and gross bilateral visual field constriction. VEP examination, even with a 13' check pattern, was totally normal. It was also felt that the gross field constriction was not consistent with the ease with which she avoided obstacles placed in her path. All other investigations including E.M.I scan and air encephalography were normal.

viii) M.P. This 56 year old lady was admitted for investigation of headache, blackouts and blindness in the right eye. The failure to perceive light in the right eye followed a head injury three months earlier. There was a history of psychiatric illness which had resulted in her undergoing a stereotactic subcaudate tractotomy for chronic depression. On examination there was no perception of light in the right eye but the pupils were equal and reacted equally to light and accommodation. Despite the reported lack of light perception in the right eye normal responses to a 40' check pattern and a diffuse flash stimulus were recorded which were identical to those from the normal eye. All other investigations, including E.M.I scan and examination of the cerebrospinal fluid, were normal.

ix) M.H. This 59 year old hospital orderly was initially seen by the ophthalmologists in 1973 with reduced vision in the right eye. A microaneurysm near the right macula was found but as fluorescein angiography showed very little, it was not felt that this totally accounted for the reduced visual acuity which, at that time, was 6/36. Continuing complaints of visual impairment followed and by 1976, following negative (other than the right macular lesion) investigation at various hospitals, she was found to have a visual acuity of 6/60 on the right, 6/18 on the left with bilaterally constricted fields. Pattern evoked potentials were mildly delayed on right eye stimulation compared with the left; flash evoked potentials and electroretinography were normal. Pattern responses to a 13' pattern were well formed. It was concluded that there was a right macular lesion with overlay and non-organic left visual loss.

x) E.K. This 59 year old lady was referred for assessment of gross bilateral field constriction which was confirmed on perimetry. VEP and ERG examination were normal and following this it was noted by the referring ophthalmologist that her fields to confrontation, with much persuasion, were thought to be considerably fuller than on perimetry.

xi) K.H. This 65 year old lady was admitted with a two year history of virtually total blindness following a 'stroke'. She was very dependent on her husband who did virtually everything for her. Initial examination showed acuities of 6/60 on the right, C.F. on the left. She was depressed, hypertensive and had a past medical history of rectal carcinoma treated with diathermy. It soon became clear that the visual deficit was nowhere near as bad as she maintained, for although she said she could hardly see anything she was able to describe fine details of the doctor's clothing. She spent a lot of time watching television. E.M.I scan showed a small right posterior lesion compatible with a previous infarct. There was a mild latency increase in the right eye PVEP but FVEP and ERG examination were normal. Ophthalmological examination showed colloid degeneration of the maculae but no serous elevation or other features of disciform degeneration. The ophthalmoscopic appearances were not thought compatible with the degree of visual loss. She was seen by the psychiatrists who agreed that there was marked hysterical overlay.

In most of these patients the relevant neurophysiological finding is that of normal VEP's despite markedly reduced visual acuity, gross visual field constriction or denial of perception of the stimulus by the patient. In others a mild abnormality was seen despite severe apparent loss of visual function, strongly suggesting hysterical overlay. The objective assessment of the visual system by the VEP in patients with communication difficulties is also demonstrated. Here of course the VEP is also relevant in the detection of abnormalities <u>not</u> communicated by the patient e.g the

ethambutol toxicity in immigrants described by Harding et al. (1979).

The normal FVEP in the patient (M.P., e, viii) with no perception of light in one eye of presumed psychogenic aetiology confirms similar findings by previous authors (Harding, 1974; Beck et al., 1975). Similarly, normal FVEP and ERG in patients with grossly constricted visual fields is not suggestive of an organic aetiology.

However, in many of the patients in this series the complaint was of impaired visual acuity in one eye. Here, where perception of light is not in doubt, the FVEP is of less value and the PVEP comes to the fore. If a patient has markedly reduced visual acuity in one eye an interocular PVEP asymmetry may be expected. If no such asymmetry is seen, particularly with small (e.g 10' - 13') check patterns, then there is strong evidence to support a non-organic aetiology, the 6/18 line on a Snellen chart subtending a visual angle of some 15' at the eye (Allen, 1968). These findings confirm the previous report of PVEP in psychogenic visual loss (Halliday, 1973).

A marked interocular asymmetry in the patient's perception of the stimulus unaccompanied by an asymmetry in the PVEP, or intact PVEP's to a small check stimulus with severely reduced visual acuity bilaterally are therefore considered to be strongly suggestive of at least a substantial amount of non-organic visual dysfunction. The reader is however reminded of the cautionary warning of Halliday (1973) that a normal VEP does not preclude the presence of some organic disease. The reader is also reminded, although no such patient is included in the present series, that the PVEP is dependent on fixation and, to a lesser extent, accommodation of the stimulus. In patients where this is not obtained the FVEP remains an extremely useful tool in the objective assessment of the visual system.

CHAPTER FOUR

C O N C L U S I O N S

4.1 Overall Discussion and Conclusions

Throughout the course of this thesis it has become apparent that the averaged cortical potentials evoked both by diffuse flash (FVEP's) and pattern reversal (PVEP's) stimulation are sensitive indicators of the functional state of the pre-chiasmal, chiasmal and post-chiasmal visual pathways. It now remains to re-examine some of those findings and assess the roles and effectiveness of the two types of stimulation.

The most obvious roles for the FVEP are in the examination of the uncooperative or non-cooperative patient, and in those patients in whom the PVEP is absent. The cooperation and ability of the patient to fixate on the centre of the pattern and accommodate to the pattern is required for PVEP assessment. Certainly comatose patients are incapable of fixating a pattern and flash stimulation is the only practical means of evaluating the intracerebral visual pathways after the pupillary reflexes have been clinically examined. There may also be an absence of fixation in patients who are malingering and the FVEP again may provide valuable information concerning the state of visual function. Equally patients with severely reduced visual acuity (organic) may be incapable of perceiving the pattern stimulus and thus provide absent PVEP's which add little to the state of clinical knowledge other than by providing neurophysiological confirmation of the reduction in central vision. The reader will no doubt recall that in chiasmal compression the typical interhemispheric asymmetry usually seen with monocular pattern stimulation could occasionally only be elicited with flash stimulation, the absent PVEP representing the marked loss of visual acuity in severely affected eyes.

Patients with acute optic or retrobulbar neuritis, though not specifically described in this thesis, can also display absent PVEP's and the FVEP changes may assist the clinician with his diagnosis. In older patients the marked abnormalities seen in the FVEP's of patients with

ischaemic optic neuropathy associated with giant cell arteritis of distorted waveform, highly reduced amplitude and a substantial delay in the early negative component, may, when further research has been performed to confirm these findings, become a factor in the decision whether to perform temporal artery biopsy, the PVEP being absent and therefore relatively uninformative.

We have also seen that the FVEP may be an accurate indicator of optic nerve function in eyes which have suffered major trauma and can provide, in conjunction with the ERG, a good prediction of the eventual functional state of the eye when conventional clinical methods of examination such as ophthalmoscopy are impractical due to the physical condition of the eye.

There are also situations in which the PVEP supplies most information. In non-acute optic nerve demyelination, which can also be sub-clinical, the characteristic evoked potential delay, first described by Halliday et al. (1972, 1973) and since confirmed by numerous subsequent authors (see sections 1.4 and 3.3 for details) is often not seen in the FVEP which can even be normal. It is possible that this represents the greater propensity of the central visual fibres for demyelination, clinically reflected in the not uncommon finding of a central scotoma. Pattern reversal, where there is no change in luminance, stimulates the macula or fovea, particularly with relatively small check sizes, whereas a flash stimulates the whole retina due to the diffusing power of the globe of the eye.

While the much lower variability inherent in the PVEP may be responsible for its greater sensitivity in optic nerve demyelination, the differences in stimulated retinal area may account for the increased effectiveness of combined PVEP and FVEP examination compared with the individual findings of either investigation in some of the other conditions described. In the non-demyelinating pre-chiasmal lesions it is often the

combined PVEP and FVEP findings which enable the differential diagnoses to be correctly assessed and this author has even observed cases of optic nerve demyelination where an equivocal PVEP waveform has been resolved by the finding of delayed FVEP, This equivocality generally consisted of either an enhanced, delayed P1 component, at a latency equivalent to a normal P2, followed by a delayed P2; or a normal latency P2 followed by a later positivity.

Indeed the complementary nature of the two stimulus forms is also in evidence in the patients with post-chiasmal lesions, both with and without direct visual pathway involvement. Here the advantages of combining the findings from the FVEP and PVEP appear to be twofold. Firstly the FVEP was shown to be more sensitive to generalised neurophysiological disturbances than the PVEP, abnormalities being seen when no clinical involvement of the visual pathways was present, and even to have a possible pathognomic waveform in cases of 'suprastriate hemianopia' (see also Feinsod et al., 1974, 1975). The second advantage of a combination of flash and pattern reversal stimulation appears to be in the detection of visual field defects. Patients were described with homonymous hemianopia and macular sparing in whom the PVEP was normal, the FVEP abnormal; with homonymous hemianopia and macular involvement in whom both the PVEP and the FVEP were abnormal; and a single patient with an homonymous scotomatous hemianopic field defect had a normal FVEP but an abnormal PVEP. This strong dependence of the PVEP on the central visual field has previously been suggested by Regan and Heron (1969) who described a single patient with a macular sparing homonymous hemianopia in whom the potentials evoked by sine wave modulated pattern were normal, but those evoked by sine wave modulated flash were abnormal.

This combined usefulness of the FVEP and PVEP in a wide variety of clinical conditions is not compatible with the increasing disuse of the FVEP detailed in the introductory section of this thesis and it is the

conclusion of this author that such disuse is not justified. Since the introduction of the PVEP to the clinical field (Halliday et al., 1972, 1973) there has been a growing tendency to regard the PVEP as a panacea for neurophysiological ills. It is suggested however that the findings presented in this thesis clearly indicate that any department offering a clinical VEP service should at least have FVEP facilities available and there is a strong argument for routinely examining the FVEP in clinical VEP investigation. It is recognised however that the rewards from this may be relatively small in those departments purely advising on optic nerve conduction in patients with clinically suspected multiple sclerosis.

The extent to which the findings presented in this thesis agree or disagree with those of previous authors also merits some attention in this discussion. The reader no doubt recalls that although the findings presented generally support those of previous authors in those conditions where an adequate description of VEP findings has previously appeared, there are some exceptions to this. Equally the VEP findings in a number of conditions are described in this thesis, albeit in a small number of patients, where little or no previously published work is available for comparison.

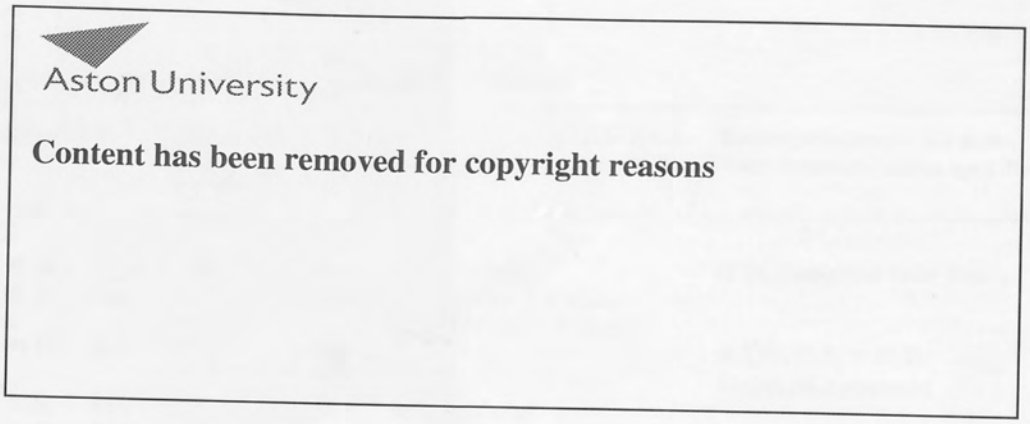
Possibly the most important discrepancy between the present report and those of previous authors is that concerning the PVEP findings in patients with hemianopic visual field defects where the consistent localisation of the abnormality contralateral to the field defect described in this thesis, findings that are in agreement with those that would be predicted on a purely neuroanatomical basis, is in marked disagreement with the ipsilateral abnormality localisation suggested by Halliday and his co-workers (Halliday et al., 1976; Blumhardt et al., 1977). It seems likely from additional recordings in three suitable patients that this discrepancy is caused by differences between the stimulus and

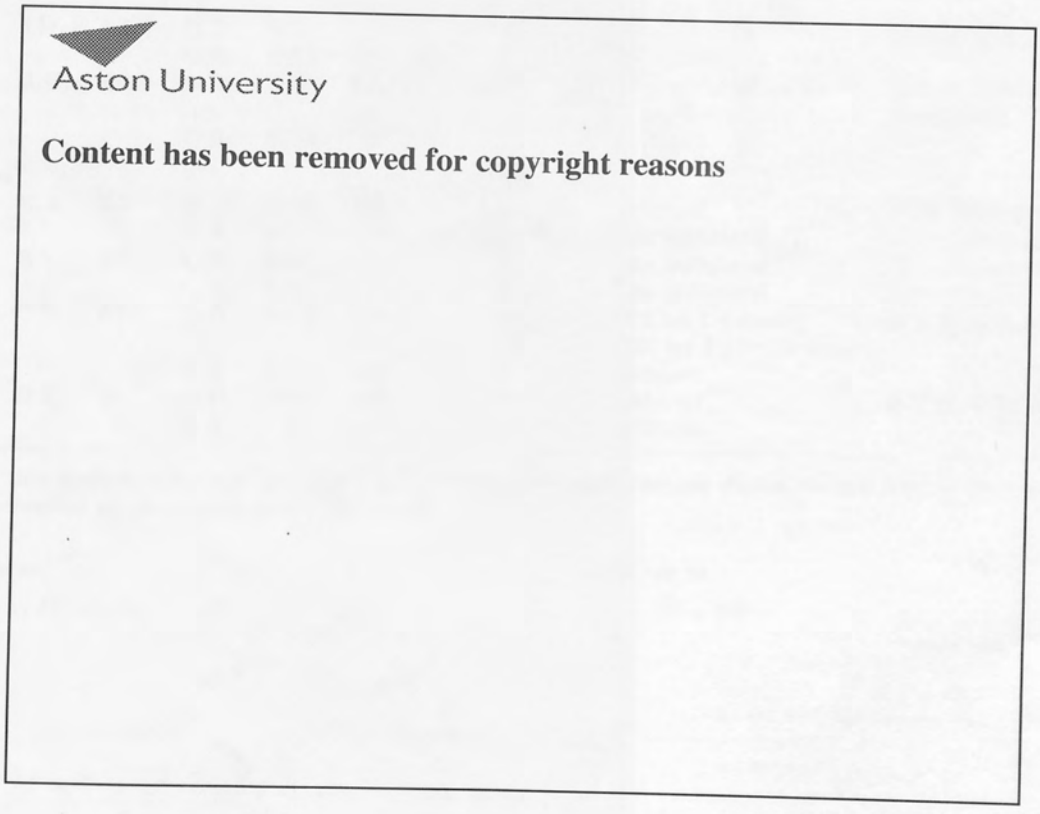
recording parameters used by Halliday and his colleagues (op. cit.) and those used in this study. These additional recordings showed that the findings obtained using the recording parameters of Halliday and his colleagues (active electrodes 5 cm anterior and 5 cm lateral to the inion with a mid frontal reference) are so susceptible to changes in stimulus parameters that changes in the size of the stimulus produced different abnormality localisations in the same patient. It is again noted that the findings obtained using the recording parameters of this author (active electrodes 2 cm anterior and 2 cm lateral to the inion with ipsilateral sylvian reference electrodes) were unaffected by changes in stimulus parameters, always correctly localising the abnormality to the hemisphere contralateral to the visual field defect. The clinical implications of not being able to localise to one hemisphere or the other an underlying dysfunction when presented with a PVEP abnormality at the scalp are both serious and extremely undesirable and the importance of adequate consideration of stimulus and recording parameters cannot then be overemphasised. Indeed, it may be the influence of these parameters on the PVEP which is responsible for other relatively minor discrepancies between the findings of this study and those of previous authors.

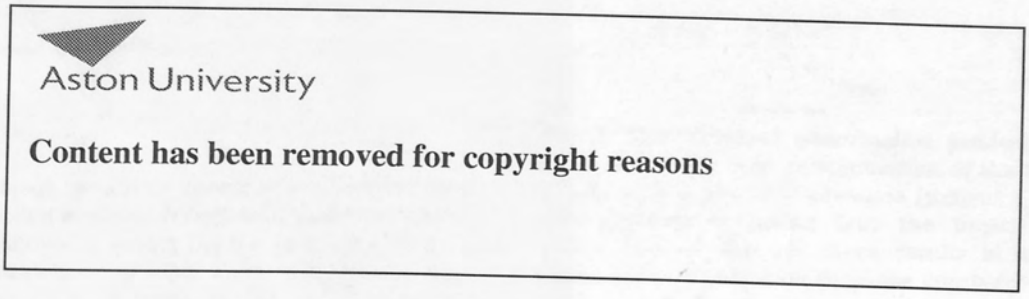
Although much further research is necessary to ascertain why particular combinations of stimulus and recording parameters can influence the PVEP so drastically, it seems possible that the degree of infolding of the occipital cortex and the projection of the retina in the cortex may be relevant factors. It must however be considered possible that the limitations of the spatial average provided by the VEP may not enable these problems to be adequately resolved. It is nonetheless hoped that this thesis, by raising these problems and by evaluating the respective merits of the PVEP and the FVEP in a wide variety of clinical conditions, has made a significant contribution to our knowledge of the clinical visual evoked potential.

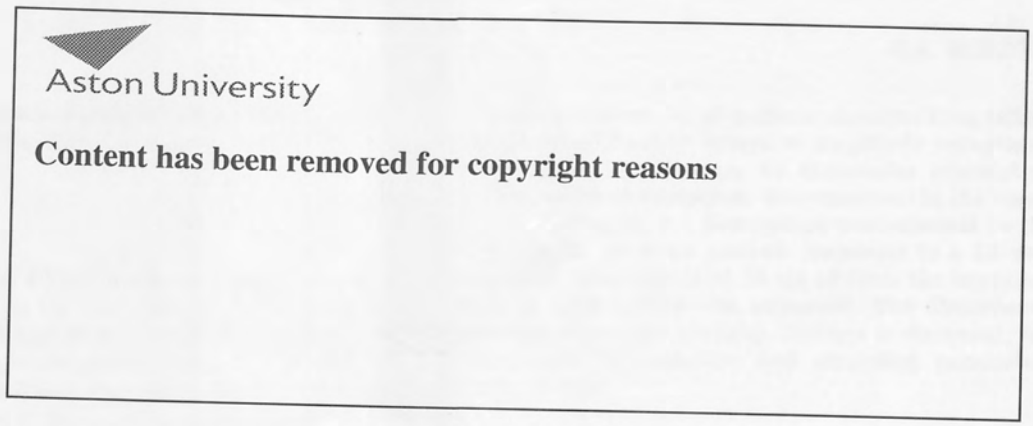
APPENDIX

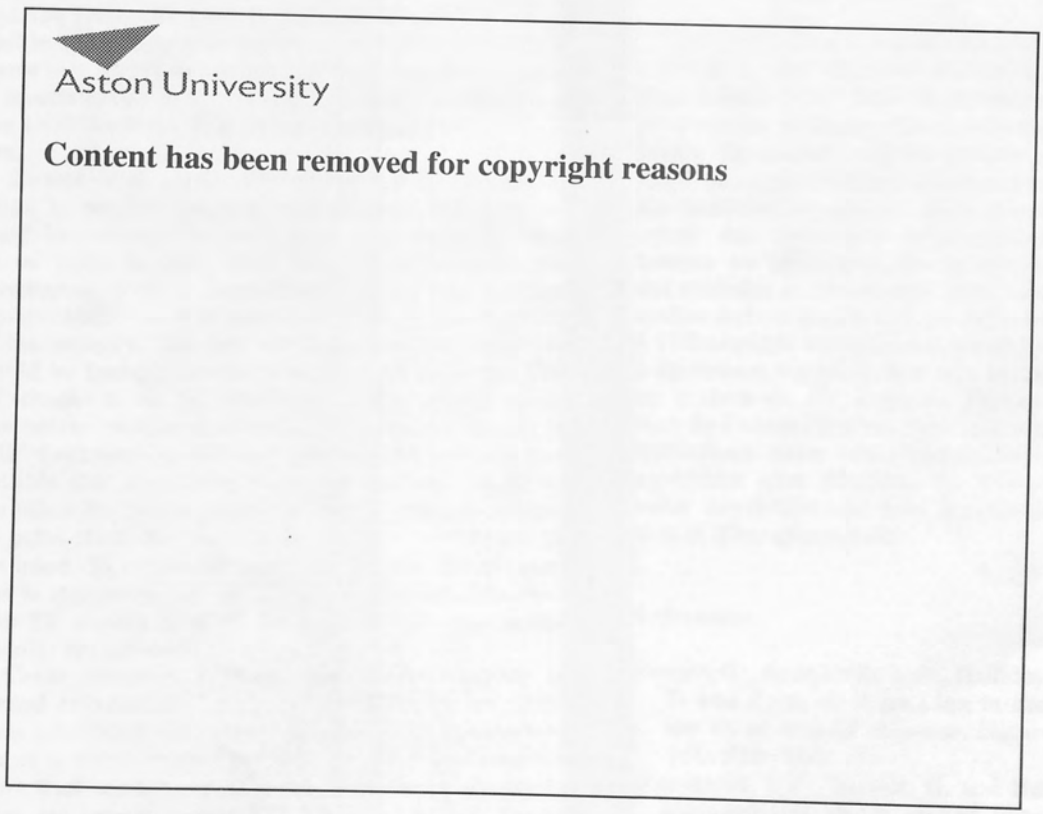
P U B L I C A T I O N S

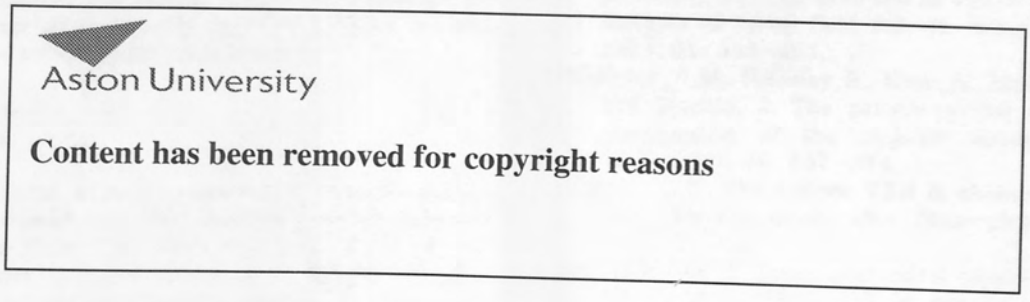

Aston University
Content has been removed for copyright reasons


Aston University
Content has been removed for copyright reasons


Aston University
Content has been removed for copyright reasons


Aston University
Content has been removed for copyright reasons


Aston University
Content has been removed for copyright reasons


Aston University
Content has been removed for copyright reasons

Abnormalities of the pattern visual evoked potential in patients with homonymous visual field defects.

G. E. Holder

Regional Department of Clinical Neurophysiology
Brook General Hospital,
Shooters Hill Road,
Woolwich, S.E.18.

Abnormalities of the pattern visual evoked potential in patients with homonymous visual field defects.

This report describes the type of abnormality found on pattern visual evoked potential (PVEP) examination in patients with homonymous visual field defects. In previous reports by this author[1,2] PVEP abnormalities have been described in patients with bitemporal hemianopia. As would be predicted on purely neuroanatomical grounds, these were invariably maximal over the hemisphere contralateral to the field defect. These findings were, however, in disagreement with those of Halliday and colleagues[3] who reported maximal abnormalities ipsilateral to the field defect in patients with chiasmal compression. The apparent discrepancy between these two reports has been attributed to the use of differing stimulus and recording parameters in the two studies[2].

In homonymous hemianopia Halliday and his co-workers[4] have described abnormality localisation ipsilateral to the field defect in a patient following occipital lobectomy, and although Wildberger et al.[5] found contralateral abnormality localisation in 6 patients, this was using higher frequency (8/sec) stimulation.

Method and Materials.

Nineteen patients with homonymous visual field defects are reported (see Table 1), the site and nature of the lesion being established by angiography, CAT scan or at operation.

Bipolar occipital-sylvian and occipital-parietal recordings were taken over both hemispheres using silver/silver chloride electrodes placed according to the Modified Maudsley system[2]. The occipital electrodes were therefore situated 2 cm anterior and 2 cm lateral to the inion. On-line averaging was performed

by a Datalab Biomac 1000 receiving its input via an SLE machine which was used to monitor eye movements, etc., in addition to the primary EEG trace. Pattern reversal stimulation was provided by a Digitimer stimulator (moving mirror) situated 80 cm from the patient. The total field subtended at the eye was usually 11^{o} with an individual check subtense of 26', but variations in stimulus parameters were used on occasions. Movement of the pattern and initiation of the Biomac sweep were controlled by a Digitimer 4030 pulse generator. Two reversals per second were used with an analysis time of 320 m.sec. Responses were generally the result of 128 reversals but on occasions 256 or 512 reversals were used to obtain a satisfactory trace. Each eye was examined at least twice in all patients, the findings being assessed in relation to an extensive normal control group.

In two patients (1 and 12) further recordings were taken using additional electrodes placed 5 cm anterior and 5 cm lateral to the inion as used by other workers[3,4]. These were referred to a mid-frontal reference. The purpose of these additional recordings was to investigate the relative importance of stimulus and recording parameters on the localisation of the abnormality. Patient 1 was initially seen prior to surgery, and later following occipital lobectomy for glioma. Patient 12 was examined after partial occipital lobectomy for adenocarcinoma.

Results.

The main results are documented in Table 1. As in earlier reports[1,2], P2 has been used to describe the major positive component normally seen at approx. 100 m.sec, N2 the immediately preceeding and N3 the immediately following negative components. All latency measurements were taken from the peak

of the relevant component. In some instances there was a marked disturbance in PVEP morphology on the affected side. Whilst it is recognised that this is a subjective evaluation, the term waveform distortion (WFD) has been used to indicate a relative loss of normal morphology.

It is noted that, without exception, the abnormalities were localised over the affected hemisphere, i.e. contralateral to the field defect, as would be predicted on neuroanatomical grounds. Examples of the type of abnormality seen are shown in Figs 1 and 2.

In the three patients with involvement of both hemispheres (17-19), the more abnormal reponse was in each case recorded over the hemisphere contralateral to the side of maximum visual field defect.

An example of the effects of variations in stimulus parameters on the potentials recorded by electrodes placed 2 cm anterior and lateral to the inion (as normally used by this author) and 5 cm anterior and lateral to the inion (used by Halliday and his colleagues) is shown in Fig. 3 in a patient following left occipital lobectomy. As these findings are relatively complex they have been summarised in Table 2. The clear reversal of abnormality localisation induced in the '5 cm' electrodes by altering stimulus parameters was not as clear in the other patient. In patient twelve although abnormality localisation could be markedly affected, the changes occurred at differing parameters suggesting an interindividual difference factor. The abnormalities recorded by the '2 cm' electrodes were, however, relatively unaffected by changes in stimulus parameters, the abnormality consistently being localised over the involved hemisphere.

Discussion.

The value of PVEP examination in homonymous hemianopia is established. In each case the abnormalities occurred over the affected hemisphere i.e. contralateral to the visual field defect. In 3 patients with bilateral lesions the PVEP correctly localised the more abnormal hemisphere. These findings of abnormality localisation contralateral to the field defect are consistent with previous reports by this author[1,2] on patients with chiasmal compression and bitemporal hemianopia.

The type of abnormality seems to be at least partially dependent on the pathological nature of the lesion. In three cases (7, 11, 17) a significant amplitude reduction over the affected hemisphere was the only abnormal finding, and in each of these cases infarction had caused the field defect. In cases (e.g. 1, 2, 5, 10, 12, 13, 15) where the waveform was more drastically altered, the lesions were space-occupying (6 tumours, 1 haematoma).

These results are however apparently discrepant with those of Halliday and his colleagues[3,4] who suggest, using a 32° stimulating field with 50' checks, an abnormality localisation ipsilateral to the field defect. They use recording electrodes 5 cm anterior and lateral to the inion referred to a mid-frontal reference. The findings (Fig.3, Table 2) in a patient following occipital lobectomy suggest that this apparent discrepancy is due to the position of their recording electrodes in conjunction with a large stimulating field. In Fig. 3, channels 3 and 4 show a contralateral abnormality localisation using the stimulus parameters regularly used by this author (11°, 26'). Increasing the field and check size to 22° and 57' (approximating to 32°, 50') produces an ipsilateral localisation, the abnormality changing sides! Use of 16° and 30' (30' ≃ 26')

probably gives ipsilateral localisation. Reduction to 8° and 13' then further changes the abnormality localisation which reverts to contralateral. The similarity between 26' and 30' and the markedly different PVEP's suggests the total size of the stimulating field as the most relevant factor. Electrodes 2 cm anterior and lateral to the inion are however relatively unaffected by changes in stimulus paremters, and correctly localise the abnormality to the affected hemisphere throughout.

The mechanisms of the lateralisation reversal described here in response to change in stimulus parameters may well be related to the cortical representation of the macula at the occipital pole (generator neurones posteriorly orientated) and of the peripheral retina on the medial surface of the hemisphere. This was suggested by Barrett et al.[6], who, using half-field stimulation in normals and with recording electrodes 5 cm anterior and lateral to the inion, found that their normally ipsilateral response could in fact have a contralateral predominance if stimulation was confined to the macular area.

A marked susceptibility to change in stimulus parameters is extremely unsatisfactory from a clinical point of view, and it is therefore suggested that centres using electrodes 5 cm anterior and lateral to the inion pay very close attention to their stimuli so as to avoid the false or equivocal abnormality localisation which can be obtained with such recording parameters. This seems particularly relevant to those centres using stimulus parameters similar to the ones readily obtained from the commercially available stimulator used in this study.

TABLE 1 CLINICAL MATERIAL

	Pt.	aet	Diagnosis	Fields/VEP findings
FEMALES	1. G.K.	55	L occ. glioma	RHH L amp ↓, P2 lat ↑ (0-10 ms) WFD (occasional)
	2. J.B.	61	L temp-par-occ. glioma	RHH L amp ↓, WFD
	3. V.M.	68	L post. cer. art. thrombosis	RHH L amp ↓, P2 lat ↑ (0-20 ms)
MALES	4. C.S.	23	L post. cer art. occlusion	RHH L P2 lat ↑ (4-10 ms)
	5. D.W.	38	R temp. astrocytoma	LHH R P2 absent. WFD
	6. C.S.	41	L occ. infarction	RHH L amp ↓, N3 lat ↑ (0-10 ms)
	7. P.R.	46	L occ. infarction	RHH L amp ↓
	8. K.S.	52	R par. melanoma	LHH R variable amp ↓ lat ↑ (P2 0-8 ms, N3 0-10 ms)
	9. E.P.	54	R par. astrocytoma	LHH R P2 lat ↑ (4-10 ms). Early components ↓.
	10. C.W.	55	L temp. glioma	RHH L N2 absent. Lat ↑ (P2 0-6 ms, N3 15-30 ms). WFD.
	11. J.T.	56	R occ. infarction	LHH R amp ↓
	12. A.B.	58	R par-occ. adenocarcinoma*	LHH R amp ↓ , P2 lat ↑ (5-20 ms). WFD.
	13. H.W.	63	R par-occ. haematoma	LHH R amp ↓ , P2 lat ↑ (5-12 ms). WFD (often).
	14. W.S.	64	L int. carotid occlusion	RLQ L amp ↓ lat ↑ P2 (0-6 ms), N3 (0-12 ms).
	15. J.S.	67	L post. temp. astrocytoma	RHH L lat ↑ P2 (6-10 ms), N3 (15-30 ms); amp often ↓. WFD.
	16. F.B.	70	L occ. infarction	RHH L amp ↓ , P2 lat ↑ (variable) (5-8 ms).
	17. R.H.	59	Bilat. occ. infarction R > L	Preserved R lower field. R amp ↓
	18. J.M.	63	Bilat. occ. infarction L > R	Preserved L lower field. R, L amp ↓ L P2 lat ↑ (10 ms).
	19. G.S.	71	Bilat. occ. infarction R > L	V. small field preservation L > R. Bilat lat ↑ , amp ↓. Often absent R.

TABLE 1 continued

* Patient examined following craniotomy

(R)HH.	(Right) homonymous hemianopia
LQ	lower quadrantanopia
lat.	latency
amp.	amplitude
temp.	temporal
occ.	occpital
par.	parietal
WFD	waveform distortion
cer.	cerebral

Table 2. The effects of variations in stimulus and recording parameters on PVEP abnormality localisation (Pt. 1, see Fig. 3).

	Total field/individual check subtense			
	11°/26'	22°/57'	16°/30'	8°/13'
Channels 1 + 2	L*	L*	L*	L*
Channels 3 + 4	L**	R**	(R)***	L**

L and R represent the hemisphere over which the abnormality is seen (Fig. 3.)

* amplitude reduced ** latency extended

*** here, although the L hemisphere potential is of reduced amplitude, the R hemisphere potential is delayed and it is felt that this delay is probably more significant.

Legends to figures

Fig.1. Findings typical of right homonymous hemianopia in a 46 year old man following left occipital infarction. The left hemisphere traces (channels 2 and 4) show a marked amplitude reduction compared with the right. No inter-hemispheric latency asymmetry is present and no significant interocular asymmetry is seen.

Fig.2. Findings in a 38 year old man with an extensive right temporal astrocytoma and left homonymous hemianopia. The notable feature is the total absence of the major positive (P2) component on the right (channels 1 and 3). P2 is however clearly seen on the left and is of normal latency. No interocular asymmetry is seen.

Fig. 3. (see also Table 2 and Discussion). The effects of variations in the total field and individual check subtense on the potentials recorded by electrodes 2 cm anterior and lateral to the inion (channels 1 and 2) and 5 cm anterior and lateral to the inion (channels 3 and 4) in a 55 year old lady following left occipital lobectomy for glioma. Note particularly the marked changes seen in channels 3 and 4 in response to variations in stimulus parameters compared with the relative stability of channels 1 and 2.

SUMMARY

Abnormalities of the potentials evoked by pattern reversal stimulation (PVEP) are described in nineteen patients with post-chiasmal lesions giving rise to homonymous visual field defects. The pathological nature of the lesions was mostly intracranial tumour or cerebrovascular accident, but in all cases the site and nature of the lesion was established.

Pattern reversal stimulation (26' individual check subtense, 11° total field) was performed using a commercially available (Digitimer) moving mirror stimulator, the PVEP's being recorded with electrodes applied according to the modified Maudsley system of electrode placement (occipital electrodes situated 2 cm anterior and 2 cm lateral to the inion).

In all patient the abnormalities of amplitude and/or latency were seen over the hemisphere contralateral to the visual field defect, as would be predicted on a purely neuroanatomical basis. The results are discussed with reference to previous findings, stress being placed on the contribution of stimulus and recording parameters to the abnormality localisation. Additional studies performed to assess the relative importance of these parameters suggest that centres using electrodes 5 cm anterior and 5 cm lateral to the inion pay particular attention to their stimuli so as to avoid the false or equivocal abnormality localisation which can be obtained with such recording parameters.

References

1. Holder, G. E. (1977). The pattern VER in chiasmal compression. Electroenceph. clin. Neurophysiol. 43, 772-773.

2. Holder, G. E. (1978). The effects of chiasmal compression on the pattern visual evoked potential. Electroenceph. clin. Neurophysiol. 45, 278-280.

3. Halliday, A. M., Halliday, E., Kriss, A., McDonald, W. I. and Mushin, J. (1976). The pattern evoked potential in compression of the anterior visual pathways. Brain, 99, 357-374.

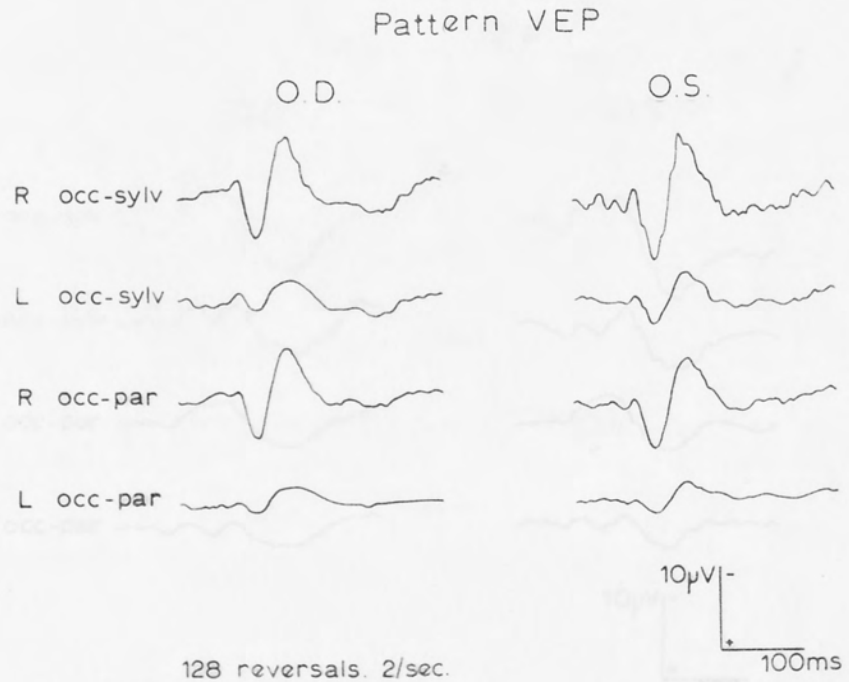
4. Blumhardt, L. D., Barrett, G. and Halliday, A. M. (1977). The asymmetrical visual evoked potential to pattern reversal in one half field and its significance for analysis of visual field defects. Brit. J. Ophthal., 61, 454-461.

5. Wildberger, H. G. H., Van Lith, G. H. M., Wijngaarde, R. and Mak, G. T. M. (1976). Visually evoked cortical potentials in the evaluation of homonymous and bitemporal visual field defects. Brit. J. Ophthal., 60, 273-278.

6. Barrett, G., Blumhardt, L. D., Halliday, A. M., Halliday, E. and Kriss, A. (1976). A paradox in the lateralisation of the visual evoked response. Nature (Lond.), 261, 253-255.

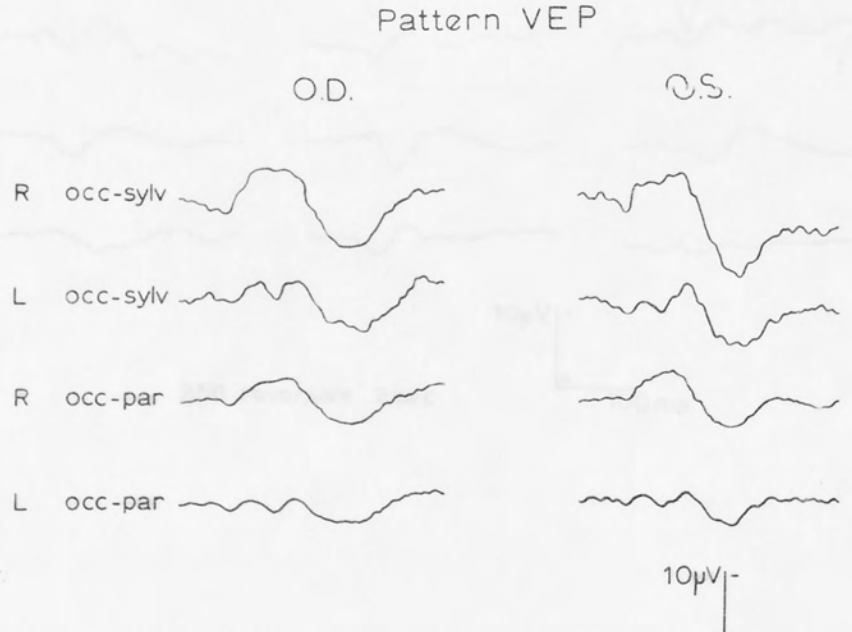
P.R. aet 46

L occipital infarct
V.O.D. J1 V.O.S. J4



D.W. aet 38

R temporal astrocytoma
V.O.D. 6/9 V.O.S. 6/9

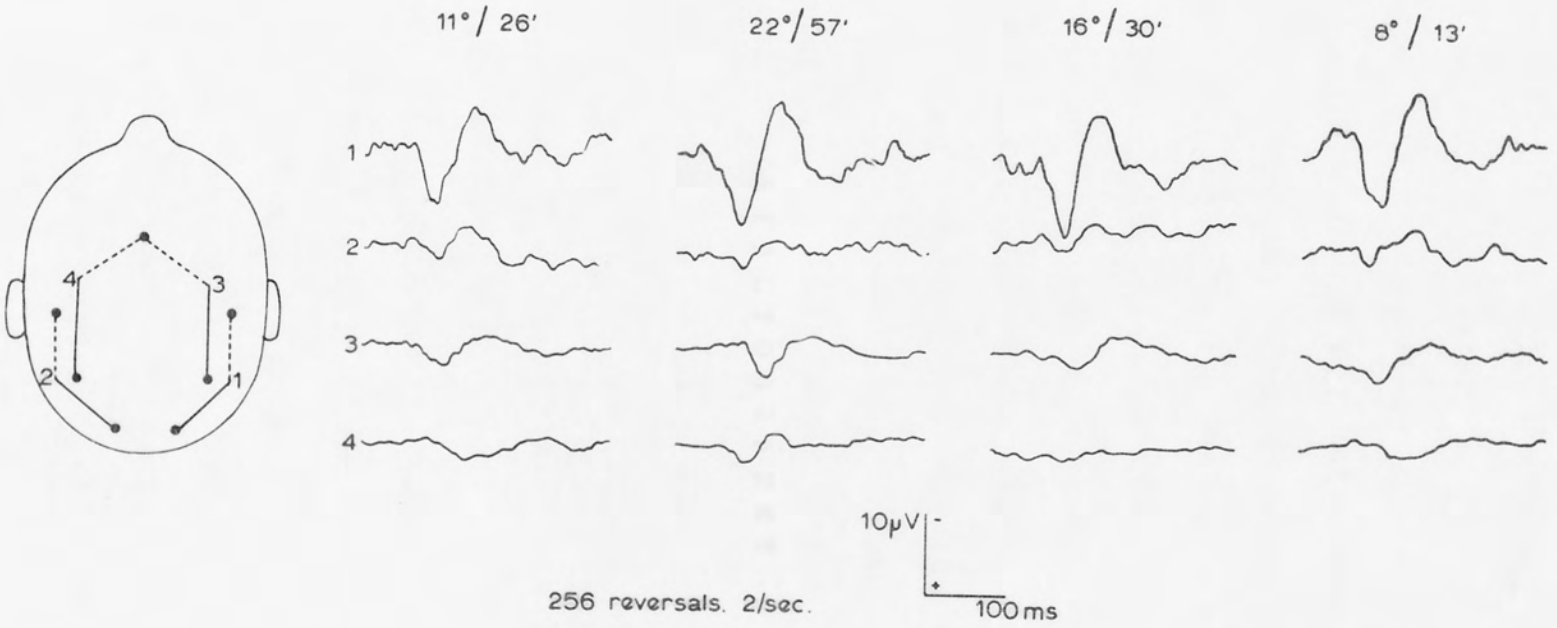


128 reversals. 2/sec.

G.K. aet 55

L occipital lobectomy
V.O.D. J6

Pattern VEP



256 reversals. 2/sec.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Abraham, F.A., Cohen, D. and Sohmer, H. (1977). "Usher's syndrome: electrophysiological tests of the visual and auditory systems." Docum. ophthal. (Den Haag), 44, 435 - 444.

2. Abraham, F.A., Melamed, E. and Lavy, S. (1975). "Prognostic value of visual evoked potentials in occipital blindness following basilar artery occlusion." Appl. Neurophysiol., 38, 126 - 135.

3. Adachi-Usami, E., Kellerman, F-J. and Makabe, R. (1973). "Clinical evaluation of the visual evoked response in a case of optic neuritis." Ophthal. Res., 4, 343 - 354.

4. Adams, W.L., Arden, G.B. and Behrman, J. (1969). "Responses of human visual cortex following excitation of peripheral retinal rods. Some applications in the clinical diagnosis of functional and organic visual defects." Brit. J. Ophthal., 53, 439 - 452.

5. Adrian, E.G. and Matthews, B.H.C. (1934). "The Berger rhythm; potential changes from the occipital lobes of man." Brain, 57, 355 - 385.

6. Allen, J.H. (Ed.) 'May's Manual of the Diseases of the Eye', Williams and Wilkins, Baltimore, 1968, p. 265.

7. Andreassi, J.L., Okamura, H. and Stern, M. (1975). "Hemispheric asymmetries in the visual evoked potential as a function of stimulus location." Psychophysiology, 12, 541 - 546.

8. Arden, G.B. (1973). "The visual evoked response in ophthalmology." Proc. roy. Soc. Med., 66, 1037 - 1043.

9. Arden, G.B., Barnard, W.M. and Mushin, A.S. (1974). "Visually evoked responses in amblyopia." Brit. J. Ophthal., 58, 183 - 192.

10. Arnal, D., Gerin, P., Salmon, D., Ravault, M.P., Magnard, P. and Hugonnier, R. (1972). "Intérêt des potentiels évoqués moyens

visuels en ophtalmologie." Electroenceph. clin. Neurophysiol., 32, 615 - 622.

11. Ashworth, B., Maloney, A.F.J. and Townshend, H.R.A. (1978). "Delayed visual evoked potentials with bilateral disease of the posterior visual pathway." J. Neurol. Neurosurg. Psychiat., 41, 449 - 451.

12. Asselman, P., Chadwick, D.W. and Marsden, C.D. (1975). "Visual evoked responses in the diagnosis and management of patients suspected of multiple sclerosis." Brain, 98, 261 - 282.

13. Balen, A. Th. M. van (1971). "Toxic damage to the optic nerve caused by iodochlorhydroxyquinoline." Ophthalmologica (Basel), 163, 8 - 9.

14. Barrett, G., Blumhardt, L., Halliday, A.M., Halliday, E. and Kriss, A. (1976 a). "Paradoxical reversal of lateralisation of the half-field pattern evoked response with monopolar and bipolar electrode montages." J. Physiol. (Lond.), 258, 63P - 64P.

15. Barrett, G., Blumhardt, L., Halliday, A.M., Halliday, E. and Kriss A. (1976 b). "A paradox in the lateralisation of the visual evoked response." Nature, 261, 253 - 255.

16. Bartl, G. (1978). "Das Elektroretinogramm und das evozierte Sehrindenpotential bei normalen und an Glaukom erkrankten Augen". Albrecht v. Graefes Arch. Ophthal., 207, 243 - 269.

17. Bartl, G., van Lith, G.H.M. and van Marle, G.W. (1978). "Cortical potentials evoked by a TV pattern reversal stimulus with varying check sizes and stimulus field." Brit. J. Ophthal., 62, 216 - 219.

18. Beck, E.C., Dustman, R.E. and Lewis, E.G. (1975). "The use of the averaged evoked potential in the evaluation of central nervous system disorders." Int. J. Neurol., 9, 211 - 232.

19. Behrman, J., Nissim, S. and Arden, G.B. (1972). "A clinical method

obtaining pattern visual evoked responses." Adv. Exp. Biol. Med., 24, 199 - 206.

20. Bergamini, L. and Bergamasco, B. (1967). "Possibility of the clinical use of sensory evoked potentials recorded transcranially in man." Electroenceph. clin. Neurophysiol., Suppl. 26, 114 - 122.

21. Berger, H. (1929). "Uber das Elektrencephalogramm das Menschen." Arch. Psychiat. Nervenkr., 87, 527 - 570.

22. Bergström, L. and Nyström, S.H.M. (1970). "Visually evoked potentials in patients with brain lesions with or without disturbances of consciousness." Acta Neurol. Scand., 46, 562 - 572.

23. Berman, M.S. and Levi, D.M. (1975). "Hysterical amblyopia: electrodiagnostic and clinical evaluation." Amer. J. Optom. Physiol. Opt., 52, 267 - 274.

24. Berry, R.G. and Alpers, B.J. (1957). "Occlusion of the carotid circulation." Neurology (Minneap.), 7, 223 - 237.

25. Bishop, G.H. and Clare, M.H. (1955). "Organisation and distribution of fibres in the optic tract of the cat." J. comp. Neurol., 103, 269 - 304.

26. Blumhardt, L.D., Barrett, G. and Halliday, A.M. (1977). "The asymmetrical visual evoked potential to pattern reversal in one half-field and its significance for the analysis of visual field defects." Brit. J. Ophthal., 61, 454 - 461.

27. Blumhardt, L.D., Barrett, G., Halliday, A.M. and Kriss, A. (1978). "The effect of experimental 'scotomata' on the ipsilateral and contralateral responses to pattern reversal in one half-field." Electroenceph. clin. Neurophysiol., 45, 376 - 392.

28. Bodis-Wollner, I. and Yahr, M.D. (1978). "Measurements of visual evoked potentials in Parkinson's Disease." Brain, 101, 661 - 672.

29. Boghen, D.R. and Glaser, J.S. (1975). "Ischaemic optic neuropathy.

The clinical profile and natural history." Brian, 98, 689 - 708.

30. Bornstein, Y. (1975). "The pattern evoked responses in optic neuritis." Albrecht v. Graefes Arch. Ophthal., 197, 101 - 106.

31. Bostock, H. and Sears, T.A. (1976). "Continuous conduction in demyelinated mammalian nerve fibres." Nature, 263, 786 - 787.

32. Bostock, H. and Sears, T.A. (1978). "The internodal axon membrane: electrical excitability and continuous conduction in segmental demyelination." J. Physiol. (Lond.), 280, 273 - 301.

33. Brazier, M.A.B. (1964). "The effect of drugs on the EEG of man." Clin. Pharmacol. Ther., 5, 102 - 116.

34. Brindley, G.S. and Westheimer, G. (1965). "The spatial properties of the human electroretinogram." J. Physiol. (Lond.), 179, 518 - 537.

35. Brontë-Stewart, J., Pettigrew, A.R. and Foulds, W.S. (1976). "Toxic optic neuropathy and its experimental production." Trans. ophthal. Soc. U.K., 96, 355 - 358.

36. Broughton, R., Meier-Ewart, K. and Ebe, M. (1969). "Evoked visual, somatosensory and retinal potentials in photosensitive epilepsy." Electroenceph. clin. Neurophysiol., 27, 373 - 386.

37. Bruesch, S.R. and Arey, L.B. (1942). "The number of myelinated and unmyelinated fibres in the optic nerve of vertebrates." J. comp. Neurol., 77, 631 - 655.

38. Bynke, H., Olsson, J-E. and Rosén, I. (1977). "Diagnostic value of visual evoked response, clinical eye examination and CSF analysis in chronic myelopathy." Acta Neurol. Scand., 56, 55 - 69.

39. Cappin, J.M. and Nissim, S. (1975). "Visual evoked responses in the assessment of field defects in glaucoma." Arch. Ophthal., 93, 9 - 18.

40. Carroll, W.M. and Mastaglia, F.L. (1978). "A combined clinical and VEP study of affected and asymptomatic members of a kindred

with Leber's Optic Atrophy." Presented at International Evoked Potentials Symposium, Nottingham, September 1978.

41. Celesia, G.G. and Daly, R.F. (1977). "Visual electroencephalographic computer analysis (VECA)." Neurology (Minneap.), 27, 637 - 641.

42. Ciganek, L. (1961). "The EEG response (evoked potential) to light stimulus in man." Electroenceph. clin. Neurophysiol., 13, 165 - 172.

43. Ciganek, L. (1971). "Binocular addition of the visual response evoked by dichoptic patterned stimuli." Vision Res., 11, 1289 - 1297.

44. Cobb, W.A. (1950). "On the form and latency of the human cortical response to illumination of the retina." Electroenceph. clin. Neurophysiol., 2, 104.

45. Cobb, W.A. and Dawson, G.D. (1960). "The latency and form in man of the occipital potentials evoked by bright flashes." J. Physiol. (Lond.), 152, 108 - 121.

46. Cobb, W.A., Ettlinger, G. and Morton, H.B. (1968). "Cerebral potentials evoked in man by pattern reversal and their suppression in visual rivalry." J. Physiol. (Lond.), 195, 33P - 34P.

47. Cogan, D.G. (1966 a). "Neurology of the Visual System." C.C. Thomas, Springfield, pp 102 - 104.

48. Cogan, D.G. (1966 b). Ibid pp 178 - 179.

49. Cohn, R. (1963). "Evoked visual cortical responses in homonymous hemianopic defects in man." Electroenceph. clin. Neurophysiol., 15, 922.

50. Crews, S.J. and Harding, G.F.A. (1978). "The VEP in optic neuropathies." J. roy. Soc. Med., 71, 550.

51. Crews, S.J., Hillman, J.S. and Thompson, C.R.S. (1975). "Electrodiagnosis and ultrasonography in the assessment of recent major trauma." Trans. ophthal. Soc. U.K., 95, 315 - 321.

52. Crighel, E. and Botez, M.I. (1966). "Photic evoked potentials in man in lesions of the occipital lobes." Brain, 89, 311 - 316.

53. Crighel, E. and Poilici, I. (1968). "Photic evoked responses in patients with thalamic and brain stem lesions." Confin. neurol. (Basel), 30, 301 - 312.

54. Crighel, E. and Sterman-Marinchescu, C. (1971). "Flash evoked responses in acute cerebro-vascular diseases. The correlation with the clinical, electroencephalographic and rheoencephalographic course." Revue Roum. Neurol., 8, 275 - 284.

55. Crighel, E., Poilici, I. and Marinchescu, C. (1966). "The influence of hypoxia on flash evoked potentials in normals and in patients with cerebral circulatory insufficiency." Confin. neurol. (Basel), 28, 348 - 354.

56. Crighel, E., Rosianu, C., Constantinescu, V. and Matei, M. (1974). "Dispersion pattern of visual evoked responses in epilepsy." Eur. Neurol., 12, 148 - 158.

57. Crighel, E., Arseni, C. and Matei, M. (1976). "Visual evoked responses and their dispersion pattern in frontal lobe tumours." Eur. Neurol., 14, 17 - 28.

58. Cullen, J.F. and Coleiro, J.A. (1976). "Ophthalmic complications of giant cell arteritis." Surv. Ophthal., 20, 247 - 260.

59. Dawson, G.D. (1947). "Cerebral responses to electrical stimulation of peripheral nerve in man." J. Neurol. Neurosurg. Psychiat., 10, 134 - 140.

60. Dawson, G.D. (1954). "A summation technique for the detection of small evoked potentials." Electroenceph. clin. Neurophysiol., 6, 65 - 84.

61. Dawson, W.W., Perry, N.W. and Childers, D.G. (1972). "Variations in human cortical response to patterns and image quality."

Invest. Ophthal., 11, 789 - 799.

62. Domino, E.F., Matsuoka, S., Waltz, J. and Cooper, I. (1964). "Simultaneous recordings of scalp and epidural somatosensory evoked responses in man." Science, 145, 1199 - 1200.

63. Dorfman, L.J., Nikoskelainen, E., Rosenthal, A.R. and Sogg, R.L. (1977). "Visual evoked potentials in Leber's Hereditary Optic Neuropathy." Ann. Neurol., 1, 565 - 568.

64. Drasdo, N. (1978). "Cortical potentials evoked by pattern presentation in the foveal region." Presented at International Evoked Potentials Symposium, Nottingham, 1978.

65. Duchowny, M.S., Weiss, I.P., Majlessi, H. and Barnet, A.B. (1974). "Visual evoked responses in childhood cortical blindness after head trauma and meningitis." Neurology (Minneap.), 24, 933 - 940.

66. Dustman, R.E. and Beck, E.C. (1969). "The effects of maturation and aging on the waveform of visually evoked potentials." Electroenceph. clin. Neurophysiol., 26, 2 - 11.

67. Duwaer, A.L. and Spekreijse, H. (1978). "Latency of luminance and contrast evoked potentials in multiple sclerosis patients." Electroenceph. clin. Neurophysiol., 45, 244 - 258.

68. Eason, R.G. and White, C.T. (1967). "Averaged occipital responses to stimulation of sites in the nasal and temporal halves of the retina." Psychon. Sci., 7, 309 - 310.

69. Eason, R.G., Groves, P., White, C.T. and Oden, D. (1967). "Evoked cortical potentials in relation to visual field and handedness." Science, 156, 1643 - 1646.

70. Eason, R.G., White, C.T. and Bartlett, N. (1970). "Effects of chequerboard pattern stimulation on evoked cortical responses in relation to check size and visual field." Psychon. Sci., 21, 113 - 115.

71. Ellenberger, C. and Ziegler, S.B. (1977). "Visual evoked potentials and quantitative perimetry in multiple sclerosis." Ann. Neurol., 1, 561 - 564.

72. Evans, B.T., Binnie, C.D. and Lloyd, D.S.L. (1974). "A simple visual pattern stimulator." Electroenceph. clin. Neurophysiol., 37, 403 - 406.

73. Feinsod, M. and Auerbach, E. (1973). "Electrophysiological examinations of the visual system in the acute phase after head injury." Eur. Neurol., 9, 56 - 64.

74. Feinsod, M. and Hoyt, W.F. (1975). "Subclinical optic neuropathy in multiple sclerosis." J. Neurol. Neurosurg. Psychiat., 38, 1109 - 1114.

75. Feinsod, M., Abramsky, O. and Auerbach, E. (1973). "Electrophysiological examinations of the visual system in multiple sclerosis." J. Neurol. Sci., 20, 161 - 175.

76. Feinsod, M., Hoyt, W.F. and Wilson W.B. (1974). "Suprastriate hemianopia." Lancet, i, 1225 - 1226.

77. Feinsod, M., Hoyt, W.F., Wilson W.B. and Spire, J-P. (1975). "Electrophysiological parameters in the evaluation of occipital apoplexy." Eur. Neurol., 13, 451 - 460.

78. Feinsod, M., Hoyt, W.F., Wilson, W.B. and Spire, J-P. (1976). "Visually evoked response. Use in neurologic evaluation of post-traumatic subjective visual complaints." Arch. Ophthal., 94, 237 - 240.

79. Ferry, A.P. (1963). "Macular detachment associated with congenital pit of the optic nerve head: pathologic findings in two cases simulating malignant melanomas." Arch. Ophthal., 70, 346 - 357.

80. Fisher, N.F., Jampolsky, A., Scott, A.B., Morris, A., Lehmann, D. and Alden, J. (1968). "Traumatic bitemporal hemianopsia. III. Nasal versus temporal retinal function." Amer. J. Ophthal.,

65, 578 - 581.

81. Fishman, R.S. and Copenhaver, R.M. (1967). "Macular disease and amblyopia. The visual evoked response". Arch. Ophthal., 77, 718 - 725.

82. Foulds, W.S., Chisholm, I.A. and Pettigrew, A.R. (1974). "The toxic optic neuropathies." Brit. J. Ophthal., 58, 386 - 390.

83. Francois, J. (1976). "Vascular pseudopapillitis: ischaemic optic neuropathy." Ann. Ophthal., 8, 901 - 919.

84. Freeman, R.D. and Thibos, L.N. (1975). "Visual evoked responses in humans with abnormal visual experience." J. Physiol. (Lond.), 247, 711 - 724.

85. Galambos, R. and Davis, H. (1943). "The response of single auditory nerve fibres to acoustic stimulation." J. Neurophysiol., 6, 39 - 57.

86. Galkina, N.S., Gnezditskii, V.V., Aleksandrova, A.A. and Kozlova, A.I. (1975). "Investigation of evoked potentials to photic stimulation in man after deafferentation of the visual cortex." Byull. eksp. Biol. Med., 79, 23 - 26.

87. Gass, J.D.M. and Olsen, C.L. (1976). "Sarcoidosis with optic nerve and retinal involvement." Arch. Ophthal., 94, 945 - 950.

88. Gastaut, H. and Regis, H. (1965). "Visually evoked potentials recorded transcranially in man." in Proctor, L.D. and Adey, W.R. (Eds.) "The analysis of central nervous system and cardiovascular data using computer methods." N.A.S.A., Washington, 1965, pp 7 - 34.

89. Giltrow-Tyler, J.F., Crews, S.J. and Drasdo, N. (1978). "Electroretinography with corneal and non-corneal electrodes." Invest. Ophthal. Vis. Sci., 17, 1124 - 1127.

90. Goff, W.R., Rosner, B.S. and Allison, T. (1962). "Distribution of cerebral somatosensory evoked responses in normal man."

Electroenceph. clin. Neurophysiol., 14, 697 - 713.

91. Gould, H. and Kaufmann, H.E. (1961). "Sarcoid of the fundus." Arch. Ophthal., 65, 453 - 456.

92. Halliday, A.M. (1973). "Evoked responses in organic and functional sensory loss" in Fessard, A. and Lelord, G. (Eds.) "Activités evoquées et leur conditionnement chez l'homme normal et en pathologie mentale." INSERM, Paris, pp 189 - 212.

93. Halliday, A.M. (1976). "Visually evoked responses in optic nerve disease." Trans. ophthal. Soc. U.K., 96, 372 - 376.

94. Halliday, A.M. and Michael, W.F. (1970). "Changes in the pattern evoked response in man associated with the vertical and horizontal meridians of the visual field." J. Physiol. (Lond.), 208, 499 - 513.

95. Halliday, A.M., McDonald, W.I. and Mushin, J. (1972). "Delayed visual evoked response in optic neuritis." Lancet, i, 982 - 985.

96. Halliday, A.M., McDonald, W.I. and Mushin, J. (1973). "Visual evoked response in the diagnosis of multiple sclerosis." Brit. med. J., 4, 661 - 664.

97. Halliday, A.M., McDonald, W.I. and Mushin, J. (1974 a). "The dissociation of amplitude and latency changes in the pattern evoked response following optic neuritis." Electroenceph. clin. Neurophysiol., 36, 218.

98. Halliday, A.M., McDonald, W.I. and Mushin, J. (1974 b). "Delayed visual evoked responses in progressive spastic paraplegia." Electroenceph. clin. Neurophysiol., 37, 328.

99. Halliday, A.M., McDonald, W.I. and Mushin, J. (1974 c). "Delayed pattern evoked responses in optic neuritis in relation to visual acuity." Trans. ophthal. Soc. U.K., 93, 315 - 324.

100. Halliday, A.M., Halliday, E., Kriss, A., McDonald, W.I. and

Mushin, J. (1976). "The pattern evoked potential in compression of the anterior visual pathways." Brain, 99, 357 - 374.

101. Harden, A. and Pampiglione, G. (1972). "ERG, VER and EEG in twelve children with late infantile neuronal lipidosis." Adv. Exp. Biol. Med., 24, 287 - 293.

102. Harding, G.F.A. (1974). "The visual evoked response." Adv. Ophthalmol., 28, 2 - 28.

103. Harding, G.F.A., Thompson, C.R.S. and Panayiotopoulos, C.R. (1970). "Evoked response diagnosis in visual field defects." Proc. electrophysiol. Technol. Ass., 16, 159 - 163.

104. Harding, G.F.A., Smith, G.S. and Smith, P.A. (1978). "The effects of various stimulus parameters on the lateralisation of the VEP." Presented at International Evoked Potentials Symposium, Nottingham, September, 1978.

105. Harding, G.F.A, Crews, S.J. and Good, P. (1979). "The VEP as a diagnostic aid in neuroophthalmic disease." in Barber, C. (Ed.) "Evoked potentials: Proceedings of the Nottingham Symposium". M.T.P. Press, Lancaster, 1979 (in press).

106. Harmony, T., Ricardo, J., Otero, G., Fernandez, G., Llorente, S. and Valdes, P. (1973). "Symmetry of the visual evoked potential in normal subjects." Electroenceph. clin. Neurophysiol., 35, 237 - 240.

107. Harmony, T., Alvarez, A., Roche, A., Fernandez, G. and Figueredo, P. (1978). "Visual, auditory and somatosensory evoked responses in patients with cerebrovascular disorders." Activ. nerv. sup. (Praha), 20, 161 - 177.

108. Harrison, B.M. and McDonald, W.I. (1977). "Remyelination after transient experimental compression of the spinal cord." Ann. Neurol., 1, 542 - 551.

109. Harter, M.R. (1970). "Evoked cortical responses to chequerboard patterns: effect of check size as a function of retinal eccentricity." Vision Res., 10, 1365 - 1376.

110. Harter, M.R. (1971). "Visually evoked cortical responses to the on- and off-set of patterned light in humans." Vision Res., 11, 685 - 695.

111. Harter, M.R. and White, C.T. (1968). "Effects of contour sharpness and check size on visually evoked ocrtical potentials." Vision Res., 8, 701 - 711.

112. Harter, M.R. and White, C.T. (1970). "Evoked cortical responses to checkerboard patterns: effect of check size as a function of visual acuity." Electroenceph. clin. Neurophysiol., 28, 48 - 53.

113. Hennerici, M., Wenzel, D. and Freund, H-J. (1977). "The comparison of small size rectangle and checkerboard stimulation for the evaluation of delayed visual evoked responses in patients suspected of multiple sclerosis." Brain, 100, 119 - 136.

114. Hillman, J.S., Myska, V. and Nissim, S. (1975). "Complete avulsion of the optic nerve. A clinical, angiographic and electrodiagnostic study." Brit. J. Ophthal., 59, 503 - 509.

115. Hoeppner, T. and Lolas, F. (1978). "Visual evoked responses and visual symptoms in multiple sclerosis." J. Neurol. Neurosurg. Psychiat., 41, 493 - 498.

116. Holder, G.E. (1977). "The pattern VER in chiasmal compression." Electroenceph. clin. Neurophysiol., 43, 772 - 773.

117. Holder, G.E. (1978 a). "The effects of chiasmal compression on the pattern visual evoked potential." Electroenceph. clin. Neurophysiol., 45, 278 - 280.

118. Holder, G.E. (1978 b). "Abnormalities of the pattern visual evoked potential in patients with homonymous visual field defects."

Presented at International Evoked Potentials Symposium, Nottingham, September, 1978.

119. Hoyt, W.F. and Luis, O. (1963). "The primate chiasm, details of visual fibre organisation studied by silver impregnation techniques." Arch. Ophthal., 70, 69 - 85.

120. Hume, A.L. and Cant, B.R. (1976). "Pattern visual evoked potentials in the diagnosis of multiple sclerosis and other disorders." Proc. Aust. Assoc. Neurol., 13, 7 - 13.

121. Ikeda, H., Tremain, K.E. and Sanders, M.D. (1978). "Neurophysiological investigation in optic nerve disease: combined assessment of the visual evoked response and electroretinogram." Brit. J. Ophthal., 62, 227 - 239.

122. Jacobsen, J.H., Hirose, T. and Suziki, T.A. (1968). "Simultaneous ERG and VER in lesions of the optic pathway." Invest. Ophthal., 7, 279 - 292.

123. Jasper, H.H. (1958). "Report of the committee on methods of clinical examination in routine electroencephalography." Electroenceph. clin. Neurophysiol., 10, 370 - 375.

124. Jayle, G.E., Tassy, A.F., Deransart-Ferrero, J. and Cornand, A. (1971). "Un cas de cécité corticale avec conservation du potentiel évoqué visuel occipital." Rev. Oto-neuro-ophthal., 43, 229 - 232.

125. Jeffreys, D.A. (1971). "Cortical source locations of pattern-related visual evoked potentials recorded from the human scalp." Nature, 229, 502 - 504.

126. Johnson, F., Hayward, M. and Walsh, S. (1976). "Chequerboard pattern reversal using a modified television display to measure visual evoked responses." Biomed. Eng., 11, 56 - 57.

127. Jonkman, E.J. (1967). "The average cortical response to photic stimulation." Thesis, Amsterdam.

128. Kawamura, H., Kubota, S., Asakura, T. and Kitamura, K. (1975). "A clinico-physiological study of visually evoked potential (VEP) and somatosensory evoked potential (SEP) in so-called vegetative state and coma." Neurol. med. chir., 15, 75 - 86.

129. Koles, Z.J. and Rasminsky, M. (1972). "A computer simulation of conduction in demyelinated fibres." J. Physiol. (Lond.), 227, 351 - 364.

130. Kooi, K.A. and Bagchi, B.K. (1964). "Visual evoked responses in man: normative data." Ann. N. Y. Acad. Sci., 112, 254 - 269.

131. Kooi, K.A., Güvener, A.M. and Bagchi, B.K. (1965). "Visual evoked responses in lesions of the higher optic pathways." Neurology (Minneap.), 15, 841 - 854.

132. Kooi, K.A., Yamada, T. and Marshall, R.E. (1973). "Field studies of monocularly evoked cerebral potentials in bitemporal hemianopsia." Neurology (Minneap.), 23, 1217 - 1225.

133. Kooi, K.A., Yamada, T. and Marshall, R.E. (1975). "Binocular and monocular visual evoked responses in the differential diagnosis of psychogenic and disease related disorders." Int. J. Neurol., 9, 272 - 286.

134. Kristol, C., Akert, K., Sandri, C., Wyss, U.R., Bennett, M.V.L. and Moor, H. (1977). "The Ranvier nodes in the neurogenic electric organ of the knifefish Sternarchus: a freeze-etching study on the distribution of membrane associated particles." Brain Res., 125, 197 - 212.

135. Lazurus, G.M. (1975). "A clinical application of the visual evoked potential in the diagnosis of ophthalmic and neuro-ophthalmic pathology - organic and functional lesions." J. Am. optom. Ass., 45, 1056 - 1063.

136. Levi, D.M. (1975). "Patterned and unpatterned visual evoked responses in strabismic and anisometropic amblyopia." Amer. J. optom.

Physiol. Opt., 52, 455 - 464.

137. van Lith, G.H.M., van Marle, G.W. and van Dok-Mak, G.T.M. (1978). "Variation in latency times of visually evoked cortical potentials." Brit. J. Ophthal., 62, 220 - 222.

138. Lombroso, C.T., Duffy, H.F. and Robb, R.M. (1969). "Selective suppression of cerebral evoked potentials to patterned light in amblyopia ex anopsia." Electroenceph. clin. Neurophysiol., 27, 238 - 247.

139. Long, D.M., Hartmann, J.F. and French, L.A. (1966 a). "The response of human cerebral oedema to glucosteroid administration." Neurology (Minneap.), 16, 521 - 528.

140. Long, D.M., Hartmann, J.F. and French, L.A. (1966 b). "The response of experimental cerebral oedema to glucosteroid administration." J. Neurosurg., 24, 843 - 854.

141. Lowitzsch, K., Kuhnt, U., Sakmann, Ch., Maurer, K., Hopf, H.C., Schott, D. and Thater, K. (1976). "Visual pattern evoked responses and blink reflexes in assessment of MS diagnosis." J. Neurol. (Brux.)., 213, 17 - 32.

142. McAlpine, D., Lumsden, C.E. and Acheson, E.D. (1972). "Multiple sclerosis: a reappraisal." Churchill Livingstone, Edinburgh, p 202.

143. McDonald, W.I. (1963). "The effects of experimental demyelination on conduction in peripheral nerve. A histological and electrophysiological study. II. Electrophysiological observations." Brain, 86, 501 - 524.

144. McDonald, W.I. (1974). "Remyelination in relation to clinical lesions of the central nervous system." Brit. med. Bull., 30, 186 - 189.

145. McDonald, W.I. (1977). "Pathophysiology of conduction in central nerve fibres." in Desmedt, J.E. (Ed.) "Visual Evoked

Potentials in Man: New Developments", Oxford University Press, (pp 427 - 437).

146. McDonald, W.I. and Halliday, A.M. (1977). "Diagnosis and classification of multiple sclerosis." Brit. med. Bull., 33, 4 - 9.

147. McDonald, W.I. and Sears, T.A. (1970). "The effects of experimental demyelination on conduction in the central nervous system." Brain, 93, 583 - 598.

148. McInnes, A. (1977). "The visual evoked responses to a red and white checkerboard pattern in patients with suspected multiple sclerosis." Electroenceph. clin. Neurophysiol., 43, 286.

149. Marg, E., Freeman, D.N., Peltzman, P. and Goldstein, P.J. (1976). "Visual acuity development in human infants: evoked potential measurements." Invest. Ophthal., 15, 150 - 153.

150. Mastaglia, F.L., Black, J.L. and Collins, D.W.K. (1976). "Visual and spinal evoked potentials in the diagnosis of multiple sclerosis." Brit. med. J., 2, 732.

151. Mastaglia, F.L., Black, J.L., Collins, D.W., Gutteridge, D.H. and Yuen, R.W. (1978). "Slowing of conduction in visual pathway in hypothyroidism." Lancet, i, 387 - 388.

152. Matthews, W.B., Small, D.G., Small, M. and Pountney, E. (1977). "Pattern reversal evoked visual potential in the diagnosis of multiple sclerosis." J. Neurol. Neurosurg. Psychiat., 40, 1009 - 1014.

153. Mayer, R.F. (1971). "Conduction velocity in the central nervous system of the cat during experimental demyelination and remyelination." Int. J. Neurosci., 1, 287 - 308.

154. Meyer, J.S., Foley, J.M. and Campagna-Pinto, G. (1953). "Granulomatous angiitis of the meninges in sarcoidosis." Arch. Neurol. Psychiat. (Chic.), 69, 587 - 600.

155. Michael, W.F. and Halliday, A.M. (1971). "Differences between the occipital distribution of upper and lower field pattern evoked responses in man." Brain Res., 32, 311 - 324.

156. Mierdel, P. and Marre, E. (1978). "Objective detection of reversible deficiencies in glaucoma by means of VECP." Ophthalmologica (Basel), 177, 276 - 279.

157. Millodot, M. and Riggs, L.A. (1970). "Refraction determined electrophysiologically. Responses to alternation of visual contours." Arch. Ophthal., 84, 272 - 278.

158. Milner, B.A., Regan, D. and Heron, J.R. (1974). "Differential diagnosis of multiple sclerosis by visual evoked potential recording." Brain, 97, 755 - 772.

159. Muller, W. (1962). "Untersuchungen über das Verhalten der Corticalzeit bei bitemporaler Hemianopsie." Albrecht v. Graefes Arch. Ophthal., 165, 214 - 218.

160. Namerow, N.S. and Enns, N. (1972). "Visual evoked responses in patients with multiple sclerosis." J. Neurol. Neurosurg. Psychiat., 35, 829 - 833.

161. Nawratzki, I., Auerbach, E. and Rowe, H. (1966). "The electrical response in retina and occipital cortex following photic stimulation of normal and amblyopic eyes." Amer. J. Ophthal., 61, 430 - 435.

162. Nilsson, B.Y. (1978). "Visual evoked responses in multiple sclerosis: comparison of two methods for pattern reversal." J. Neurol. Neurosurg. Psychiat., 41, 499 - 504.

163. Obenauf, C.D., Shaw, H.E., Sydnor, C.F. and Klintworth, G.K. (1978). "Sarcoidosis and its ophthalmic manifestations." Amer. J. Ophthal., 86, 648 - 655.

164. Ogashiwa, M. and Saito, Y (1973). "Neurophysiological observations in two cases showing prolonged coma." Yonago Acta med., 17,

246 - 252.

165. Oosterhuis, H.J.G.H., Ponsen, L., Jonkman, E.J. and Magnus, O. (1969). "The average visual evoked response in patients with cerebrovascular disease." Electroenceph. clin. Neurophysiol., 27, 23 - 34.

166. Pampiglione, G. (1966). "Some anatomical considerations upon electrode placement in routine EEG." Proc. electrophysiol. Technol. Ass., 13, 166 - 176.

167. Panayiotopoulos, C.P., Jeavons, P.M. and Harding, G.F.A. (1970). "Relations of occipital spikes evoked by intermittent photic stimulation to visual evoked responses in photosensitive epilepsy." Nature, 228, 566 - 567.

168. Paty, J., Courcelle, L. and Faure, J.M.A. (1976). "Visual evoked response and anti-malarial drugs." Docum ophthal. (Den Haag), Proceedings Series, 10, 389 - 397.

169. Polyak, S. (1957). "The vertebrate visual system." University of Chicago Press, 1957, p 487.

170. Potts, A.M. and Nagaya, T. (1965). "Studies on the visual evoked response. I. The use of the 0.06 degree red target for evaluation of foveal function." Invest. Ophthal., 14, 303 - 309.

171. Potts, A.M. and Nagaya, T. (1969). "Studies on the visual evoked response. III. Strabismus amblyopia and hysterical amblyopia." Docum. Ophthal. (Den Haag), 26, 394 - 402.

172. Rasminsky, M. and Kearney, R.E. (1976). "Continuous conduction in large diameter bare axons in spinal roots of dystrophic mice." Neurology (Minneap.), 26, 367.

173. Rasminsky, M. and Sears, T.A. (1972). "Internodal conduction in undissected demyelinated nerve fibres." J. Physiol. (Lond.), 227, 323 - 350.

174. Regan, D. (1977 a). "Steady-state evoked potentials." J. opt. Soc. Am., 67, 1475 - 1489.

175. Regan, D. (1977 b). "Speedy assessment of visual acuity in amblyopia by the evoked potential method." Ophthalmologica (Basel), 175, 159 - 164.

176. Regan, D. and Heron, J.R. (1969). "Clinical investigation of lesions of the visual pathway: a new objective technique." J. Neurol. Neurosurg. Psychiat., 32, 479 - 483.

177. Regan, D. and Richards, W.A. (1973). "Brightness contrast and evoked potentials." J. opt. Soc. Am., 63, 606 - 611.

178. Regan, D., Milner, B.A. and Heron, J.R. (1976). "Delayed visual perception and delayed visual evoked potentials in the spinal form of multiple sclerosis and in retrobulbar neuritis." Brain, 99, 43 - 66.

179. Richey, E.T., Kooi, K.A. and Tourtelotte, W.W. (1971). "Visually evoked responses in multiple sclerosis." J. Neurol. Neurosurg. Psychiat., 34, 275 - 280.

180. Rietveld, W.J., Tordoir, W.E.M. and Duyff, J.W. (1965). "Contribution of the fovea and parafovea to the visual evoked response." Acta physiol. pharmacol. neerl., 13, 330 - 339.

181. Rietveld, W.J., Tordoir, W.E.M., Hagenouw, J.R., Lubbers, J.A. and Spoor, Th. A.C. (1967). "Visual evoked responses to blank and to checkerboard patterned flashes." Acta. physiol. pharmacol. neerl., 14, 259 - 285.

182. Ritchie, J.M. and Rogart, R.B. (1977). "The density of sodium channels in mammalian myelinated nerve fibres and the nature of the axonal membrane under the myelin sheath." Proc. nat. Acad. Sci. (Wash.), 74, 211 - 215.

183. Roper-Hall, M., Harding, G.F.A. and Thompson, C.R.S. (1971). "The visual evoked response in macular diseases." Presented at

Joint Meeting of the Ophthalmological Section of the Royal Society of Medicine with the Midland Ophthalmological Society, Birmingham, 1971. Cited in Harding, G.F.A. (1974).

184. Rosenbluth, J. (1976). "Intramembranous particle distribution at the node of Ranvier and adjacent axolemma in myelinated axons of the frog's brain." J. Neurocytol., 5, 731 - 745.

185. Rouher, F., Plane, C. and Sole, P. (1969). "Intérêt des potentiels évoqués visuels dans les affections du nerf optique." Arch. Ophthal. (Paris), 29, 555 - 564.

186. Sanders, M.D. (1976). "Diagnostic difficulties in optic nerve disease and in papilloedema and disc oedema." Trans. ophthal. Soc. U.K., 96, 386 - 394.

187. Schmidt, L.H. (1966). "Studies on the antituberculous activity of ethambutol in monkeys." Ann. N.Y. Acad. Sci., 135, 747 - 758.

188. Schneider, J. (1968). "Tumeurs cérébrales et potentiels évoqués." Rev. neurol. (Paris), 118, 443 - 458.

189. Shagass, C., Amadeo, M. and Ruemer, R.A. (1976). "Spatial distribution of potentials evoked by half-field pattern reversal and pattern onset stimuli." Electroenceph. clin. Neurophysiol., 41, 609 - 622.

190. Shahroki, F., Chiappa, K.H. and Young, R.R. (1978). "Pattern shift visual evoked responses." Arch. Neurol. (Chic.), 35, 65 - 71.

191. Sokol, S. (1972). "An electrodiagnostic index of macular degeneration." Arch. Ophthal., 88, 619 - 624.

192. Sokol, S. and Bloom, B. (1973). "Visually evoked cortical responses of amblyopes to a spatially alternating stimulus." Invest. Ophthal., 12, 936 - 939.

193. Sokol, S. and Dobson, V. (1976). "Pattern reversal evoked potentials

in infants." Invest. Ophthal., 15, 58 - 62.

194. Sokol, S. and Shaterian, E.T. (1976). "The pattern evoked cortical potential in amblyopia as an index of visual function." in Moore, S. and Mein, Y. (Eds.) "Orthoptics: past, present, future." Stratton, New York, 1976, pp 59 - 67.

195. Spehlmann, R. (1965). "The averaged electrical responses to diffuse and to patterned light in the human." Electroenceph. clin. Neurophysiol., 19, 560 - 569.

196. Spekreijse, H., Khoe, L.H. and van der Tweel, L.H. (1972). "A case of amblyopia; electrophysiology and psychophysics of luminance and contrast." Adv. Exp. Biol. Med., 24, 141 - 156.

197. Spekreijse, H., van der Tweel, L.H. and Zuidema, Th. (1973). "Contrast evoked responses in man." Vision Res., 13, 1577 - 1601.

198. Statton, R., Blodi, F.C. and Hanigan, J. (1964). "Sarcoidosis of the optic nerve." Arch. Ophthal., 71, 834 - 837.

199. Sugar, H.S. (1964). "An explanation for the acquired macular pathology associated with congenital pits of the optic disc." Amer. J. Ophthal., 57, 833 - 835.

200. Thompson, C.R.S. and Harding, G.F.A. (1978). "The visual evoked potential in patients with cataracts." Docum. ophthal. (Den Haag), Proceedings series, 15, 193 - 201.

201. Thompson, C.R.S., Harding, G.F.A. and Pearce, L. (1977). "The flash evoked potential in patients with cataracts." Electroenceph. clin. Neurophysiol., 43, 773.

202. Tsutsui, J., Nakamura, Y., Takenaka, J. and Fukai, S. (1973). "Abnormality of the visual evoked response in various types of amblyopia." Jap. J. Ophthal., 17, 82 - 93.

203. Uenoyama, K. (1971). "Visual evoked response produced by patterned light stimulus." Invest. Ophthal., 10, 664 - 671.

204. Vanzulli, A., Bogacz, J., Handler, P., Garcia-Austt, E. (1960). "Evoked responses in man. I. Photic responses." Acta. neurol. lat.-amer., 6, 219 - 231.

205. Vaughan, H.G. and Katzman, R. (1964). "Evoked response in visual disorders." Ann. N.Y. Acad. Sci., 112, 305 - 319.

206. Vaughan, H.G., Katzman, R. and Taylor, J. (1963). "Alterations of visual evoked response in the presence of homonymous visual defects." Electroenceph. clin. Neurophysiol., 15, 737 - 746.

207. Walsh, F.B. and Hoyt, W.F. (1969). "Clinical Neuroophthalmology." Williams and Wilkins, Baltimore, 1969, pp 2552 - 2555.

208. Wanger, P. and Nilsson, B.Y. (1978). "Visual evoked responses to pattern reversal stimulation in patients with amblyopia and/or defective binocular functions." Acta. Ophthal., 56, 617 - 627.

209. White, C.T. (1969). "Evoked cortical responses and patterned stimuli." Amer. Psychol., 24, 211 - 214.

210. Wildberger, H.G.H., van Lith, G.H.M. and Mak, G.T.M. (1976). "Comparative study of flash and pattern evoked VECP's in optic neuritis." Ophthal. Res., 8, 179 - 185.

211. Wildberger, H.G.H., van Lith, G.H.M., Wijngaarde, R. and Mak, G.T.M. (1977). "Differential diagnostic aspects between optic neuritis and chiasm tumours." Ophthalmologica (Basel), 174, 106 - 110.

212. Wilson, W.B. (1978). "Visual evoked response differentiation of ischaemic optic neuritis from the optic neuritis of multiple sclerosis." Amer. J. Ophthal., 86, 530 - 535.

213. Wilson, W.B., Kirsch, W.M., Neville, H., Stears, J., Feinsod, M. and Lehman, R.A.W. (1977). "Monitoring of visual function during parasellar surgery." Surg. Neurol., 5, 323 - 329.

214. Zeese, J.A. (1977). "Pattern visual evoked responses in multiple sclerosis." Arch. Neurol. (Chic.), 34, 314 - 316.

Wildberger, H.G.H., van Lith, G.H.M., Wijngaarde, R. and Mak, G.T.M. (1976 b) "Visually evoked potentials in the evaluation of homonymous and bitemporal visual field defects" Brit. J. Ophthal., 61, 454 - 461.