TOPOGRAPHIC STUDIES OF SCALP POTENTIALS EVOKED BY PATTERN PRESENTATION

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Doctor of Philosophy

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SUMMARY

The waveform and scalp distribution of the visual evoked potentials elicited by stimuli in the foveal and parafoveal regions have been investigated in a group of normal humans using a 16-channel "brain mapping" system. The waveform and topography of the responses to pattern onset and pattern reversal stimulation were investigated, using 4 x 4° full field and 4 x 2° lateral and altitudinal half-field stimuli. The responses were composed of several successive peaks which are in some respects consistent with those demonstrated by other workers using larger field sizes. The differences in the behaviour of these components with respect to the position of the stimulus in the visual field were suggestive of origins in different areas of the visual cortex and/or different visual mechanisms. Of particular interest were the major early positive components "P90" and "P95" of the responses to pattern onset and pattern reversal stimulation respectively. More detailed exploration of the behaviour of these major early positive components was carried out using "M-scaled" stimuli selected to activate one square centimetre patches of striate cortex and associated extrastriate re-projections, positioned at different points in the foveal and parafoveal area of the visual field. The inter- and intra-subject variability in amplitude and localisation of the signals elicited by these targets was considered to be a reflection of the individual variations in relationship of visual field projections with the pattern of gyri and fissures on the proximal surface of the occipital lobe. The behaviour of component P90 of the onset response is consistent with a lateral origin in extrastriate visual cortex; that of P95 of the pattern reversal response is consistent in some respects with a striate cortical origin, but in others with a partial origin in extrastriate cortex.

Key words:

foveal - generators - pattern - topography - visual evoked potentials

This thesis is dedicated, with much love, to

MY PARENTS

Marion and Alan Edwards

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CHAPTER 1
Introduction

The scalp recorded visual evoked potential is a valuable tool for the objective assessment of visual function in humans. It provides a means of determining that the pathway from the eye to the brain is intact in situations where visual standard can not be measured by subjective means. It is of great use, therefore, with patients such as infants or the mentally handicapped who can not respond subjectively and also in ocular conditions in which loss of media transparency prevents the formation of a clear image on the retina, as in cataract or vitreous haemorrhage. The VEPs elicited by both pattern and flash stimulation have been used extensively over the last twenty years in the detection and differential diagnosis of various conditions affecting the visual pathway and the visual cortex. The recording of VEPs in cases of suspected optic neuritis, for example, is now standard practice in most hospital eye departments. However, in spite of the extensive clinical use of VEPs and the large number of related studies reported in the literature the exact nature, origins and physiological significance of these signals still remains, to some extent, a mystery. Since the VEP is one of a still limited number of non-invasive methods available for studying the activity of the visual system, the determination of its "meaning" remains an important task.

Over the last twenty years, various groups of workers have attempted to determine the cortical sites of origin of the constituent components of flash and pattern VEPs by investigating the scalp distribution or topography of these signals and the way in which this is affected by the location of the stimulus in the visual field. There is still, however, no universal agreement as to what these origins might be. One of the problems involved in such interpretations lies in the position and arrangement of the visual cortical areas in the occipital lobe. These areas lie partly on the proximal surface of the cortex, which is particularly accessible to recording from scalp electrodes, but also on the mesial and tentorial surfaces of the occipital lobe, where the orientation of the cortical surface (and consequently also the VEP generators) with respect to the scalp changes in a not entirely predictable fashion. Those portions of visual cortex which lie on the proximal surface are thought to contain the representations of the most central portion of the visual field. It would seem logical, therefore, that in a study of the cortical origins of VEP components, the use of stimuli confined to the foveal and parafoveal areas would aid in the interpretation of results. The majority of studies, however, have tended to concentrate on the responses to relatively large targets. It is the purpose of the work in this thesis to study the waveform and the scalp distribution of the responses of the visual system to stimuli confined to the central few degrees of the visual field, in the hope of learning more about the cortical origins and physiological significance of the VEP.

Over the last few years, studies on the scalp distribution of evoked potentials have been assisted by the development of a technique known as "brain mapping". This involves the recording of activity from numerous electrode sites and the imaging of the distribution of signals across the scalp at a particular point in time by various means. One method involves the display of coloured equipotential contour maps, constructed by interpolation of amplitude levels between neighbouring electrode points. In the work reported in this thesis, a commercially available mapping system which uses coloured equipotential contour maps, the Bio-logic "Brain Atlas III" system, has been used for the recording and display of scalp potential distribution.

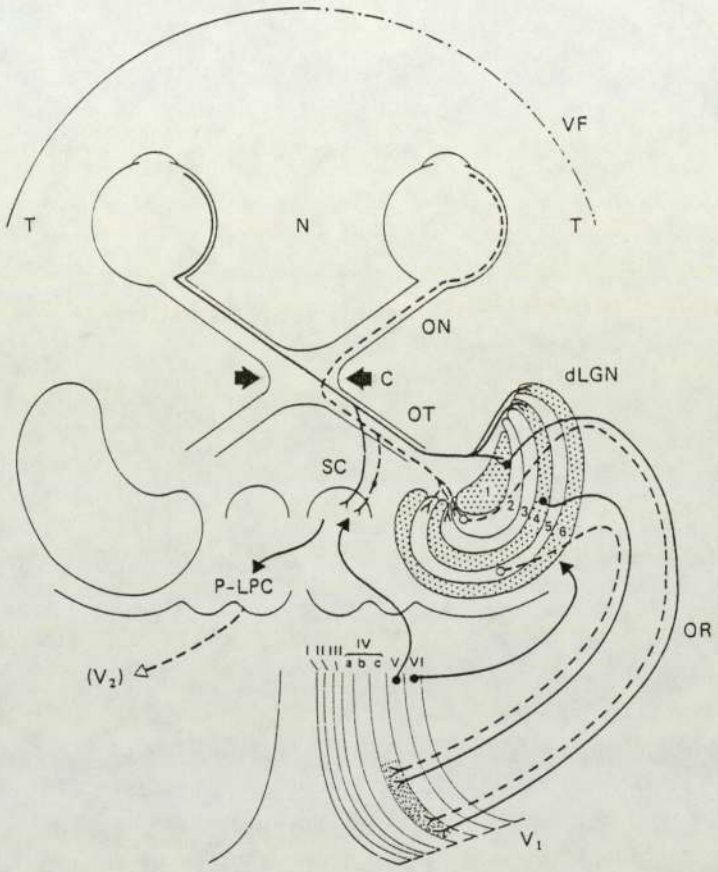


Figure 2.1

A schematic representation of the visual pathways between the retina and the right cerebral hemisphere in man. The dominant geniculate route from the retina is relayed via the thalamus to (predominantly) layer IVc of the striate (primary) cortex. The mid-brain route travels via the tectum to secondary visual cortical areas. Centrifugal connections exist between the striate cortex and the superior colliculus, and the lateral geniculate nucleus. Key: VF (visual field); N,T (nasal and temporal hemiretinae); ON (optic nerve); C (optic chiasma); OT (optic tract); dLGN (dorsal lateral geniculate nucleus); OR (optic radiations); V1, V2 (primary and secondary visual cortical areas); SC (superior colliculus); P-LPC (pulvinar-lateral posterior complex).
(After Pointer 1986)

CHAPTER 2

Anatomy and physiology of the visual system

2.1 Introduction

2.2 General anatomy of the visual pathway

Figure 2.1 shows the basic organisation of the visual pathway. This is a sensory pathway and its various stages correspond to the general pattern, as discussed by Duke-Elder (Duke-Elder and Wybar 1961) who compares it with a somaesthetic sensory tract. In the visual pathway, the first three stages of the neural pathway are represented in the retina. The receptors are the rods and cones. These cells react to light stimulation with photochemical changes, giving rise to electrical impulses transmitted to the bipolar cells, which represent the first order neurones. Impulses are then passed on to the second order neurones, the ganglion cells. These have their cell bodies and peripherial dendrites in the retina, but only the first part of their axons, which form the nerve fibre layer and come together as the optic nerve. The fibres traverse the retina and enter the optic nerve in an orderly fashion, so that fibres from adjacent points on the retina remain fairly close to each other. This "retinotopic" order is maintained for the peripheral fibres throughout the visual pathway. Fibres from the macular area, however, are widely dispersed among the other fibres between the retina and the lateral geniculate nucleus and so do not adhere to this order. In the LGN and in the striate area of the visual cortex there is an orderly arrangement of all fibres.

There are an estimated 1-1.1 x 10^6 fibres in the human optic nerve (Polyak 1957; Kupfer et al. 1967). The large number of fibres serving the macular area, which are necessary for mediation of high central visual acuity, make up around 65% of this number (Orban 1984).

The two optic nerves meet at the optic chiasma, where a partial decussation of nerve fibres takes place, about half the fibres from each optic nerve crossing over to enter the contralateral optic tract. The ratio between crossed and uncrossed fibres in human is about 53:47 (Kupfer et al. 1967). Only fibres from the nasal halves of the retinae i.e. those representing the temporal halves of the visual field, cross over. Fibres from the temporal hemi-retina of each eye, representing the nasal visual field, enter the ipsilateral optic tract. Each optic tract therefore, contains fibres from both eyes representing the contralateral half of the visual field.

An estimated 80% (Harrington 1981) of optic tract fibres terminate in the dorsal lateral geniculate body (LGNd) in the midbrain. There are also projections to various other sites in the central nervous system: These include:-

1. the suprachiasmatic nuclei of the hypothalamus (thought in lower mammals to be involved with neural control of circadian rhythms),
2. the pretectal area of the midbrain (subserving optokinetic nystagmus and the pupillary light reflex),
3. the accessory optic system,
4. the superior colliculi and
5. the pulvinar of the thalamus (all thought to play a role in co-ordination of head and eye movements in visual tracking, pursuit and fixation),
6. the ventral lateral geniculate nucleus or LGNv (the pregeniculate nucleus in primates, which may also be concerned with eye movements) (Rodieck 1979; Pearlman 1981; Shickman 1981).

About 10% of ganglion cells in the macaque project to the superior colliculus (Perry and Cowey 1984) where the visual field is mapped onto the superficial layers in an orderly fashion (Wurtz and Albano 1980).

In histological section the LGNd appears laminated. In the thickest part, in humans and primates, there are usually six separate layers of cell bodies with narrow, sparsely populated areas in between (Figure 2.2) (Chacko 1948). The four dorsal layers are parvocellular layers, in which the cells are relatively small. The two ventral layers are magnocellular layers, where the cells are larger. Anteriorly and posteriorly the parvocellular layers unite to form two layers, resulting in an overall four-layered appearance. This laminar pattern can vary between individuals (Hickey and Guillery 1979). Kaas, Huerta, Weber and Harting (1978) considered that the basic laminar pattern in primates is one of two magnocellular layers, two parvocellular layers and two ventrally located superficial layers, with the parvocellular layers dividing into leaflets to give the impression of four layers. The posterior segment of the LGNd receives fibres representing the central 10-15° of the contralateral visual hemifield. The remainder of the hemifield is represented in the anterior four-layered portion. Uncrossed fibres terminate in layers 2,3 and 5, crossed fibres projecting to layers 1,4 and 6.

Within the layers of the LGNd, the projections are arranged in a retinotopic fashion, each layer containing an orderly map of the contralateral viual hemi-field (Clark 1941). These maps are in precise register, so that an electrode passing through the LGNd perpendicular to the layers will record from cells representing corresponding areas of the two retinae (Figure 2.3).

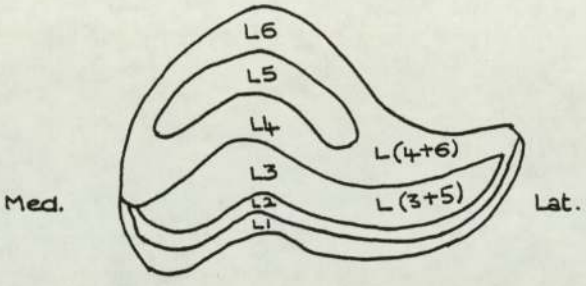


Figure 2.2

The lamination of the lateral geniculate nucleus in the human.

(From Duke-Elder and Wybar 1961)

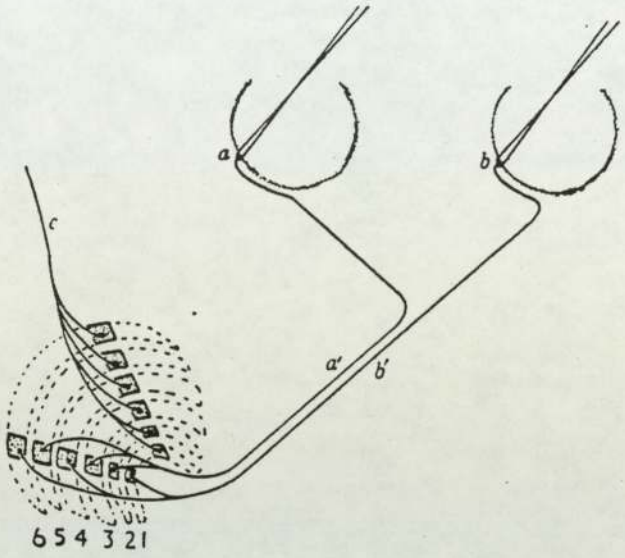


Figure 2.3

The representation of the retina on the lateral geniculate nucleus of the primate.

Impulses from corresponding points, (a, b) in the two retinae pass up the optic tract. Uncrossed impulses (a') terminate in layers 2, 3 and 5; crossed impulses (b') terminate in layers 1, 4 and 6. The projection from the LGN (c) to the visual cortex involves a band of cells from all the layers.

(From Duke-Elder and Wybar 1961)

The optic radiation fibres in primates and humans originate solely in the LGNd and form the only direct afferent visual pathway from subcortical regions to the cerebral cortex (Polyak 1957). These are the third order neurones of the visual pathway, projecting to and terminating in the striate area of the visual cortex. The striate cortex (Brodmann's area 17, the primary visual area, or V1) is situated around the pole of the occipital lobe in each cerebral hemisphere. Some of it is visible on the posterolateral surface of the hemisphere but most of it is located on the medial aspect (Figures 2.4, 2.7) around and buried in the calcarine fissure. Fibres representing central retinal areas terminate posteriorly in the striate area, with the many macular fibres occupying a relatively large area of cortex near the occipital pole. Fibres from more peripheral areas terminate successively more anteriorly. The superior retina is represented on the upper lip of the calcarine fissure, the inferior retina on the lower lip.

As a result of the partial decussation of fibres at the chiasma, the striate cortex in each hemisphere receives projections from the temporal half of the retina of the ipsilateral eye, and the nasal half of the contralateral retina. Thus each hemisphere contains the complete representation of the contralateral half of the visual field. The segregation of fibres from the two halves of the retina, however, is not a perfect one and there is evidence for a median strip of overlap, corresponding to the vertical meridian of the visual field, in which there is intermingling of ganglion cells which project to ipsilateral and contralateral optic tracts (Stone et al. 1973). This zone corresponds to about 1^{o} of visual angle except at the fovea where, due to the displacement of ganglion cells around the foveal pit it extends to about 3^{o} (Bunt et al. 1977).

The nerve cells and fibres of the striate area are arranged in several layers parallel to the cortical surface (see Figure 2.5). Optic radiation fibres terminate for the most part in layer 4. In macaque, fibres from parvocellular geniculate layers terminate in 4Cß and to a lesser extent in 4A; those from magnocellular geniculate layers terminate in 4Cα (Hubel and Wiesel 1972; Blasdel and Lund 1983).

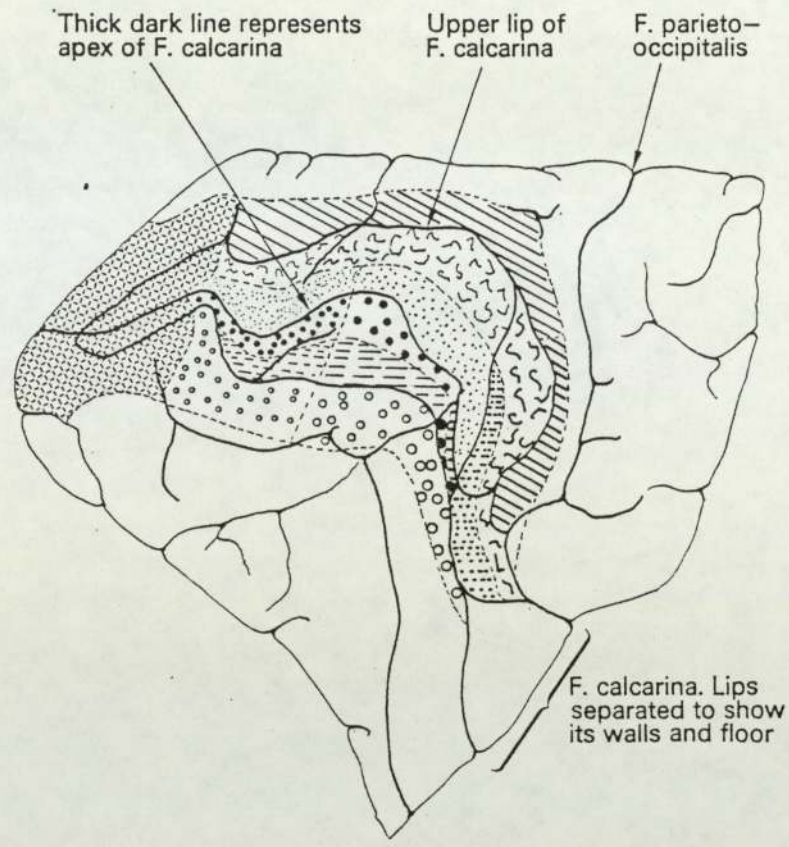
Cortical neurones have been grouped into two main types, pyramidal cells and stellate cells. The axons of pyramidal cells tend to project to targets elsewhere in the cortex or to subcortical areas, whereas those of the stellate cells form local intracortical connections (Pearlman 1981). Most cells in layer 4 are of the stellate variety.

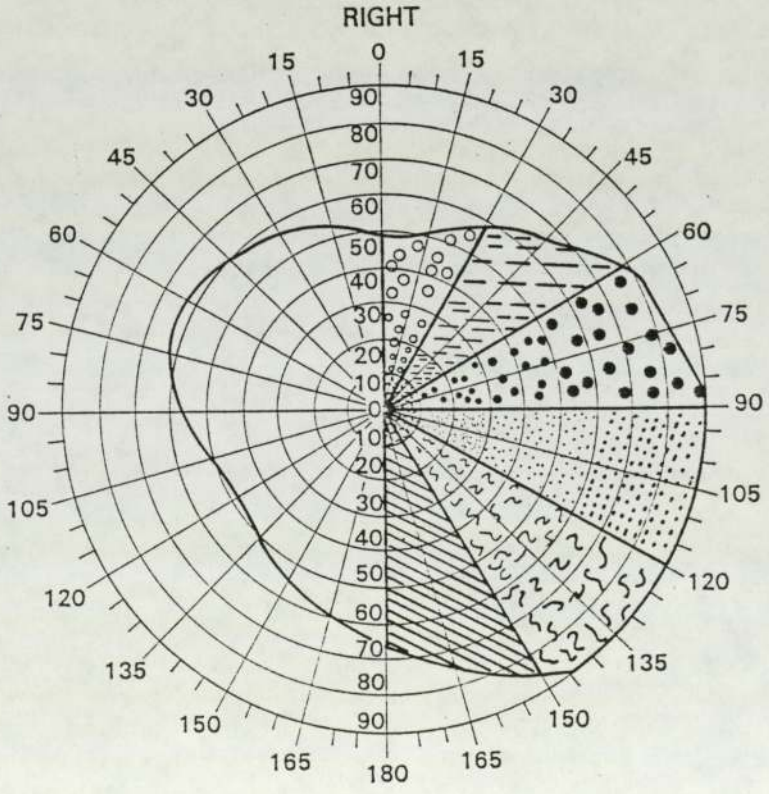
The striate area makes efferent connections with several subcortical areas, including the LGNd, the pulvinar of the thalamus and the superior colliculus. The superior colliculus makes no direct reciprocal connections although it does project to cells in the pulvinar, and the pulvinar in turn projects to the striate area.

Figure 2.4

The representation of the right visual hemi-field on the striate area of the left cerebral hemisphere in humans.

(From Brindley 1970)


Thick dark line represents apex of F. calcarina
Upper lip of F. calcarina
F. parieto–occipitalis
F. calcarina. Lips separated to show its walls and floor


RIGHT
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50
60
70
80
90

Figure 2.5

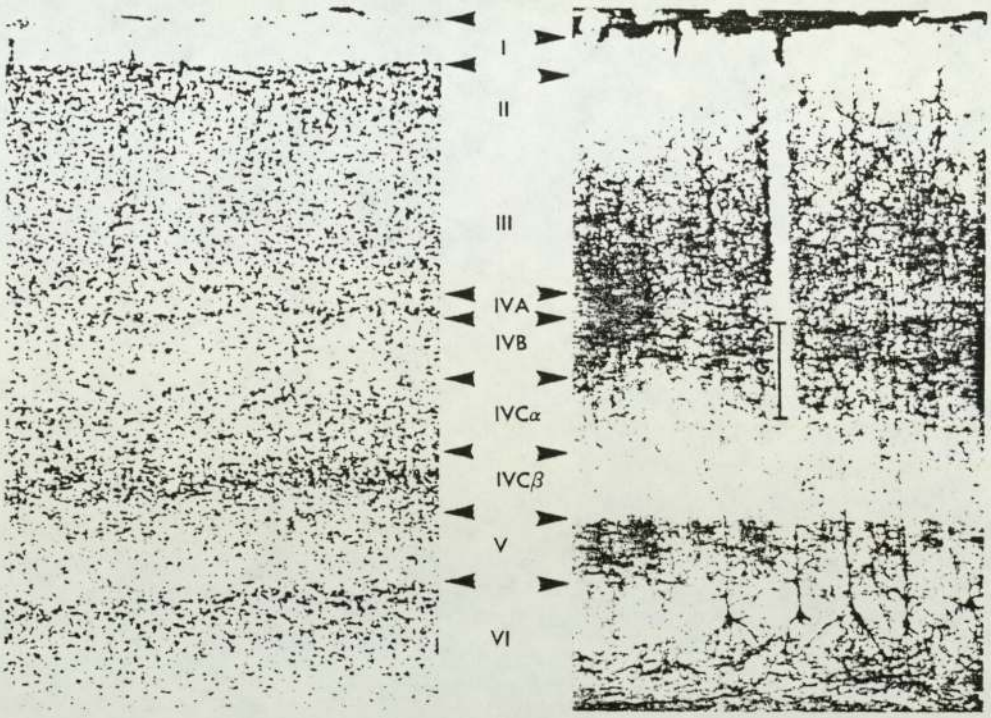
a. Two differently stained sections of area 17 of the visual cortex of the macaque. Left: stained to show cell nuclei; right: stained to show cell bodies and processes.

(From Pearlman 1981)

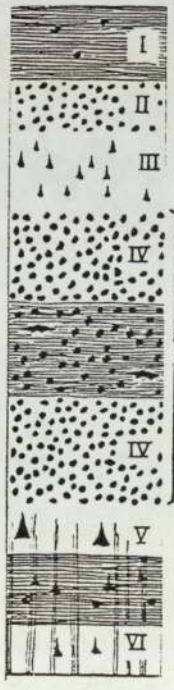
b. Schematic representation of striate cortical layers in the human.

(From Duke-Elder and Wybar 1961)

a.



b.



Cortical surface

Plexiform lamina

External granular lamina

Pyramidal lamina

Internal granular lamina

Ganglionic lamina

Multiform lamina

Cortical inter-connections of the striate area are extensive, especially with surrounding areas of the visual cortex. The visual cortex in right and left hemispheres is connected via the corpus callosum.

There is extensive variability in the shape, position and overall size of the striate cortex in man, and also in the exposed area, ie that visible on the surface of the hemispheres (Brindley 1972; Stensaas et al. 1974). Stensaas and co-workers (1974) found a threefold variation in total area and a fourfold variation in exposed area between different human brains. An average of 67% of striate cortex was found to be buried in the calcarine fissure and its branches. The exposed area in the two hemispheres of an individual were anything from mirror images to totally dissimilar. In addition, some brains were found to have a total absence of exposed cortex on the posterolateral aspect of the hemispheres. Van Essen, Newsome and Maunsell (1984) found a twofold variation in the area of striate cortex in their six macaque monkeys.

2.3 Physiological aspects of the visual system

2.3a Cell types and organization in the striate cortex: the heirarchical model

Retinal ganglion cells in the cat are found to have receptive fields with symmetrical, concentric, centre-surround type spatial organization (Kuffler 1953). These receptive fields can be classified as "on" centre, with an excitatory centre and an inhibitory surrounding region, or "off" centre, having an inhibitory centre and an excitatory surround. The receptive fields of geniculate cells in cat and in monkey have the same organization (Hubel and Wiesel 1961; Dreher et al. 1976). Both cell types respond best to a spot of light just covering their receptive field centre or an annulus positioned over its periphery. Diffuse light produces little response since the activities of centre and surround tend to cancel each other. Due to the receptive field symmetry, a bar of light produces the same response at any orientation.

The majority of cells in the striate cortex have more complicated spatial organization in their receptive fields. Hubel and Wiesel have developed a scheme for classifying visual cortical cells. Some of their findings from extensive research into cell types and organisation in the visual cortex of cats and monkeys (using combined neurophysiological and antomical techniques) are summarised in three review articles (Hubel and Wiesel 1977, 1979; Hubel 1982).

"Concentric" cells are found in layer 4 of the striate cortex in monkey but not in cat. Their receptive field properties are similar to those of ganglion cells and geniculate cells

but they are less responsive to diffuse illumination. Other cell types in the striate cortex respond best to line or bar stimuli of specific orientation. "Simple" cells have receptive fields with antagonistic areas arranged in parallel bands of on and off regions. Their optimal stimulus is a line or bar with its boundaries coinciding with those of the receptive field subdivisions. They are found mostly in layer 4. "Complex" cells are much more numerous then simple cells. They do not have distinct antagonistic regions in their receptive fields and so the position of an optimally orientated bar need not be carefully specified. They respond best if the stimulus is swept across the receptive field, about half of them responding much better to one direction of movement than the other. "Hypercomplex" cells were originally described as complex-like cells with the added feature of length specificity. When a line stimulus is elongated past a certain extent, cell response drops off, a property described as "end-stopping". Simple cells with this property have since been described and are classed as type I hypercomplex cells to distinguish them from type II cells, which are the complex-like cells first described (Dreher 1972). Complex and hypercomplex cells are found mostly outside layer 4.

Kelly and Van Essen (1974) stated that in area 17 of the cat most simple cells are found in layer 4, most complex cells in layers 2,3, 5 and 6 and most hypercomplex cells in layers 2 and 3. They also found that the majority of simple cells were stellate cells, whereas most complex and hypercomplex cells were pyramidal cells.

Some simple cells and many complex and hypercomplex cells are binocular, in that they can be stimulated through either eye, and have receptive fields in the two eyes with similar positions and characteristics. However, the response is often greater for stimulation of one eye than for the other. This effect is known as "relative ocular dominance" and ranges, between cells, from almost monocular preference to equal preference for both eyes. Geniculate cells, and concentric striate cells in monkeys, are monocular.

In areas 18 and 19 of cat and monkey the relative proportions of cell types change, with simple cells becoming less common and complex and hypercomplex cells being found in greater numbers. Also in extrastriate cortex a greater percentage of cells are binocularly driven.

The striate cortex as a whole can be divided into sections, or "columns" based on orientation preference and eye preference. An electrode penetrating through the layers of the striate complex perpendicular to its surface encounters cells with idential orientation preference and overlapping receptive fields. This vertical grouping is termed an "orientation column", and the area occupied by the overlapping receptive fields is termed

the "aggregate" receptive field of the column. An electrode penetration parallel to the surface shows a fairly orderly progression of orientation preference across the cortex from one column to the next. In addition, all cells recorded from a vertical penetration have the same eye preference. Penetration parallel to the surface shows that this changes regularly and abruptly from one eye to the other across the striate area, forming an arrangement of "ocular dominance columns". More recently, evidence has been found for the presence of colour (Michael 1981) and spatial frequency (Tootell et al. 1981) columns. Columns are of similar dimensions across the striate cortex but aggregate fields increase in size moving away from the foveal representation near the occipital pole. This is consistent with the greater area of striate cortex devoted to central vision (see Section 2.4).

It appeared to Hubel and Wiesel that the cortex might be divided into sectors, about 1x1mm in extent, each of which contains the necessary "equipment" for the analysis of a specific portion of the visual field, containing a full (180°) set of orientation columns and a pair of ocular dominance columns. They termed these units "hypercolumns". Further evidence for the organisation of striate cortex into such "modules" has been found from studies revealing a regular pattern of cytochrome oxidase "blobs", "spots" or "puffs" across the striate area (Horton and Hubel 1981; Humphrey and Hendrickson 1983). These spots reveal regions of high metabolic activity which are aligned along the centres of ocular dominance columns. The response properties of the cells in these regions suggest that they could correspond to colour columns (Hendrickson 1985).

Hubel and Wiesel considered that the properties of simple cell receptive fields could be explained on the basis of the input from several concentric (or geniculate) cells with overlapping receptive fields. Complex and hypercomplex cells could then, in their turn, receive inputs from several simple cells or complex cells respectively, each having the same receptive field orientation. This constitutes a heirarchical system in which the series of inter-connected cell types becomes more complicated at each stage, moving away from the geniculate input in layer 4. Binocular cells receive inputs from monocular cells from the two eyes, having identical characteristics and corresponding receptive field position. This idea is supported by the manner in which the striate area appears to be organized, in vertical columns with identical orientation preference, with receptive fields becoming more complex moving away from the central layer. The increasing numbers of hypercomplex and binocular cells in areas 18 and 19 suggests that further processing in these areas is at higher levels than in area 17. Although this system is feasible there has been no conclusive proof of its existence. In addition, there is much evidence for the presence of parallel, as opposed to serial, channels, in the visual system.

Table 2.1

X-, Y- and W- cell pathways in the cat visual system.

References:-

1 Enroth-Cugell and Robson 1966
3 Celand et al. 1971
4 Cleland and Levick 1974a
5 Cleland and Levick 1974b
6 Stone and Fukuda 1974
7 Peichl and Wassle 1979
8 Cleland et al. 1975
9 Hoffmann 1973
10 Derrington and Fuchs 1979
11 Stone and Hoffmann 1971
12 Stone and Dreher 1973

	X	Y	W
RETINAL GANGLION CELLS			
Receptive field organisation (ref. 1-6)	antagonistic centre/surround	antagonistic centre/surround	some as X and Y, others have unusual arrangements
Receptive field spatial summation properties (ref. 1)	linear	non-linear	
Response to standing contrast (ref. 3-6)	sustained	transient	sustained or transient "sluggish"
Morphological correlates (ref. 7)	ß	∝	γ , ε
Percentage of cell population	55%	3-4%	42%
Diameter of receptive field centre for cells in central area of retina (ref. 7)	20'	50'	
Axon conduction velocity (ref. 3-6,9)	medium	fast	slow
MIDBRAIN PROJECTIONS			
Connections in midbrain (ref. 3, 9,10)	X cells in LGNd	Y cells in LGNd	mainly (80% of fibres) with superior colliculus
Axon conduction velocities (ref. 11)	slow	fast	
Cortical projections (ref. 12)	area 17	areas 17 and 18	

2.3b Parallel channels in the visual system

Studies on receptive field properties and axon conduction velocity of cat retinal ganglion cells have shown that they can be divided into three main types, known as "X", "Y" and "W" cells. Some of the main characteristics of and distinctions between these types of cells are summarised in Table 2.1. For a more extensive review see Rodieck (1979), Stone, Dreher and Leventhal (1979), Lennie (1980) and Stone (1983).

X and Y cells were first distinguished in the retina of the cat by Enroth-Cugell and Robson (1966). These authors noted that for some cells with concentrically organised receptive fields a position could be found where the introduction of a grating stimulus elicited no response i.e. a null position. These were termed "X" cells. For the other cells ("Y" cells) no null position could be found. The authors concluded that X cells must have a linear response to the sum of excitatory and inhibitory signals from different parts of their receptive fields whereas the spatial summation shown by Y cells was non-linear. These authors also noted that the mean discharge frequency of Y cells but not X cells was greatly increased for a moving grating as compared with a stationary one. Cleland, Dubin and Levick (1971) proposed that these two groups of ganglion cells could be better described by their response to standing contrast. Both types of cell showed a sharp increase in discharge rate on initial exposure to a stimulus but whereas that for X cells was maintained, that for Y cells rapidly returned to the resting level. These two groups are alternatively known, therefore, as "sustained" and "transient" cells respectively.

Cleland and Levick (1974b) described a third class of ganglion cells in the cat. These they termed "sluggish" due to their low responsiveness compared with that of the "brisk" X and Y cells. Sluggish cells were found to have either sustained or transient response properties. Stone and his colleagues (e.g. Stone and Fukuda 1974) have termed these "W" cells. Further studies have revealed a range of cells with unusual receptive field properties (see Lennie 1980) which are normally included in the W cell category. Morphological correlates of X, Y and W cells have been described in the retina of the cat and have been termed beta, alpha and gamma cells respectively (Boycott and Wassle 1974; Peichl and Wassle 1979) X and Y ganglion cells project to the LGNd in the midbrain, where they synapse with cells which have corresponding properties (Cleland et al. 1971; Fukuda and Stone 1974). Many Y cells and the majority of W cells project to the superior colliculus (Cleland and Levick 1974a; Fukuda and Stone 1974; Hoffmann 1973).

Evidence of X- and Y-like cell systems in the monkey has been found (e.g. de Monasterio and Gouras 1975; de Monasterio 1978a; Dreher et al. 1976; Schiller and Malpeli 1977; Leventhal et al. 1981). Perry, Oehler and Cowey (1974) distinguished beta (Pß) and alpha (Pα) cells in the macaque retina which project to the LGNd. Rodieck, Binmoeller and Dineen (1985) studied the morphology of retinal ganglion cells in the human. These authors distinguished two types of cell which corresponded to the parasol and midget types described by Polyak (1957) and suggested that these cells were equivalent to Pα and Pß cells respectively. A separate W system in primate has not been as well substantiated as in the cat. Schiller and Malpeli (1977) and de Monasterio (1978b) have found ganglion cells with W-like receptive field properties in the monkey retina and Perry and Cowey (1984) have described morphological correlates (gamma and epsilon cells) which project to the superior colliculus.

Most ganglion cells and geniculate cells in the monkey are colour sensitive. Cells with "colour-opponent" receptive fields give an "on" response to one colour in their receptive field centre and an "off" response to another colour in the periphery, or vice-versa. Cells with "broad band" receptive fields do not have this centre-surround spectral opponence and respond, with excitation or inhibition, to a wider range of wavelengths (de Monasterio and Gouras 1975; Dreher et al. 1976; Schiller and Malpeli 1977). Dreher, Fukuda and Rodieck (1976) and Schiller and Malpeli (1978) found that cells in the parvocellular layers of the LGNd were mostly colour opponent whereas those in magnocellular layers had broad band receptive fields. Wiesel and Hubel (1966) divided geniculate cells in the macaque into four types. Type I cells had concentric centre-surround receptive fields with a colour opponent organisation. Type II cells had colour but not spatially opponent and type III cells spatially but not colour opponent receptive fields. The rare type IV cells had "on" centre colour opponent receptive fields. The majority of cells in the parvocellular layers were of type I, but types II and III were also found. Cells in the magnocellular layers were mostly type III with a few type IV.

Dreher, Fukuda and Rodieck (1976) and Schiller and Malpeli (1978) found that, when classified according to axon dimensions and conduction velocity, all types of cell in the parvocellular layers were X-like whereas those in the magnocellular layers were Y-like. Kaplan and Shapley (1982) classified LGNd cells as X or Y according to receptive field spatial summation and spatial resolution. On the basis of these criteria 75% of magnocellular neurones were X-like and the remainder were Y-like. Magnocellular X cells were however, distinguished from parvocellular X cells by their high contrast sensitivity and their lack of colour opponence. Perry, Oehler and Cowey (1984) found, however, that magnocellular layers received projections almost exclusively from Pα cells

and parvocellular layers from Pß cells.

The receptive field centre size of ganglion cells in the cat and monkey increases with retinal eccentricity (e.g. Cleland et al. 1971; Stone and Fukuda 1974; De Monasterio and Gouras 1975). Hubel and Wiesel (1974) and Dow, Snyder, Vautin and Bauer (1981) have shown that the dimensions of cortical cell receptive fields in the macaque also increase with visual field eccentricity.

Geniculate cells in the cat project to areas 17, 18 and 19 of the visual cortex and also to the lateral suprasylvian area (Wilson and Cragg 1967). Stone and Dreher (1973) found that X cells project to area 17 and Y cells to areas 17 and 18. Stone, Dreher and Leventhal (1979) concluded, from their review of the literature, that X cells appear to project mainly to area 17, Y cells to area 18 and W cells to area 19.

Cells in the monkey LNGd project solely to area 17 of the cortex (Wilson and Cragg 1967). Parvocellular layers project mainly to layers 4Cß and 4A; magnocellular layers project mainly to layer 4Cα (Hubel and Wiesel 1972; Blasdel and Lund 1983). Accepting that cells in parvocellular layers are X-like and those in magnocellular layers are Y-like, it appears that X and Y systems in the monkey have distinct, maybe separate, cortical connections. The finding that both simple and complex cells can have X-like or Y-like properties (see Lennie 1980; Ikeda and Wright 1975) suggests however, that there is no straightforward distinction between parallel channels at cortical level in either cat or monkey. Stone, Dreher and Leventhal (1979) considered the possibility that there may be X-, Y- and W-like channels in the cortex which each involve simple, complex and hypercomplex cells. Further evidence has been found for the existence of parallel and heirarchical mechanisms in extrastriate cortex, as discussed in section 2.5.

Psychophysical investigations have provided evidence of parallel channels in the human visual system which perhaps correspond to the X and Y channels in the cat and monkey. Tolhurst (1973) and Kulikowski and Tolhurst (1973) have postulated two such independent systems, one responsible for discrimination of spatial structure in the visual environment, more sensitive at high spatial frequences, and the other mediating flicker and movement detection, more sensitive at lower spatial frequences. They compared these two systems with X and Y ganglion cells in the cat. In addition, Tolhurst (1975) found that at low spatial frequencies, response to short exposures of sinusoidal gratings tended to be transient, whereas at high spatial frequences responses tended to be sustained. Movshon, Thompson and Tolhurst (1978), working on the cat visual cortex, found that neurones in area 17 were more sensitive to higher spatial frequencies than those in area 18, and were less sensitive at higher temporal frequences than at low ones.

They suggested that this was consistent with the idea of "pattern" and "movement" channels, based in areas 17 and 18 respectively.

Many studies on parallel visual channels in humans have been based on the hypothesis that the visual system contains a number of channels, each responding to a selective range of spatial frequencies, and that it performs a kind of Fourier analysis on the visual environment. Campbell and Robson (1968) found that contrast sensitivity and visbility for gratings of different luminance profiles were dependent upon the Fourier components of the grating waveforms. Blakemore and Campbell (1969) found that after adapting one eye to a sinusoidal grating of a particular spatial frequency there was a temporary rise in contrast threshold to gratings of the same orientation over a range of spatial frequencies centred on that of the adapting grating. The effect was transmitted to the non-adapted eye. They concluded that these findings supported the existence of neurones sensitive to spatial frequency and suggested that the orientation specificity and interocular transfer of the effect pointed to a cortical location for these neurones. These results have been confirmed using electrophysiological techniques (Campbell and Maffei 1970).

Maffei and Fiorentini (1973) found that simple cells in the striate cortex of the cat behaved like spatial frequency filters. They also showed that the spatial frequency range over which cells were sensitive became progressively narrower for cells higher along the visual pathway from retina to cortex. These authors suggested that this spatial frequency selectivity could be the neural basis of psychophysical findings. De Valois, De Valois and Yund (1979) investigated responses of single cells in the striate cortex of the cat and the macaque to various types of pattern, including sinusoidal gratings, square wave gratings and checkerboards. They found that contrast sensitivity, orientation selectivity and spatial tuning of cortical cells could be much better predicted from the Fourier components of a pattern than from the arrangement of contrasts and edges in it.

From the evidence presented in this section and the previous one it is clear that both parallel and heirarchical mechanisms must operate within the visual system. However, their relative importance in the processing of visual information is uncertain.

2.4 The neural representation of visual space: cortical magnification studies

The manner in which the visual field is represented on the human striate cortex has been long established from studies of the visual field defects resulting from cerebral injuries, these being mainly war wounds (Holmes 1918, 1945; Spalding 1952) (Figure 2.4). Roughly, central areas of each hemifield are represented at the occipital poles, with more peripheral points projected progressively more anteriorly along the medial aspect of each hemisphere. The monocular temporal crescent is represented at the most anterior part of area 17 in the contralateral hemisphere. Vertical visual field quadrants are projected near to the border with area 18, which in fact represents the vertical meridian. Horizontal quadrant representation is found on the buried portion of striate cortex within the calcarine fissure. The upper visual field is represented below the calcarine fissure, the lower field above it. The fovea is disproportionately represented, its projection occupying relatively more cortical area than the periphery.

Further studies on humans have used phosphenes, elicited in the visual field by electrical stimulation of the visual cortex in blind subjects (Brindley and Lewin 1968; Brindley 1973; Dobelle et al. 1979). By relating the position of a phosphene in the visual field to the site of stimulation in the cortex, a picture of the cortical field representation can be built up. The results of both groups cited tended to confirm the classical map for striate cortex. In addition, there was evidence suggesting a second map, superimposed on the first. Dobelle and co-workers (1979) considered that this might be due to a separate representation of the visual field on an extrastriate visual area, possibly area 18. This idea is consistent with neurophysiological findings in monkeys (Zeki 1978a) (see section 2.5).

Early work using neurophysiological and anatomical techniques revealed a similar visual field mapping to that in humans on the striate cortex in the monkey (Talbot and Marshall 1941; Daniel and Whitteridge 1961). Daniel and Whitteridge (1961) devised an index which quantified cortical visual field representation in terms of the number of millimetres of cortex devoted to each degree of visual field. This is the "cortical magnification factor" -usually termed "M"- which is measured in mm/deg. These authors pointed out that the value of M decreases monotonically from the central visual field to the periphery. This finding is consistent with the large foveal representation on the classical map for humans. The maximum value of M was found to be about 6mm/^{o}, at the fovea. Talbot and Marshall (1941) quoted a representation of 0.5mm on the cortex for a target of 1' of arc at the fovea. Daniel and Whitteridge (1961) and also Dow, Snyder, Vautin and Bauer (1981), have interpreted this measure as being equivalent to a maximum value of 30mm/deg for M_0 (foveal M). As remarked by Pointer (1986) however, it is not

appropriate to take a direct reciprocal of the value measured by Talbot and Marshall. A more accurate approximation would be 6mm/° which is in fact the value found later by Daniel and Whitteridge (1961).

It has long been held that there is a relationship between the density of retinal ganglion cells and visual acuity or the reciprocal of VA, minimum angle of resolution or MAR in humans (e.g. Weymouth 1958). Daniel and Whitteridge (1961) postulated on the relationship between VA, retinal ganglion cell density and cortical magnification. They found a reasonable agreement between plots of 1/M in monkey and VA in man against eccentricity. Rolls and Cowey (1970) showed that in monkey the decline in M with eccentricity was approximately proportional to the decrease in retinal ganglion cell density in the area 10-50° from the fovea. At lower eccentricities cell displacement in the retina caused the relationship to break down. The authors extended the function to the fovea using estimates of cone density, on the assumption that the ratio of ganglion cells to cones near the fovea is about one.

Cowey and Rolls (1974) used the phosphene data provided by Brindley and Lewin (1968) to calculate values of cortical magnification factor in man. They did this by dividing the angular distance between phosphenes in the visual field by the linear distance between corresponding electrodes on the cortex. Cowey and Rolls (1974) found that, as in monkey, M decreased with increasing eccentricity being 4mm/° at 2° declining monotonically to 0.5mm/° at 25° eccentricity. The subsequent comparison of data on minimum angle of resolution (MAR) at different eccentricities (Weymouth 1958) revealed that M was inversely proportional to MAR and therefore must be directly proportional to visual acuity. Using this relation, Cowey and Rolls predicted a value of 15.1mm/° for M_o. Dobelle, Turkel, Henderson and Evans (1979) applied a similar method of analysis to their own phosphene data and had similar findings.

The estimation of M values from data on retinal ganglion cell density has been carried out in man. Drasdo (1977) stated that M^2 (rather than M) is proportional to ganglion cell density per solid degree of visual space at eccentricities greater than 10°. He surmounted the problem of cell displacement at the fovea by considering density of ganglion cell receptive fields, which presumably must be proportional to M^2 at all eccentricities. Estimations of D_r were made from the data of several other workers and modified to take into account the projection of retinal area into the visual field, using a specially designed schematic eye (Drasdo and Fowler 1974). On a plot of $1/\sqrt{D_r}$ (which should be proportional to 1/M) against eccentricity the function was extended to the fovea using Polyak's (1957) estimation of foveal cone separation, by a similar logic to that applied

by Rolls and Cowey (1970), to reveal a value of 11.5mm/° for M_0.

Drasdo (1977) compared values of $1/\sqrt{D_r}$ with computations of 1/M from the data of other workers on visual acuity, cortical phosphenes and migraine scotomata and found a high correlation in all cases. He went on to present a set of equations which can be used to estimate M at a peripheral angle along the principle meridians of the visual field. The approximate general relation

$$V = k(1+ s\theta)$$

can be applied, where V = 1/M, k = M_0 and s is a constant which depends on the meridian. The following values of s and limits of eccentricity are appropriate for the different meridians:- temporal s = 0.46, θ <35°; nasal s = 0.50, θ <20°; superior s = 0.62, θ <10°; inferior s = 0.66, θ <20° . For eccentricities within 30°, data from all meridians may be combined to give the further approximated relation

$$V = k(1+ 0.59\theta)$$

Rovamo and Virsu (1979) also used ganglion cell receptive field densities to estimate M in the human. These authors used a method based on that of Drasdo (1977) to determine the relationship of D_r with eccentricity but the application of slightly different data led to the slightly lower estimate of 7.99 mm/° for M_0. In particular, Rovamo and Virsu (1979) disagreed with Drasdo (1977) on the value used for foveal cone separation, which they said was too low. These authors produced their own set of equations for calculation of M along the four principal meridians. Applying the same method, M_0 for rhesus monkey was calculated as 5.66mm/deg. This value was found by these authors to be consistent with that predicted from the ratio of striate cortical area in man and monkey, which is 5.46mm/deg. Rovamo and Virsu (1979) also showed that VA at different eccentricities could be predicted from M.

Hubel and Wiesel (1974) studied the relationship between magnification, receptive fields and columns in the primate striate cortex. They showed that there was a parallel increase in receptive field size and scatter and 1/M out to an eccentricity of 22°. These authors also found that displacement of a recording electrode 2mm along the cortex was sufficient to move from one set of cells with overlapping receptive fields (or one

"aggregate" receptive field) to another. Hubel and Wiesel (1974) commented that such a displacement corresponded to the extent of a pair of ocular dominance columns or a 180° set of orientation columns. A 2 x 2mm block of cortex might therefore contain all the cortical "machinery" necessary for dealing with a particular area of the visual field, being roughly equivalent to an aggregate receptive field. These authors later reduced their estimate for the cortical displacement equivalent to an aggregate receptive field to 1-2mm (Hubel and Wiesel 1977). Van Essen, Newsome and Maunsell (1984) quoted a value of 1mm.

Such a block of cortex as that described by Hubel and Wiesel (1974) has been termed a cortical "module" (e.g. Schein and de Monasterio 1987). These modules would appear to represent a larger portion of the visual field in the periphery than in the centre, an observation which is clearly consistent with the decrease in M at increasing eccentricities. The suggestion of cortical modular organisation has received support from anatomical studies which have shown that cytochrome oxidase blobs are arranged in a regular pattern over the striate cortex (e.g. Horton and Hubel 1981).

Dow, Snyder, Vautin and Bauer (1981) found that the parallel relationship between cortical receptive field size and inverse magnification breaks down at the fovea. At visual field angles of less than 5° the rate of falloff of receptive field size with decreasing eccentricity is less than that of 1/M. Receptive field size at the fovea is, therefore, larger than expected and the degree of overlap is higher. Consequently the portion of cortex related to an aggregate receptive field was higher at the fovea than that measured by Hubel and Wiesel (1974) for more peripheral regions and a displacement of 2mm was not sufficient to reveal non-overlapping receptive fields. Dow and co-workers (1981) looked at the relationship between cortical "point image size" and eccentricity using their own foveal data and the peripheral data of Hubel and Wiesel (1974). Point image size, which is the extent of cortex activated by a stimulus at a point in the visual field, was estimated by taking the product of aggregate receptive field size (mean field size plus scatter) and 1/M. Since, according to these authors, field size and M do not have a fixed constant of proportionality it follows that point image size can not be constant at all eccentricities. As expected, point image size was found to increase in the foveal area. Dow et al. (1981) quoted a value of 30mm/° for M_0 which they suggested is equivalent to the reciprocal of the 2min/mm for foveal representation found by Talbot and Marshall (1941). Such an inversion, as commented above, is not appropriate. Later workers have queried the accuracy of Dow et al.'s (1981) computations (Van Essen et al. 1984; Levi et al. 1985; Schein and de Monasterio 1987). Van Essen, Newsome and Maunsell (1984) re-evaluated the data of Dow et al. (1981) and suggested a value of 15-20mm/° as

a better estimate. Dow, Vautin and Bauer (1985), using new data, gave a reduced estimate of about 16-25mm/°.

Van Essen, Newsome and Maunsell (1984) found a marked decease in the rate of change of receptive field size at eccentricities of less than 5.5°. These authors calculated point image area, being the product of aggregate receptive field area and areal magnification (mm^2/deg^2), for eccentricities out to 80°. They found that point image area reached a minimum at around 5°, increasing steeply at lower eccentricities and much more gradually towards the periphery. These authors speculated on the relationship between point image size and cortical modules, commenting that the variability in point image area is much greater than that in the dimensions of hypercolumns (or at least ocular dominance columns) or cytochrome oxidase blobs (Horton and Hubel 1981; Connolly et al. 1982; Le Vay et al. 1984). They suggested that these three parameters might represent separate bases for defining modules and that point image size was perhaps the least appropriate.

The results of investigations into the projection of the visual field on the primate LGNd have cast some doubt on the applicability of retinal ganglion cell densities to the estimation of cortical magnification. These studies have shown that the representation of the central portion of the visual field on the LGNd is already enhanced compared with that in the retina (Malpeli and Baker 1975; Connolly and Van Essen 1984; Perry and Cowey 1985), possibly indicating a two-stage magnification process. Recently, it has been suggested that there were certain inaccuracies in the computations of these authors. Schein and de Monasterio (1987) have applied their own analyses to the data from a number of studies in an attempt to discover, amongst other things, the relationship between ganglion cell density, geniculate cell density and cortical mapping in the macaque. These authors considered that the ratio between numbers of ganglion cells which project to the LGNd and geniculate cells is constant and essentially unity, at least for eccentricities greater than 5° and possibly also in the foveal area. This implies that retinal ganglion cell estimates can be used in the determination of cortical magnification.

Schein and de Monasterio (1987) applied their computaions to LGNd parvocellular (P cells) and magnocellular (M cell) neurones to reveal different properties of these two types of cells in terms of cortical representation. Comparison of the density of P and M cells with areal cortical magnification revealed the number of afferents per mm^2 of striate cortex or "afferent density" for each cell type. The afferent density for P cells was found to be relatively constant with increasing eccentricity whereas that for M cells showed a steep incline. It was suggested by the authors that P cells might be the neural substrate of cortical magnification. Comparison with the density of cytochrome oxidase puffs at

different eccentricities also showed a constant relationship for P cells. For M cells however, the number projecting to each puff increased markedly with increasing eccentricity. On the other hand, afferent density of M cells but not P cells was shown to have a constant relationship with cortical point image size. These results suggested that the projection of P cells might be related to cortical modular organisation, whereas that of M cells might be related to point image size and aggregate receptive fields.

Schwartz (1977) considered that the visual field projection in primate V1 could be represented by a logarithmic conformal map. In this type of representation, magnification is proportional to the inverse of eccentricity, and distance along the cortex related to a region of visual field is proportional to the log of inverse eccentricity. As pointed out by Van Essen, Newsome and Maunsell (1984) the V1 representation cannot be a perfect logarithmic conformal mapping since this would require that the foveal projection be infinite in size. The application of an additive constant is required to account for the decreased rate of change in M towards the fovea (Schwartz 1980). Further requirements of such a map are that M should be meridionally symmetric i.e. independent of polar angle and locally isotropic i.e. independent of the direction within the cortex along which it is measured. Van Essen and colleagues (1984) found that the inferior visual field representation was slightly greater than that of the superior field, and that regions near the horizontal meridian were much better represented than those near the vertical meridian. The meridional asymmetry of M is, as commented by Rovamo and Virsu (1979), to be expected on the basis of differences in retinal ganglion cell density.

Van Essen et al. (1984) also reported ratios of up to 3:1 between M measured along visual field meridians and orthogonal to them. This ratio varied between regions of the visual field, being smallest near the horizontal meridian, where representation was almost perfectly isotropic, and largest at the superior extreme of the vertical meridian. Over most of the cortex however the ratio was less than 2:1. Sakitt (1982) predicted a similar ratio based on the geometric shape of the cortex. Hubel and Freeman (1977) suggested that M measured along ocular dominance columns should be twice that measured across them. Other workers have calculated this ratio to be in the region of 1.5:1 (Tootell et al. 1982; Dow and Bauer 1984; Dow et al. 1985). Schwartz (1985) has commented that these local anisotropies do not affect the overall picture of the visual field representation in V1.

The implications of cortical magnification with regard to the decline in level of visual performance towards the periphery of the visual field have been studied. Rovamo and Virsu (1979) studied the effect of retinal eccentricity on contrast sensitivity. Using stimuli of constant angular subtense, contrast sensitivity was found to decrease with

increasing eccentricity. The authors then adjusted the size of stimuli at different eccentricities so that they had equivalent cortical representations, a process termed "M-scaling". The contrast sensitivity functions measured using these cortically equivalent stimuli were similar at all eccentricities. The principle of invariance with eccentricity when stimuli are made cortically equivalent has been found to apply for other aspects of photopic vision e.g. temporal contrast sensitivity (Virsu et al. 1982;Wright and Johnston 1983), visual motion (Wright and Johnston 1985; Johnston and Wright 1986) and pattern reversal visual evoked potentials (Meredith and Celesia 1982).

Drasdo (1983) has produced a schematic map of the average projection of the visual field on the striate cortex in man. Using his own equations (Drasdo 1977) he calculated M at different eccentricities in the visual hemi-field. He used the values found to calculate the separation, on the cortex, of points representing the projection of points at these different eccentricities. Drasdo then constructed wire models of corresponding dimensions to represent the actual shape of the projection on the striate cortex. A similar method was used by Daniel and Whitteridge (1961) to represent striate cortical projections in the monkey. By comparing his models with the striate area on a plaster replica of a human brain, Drasdo (1983) produced his schematic map (Figure 2.6). This map was extrapolated to cover extrastriate visual areas, where Drasdo assumed further representations of the visual field occur, each being a mirror image of the last (see section 2.5)

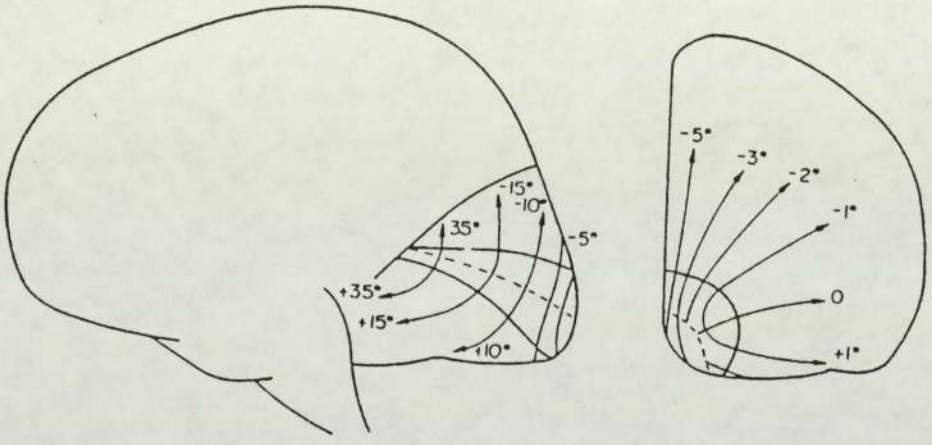


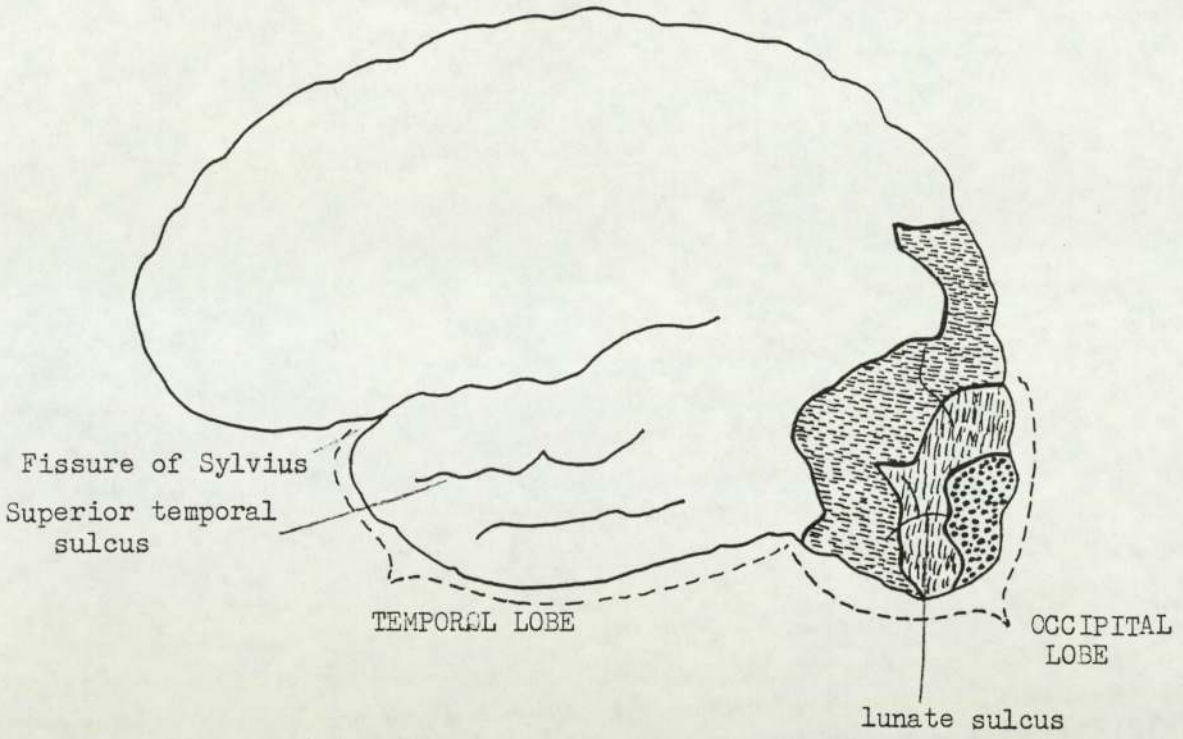
Figure 2.6

A schematic map of the average human cortical projection of the visual field.

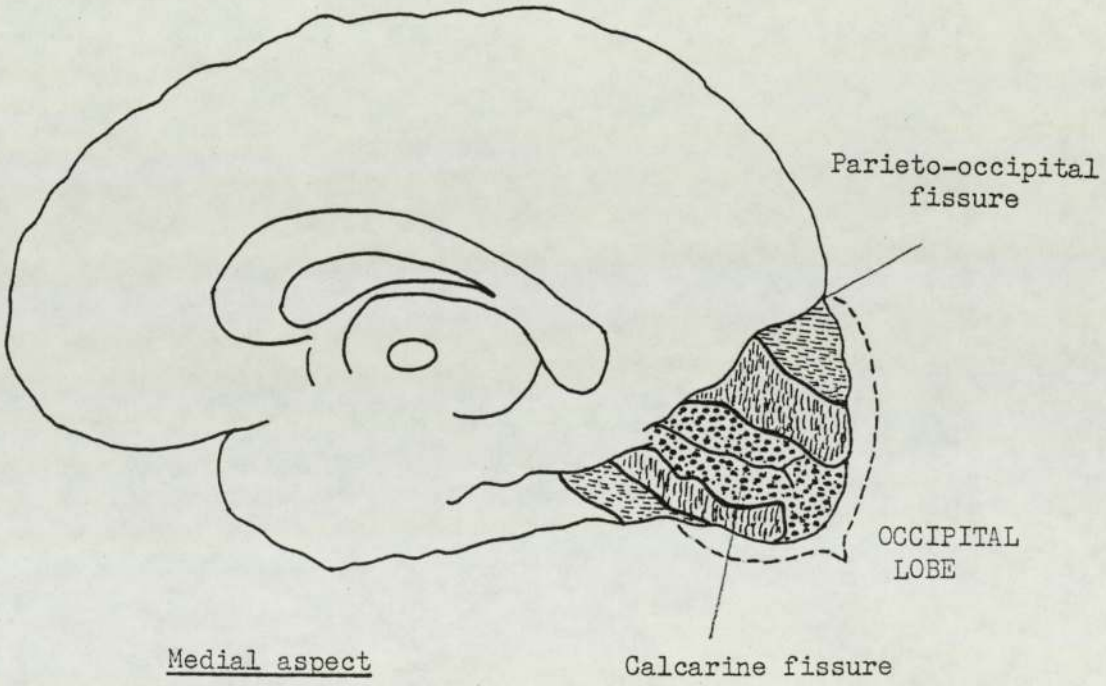
(After Drasdo 1983)

Figure 2.7

Areas of the visual cortex in the human, according to the cytoarchitectonic classification of Brodmann (1909).



Lateral aspect



Medial aspect

Area 17

Area 18

Area 19

2.5 Extrastriate visual cortical areas

The primary functions of striate cortex in man and monkey as suggested by the work reviewed in previous sections are a degree of form analysis (whether it be using contours or Fourier components) and a bringing together of the inputs from the two eyes. In addition to the striate area, there are extensive surrounding cortical areas, also with visual functions, which can be referred to as extrastriate visual cortex.

Cytoarchitectonic studies (Brodmann 1909) divide the region into two sections, areas 18 and 19, forming two concentric rings around area 17 (Figure 2.7). However, studies on higher mammals, particularly monkeys have revealed subdivisions in these areas and also confirmed the involvement of surrounding areas e.g. the inferotemporal cortex in visual function. Zeki (1978a,b,c) using combined anatomical and physiological techniques, has done much to illustrate these divisions in the visual cortex on the rhesus macaque. Allman and Kaas have conducted similar studies on the owl monkey (see Kaas 1977; Allman et al. 1981).

Zeki (1978a) divides the visual cortex in the macaque into six areas (Figure 2.8). Each has its own anatomical connections, both intra- and inter-hemispheric (the latter via the corpus callosum), and its own mapping of the visual field. Evidence for separate visual areas comes from the finding of distinct patches of callosally connected extrastriate cortex, each of which is related to the representation of the vertical meridian of the visual field in a separate visual area. In the striate cortex (V1) the contralateral hemi-field is completely mapped once, with adjacent areas on the retina represented at adjacent areas on the cortex. This has been called a topological or "first order "representation of the visual hemi-field (see Kaas 1977). The next two areas, V2 and V3, each have a split representation of upper and lower visual quadrants (Van Essen and Zeki 1978) known as a second order representation (Kaas 1977). However, within these split representations mapping is orderly and single and there is a tendency for each map to be a mirror image of the preceding one (Zeki 1978a).

In the "motion area" of the superior temporal sulcus (STS) which is part of area MT (Van Essen and Maunsell 1983) and in area V4, parts of the visual field are represented multiply in a complicated fashion (Van Essen and Zeki 1978). In V4 only central fields appear to be represented, but in the motion area more emphasis is placed on the peripheral field. Area 3A does not have a split representation, and topographically resembles V1 more than it does V2 or V3 (Van Essen and Zeki 1978). All of the areas described except V1 and the motion area lie within Brodmann's area 18.

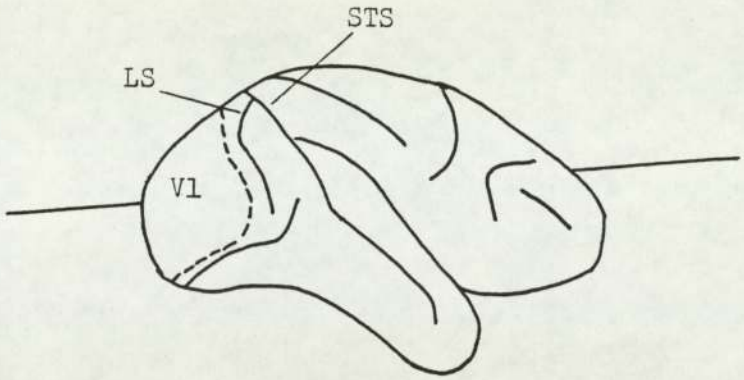
Figure 2.8

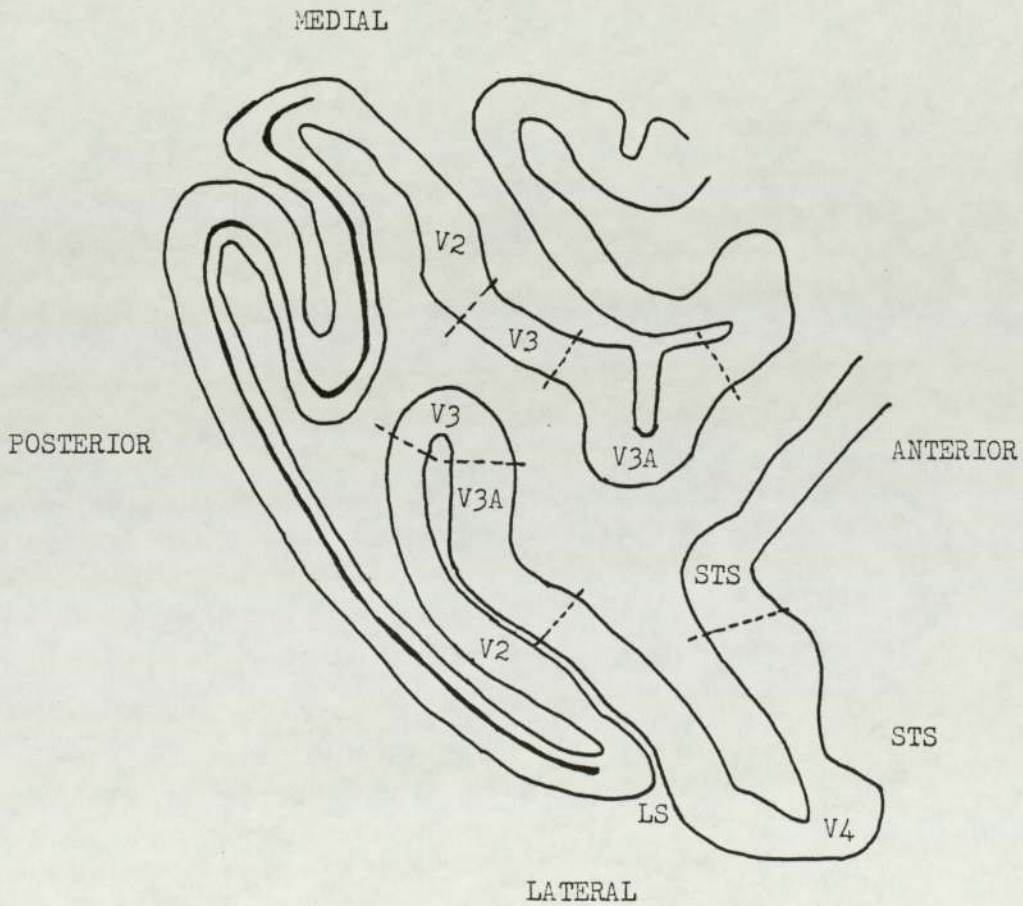
Visual cortical areas in the rhesus monkey.

The upper diagram shows a lateral view of the brain of the rhesus monkey. The lower diagram shows a horizontal section through the striate and extrastriate cortex, at the level shown by the line on the upper diagram. The boundaries of the different areas are shown by dashed lines. The continuous line in the cortex represents VI.

LS = Lunate sulcus
STS = Superior temporal sulcus

(After Zeki 1978a)


STS
LS
V1


MEDIAL
V2
V3
V3
V3A
POSTERIOR
ANTERIOR
V3A
STS
V2
STS
LS
V4
LATERAL

Functional specialization in these different extrastriate areas has been investigated by examining distribution of cells with different receptive field properties, notably orientation selectivity, direction selectivity and colour sensitivity (Zeki 1978b). The majority of orientation selective cells are found in V2, V3 and V3A. Receptive field sizes are smaller in V2 than in V3 or V3A (and in turn are larger than in V1 - Zeki 1978a). Directionally selective cells are most concentrated in the motion area of the STS, where even orientation selective cells are directionally selective. Colour sensitive cells are grouped mainly in V4. Most cells in all areas are binocularly driven. Cells in inferotemporal cortex have large receptive fields which usually include the centre of fixation and often extend across the vertical meridian of the visual field (Gross et al. 1974, 1981). They respond better to features such as shape, texture or colour than to bars or slits, even to the extent of being selective for specific objects such a hand or a face.

Some extrastriate areas have separate anatomical inputs from V1 (Zeki 1978c), and each projects to more than one further area (Zeki 1978a). There is evidence, therefore, for simultaneous analysis of separate types of information in the different visual cortical areas. However, there is also a suggestion of a heirarchical system, where an area analyses the same type of information as the previous area but at a higher level. Van Essen and Maunsell (1983) studied the connections between twelve areas of visual cortex in the macaque (including connections with the frontal areas), in order to determine the extent to which heirarchical and parallel systems are represented. The authors divided these areas into six heirarchical levels based on ascending and descending connections, in which V1 is at the lowest level and the areas in temporal, parietal and frontal lobes are at the highest levels. Analysis of receptive field properties in each area revealed that receptive fields were smallest in V1, increasing in size towards higher levels. It appeared that in addition to this serial arrangement, two distinct functional streams, mediating on the one hand motion analysis, involving regions such as MT, and on the other hand form and colour analysis, involving V4 and inferotemporal cortex, could be identified in these cortical areas. Ablation studies in primates have shown that inferotemporal cortex is involved in visual learning and recognition and bilateral loss of this area in humans leads to a characteristic visual cognitive disorder (Gross 1973). Such a role would be logical considering the position of this area at the top of the form and colour heirarchy of Van Essen and Maunsell (1983). Knowledge of human extrastriate areas is otherwise largely limited to that found by cytoarchitectonic studies but there have been suggestions of multiple visual field mappings from phosphene studies (Brindley and Lewin 1968; Dobelle et al. 1979).

2.6 Generators of electrical activity in the brain: neuronal sources of evoked potentials and the dipole model.

2.6a Activity in neurones and neuronal populations: action potentials and synaptic potentials.

Electrical activity occurring in neurones and neuronal populations, and its relation to surface recorded potentials, is discussed by Schlag (1973) and Nunez (1981). The membrane of a nerve cell in its resting state is normally polarized, so that there is a potential difference of around 70mV across it, the cytoplasm being negative with respect to the extracellular fluid. This resting potential arises as a result of the concentrations of ions inside and outside the cell. Inside the cell there is an excess of large organic anions, which cannot cross the semi-permeable membrane. As a result of active transport (sodium pump) the extracellular fluid contains an excess of sodium ions. Alterations in membrane potential are brought about by changes in permeability to particular ions, the most important being sodium, potassium and chloride ions. A localised increased permeability to sodium ions results in a net flow into the cell along the concentration gradient. This results in a reduced membrane potential in that region. The change in permeability is itself dependent on membrane potential, and when this decreases to a critical level, the voltage threshold, further increase in permeability is initiated which leads to further depolarization. This process rapidly accelerates until the membrane becomes completely depolarized. Due to the effects of other ions, particularly potassium ions, this process overshoots and the cell membrane becomes slightly hyperpolarized, so that the inside is positive with respect to the extracellular fluid. These increases in permeability are followed rapidly by decreases in permeability (inactivations) and the resting membrane potential is soon restored. Such events constitute a neuronal spike or action potential. If the neighbouring part of the cell membrane is electrically exciteable as, for example, in an axon, the action potential is normally sufficient to depolarize it to its threshold level and another spike is initiated. This process is repeated at intervals along the axon membrane, as a nerve impulse. If the axon is myelinated it is only exciteable at the nodes of Ranvier and so the impulse is transmitted from one node to the next.

Changes in permeability are not necessarily such that threshold is reached and complete depolarization occurs. Particularly at the junctions of neurones, limited depolarizations and also hyperpolarizations can arise, as the result of excitatory and inhibitory postsynaptic potentials (EPSPs and IPSPs) respectively. Unlike action potentials, which are rapid, marked changes, PSPs are slow, graded alterations in membrane potential which remain localised.

Such localised changes in membrane potential result in extracellular current flow between polarized and unpolarized parts of the cell. For example, if an IPSP at the tip of a

dendrite causes it to become hyperpolarized with respect to the soma, current will flow through the extracellular fluid from the dendrite to the soma. The dendrite therefore behaves as a current source and the soma as a sink, forming a source-sink pair or current "dipole source" . Microelectrodes placed in the vicinity of the dendrite and the soma would record a potential difference between the two sites.

The detection of such potential differences at a distance depends on the spatial configuration of the neurone. Darcey (1979) discusses two idealised models of neurone symmetry. In a radially symmetric cell the soma is surrounded by dendrites extending in all directions. A preponderance of excitatory or inhibitory activity in either dendrites or soma will cause the formation of multiple radial dipoles. In an axially symmetric neurone, multiple axial dipoles will arise. The potential field associated with these neurones will, at a distance, approximate to that of a current dipole having the same characteristics as the resultant of all the source-sink pairs. This resultant dipole will be much more effective for the axially symmetric cell, than that for the radially symmetric cell since the latter will obviously suffer from cancellation effects. For an axially symmetric cell the resultant dipole will be parallel to the axis of symmetry whereas that for the radially symmetric cell may be indeterminate. Although these are idealised types, the configuration of cortical stellate and pyramidal neurones can be approximated by the radially and axially symmetric models respectively. Pyramidal cells then, would be expected to play a more important role in the generation of surface recorded potentials.

The activity associated with single neurones is very small, but if the same events occur simultaneously in large numbers of cells the activity can be picked up by electrodes at a distance. In the cerebral cortex the orientation of neurones, particularly of pyramidal cells and their connections, is parallel, and orthogonal to the cortical surface. Consequently a portion of active cortex can be represented as a "dipole layer", of which the inner and outer extremes are of opposite polarity.

Scalp recorded evoked potentials are generally considered to arise as a result of synchronous PSPs in large populations of cortical neurones, mainly pyramidal cells. There may also be a limited contribution from glial cells. The time course of action potentials which is of the order of 1 or 2msecs makes it unlikely that these play much part in the genesis of evoked potential components which have a rise time of tens of milliseconds.

Several groups of workers have investigated VEP origins using intracellular recordings. Creutzfeldt and Kuhnt (1967, 1973) considered that excitatory and inhibitory PSP inputs to pyramidal cells were involved. These authors put forward an explanation as to how surface recorded evoked potential components related to the activity in cortical pyramidal

cells acting as dipole source generators. Goff, Allison and Vaughan (1978) gave a simplified version of this theory as illustrated in Figure 2.9. Pyramidal cell bodies are concentrated mostly in the lower (infragranular) layers of the cortex whereas their apical dendrites terminate in the outer (supragranular) cortical layers. An EPSP generated on or near the soma results in a local sink and a corresponding source in the apical dendrite. An electrode at the surface therefore records a positive potential. Subsequent depolarization of the apical dendrite will again result in a local sink, this time near the cortical surface, and a source at the soma. The surface recorded potential will in this case be negative. For IPSPs the opposite situation applies, whereby hyperpolarization first of the apical dendrites and then of the soma will give rise to surface positive and then negative activity. An electrode on the under-surface of the cortex will obviously record signals which are phase reversed with respect to those at the upper surface. Intracortical recordings would be required to determine whether surface recorded activity arises as a result of EPSPs, IPSPs or a combination of the two.

Vaughan's group (Kraut et al. 1985; Schroeder et al. 1988) have recently investigated the flash and pattern evoked activity of striate cortical neurones in the alert primate, using surface cortical and intracortical recordings. Kraut, Arezzo and Vaughan (1985) suggested human counterparts to the components recorded in monkey to flash stimulation, and as a result were able to comment on the possible cellular origins of the human flash VEP. The components P18, N40, P65, N95, and the late positivity of the simian VEP were thought to be the possible equivalents of the P40, N70, P100, N130 and P170 in the human. P40 was, therefore, thought perhaps to be associated with subcortical activity within the optic radiations. The subsequent components N70 and P100 were related to initial excitatory and subsequent inhibitory activity respectively in parvocellular thalamorecipient layer IVcß. N130 was thought to arise from subsequent input from stellate neurones to pyramidal cells in the supragranular cortical layers. Since no activity corresponding to P170 was recorded in the striate area, this component was presumed to perhaps arise from extrastriate cortex. Recordings of responses to pattern stimuli however, showed that activity was more prominent in the supragranular layers, particularly when chromatic stimulation was used (Schroeder et al. 1988).

2.6b The relation of cortical sources to scalp potential distribution; effects of head geometry and media properties.

Surface recorded potential distributions are dependent on the position of the recording electrode with respect to a cortical source or sink. The potential due to a dipole source obeys an inverse square law i.e. potential decreases in proportion to the square of the distance from the axis of the dipole source (Nunez 1981). Apparent distribution also

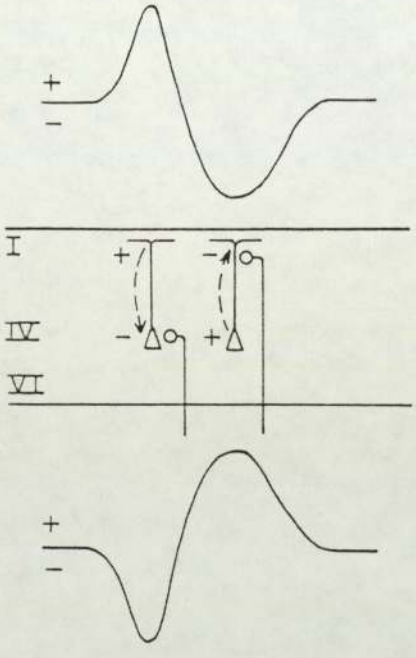


Figure 2.9

Simplified model of electrogenesis of the primary positive and negative potentials in sensory cortex. Afferents from the thalamic relay nucleus terminate directly (or via stellate interneurons) on or near pyramidal cell bodies whose depolarization by excitatory synaptic action is recorded as a positive potential at the cortical surface (upper EP). Slightly later, depolarization of apical dendrites by axodendritic synapses (shown), or by electrotonic invasion from the cell body, evokes a surface negative potential. Beneath the cortex a potential of similar waveform but opposite polarity is recorded (lower EP). For illustrative purposes separate neurons are shown as generating the surface positive and negative potentials; while there is evidence of some spatial differentiation of this sort, most neurons probably generate both potentials sequentially. Hyperpolarization of the cell body or dentrites via inhibitory synaptic action would evoke surface negative and positive potentials respectively. Other neural elements are also activated by an afferent volley, for example stellate cells and the basal dendrites of pyramidal cells. However, their random orientation is thought to minimize the potential field produced by their activation.

(From Goff et al. 1978)

depends on the distance of the recording electrode measured orthogonal to the dipole axis. Increasing displacement leads to a broader distribution with a lower amplitude centrally. These effects have been described by Goff, Allison and Vaughan (1978). The finite distance between cortical surface and scalp electrodes (which amounts to several millimetres) inevitably leads to "spatial averaging" of signals from multiple dipole sources. In fact, the effective generator can be considered as the net or equivalent dipole resulting from the summation of activity related to a single dipole. This is an adequate approximation if the active area of cortex is small compared to the distance at which the potential is measured. Where the area of active cortex is large it must be represented as a dipole layer or "sheet". In general, a small dipole sheet gives rise to localised scalp potentials which attenuate rapidly with distance whereas a sheet of large angular extent produces larger amplitude signals which are more widespread.

It would appear that scalp electrodes should record attenuated versions of potentials on the cortex directly beneath them. Creutzfeldt and Kuhnt (1967, 1973) and Heath and Galbraith (1966) have found experimentally that this is the case. The surface distribution of evoked potentials is however also affected by the orientation of dipole sources with respect to the scalp. The effective orientation of neuronal generators is not constant since the cortex is folded into gyri and fissures. Very simply, dipole sources lying in fissures where the cortical surface generally lies at right angles to the scalp might be expected to have a tangential orientation whereas those related to gyral cortex will tend to be oriented radially with respect to the scalp. Vaughan (1974) considers that the majority of cortical sources can be represented by one of two simple dipole source configurations, which are based on the geometry of cortical gyri and fissures, or a combination of the two. The first is a radial segment or "cap" concentric with the centre of a sphere representing the brain. This could be used to model gyral cortex on the outer surface of the brain which is concentric with the skull and scalp, for example the portion of striate cortex extending onto the posterior surface of the occipital lobe. The second model is an angular sector perpendicular to the brain surface, representing sulcal cortex such as that lying within the calcarine fissure. The two models are associated with radial and tangential equivalent dipoles respectively. For dipoles of similar strength, one with a radial orientation is much more effective at the scalp. Consequently, the cortical gyri are much more important in the generation of surface recorded potentials. This effect is emphasised by the effective "cancellation" of potentials of the same polarity which arise on the two sides of a fissure.

In computations of surface potentials related to sources of electrical activity in the brain, the head is often regarded as a spherical volume conductor. Darcey (1979) discusses the various assumptions made in the modelling of neuronal generators in the brain and the calculation of the related surface potential distributions. As far as the geometry of the

head is concerned, it would be more accurately represented by an ellipsoid. Although the brain and its coverings (meninges, skull and scalp) are irregular in shape and thickness, the deviation from regularity is only significant, with regard to generator effectivity, for the lower half of the brain. In particular, around the portion of the brain occupied by visual cortical areas deviations from spherical are generally considered to be not too severe, although a recent report by Srebro (1988) shows that the increased thickness of the skull in the area near the inion causes an anterior and lateral shift of peaks in scalp recorded activity related to modelled striate cortical generators.

Over the range of frequencies present in EEG and EP waveforms the reactivity of the media of the head is negligible. The head can therefore be regarded as being purely resistive, so that signals are volume conducted instantaneously. This means that simultaneous activity related to sources at different depths will be recorded at scalp electrodes at the same time.

The equations governing the behaviour of current flow and therefore potential distributions, of which the most important are those of Poisson and Laplace, are valid only if a volume conductor is homogeneous and isotropic. The head is obviously not homogeneous, being composed of several layers of media with different resistive properties. If each of these layers is considered separately however, these equations can be applied. In a "three sphere" model the effects of brain, skull and scalp are considered. A more accurate model uses five spheres in which the skull, which is itself not homogeneous, is regarded as three separate layers. The head media are also anisotropic, that is the resistive properties, particularly of the brain and skull, are not the same measured normal and parallel to the surface. This factor has, in fact, very little effect on potentials generated in the cortex and it is therefore often ignored, although correction factors can be applied. The effects of inhomogeneity are to attenuate and smear scalp recorded potentials, so that if calculations are used for a homogeneous model (single sphere) the sources computed from the same potential distributions are deeper and weaker than if inhomogeneity had been taken into account. In practice, these effects do not appear to alter qualitative generator characteristics significantly.

CHAPTER 3

The visual evoked potential. I. General aspects and stimulus related properties of VEPs in the normal subject.

3.1 Introduction

The properties of the scalp recorded VEP waveform are dependent upon many factors. These include both inter- and intra-individual variables. It is the purpose of this chapter to outline the basic waveforms of the signals elicited by the different methods of visual stimulation and to show how these patterns are modified by various stimulus characteristics and to discuss the implications of these properties in terms of what they suggest or reveal about the nature of VEPs and their sources. The primary purpose of the present study is to investigate the scalp topography of the VEP and its relation to the part of the visual field which is stimulated. These factors will be discussed at length in the following chapter, and will only be mentioned here in passing. In addition to normal variations, characteristic modifications of the normal VEP waveform can be caused by various pathological conditions of the brain and the visual system The VEP, therefore, has become an important tool for clinical diagnosis and as such has been the basis of a great wealth of literature. In a report such as this, which is based on research carried out on normal individuals, it is considered inappropriate to attempt to review this work. Clinical aspects of the VEP will, therefore, be discussed only where they are believed to be particularly relevant.

3.2 Methods of stimulation and basic waveforms

3.2.a Flash stimulation

Early workers in the field of visual evoked potentials used the brief, diffuse, spatially unstructured flashes of light produced by a stroboscope as stimuli. The waveform of the response to such a stimulus is quite variable, but several components which are common to a large portion of the population can be described. Figure 3.1 shows the normal flash response as described and labelled by Harding (1974). Also shown is the nomenclature of comparable components described by other workers. The most commonly observed component in this response is the large positivity occurring at a latency of around 100-120 msec, labelled by Harding as P2. Although the clinical value of flash stimulation is immense (Harding 1974, 1982; Halliday 1982; Wright et al. 1987), more recent studies on the nature and sources of the VEP have concentrated largely on responses to spatially structured or "pattern" stimuli. A patterned target is, as described in Chapter 2, a much more effective stimulus for cortical cells than a light flash, and is

better related to the appearance of the normal visual environment.

3.2.b Patterned flash stimulation

If a spatially structured target, such as a black and white checkerboard pattern, is superimposed on a diffuse flash, the response morphology is altered (Spehlmann 1965; Rietveld et al. 1967). The two major components of the patterned flash response so elicited are a large negative wave appearing at a similar latency to the flash P2 component and a large positive wave at the same latency as P3. Many early pattern VEP studies used this type of stimulation (Spehlmann 1965; Rietveld et al. 1967; Harter and White 1968, 1970; Harter 1970). For those workers interested in the physiological significance of the VEP, this type of stimulus presented a problem in that it contains elements related to both "contrast" and "luminance" effects on the visual system. Some workers have attempted to separate these two elements by "subtracting" a pure flash VEP from the combined response (Jeffreys 1968; Harter 1977). This procedure, however, could lead to problems in that it is likely that these elements interact to some degree, rather than summating linearly (MacKay and Jeffreys 1973). Consequently, patterned flash stimulation has been largely superceded by those methods in which the mean luminance across the stimulus field remains constant throughout the stimulus cycle.

3.2.c Pattern reversal stimulation

This method of stimulation involves the rhythmic interchange, or "reversal", of two sets of pattern elements within a target. It follows that in order for the mean stimulus luminance to remain constant the two sets of elements must be symmetrical. Hence the patterns used are normally black and white checkerboards, or, less frequently, sine wave or square wave gratings. Changeover is usually abrupt, taking only a few milliseconds. In pattern reversal, one stimulus cycle consists of two reversals, such that stimulus temporal frequency in Hz is half the number of reversals per second. The form of the pattern reversal response in most normal subjects is dominated by a major positive component at a latency of around 100 msecs (Figure 3.2b). Halliday and co-workers have termed this component "P100" (e.g. Barrett et al. 1976). This positivity is often preceded and followed by negative components at latencies of around 75 and 145 msecs (Blumhardt and Halliday 1979).

3.2.d Pattern onset-offset stimulation

Alternatively known as pattern appearance-disappearance, this method involves the periodic presentation of a patterned target into a blank field, which is normally of equal mean luminance. A stimulus cycle consists of the onset or appearance of the pattern

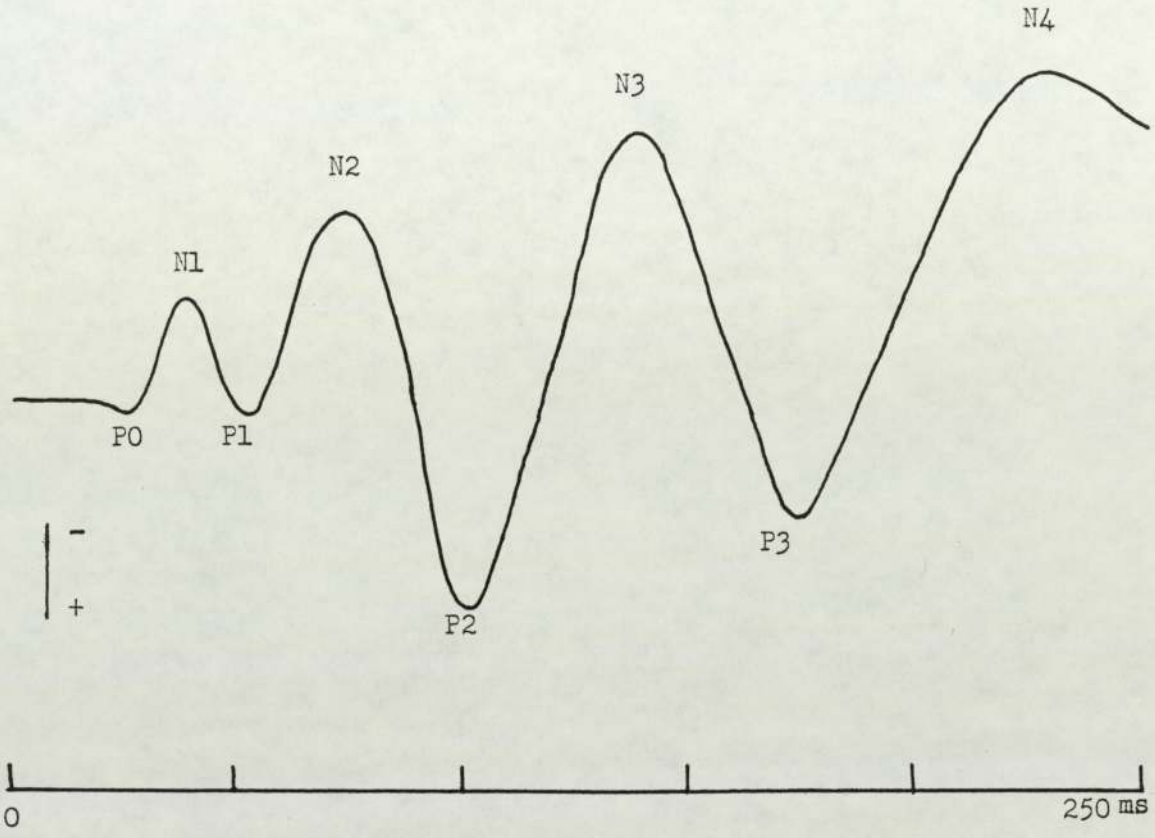


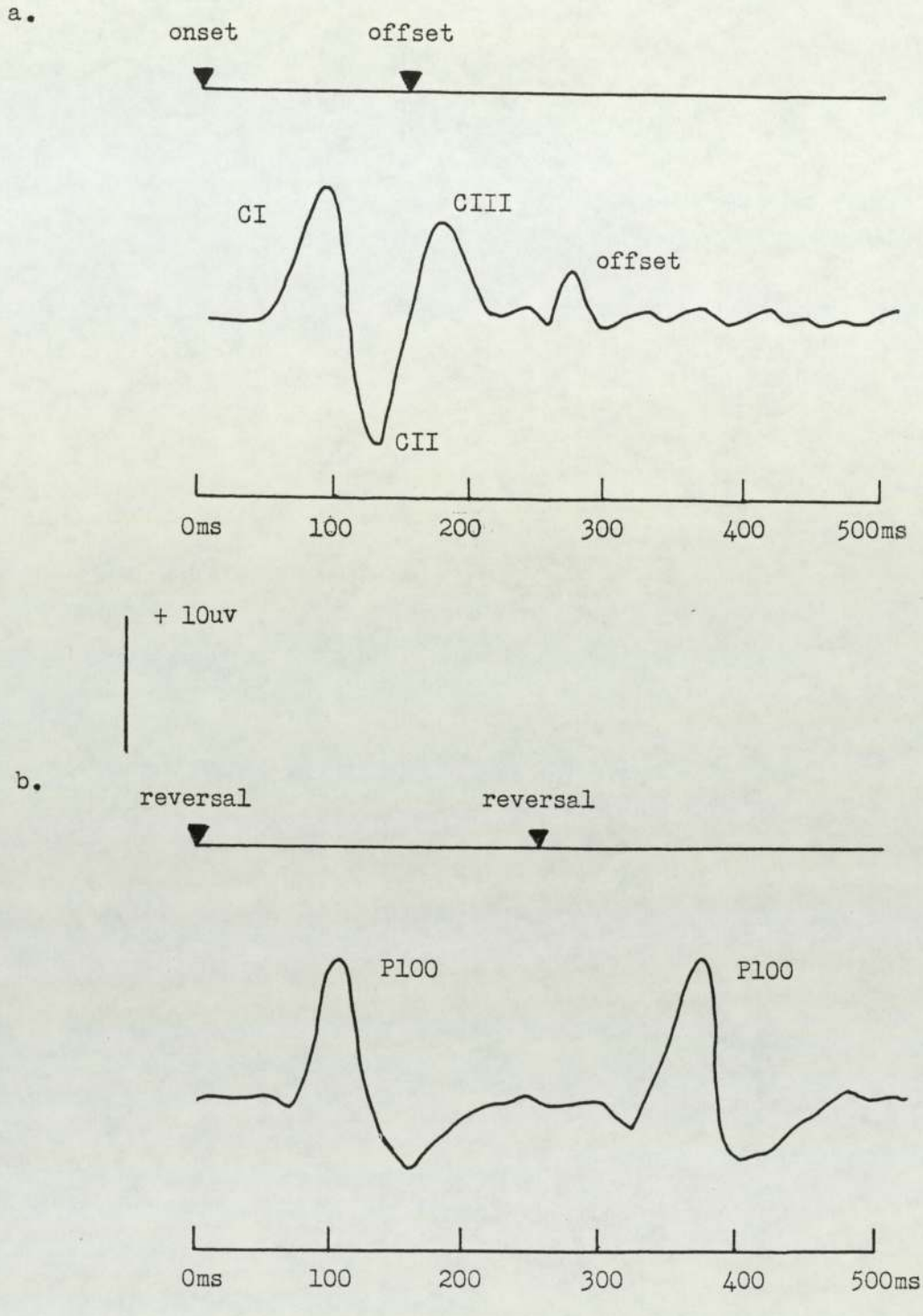
Figure 3.1

The waveform of the visual evoked potential elicited by flash stimulation in the normal subject.

(After Harding 1974)

Figure 3.2

The waveform of the visual evoked potential elicited by a. pattern onset-offset and b. pattern reversal stimulation in the normal subject.


a.
onset
offset
CI
CIII
offset
CII
0ms
100
200
300
400
500ms
+ 10uv
b.
reversal
reversal
P100
P100
0ms
100
200
300
400
500ms

followed by its disappearance or offset. Both onset and offset of the stimulus produce a specific response, but a separate offset response can only be distinguished if the duration of pattern exposure is 100 msecs or longer (Spekreijse and Estevez 1972). The generally accepted form of the pattern onset response was described by Jeffreys (1970). It has a triphasic waveform, being comprised of a negative peak with preceding and following positive peaks (see Figure 3.2a). Jeffreys termed these components CI, CII and CIII and gave their latencies as about 75, 100 and 150 msecs respectively (James and Jeffreys 1975). In addition to these components, under some stimulus conditions an early negative component has been described which normally precedes CI (Kulikowski 1977a; Lesevre and Joseph 1979; Drasdo 1980). Drasdo (1980) has termed this component C0. The response to pattern offset is generally less consistent than that to pattern onset. The most prominent component is a positive peak at about 100 msecs which is often preceded by a negative deflection (Spekreijse et al. 1973; Jeffreys 1977; Kriss and Halliday 1980).

3.2.e Steady-state stimulation.

The VEP waveforms described above are only observed in conditions of "transient" stimulation, where the presentation rate is relatively low e.g. 1-2 Hz. Under these conditions, each response is more or less complete and the visual system has returned to its "resting state" before the arrival of the next stimulus. As stimulation rate is increased the shape of the response becomes more regular and eventually, at high temporal stimulus frequencies (e.g. 10 Hz), appears quasi-sinusoidal. Such signals are termed "steady-state" responses. These responses may be processed using averaging techniques and interpreted in terms of amplitude and peak latency in the same way as transient responses. They are, however, more appropriately processed using band-pass filters and analysed using Fourier techniques. Their relatively simple waveforms are easily quantified in terms of peak-to-trough amplitude and phase (Regan 1972, 1977; Kulikowski 1977a). As a result of this, steady-state techniques have been found to be useful when studying stimulus related properties of the VEP. (e.g. Campbell and Maffei 1970; Kulikowski 1977a). The use of Fourier analysers improves resolution at low signal amplitudes (Regan 1977), rendering the technique particularly useful when operating at threshold or near-threshold conditions. In studies in which the physiological significance of individual response components is to be investigated, however, steady-state VEPs are of relatively little value.

3.3 The effects of spatial and temporal stimulus parameters on the VEP

3.3a Spatial configuration of the stimulus elements

The waveform of the pattern onset response can vary markedly with different types of pattern element (Spekreijse and Estevez 1972; MacKay and Jeffreys 1973; Jeffreys 1977). Similar components have, however, been described for isolated squares (Jeffreys 1970), checkerboards (e.g. Spekreijse and Estevez 1972; Barber and Galloway 1979; Drasdo 1980) and grating stimuli (e.g. Kulikowski 1977a; Parker and Salzen 1977a; Drasdo 1980), although Jeffreys (James and Jeffreys 1975; Jeffreys 1977) finds that onset components are larger in amplitude when the pattern consists of discontinuous contours. This applies particularly to CII and CIII so that these components are smaller with grating stimuli than with checks or squares. Spekreijse, van der Tweel and Zuidema (1973) describe the horizontal or vertical grating VEP as being "sluggish" i.e. rising and falling slowly. The pattern offset response changes in amplitude rather than waveform with different stimulus elements, with larger amplitude signals being elicited by diamonds than by checks (Spekreijse et al. 1973).

Transient pattern reversal VEPs recorded using stimuli other than checkerboards are rarely reported. Plant, Zimmern and Durden (1983) used reversing sinusoidal gratings and elicited responses with a very similar waveform to that described by Halliday and co-workers (e.g. Blumhardt and Halliday 1979) for the checkerboard reversal response.

3.3b Spatial frequency

Studies on variation of latency of pattern onset components with spatial frequency have used, in the main, sinusoidal grating stimuli. Parker and Salzen (1977a and b) found that the latencies of the major components of the pattern onset response to sinusoidal gratings show a monotonic increase with increasing spatial frequency. A similar relationship has been demonstrated by other workers (Jones and Keck 1978; Vassilev and Strashimirov 1979; Vassilev et al. 1983; Plant et al. 1983; Musselwhite and Jeffreys 1982). Most studies have shown, however, that latency reaches a minimum at around 2-4 cycles per degree (Jones and Keck 1978; Parker et al. 1982a; Plant et al. 1983; Musselwhite and Jeffreys 1985). For coarser gratings the picture becomes less clear, latencies being much more variable and tending to increase again. Jones and Keck (1978) and Plant, Zimmern and Durden (1983) attribute this behaviour to the appearance of additional early components in the responses at these low spatial frequencies.

The magnitude of this latency change has been found to depend on which component is measured. Parker and Salzen (1977b) found that the latency increase was clearer for the

earlier components in the response (occurring before 200 msecs) than for later ones. Plant, Zimmern and Durden (1983) found no consistent effect at all on their late positive component. Vassilev, Manahilov and Mitov (1983), however, showed a greater effect on the later components, producing a "widening" effect on the response waveform at high spatial frequencies. This is in contrast to the findings of Drasdo (1980), who shows that at high spatial frequencies, the first prominent positive component in the response may actually appear on the descending slope of the ensuing negative component, indicating a latency increase of the first component with respect to the second, causing a crowding effect.

Parker and Salzen (1977b) commented that the latency increase with increasing spatial frequency might reflect a delay in cortical processing related to the lower contrast sensitivity of the visual system for finer details. Jones and Keck (1978) suggested that if the behaviour of the VEP were related solely to contrast sensitivity, then component latency ought to show a minimum and component amplitude a maximum at around 4 cycles per degree, which is at the peak of the human psychophysical CSF (when measured with small, static gratings). They showed that although this was indeed the case, if grating contrast was manipulated to produce VEPs of the same amplitude at different spatial frequencies there was still a latency increase with finer gratings. Vassilev and Strashimirov (1979) and Vassilev, Manahilov and Mitov (1983) showed that if grating contrast is a constant multiple of the threshold value at each spatial frequency, the relationship still holds. Musselwhite and Jeffreys (1985), however, also using constant suprathreshold contrast levels, found no effect of spatial frequency on the latency of their Cl component.

The effect of spatial frequency on the latency of the pattern reversal response to grating stimuli is similar to that for the pattern onset response (Plant et al. 1983), that is, an increase in latency with increased spatial frequency above 2 cycles per degree. Vassilev and co-authors (1978) report that the latency of the offset response also tends to increase with increasing spatial frequency.

The amplitude of the VEP elicited by the onset, reversal and flash presentation of checkerboard patterns appears to show spatial tuning characteristics, being maximal for a particular check size (Harter 1970; Eason et al. 1970; Armington et al. 1971; Regan and Richards 1971; Spekreijse and Estevez 1972; Drasdo 1980). Most studies have found that for the central few degrees of the visual field, check sizes of between 10 and 20 minutes of arc produce the maximum response. The optimum check size increases with increasing retinal eccentricity (Harter and White 1970; Meredith and Celesia 1982). This spatial tuning property has been attributed to sizes and arrangements of ganglion cell receptive fields (Harter 1970; Eason et al. 1970; Armington et al. 1971).

Plant, Zimmern and Durden (1983) demonstrated spatial tuning functions for the early and late components of the pattern onset response to sinusoidal gratings. For grating reversal, however, only the early components showed spatial selectivity. These authors also noted that the optimum spatial frequency for the early pattern onset components tended to be higher than that for those elicited by pattern reversal.

Parker and Salzen (1977a) were able to demonstrate a tuning function for their early onset component with high contrast gratings, but the results were much less convincing when moderate contrast levels were used. Both of these authors found that the optimum spatial frequency showed an increase with increasing field size or eccentricity. Jones and Keck (1978), as commented previously, found that for gratings of constant contrast, the amplitude of their main negative component was maximal at around 4 cycles per degree i.e. the peak of the psychophysical contrast sensitivity function.

Parker and Salzen (1982a) and Vassilev and co-workers (1983) found that the response to the offset of sinusoidal grating patterns is poor or even absent at high spatial frequencies. This is not, however, consistent with the observation of Spekreijse and Estevez (1972) that the response to checkerboard offset becomes stronger relative to the onset response as check size decreases.

For sinusoidal gratings of low spatial frequency, the waveform of the response to pattern onset and pattern reversal tends to appear very similar (Plant et al. 1983). Also at low spatial frequencies, responses to grating onset and offset tend to be of comparable waveform and amplitude (Vassilev et al. 1983). Kulikowski (1977b) states that at moderate frequencies the responses to grating offset and reversal are similar whilst for coarse gratings the early components are almost identical in all three types of response.

Tyler, Apkarian and Nakayama (1978), using steady-state reversal of sinusoidal gratings, found that the VEP shows a fairly narrow-band spatial tuning function with two peaks. They suggested that the two peaks, which occur at different spatial frequencies when the temporal frequency of pattern reversal is changed, may be related to the resonance characteristics of different types of neural circuitry in the visual cortex.

At high spatial frequencies the pattern onset response to sinusoidal gratings is dominated by a single early negative component (Plant et al. 1983; Russell et al. 1986). This is probably equivalent to Drasdo's "C0" (Drasdo 1980).

3.3.c Spatial contrast

Spatial contrast within pattern stimuli is normally monochromatic luminance contrast i.e. black and white elements are used. Sometimes chromatic contrast is used e.g. red and green elements. Responses to chromatic stimuli are difficult to evaluate, due to the possible interplay between "luminance" and "colour" mechanisms in the visual system. This is likely to be a problem even with chromatic stimuli which have been luminance balanced subjectively (Paulus et al. 1984).

The amplitude of the VEP elicited by steady-state pattern reversal stimulation is proportional to the logarithm of the suprathreshold contrast of the target. Extrapolation of the function to zero amplitude predicts the psychophysical contrast threshold (Campbell and Maffei 1970; Campbell and Kulikowski 1972; Wright and Johnston 1982). Campbell and Maffei (1970) found that for spatial frequencies below 3 cycles per degree the results were best fitted by two regression lines, the function becoming less steep at low contrasts.

Kulikowski (1977a) studied the relationship between the pattern onset-offset response and contrast, confirming the amplitude-log suprathreshold relationship. He found that for presentation times of up to 50msecs both early and late VEP components are correlated with the psychophysical contrast threshold. For pattern durations greater than 50msecs, only late components show this property, the early components being less resistant to contrast reduction. For low contrast levels, just above threshold, VEP amplitude may show a linear relationship with contrast (Kulikowski 1977a; Wright and Johnston 1982). Kulikowski (1977a) also found that the latencies of the early pattern onset components show an approximate inverse proportionality with suprathreshold contrast. The latency of components CI and CII of the pattern onset response decreases monotonically with increasing contrast (Musselwhite and Jeffreys 1982). The relationship is not affected by an increase in stimulus duration up to 100msecs. The extrapolated VEP component threshold corresponds well with the psychophysical threshold.

Spekreijse and co-workers (Spekreijse et al. 1973; 1977) maintain that, for the CII pattern onset component, the linear amplitude to log contrast relationship is valid only up to contrast levels of about 20-30%. After this the response amplitude appears to saturate and the function levels out. They found that the level at which saturation occurs is dependent on check size, the response to checks greater than 20 minutes of arc saturating at a lower contrast than that to smaller checks. Saturation level was also found to be luminance dependent, occurring at a lower contrast the higher the mean luminance.

Jones and Keck (1978) found that both the amplitude and latency of the major negativity in their pattern onset response showed saturation with increasing contrast. Manahilov and Vassilev (1986) found that their N2 component saturated at a contrast of 10%. Katsumi, Tanino and Hirose (1985) showed a saturation effect on the latency of the pattern reversal steady-state VEP at higher contast levels. Jeffreys (1977) studied the behaviour of the transient pattern onset response with respect to spatial contrast. He found that the saturation characteristics of the components of the onset response differed. Components CII and CIII developed more rapidly than CI as contrast was increased from threshold, and saturated earlier.

A steady contrast throughout the stimulus cycle normally attenuates the onset response, as if this initial contrast level sets a starting point some way up the amplitude scale (Spekreijse et al 1973). There are, however, situations in which standing contrast can actually enhance the response. There is a "dead zone" in the amplitude versus contrast curve where the stimulus contrast is less than the threshold value needed to elicit a VEP. A small initial contrast could take up this dead zone so that the additional contrast associated with stimulus onset would have more effect. This effect is more pronounced at low luminances. Pattern offset responses are much less affected than pattern onset responses and appear to depend on the change in contrast and not on absolute initial and final values. Jeffreys (1977) also found that standing contrast attenuates the onset response although this reduction was more marked for CII and CIII than for CI. There appeared to be an association with the subjective definition of the outlines of the pattern elements in that when the resting contrast was increased to such a level that the pattern could be clearly seen, CII and CIII were markedly attenuated whereas CI could still be fairly large. This also applied to the effects of defocus. When the amount of blur was sufficient to make the edges in the pattern indistinct, CII and CIII were always attenuated, whereas CI was much more resistant.

Vassilev and co-authors (1978) showed that at low spatial frequencies the onset response was most prominent at intermediate contrast levels. Also at low spatial frequencies they found that the amplitude of the offset response was affected more markedly by decreasing contrast than that of the onset response, indicating a lower contrast sensitivity for pattern offset than pattern onset with coarse stimulus details. At higher spatial frequencies these authors found, in general, an increase in amplitude and decrease in latency of pattern onset components, and a decrease in latency of pattern offset components, with increased contrast. Parker, Salzen and Lishman (1982a) showed that the amplitude of their N1-P1 component increased steadily with increasing contrast. They fitted their data with two linear functions, that for contrasts of less than 12% being less steep than that for higher contrasts. Increasing contrast also caused a steady increase in P1 latency.

For presentation durations of up to 50msecs the contrast threshold of the pattern onset VEP is inversely proportional to stimulus duration ie. response amplitude behaves according to the contrast equivalent of Bloch's law (Spekreijse et al. 1973; Kulikowski 1977a; Musselwhite and Jeffreys 1982). This relationship does not hold for pattern onset latency (Musselwhite and Jeffreys 1982) nor for the response to pattern offset (Spekreijse et al. 1973).

Investigations of the VEP contrast sensitivity function (VEP CSF) have been conducted using steady-state techniques (Cannon 1983; Katsumi et al. 1985) The VEP CSF has an inverted "U" shape, similar to that for the psychophysical function, peaking around 2-6 cycles per degree, but psychophysical contrast sensitivity is always higher. The VEP curve tends to show less of a low spatial frequency falloff. VEP amplitude decreases as a log function of decreasing contrast modulation depth and the extrapolated function predicts subjective threshold (Bodis-Wollner and Hendley 1977). The slope of the function depends upon the mean contrast level, being steeper for higher mean contrast levels.

3.3.d Luminance and illuminance

A decrease in average brightness of the stimulus leads to a decrease in amplitude and an increase in latency of the P100 of the pattern reversal response (Halliday 1982). The latency of the flash response is also found to increase with decreased luminance (Vaughan et al. 1966; DeVoe et al. 1968; Whittaker and Siegfried 1983) and van der Tweel, Estevez and Cavonius (1979) found a similar effect on the pattern onset response.

Spekreijse, van der Tweel and Zuidema (1973) commented that under conditions of low luminance and contrast the response to checkerboard onset appeared "sluggish", being low in amplitude and long in latency. Van der Tweel and co-workers (1979), however, found that if pattern contrast was adjusted to be a constant multiple of threshold contrast, the shape and amplitude of the onset response showed little variation over a wide range of retinal illuminance levels.

Ermolaev and co-authors (1978) found that reducing background illumination and allowing the subject to dark adapt caused a change in the waveform of the patterned flash response. The major negative component at around 100 msecs was replaced by a negativity at around 130 msecs. Ermolaev and Kleinman (1983) found a similar effect on the pattern onset VEP. Decreasing target luminance caused a steady decrease and a steady increase respectively in the amplitudes of N100 and N130. At intermediate

luminances, both components could be distinguished in the response.

3.3.e Temporal factors: stimulus duration, interstimulus interval and adaptation studies

As has already been mentioned, the duration of pattern exposure in pattern onset-offset stimulation is important in relation to the recognition of separate onset and offset responses. With short exposure durations it is possible that the offset response may overlap temporally with the later components in the onset response. Van Lith and co-authors (1981) consider that the second positive peak in the pattern onset response (probably equivalent to Jeffreys' CIII) to a stimulus of duration 80msecs or less contains at least some contribution from the offset response. Spekreijse and Estevez (1972) suggested that a gap of 100msecs was required to separate the two responses. Jeffreys, who has conducted much of his work using a 25msec onset period, acknowledges that there may be a contribution from pattern offset, but finds that the response for longer durations (greater than 100msecs) contains the same basic components (Jeffreys 1977, 1980).

Barber and co-workers (Barber and Galloway 1979,1982; Jackson and Barber 1980) have studied the effects of varying temporal stimulus parameters on the pattern VEP. They found that adjusting stimulus duration and time between stimuli (inter-stimulus interval or ISI) affected the response components in a different manner. Increasing stimulus duration at a constant ISI caused an increase in the amplitude of component CI and, to a lesser extent, CIII. CII, however, showed a decrease in amplitude and pattern reversal P100 showed little change. The behaviour of CI, and to a certain extent CIII, can be explained by the concept of "residual contrast". Barber and Galloway (1979) suggested that increasing stimulus duration without changing ISI might lead to a persistence of "contrast representation" in the visual system between one stimulus and the next. This would have the same effect as a small standing contrast, which is to enhance the pattern onset response (Spekreijse et al. 1973). The reduction in amplitude of CII, on the other hand, showed an adaptive type of behaviour. If pattern duration was kept constant and ISI increased, CII showed a clear increase in amplitude. CI and CIII showed an initial increase and then a levelling off, with CIII reducing slightly in amplitude at extreme values. No overall effect was found for P100. The effects on the onset response components appeared to be modified by using randomised ISIs. In particular this caused the amplitude of CII to decrease at high values of ISI.

Barber and Galloway (1979) found that the plot of CII amplitude against ISI was best fitted by two linear functions, the slope at higher values of ISI (greater than 1-2 seconds) being flatter. They have derived a model with exponential adaptation and linear recovery characteristics which gives a reasonable prediction of CII behaviour (Barber and

Galloway 1982). The modification of the amplitude-ISI function by irregular and prompted stimulation caused Jackson and Barber (1980) to suggest that CII is influenced by both physiological and psychological factors.

The different behaviour of the pattern onset components with respect to temporal stimulus parameters had been demonstrated previously by Jeffreys and co-workers (James and Jeffreys 1975; Jeffreys 1977). They found that pre-exposure to a pattern causes ready adaptation of CII and CIII whereas attenuation of CI is not nearly so marked. Increasing stimulus duration also caused a reduction of amplitude of CII and CIII without affecting CI, although CII recovers if the ISI is increased. The fact that increasing onset duration attenuates later components in the response may suggest that there is in fact some contribution from the offset response with short pattern exposure periods but Jeffreys did not comment on this point.

Barber and Galloway (1979) also looked at the effects of prolonged stimulus sequences with large numbers of averages. They found that the amplitude of CII showed an initial sharp drop, up to six presentations, after which time it levelled out. CI was little affected and CIII showed a slight decrease over extended stimulus sequences. Barber and Galloway (1979) suggested that by discarding the responses to the first few stimuli a stably adapted VEP would be obtained.

Ochs and Aminoff (1980) investigated the effects of adaptation to pre-exposed patterns on the responses to pattern reversal and pattern onset stimulation, using high contrast line gratings. They found that adapting to an identical stimulus for several minutes prior to recording had very little effect on either response. They discovered, however, that extending the stimulus duration and reducing the interstimulus interval until the pattern was almost continuously present affected the principal positive and negative components in the pattern onset response. Both components were found to increase in latency by around 14msecs, and in addition the negative peak was markedly reduced in amplitude. As a result, the adapted pattern onset response appeared to resemble the normal response to pattern reversal.

The presence of steady outlines around the stimulus elements appears to reduce the amplitude of the pattern onset response to isolated squares and to checks (Jeffreys 1977; Spekreijse et al. 1973). Jeffreys (1977) finds that, as with pattern pre-exposure, attenuation of CII and CIII is marked, whereas there is relatively little effect on CI. Jeffreys (1977) and Jeffreys and Musselwhite (1984) looked at the effects of pattern pre-exposure on the pattern onset VEP using different spatial configurations of pattern and different types of contour composition. For example, they used continuous outlines, dotted outlines and surface texture discontinuities as well as edges of positive

and negative contrast polarity. They found that so long as the form was the same, pre-exposure to a pattern with a different type of contour still caused attenuation of components CII and CIII. Attenuation of CI however was specific to both form and contour composition.

Campbell and Maffei (1970) explored the relationship of adaptation effects in the VEP to spatial frequency and orientation. Using steady-state reversal of sinusoidal gratings they discovered that these effects had a specificity similar to that found in psychophysical studies (Campbell and Kulikowski 1966; Blakemore and Campbell 1969) i.e. the effects were limited to bandwidths of less than one octave and to orientation differences of 15 degrees.

Smith and Jeffreys (1978a) showed that adaptation of components CI and CII of the transient pattern onset response, but not CIII, was spatial frequency specific. In addition, they showed that CI adaptation was orientation specific. These effects were transferred interocularly. Kulikowski (1977b) has also described orientation specific adaptation for pattern reversal and pattern onset VEPs. Smith and Jeffreys (1978b) showed that adaptation effects on the CI component of the pattern onset response to lcheckerboard patterns were more related to the orientation of the fundamental Fourier components i.e. at 45 degrees to the edges, than to the orientation of the edges themselves.

Manahilov and Vassilev (1986) found that at low spatial frequencies the pattern onset VEP elicited by sinusoidal gratings did not show adaptation effects to stationary gratings but was attenuated by drifting gratings. Both early and late negative components were, however, reduced by adaptation with medium and high spatial frequencies. This adaptation was spatial frequency specific for N1 but not for N2, an observation which does not tie in with Smith and Jeffreys' (1978a) findings for CII. Manahilov and Vassilev (1986) also found that the adapted pattern onset VEP resembled the response to pattern offset.

3.4 The nature of VEPs and their relation to visual processing: contour, contrast, luminance and motion

3.4.a Local luminance and contrast and origins of the pattern VEP

The relation of VEPs to the mechanisms involved in visual processing has been debated at length in the literature. The VEP which results from pure luminance stimulation can, of course, be explained on the basis of the response of the visual system to changes in the overall level of retinal illumination. By studying the temporal properties of the signals produced by sine-wave and Gaussian noise modulated luminance stimulation, Spekreijse, Estevez and Reits (1977) constructed mathematical models to represent the operation of these mechanisms. On the introduction of a "pattern" or "contrast" element, however, the situation becomes much more complex.

Superimposing a pattern on a flash of light causes a change in VEP waveform. The effects of defocus and check size or number of edges in a pattern on this patterned flash VEP led to speculation as to whether the presence of sharp borders or contours in the stimulus was the determining factor (Spehlmann 1965; Harter and White 1968). Some authors have advocated the separation of the flash and pattern elements of this combined response by "subtraction" techniques, in which the pure luminance response is subtracted from the patterned flash waveform to leave the isolated pattern response (Jeffreys 1968, 1977; Harter 1977). It is likely, however, that these two elements interact to some degree rather than directly summating. Spekreijse, van der Tweel and Zuidema (1973) report that the response to flash stimulation can be enhanced by the presence of a constantly visible steady pattern.

Padmos, Haaijman and Spekreijse (1973) proposed three models for the generating mechanisms of the pattern onset-offset VEP. In the luminance model, it is considered that the retina contains elements of finite size which are sensitive only to the local temporal luminance changes associated with the onset and offset of a pattern. The visual system processes the summed responses from many of these units operating in parallel. In the spatial frequency specific or SFS model, retinal units with antagonistic centre-surround receptive fields are sensitive to the differential stimulation of centre and surround. Again, signals are summed and processed by the visual system. In both these models, the visual system responds to the presence of contrast in the stimulus i.e. changes in luminance across the target. In the contour model the visual system contains elements which are sensitive to the onset and offset of contrast borders or edges. It is possible that these elements represent "line-detectors", input to which is derived from several units with overlapping centre-surround receptive fields.

Padmos and co-authors (1973) used these models to predict the behaviour of the onset-offset VEP under different stimulus conditons. They tested these predictions against responses recorded in the monkey and also in man, with particular reference to the behaviour of a prominent negative onset component which is probably equivalent to Jeffreys' CII. Both the local luminance and the spatial frequency specific models predicted that the responses to the onset and offset of a pattern should be symmetrical, since in each case half the retina receives an increase and the other half an equivalent decrease in illumination. Although such symmetry can be observed in the monkey VEP, human onset and offset VEPs are normally quite different. Indeed, Spekreijse and Estevez (1972) and Spekreijse et al. (1973) have shown that cortical onset and offset responses in humans have quite different stimulus-related properties.

Spekreijse and co-workers (1973) described a similar "luminance" model to that of Padmos et al. (1973) based on spatial summation in the goldfish retina. They commented that any response to a patterned stimulus based solely on local luminance responses could never be larger than the response to equivalent homogeneous field modulation. This, they found, was not the case, pattern responses being clearly larger than those to blank field modulation. The authors concluded, therefore, that pattern responses were specific to changes in spatial contrast and not merely to changes in local luminance. These authors studied the relation between "luminance" and "contrast" VEPs further (Spekreijse and Estevez 1972; Spekreijse et al. 1973) using onset, offset and contrast modulation of low contrast checkerboards accompanied by change in overall luminance. In each case, identical changes in spatial contrast produced very similar responses, independently of whether this change was achieved by luminance increase or decrease. They concluded that these responses were mainly the result of the change in spatial contrast.

Both the spatial frequency specific and the contour models of Padmos and co-workers (1973) predicted that the response to pattern stimulation would be optimum for a particular spatial frequency. It might be expected, therefore, that a plot of response amplitude against spatial frequency would show a bandpass or spatial tuning function. All types of pattern VEP have been shown to contain at least some components which demonstrate this property (see section 3.3.b). The contour model of Padmos and co-authors (1973) predicted spatial tuning by virtue of the amount of contour in the stimulus. Response amplitude would rise with an increase in the amount of contour (i.e. a decrease in check size) up to a point beyond which contours (i.e. high spatial frequency edges) are no longer visible, beyond which amplitude would drop. The luminance model, however, would predict that the amplitude/spatial frequency function should show a low pass characteristic. The response amplitude would be constant over a range from the largest check size (lowest spatial frequency) down to a value determined

by the size of the luminance sensitive summating elements. Individual checks which were much smaller than the summating elements would not elicit a response since the summated responses to the light and dark areas would cancel out. Therefore, once spatial frequency was in excess of this critical level, response amplitude would rapidly decrease. These workers found that the response to checkerboard onset showed evidence both of spatial tuning and of dependence on the presence and number of contours in the stimulus. Since the response did not show the onset-offset symmetry which might be expected from the SFS model, they proposed that the contour model gives a better representation of the behaviour of the pattern onset-offset response in man. They considered, however, that the properties of this response in the monkey were better related to the SFS model. The differences between man and monkey were thought perhaps to be the result of the differently organised architecture of the visual cortex in the two species.

From the above, it would appear that the "contrast" or "pattern" origin of at least the pattern onset response has been established. There is, however, much evidence of differences in behaviour of the responses to pattern onset, pattern offset and pattern reversal, and even of different components within each response (see section 3.3). This suggests that there may be several mechanisms involved in the generation of the pattern VEP.

3.4b Contour- and contrast-specific mechanisms and non-pattern-specific components in the pattern onset-offset VEP

Jeffreys' observations on the stimulus related properties of the pattern onset-offset components led him to propose the involvement of two mechanisms in the generation of the pattern onset-offset response (Jeffreys 1977). Contrast-specific processes are sensitive to the presence of pattern or "spatial contrast" in the stimulus but do not depend on the presence of well defined contours or edges. They show a definite relationship with stimulus contrast over a wide range and show saturation at relatively high levels. They are comparatively resistant to attenuation by defocus, pattern pre-exposure and presence of steady outlines. Contrast-specific processes contribute to component CI of the onset response and also to the offset response. Contour-specific processes are very responsive to and dependent on the presence of sharp contours or edges in the stimulus. They are very sensitive to structural detail and respond best to discontinuous pattern elements. They are relatively insensitive to actual contrast levels, saturating at lower levels than contrast-specific processes. They are markedly affected by pattern pre-exposure, adaptation, defocus and the presence of steady outlines. Contour-specific processes form part of the pattern onset response only, contributing predominantly to components CII and CIII but also to a lesser extent to CI.

Jeffreys (1977) attempted to draw parallels between these processes and populations of neurones in the visual cortex. He suggested that the contrast-specific portion of CI might be related to the activity of simple cells in the striate cortex. He commented on Maffei and Fiorentini's (1973) finding that such cells in the cat showed a linear relationship between response amplitude and log stimulus contrast. The sensitivity of CII and CIII, i.e. the contour-specific processes, to discontinous borders suggested to Jeffreys (1977) that they might originate in hypercomplex cells. The form-specific adaptation properties of CII and CIII (see Section 3.3d), caused Jeffreys to suggest later (Jeffreys and Musselwhite 1986) that these components might be related to contour-sensitive cells found in the monkey.

In addition to these pattern-related components, Jeffreys (1977; 1982) has also demonstrated the presence of small, independent non-pattern-specific components in the pattern onset VEP. These are a negativity at 150msecs and positivities at 100 and 200msecs. The P100 component was actually only found to be present when pattern onset was accompanied by a change in mean luminance but the P200 and the more prominent N150 were found under conditions of constant luminance.

3.4.c The relationship between the responses to pattern onset, pattern offset and pattern reversal

Several groups of workers have looked at the relationship between the signals elicited by these different forms of pattern stimulus. Estevez and Spekreijse (1974) conducted a series of experiments in which the initial mode of stimulation was that of checkerboard onset-offset. In successive runs the luminance levels of the two sets of checks were gradually adjusted until the stimulus had changed to pattern reversal. The data showed an apparent relationship between the pattern reversal response and the pattern offset or "contrast decrease" response. The pattern reversal VEP was thought to contain a contribution from the pattern onset or "contrast increase" response although no contribution analogous to component CII was found.

Jeffreys (1977) found that the response to pattern offset contained a component which was possibly related to the contrast-specific portion of CI. Neither his offset response nor the response to pattern reversal, however, showed evidence of components analogous to CII or CIII. From Jeffreys' (1977) results it appeared that the major positivity of the pattern reversal response contained two superimposed positive peaks. Ochs and Aminoff (1980) also found sub-components in the pattern reversal response of one of their subjects. In an experiment similar to that of Estevez and Spekreijse (1974), Jeffreys' (1977) findings indicated that these two components may be related to

component CI of the onset response and the major positive peak of the response to pattern offset.

The absence of components analogous to the contour-related CII and CIII in the offset response might be expected considering the effects on these components of standing contrast (Jeffreys 1977; Spekreijse 1980). It may be that the presence of the pattern during the onset period is enough to cause adaptation of the contour-related processes. For the same reason Jeffreys (1977) considers that there is unlikely to be much contribution from these components when using steady-state onset-offset stimulation or contrast modulation about a steady mean vlaue.

Similarities between responses to pattern offset and pattern reversal have been found by other authors (Kriss and Halliday 1980; Ochs and Aminoff 1980; Van Lith et al. 1981). Ochs and Aminoff (1980) commented that adaptation to a checkerboard pattern caused the pattern onset response to resemble that elicited by pattern reversal in waveform and latency. They considered also that exposure to the pattern during the onset period might cause enough adaptation of the visual system to affect the response to pattern offset. This might explain the similarity between offset and reversal responses. Spekreijse (1980) commented that the behaviour of the pattern reversal response in relation to various stimulus parameters such as check size was more like that of the pattern offset response than pattern onset.

3.4.d Contrast, motion and the pattern reversal response

In the last section, the relationship between pattern onset, pattern offset and pattern reversal responses were discussed and it appeared that the pattern reversal response could be explained on the basis of an interaction between mechanisms responsive to pattern onset (contrast increase) and pattern offset (contrast decrease). There is, however, a growing body of evidence to suggest that the response to pattern reversal might be more closely related to the activity of mechanisms which detect motion than of those detecting spatial contrast.

Clarke (1973) looked at the responses elicited by stationary and moving visual noise patterns. He studied the waveforms and scalp distributions of the responses to onset, offset and reversal of pattern motion and to appearance and disappearance of stationary and moving patterns. He found strong relationships between, on the one hand, motion offset, motion reversal and pattern appearance VEPs, and on the other hand, between motion onset and pattern disappearance responses. Clarke considered the possibility that the signals elicited by the motion stimuli were related to the effects of movement on the effective contrast of the pattern. The response to motion onset would then be the result

of the decrease in contrast caused by smearing of the image on the retina, and that to motion offset would be related to the effective increase in contrast occurring on cessation of movement. Similarly, the motion reversal response might be elicited by the periodic appearance of a stationary pattern at each point of reversal. Clarke found, however, that the behaviour of the motion responses was difficult to explain in these terms. In particular, earlier work (Clarke 1972) had shown that the motion reversal response was almost certainly not the result of the reduction of stimulus velocity at the point of reversal. Clarke (1973) therefore rejected this idea, concluding that the motion responses do in fact originate in movement detecting mechanisms.

Spekreijse, Dagnelie, Maier and Regan (1985) investigated responses to pattern displacement in addition to those to motion onset and offset, using checkerboard patterns. They discovered that abrupt displacement of a checkerboard in increasing amounts up to one check width generated a response which was qualitatively similar to the pattern reversal VEP. They also showed that the onset and offset of motion elicited separate signals which, when the time interval between onset and offset was small, interacted to produce a response waveform very much like that of the displacement VEP. They concluded, therefore, that the pattern reversal VEP is equivalent to a response to motion onset closely followed by a response to motion offset. These authors considered that the interaction of motion onset and motion offset detecting mechanisms as an origin for the pattern reversal VEP is a much more satisfactory explanation than that put forward earlier (Estevez and Spekreijse 1974), i.e. the interaction between mechanisms responsive to contrast increase and decrease. Fenwick and Turner (1977) demonstrated a linear relationship between pattern displacement (in terms of percentage of check size) and the amplitude of the VEP elicited.

Dagnelie, Vries, Maier and Spekreijse (1986) conducted experiments on contrast and motion responses in the macaque, using pattern appearance-disappearance and motion onset-offset stimuli. They implanted subdural electrodes in foveal and peripheral regions of area 17 of the visual cortex in order to test the contribution of these regions to the motion response. They found that in the periphery pattern reversal VEPs could, as in man, be synthesised from the responses to onset and offset of motion. In the foveal region, however, a response to motion as such was not found. Responses to motion onset and offset at the fovea could be attributed entirely to, respectively, responses to pattern disappearance (contrast decrease) and pattern appearance (contrast increase). The authors concluded, therefore, that although both motion and contrast detecting mechanisms are present in the periphery, the responses of the foveal area to both motion and pattern reversal stimuli are the result of the operation of mechanisms sensitive to contrast. It would appear, therefore, that both contrast and motion sensitive mechanisms are involved in the pattern reversal VEP.

3.4.e Pattern and movement sensitive mechanisms in VEP generation; relation to sustained and transient parallel visual channels

As discussed in Chapter 2, psychophysical and electrophysiological studies have shown that there are independent mechanisms or "channels" in the visual system which are sensitive to spatial frequency and orientation (Campbell and Kulikowski 1966; Blakemore and Campbell 1969; Campbell and Maffei 1970; Tolhurst 1973; Kulikowski and Tolhurst 1973). It is generally considered that there are two sets of channels which are selectively responsive to the qualities of pattern and movement in a visual stimulus. "Pattern" or "sustained" mechanisms appear to be sensitive to stationary stimuli containing high spatial frequencies, whereas "movement" or "transient" detectors are more responsive to low spatial frequencies, moving stimuli and high repetition rates.

Psychophysical studies show that transient processes are responsive to changes in contrast i.e. modulation depth and are independent of mean or steady contrast levels (Kulikowski and Tolhurst 1973; Bodis-Wollner and Hendley 1977). Kulikowski (1977b) has used this criterion to separate pattern and transient components in the VEP. Bodis-Wollner and Hendley (1977) have demonstrated that psychophysical and electrophysiological responses to reversing sine wave gratings are affected both by mean contrast and contrast modulation depth. They consider, therefore, that there are visual mechanisms represented in the VEP which are responsive to steady contrast as well as those responsive to contrast changes.

Kulikowski (1977b) has proposed that at medium spatial and temporal frequencies e.g. 6 cycles per degree at 1.67Hz, pattern onset and pattern reversal VEPs are dominated, respectively, by pattern related/sustained and movement-related/transient mechanisms. At low spatial frequencies, both responses are dominated by transient mechanisms, hence their similarity in shape. In addition, the subjective appearance of the two types of stimulus is very much alike, both giving the impression of movement. Such similarities are abolished when any element of high spatial frequency is introduced, whether it be a grating with a high frequency fundamental, or lines and/or edges, such as are present in line gratings or checkerboard patterns (Kulikowski 1977b).

Although the pattern onset response appears to be related mainly to pattern mechanisms, there is evidence to suggest that the major positive component in the offset response is influenced by motion sensitive processes. The fact that this component is maximally sensitive to lower spatial frequencies and also its apparent links with the pattern reversal response support this argument (Kulikowski 1977b; Biersdorf et al. 1979; Vassilev et al. 1983).

Some authors recognise the distinction between VEPs related to pattern (or "contrast") and "local luminance" detecting mechanisms e.g. Bodis-Wollner and Hendley (1977). Kulikowski (1977b) considers that responses related to local luminance changes could be better termed "contrast transient" VEPs since they are in fact related to contrast change or modulation which can be expressed as a change in local luminance. Both Kulikowski (1977b) and Bodis-Wollner and Hendley (1977) suggested the possibility that these pattern and movement (or luminance) detecting mechanisms may be related to the parallel X- and Y-cell systems which have been found in mammals (see Chapter 2).

Other workers have related their findings to the operation of parallel visual channels. Vassilev and co-workers (Vassilev and Strashimirov 1979; Vassilev et al. 1983) suggested that the increase in latency of the pattern onset response associated with increased spatial frequency can be attributed to a change in balance between the operation of faster transient and slower sustained systems. They consider that the absence of a clear pattern offset response at high spatial frequencies lends weight to this argument. Parker and Salzen (1977a, 1977b), however, regard the change as taking place within the transient system only. Both of these groups relate the latency increase to the increase in visual simple reaction time (RT) which occurs with an increase in spatial frequency. A relationship between the two seems unlikely in the light of Musselwhite and Jeffreys' (1985) finding that there is no effect on pattern onset CI latency comparable to that on RT with gratings of equivalent suprathreshold contrast. Jones and Keck (1978) consider that their additional early negative component appearing at low spatial frequencies may represent the activity of the transient system, whereas their main negative component reflects the operation of sustained mechanisms.

As described in Section 3.3.b, a plot of VEP amplitude against contrast appears to consist of two linear functions, one for high and one for low contrast. Campbell and Maffei (1970) associated this phenomenon with foveal and parafoveal contributions to the VEP. Nakayama and Mackeben (1982), working on the alert primate, also found a change in gain. They rejected the suggestion made by Campbell and Maffei (1970) on the grounds that they were able to demonstrate both high and low contrast functions with a small (2 x 2°) target, and also with high spatial frequency gratings which would be expected to elicit little response from peripheral retinal areas. They attributed the phenomenon to the operation of separate neural mechanisms. Kulikowski's group (Bain and Kulikowski 1976; Murray and Kulikowski 1983) have suggested that the change in gain is the result of the alteration in dominance of movement detecting mechanisms to that of those detecting pattern.

CHAPTER 4

The visual evoked potential. II. Topographic aspects and relation to stimulus visual field location

4.1 Introduction

The determination of the location of cortical sources of the VEP and its individual components is a longstanding problem. Since, in general, intracortical recordings on humans are not possible, the investigation of source locations has been carried out largely by means of the study of the scalp topography of the response and the manner in which waveform and distribution vary according to the location of the stimulus in the visual field. The first part of this chapter discusses some of the methods used in topographic recording and the problems involved. Section 4.3 outlines some of the approaches taken to the interpretation of the recorded data in terms of source locations. In section 4.4 the results and interpretations of a number of VEP studies using different types of stimulus are described. Finally, section 4.5 adds to the discussion of physiological significance of VEPs begun in section 3.4 For a detailed account of the more technical aspects of VEP recording and interpretation the reader is referred to Regan (1972) and Colon, Visser, Weerd and Zonneveldt (1983).

4.2 Topographic recording methods and associated problems

4.2a Number and location of recording electrodes

The number of recording channels used in the study of the scalp distribution of the VEP has varied enormously. Particularly in early studies (e.g. Cobb and Morton 1970) as few as four channels have been used and in several cases more than 40 (e.g. Lehmann et al. 1977; Darcey et al. 1980a). Electrode positions have often been determined according to a percentage scale such as the International 10-20 System (Jasper 1958) (e.g. Haimovic and Pedley 1982a; Harding et al. 1980) or they may have been placed at set distances from scalp landmarks as in the "Queen Square" system (e.g. Halliday et al. 1977). In some instances where large numbers of electrodes have been used, positions have been determined by angular separation (e.g. Darcey et al. 1980a; Thickbroom et al. 1984b). Workers using 5-16 channels have tended to restrict the electrode montage to occipital and parietal areas. Some investigators have used midline longitudinal (sagittal) and/or single horizontal (transverse) rows of electrodes, particularly in the study of altitudinal and lateral hemifield responses respectively (e.g. Jeffreys and Axford 1972a and b; Lesevre and Joseph 1979). Others have used several horizontal rows of electrodes placed mainly over the occipital area (e.g. Hoeppner et al. 1984; Drasdo

1982). The exact position of recording electrodes can influence the apparent distribution of response components. Of particular importance is the location of the reference electrode in monopolar recordings and this problem is discussed below.

Obviously, if large numbers of electrodes are used a more accurate representation of the scalp distribution of a response may be obtained than if only a few derivations are employed. The use of extensive electrode arrays does, however, lead to several problems. Firstly, there are the physical restrictions imposed by numbers of available recording channels and the data handling capacity of the averaging system. Some authors operating with limited numbers of channels have split their montage into sections and recorded over two or more sessions (e.g. Thickbroom et al. 1984b; Butler et al. 1987). There is, of course, the problem of inter-session repeatability but quite often electrode positions have been used which are common to all sessions as a check on consistency.

4.2b Representation of scalp distribution data

The second major problem is the difficulty of visualising the distribution of response components across the scalp directly from voltage-time plots. Workers using lines of electrodes have often represented their data as component amplitude profiles across these lines, which give some impression of spatial variation (e.g. Jeffreys and Axford 1972a and b). The disadvantage of such displays is that they can only provide information in a single dimension at one time. Quite early on in topographic VEP recording, investigators started to use equipotential lines to represent scalp distribution two-dimensionally, in the form of contour maps. Lehmann and co-workers (e.g. Lehmann et al 1977; Lehmann and Skrandies 1979b; 1980b) have used mapping techniques extensively since the early 1970s. Although many workers have used lines to represent the contours (e.g. Biersdorf and Nakamura 1973; Lehmann et al. 1977; Kooi et al. 1973), more recently mapping display systems have been developed which utilize colour scales to represent voltage levels (e.g. Duffy et al. 1979; Thickbroom et al. 1984b). Determination of potential levels between electrode positions on the map has usually been by means of a four nearest neighbours linear interpolation (Buchsbaum et al. 1982). Some workers considered, however, that the possibility of peak activity occurring between electrode positions should be accounted for. This is done by application of an algorithm which produces a more realistic curved interpolation similar to that which might be drawn by eye (Townsend 1987; Butler 1987).

Although maps enable the two-dimensional visualisation of response distribution at a particular latency, a series of such maps is required to show how the scalp potential field varies with time. Another method of representing temporal changes in spatial

distribution has been developed by Remond's group (e.g. Lesevre and Joseph 1979). In "chronotopographical" analysis of response topography, contours are used to represent the changes in potential along a line of electrodes, usually transverse or sagittal, over a period of time. Again, voltage levels between electrodes are found by interpolation. This method has the advantage that the display can be compared readily with a voltage-time plot and normal "components" identified. The fact that it is limited to a line of electrodes could be a disadvantage in that the choice of location for this line may not be appropriate for the study of all components, a criticism which can be levelled equally at all studies using vertical and/or horizontal electrode rows.

The localisation of scalp responses is also influenced greatly by the recording method. Many topographic studies have employed common reference recording (e.g. Michael and Halliday 1971; Jeffreys and Axford 1972a and b), quite often using an average reference (e.g. Lehmann and Skrandies 1979b; Darcey et al. 1980a and b). Others have used bipolar recording (e.g. Cobb and Morton 1970) or source derivation (e.g. Clement et al. 1985; Srebro 1985) techniques. The lateralisation of the hemifield pattern reversal response is particularly affected by whether a recording is monopolar or bipolar, as discussed below.

4.2c Identification of components

One difficulty which arises in VEP recording in general but is particularly problematical with extensive electrode arrays is that of identification of individual components within the response. The interactions between components in space and time mean that it is difficult to separate them for the purpose of locating their generators (Vaughan 1982). Jeffreys (1977, 1980) has stressed the importance of distinguishing between peaks and underlying components. In order to study the stimulus related properties of components CI and CII of the pattern onset response, he uses stimulus visual field locations and electrode arrangements which selectively enhance each component in turn whilst minimising the other. A left half-field target, according to Jeffreys' findings will, in most subjects, produce a distinct positive CI on the right (contralateral) side of the head which often inverts across the midline (Jeffreys and Axford 1972a). CII, however, is relatively small and fairly symmetrical about the midline. A recording between two electrodes 5 cm to either side of the midline shows a large positive CI with little contribution from CII. In the lower half-field VEP, the negative CII peaks on the midline and falls off rapidly to either side. CI, however, has a much flatter distribution. A recording between electrodes on the midline and 5 cm to one side shows an enhanced CII with little apparent contribution from CI. Lehmann and associates (e.g. Lehmann and Skrandies 1979b, 1980b) have devoted a great deal of attention to the problem of identifying components and determining their latency. Lehmann and Skrandies (1980b)

suggested that a "component" could be considered as "a reflection of synchronous (or almost synchronous) activity of a large neuronal population in a given area". At times of maximum neuronal activity this should be reflected as a maximum in electrical field power on the scalp. The times at which such maxima in field power occur can therefore be considered as the latencies of the response components.

These authors suggested several means by which times of maximum field power could be assessed. The first involves determination of the root mean square (RMS) of the potential differences between all possible electrode pairs in the montage. This RMS measure of field power is reference-free but it can also be related to a common average reference. The "hilliness" of the field is determined by calculating the mean of the absolute voltage deviations at all electrodes from the average reference. A reference-free mean of the absolute potential differences between all possible electrode pairs can also be calculated. A final measure is the voltage range i.e. the maximum potential difference between any two electrodes. These methods give similar although not identical times of maximal field power.

For the lower half-field pattern reversal response, maximal field power occurs at three distinct time periods, these being 50-85 msecs, 85-120 msecs and 120-155 msecs. Of these, the latter two are the most clear and consistent and usually show peak activity at around 100 and 140 msecs respectively. During these time periods, the scalp distribution of the response remains fairly stable, undergoing rapid changes in the intervals between. Such components, which manifest themselves as an occipital positivity at 100 msecs and an occipital negativity at 140 msecs, are consistent with those distinguished by other authors (e.g. Blumhardt and Halliday 1979; Shagass et al. 1976; Haimovic and Pedley 1982a).

Recently, several groups of workers have employed principle component analysis (PCA) in the study of VEP topography. This mathematical technique, when applied to scalp distribution data, breaks down the signals into a series of underlying statistically independent components, the generators of which can then be studied. Skrandies and Lehmann (1982) have used PCA to study the hemifield pattern reversal response and Maier, Dagnelie, Spekreijse and Dijk (1987) have used it in the investigation of the cortical origins of VEPs elicited by a range of stimulus types.

4.2d Baseline determination

The observed waveform and distribution of a response can be affected markedly by the baseline against which amplitude is measured. Some workers have used the pre- or post-stimulus voltage level as a baseline (e.g. Jeffreys and Axford 1972a). This type of

approach suffers from the problem that arfifacts such as DC drift and other noise may not be constant across channels and can distort the apparent distribution of the response considerably. Lehmann and Brown (1980) advocate the use of "technical zero" as a baseline i.e. that level obtained by averaging the output of the system with short-circuited preamplifier inputs. Other authors have preferred to measure transients i.e. peak-to-peak amplitudes (e.g. Michael and Halliday 1971) but this method has the inherent problem of confounding "components" in the response (Goff et al. 1969).

4.2e Location of the reference electrode

The problem of where to place the reference electrode has no easy solution and is considered by Nunez (1981) and Katznelson (Chapter 6 in Nunez 1981). A reference electrode might be considered "inactive" if it is positioned at a relatively large distance compared with the size of the generator(s). It would seem to make sense, therefore, to place the reference as far away as possible i.e. at an extreme part of the body such as the wrist. It turns out, however, that there is no point in using such a "distant" location. Current flow due to generators in the brain is actually almost confined to the head, and as a result there is no effective difference between a reference position on the neck and elsewhere in the body.

Non-cephalic reference locations do, however, suffer from EKG artifact contamination. Some workers have used the balanced non-cephalic reference of Stephenson and Gibbs (1951) to get around this problem. In this method, electrodes are placed on opposite sides and therefore opposite "poles" of the heart, one over the right sternoclavicular junction and the other over the tip of the seventh cervical vertebra. The two leads are connected through variable resistors (maximum 20kΩ). By adjustment of these resistors it is possible to neutralise, to some degree, the activity picked up at the two leads. The output, which is used as the "reference", is therefore contaminated by the minimum amount of EKG. Some investigators object to the use of non-cephalic references since the effective "baseline" potential against which all others are measured is an unknown quantity and therefore cannot be accounted for (e.g. Lehmann 1987).

The use of cephalic reference positions does, however, have its inherent difficulties. One of these is that the skull is not a closed "shell"; it has openings and irregularities which distort the potential patterns because of the tendency for current to flow along the path of least resistance. This often means that current will follow a longer path in order to go through an opening rather than one directly through the high resistivity skull. This factor should be borne in mind particularly when using ear and nose reference sites.
Many investigators have used two-ear or mastoid electrodes linked through a conductor as a common reference. This method minimises the effects of EKG on the scalp

recordings since it provides a lower resistance pathway for cardiac current, reducing its flow through the scalp. This also has the effect, however, of "shorting" the two ears and forcing their potentials to be equal. This causes "arching of equipotential lines" around the ears, making the contours more symmetrical about the midline and so reducing any hemispheric differences. One way around this problem is to connect the two ears through a variable resistor. If the resistance is high enough, little current will flow through it and the scalp potentials will be undistorted. The reference potential can then be modified so that it has a value anywhere between that of the two ears. Although this may minimise EKG artifact, the appropriate setting varies for electrodes at different scalp locations. In addition, the same comment applies to this arrangement as to a non-cephalic reference in that the "meaning" of the reference is not known and it might present problems in the determination of generator locations.

Another popular method of surmounting the problems of reference location is that of "average reference" recording, in which the average of the potentials recorded at each electrode is computed for each moment in time, and the potential difference between each active electrode and this "average" displayed. Again, interpretation of such recordings requires caution since the voltage level recorded at one scalp position is affected by both the signals and the noise picked up by all other electrodes. Also, as with the non-cephalic reference, the "meaning" of the reference level is uncertain and so deductions about possible generator locations are more difficult to make.

Bipolar derivations are normally considered to be the differential recordings from two relatively close electrodes, particularly when they form part of a chain. Although the need for a single common reference electrode is eliminated these differential recordings can give ambiguous results regarding polarity of a response. A slight lateral shift in position of a dipole generator can lead to an apparent polarity inversion. This property has been made use of in clinical VEP recording where bipolar derivations are arranged in such a manner that "phase reversal" occurs between channels on the two hemispheres, as explained by Harding (1974). Bipolar recordings can also demonstrate markedly different scalp localisation of responses than that found with common reference derivations.

The importance of the placement of both active and reference electrodes on the scalp was highlighted in a study by Holder (1980) and the discussion by Holder, Harding and Halliday which followed it. Holder (1980) investigated the lateralisation of the half-field pattern reversal response in patients with homonymous visual field defects. He used a "modified Maudsley "montage which consists of bilateral occipital-Sylvian and occipital-parietal derivations, in which the occipital electrodes were placed 2 cm anterior and lateral to the inion. Recordings with full field stimuli demonstrated maximum

i.e. over the "correct" side. Recordings from electrodes 5 cm anterior and lateral to the inion, such as those used by Halliday's group (Barrett et al. 1976a) referred to more anterior ipsilateral electrodes showed variable lateralisation depending on the stimulus visual field radius and check size used. Such an effect was first demonstrated by Halliday's group (Barrett et al. 1976a and b) and is discussed in section 4.4b(iii). Holder (1980) suggested, therefore, that the use of a montage such as that used by Halliday ("Queen Square") in which electrodes 5 cm anterior and lateral were referred to a common midfrontal reference, could produce ambiguous results concerning the lateralisation of hemispheric defects. In the discussion following Holder's (1980) paper, Halliday suggested that Sylvian and parietal references were unsuitable since they would pick up activity from the ipsilateral hemisphere reducing effective signal amplitude. He also considered that active electrodes so close to the midline were more likely to be contaminated by the spread of the response across the midline from the opposite hemisphere. Harding commented that C3 and C4 were relatively inactive ipsilateral reference sities and that Fz was subject to contamination by eye movement potentials and by the ERG in flash stimulation. Although Halliday agreed that Rolandic sites were not particularly active he considered that when comparing responses between the two sides of the head it was better to use the same reference electrode rather than referring to separate ipsilateral electrodes. Nunez (1981) suggested that a common reference on the midline is unsuitable since it is guaranteed to contaminate recordings from one side of the brain with activity picked up from the other side. He considered that a series of well chosen bipolar derivations was more appropriate for localising activity to one hemisphere.

Michael and Halliday (1971) studied the effect of reference position on the responses to upper and lower field pattern reversal stimulation. They discovered that although polarity and distribution of responses was comparable with both of these references for lower field stimulation, targets in the upper field demonstrated differences between the two. Recording with linked ears produced a negativity at 105-110msecs peaking about 7.5 cm above the inion. With a midfrontal reference, however, a smaller negativity was observed anteriorly which disappeared in intermediate channels and was replaced by a positivity at 105msecs below the inion. This positivity was found to be particularly associated with the central (0-2°) part of the stimulus. The authors considered that one or other of these references must be picking up activity from the generators of the upper field foveal response. To study this problem they recorded responses from occipital electrodes referred to a chain of six alternative reference electrode positions running down the side of the head from the midfrontal position to the neck. For active electrodes above the inion, an upper field stimulus produced the largest negativity for the lowest reference points, its amplitude decreasing to a minimum for the midfrontal electrode. On an active electrode below the inion, a positivity was recorded at a similar latency which was largest with the midfrontal electrode, decreasing rapidly towards lower reference positions.

an active electrode below the inion, a positivity was recorded at a similar latency which was largest with the midfrontal electrode, decreasing rapidly towards lower reference positions. These effects fit in well with the predicted position and orientation of the upper field dipole generators, as shown in Figure 4.1. The foveal generator is positioned so that electrodes below the inion would record a positivity when referred to midfrontal and upper reference electrodes which face the opposite end of the dipole. Ear and lower references are, however, on the same side of the dipole as the active electrodes below the inion and so little response would be recorded. Anterior electrodes would, however, show a negativity as they are closer to the upper, negative, side of the dipole. The proximity of the ear reference to the upper field generators suggested to the authors that this reference was more active than the midfrontal electrode and therefore less suitable.

The fact that the midfrontal reference is at the opposite end of the dipole generator from occipital electrodes means that positive signals tend to be enhanced. This effect can also be seen clearly in the recordings of Lehmann and Skrandies (1979b Figure 1). It may be that occipital positivity is in fact further exaggerated by independent negative activity occurring in the frontal regions at a similar latency (Spitz et al. 1985).

Other workers who have made recordings using more than one reference position have found that there is little effect on their results (Jeffreys and Axford 1972a; Lesevre and Joseph 1979; Ermolaev and Kleinman 1983). Lehmann (e.g. Lehmann and Skrandies 1979b) has commented that moving the reference electrode only alters the absolute voltages measured at each electrode and does not affect the shape of the potential distributions on the scalp. The results of Jeffreys and Axford (1972a) and of Michael and Halliday (1971) bear this out. In the case of equipotential contour maps only the labelling of each line or its position on the colour scale changes, the shape of the contours remains the same (Lehmann and Skrandies 1979b).

A more recently developed method of recording and analysing EEG and EP data which eliminates the effect of reference location whilst retaining the power of generator localisation is "source derivation" which is discussed below.

4.3 Interpretation of topographic recordings

4.3a Dipole source localisation

Several investigators, particularly those conducting earlier studies, have used VEP waveforms and scalp distribution characteristics and their modification according to stimulus visual field conditions to predict directly the most likely locations of cortical generators. By making reasonable assumptions about the anatomical configuration of visual cortical areas and the arrangement of visual field projections on them these authors have attempted to explain the behaviour of responses on the basis of dipole sources. (The applicability of the "dipole" approximation has been discussed in Chapter 2). For example, Halliday and Michael (1970) and Michael and Halliday (1971) explained the polarity inversion of the pattern reversal P100 recorded in upper and lower hemifield responses on the basis of dipole generators on the lower and upper surfaces of the occipital lobe (see section 4.4b(iii)). Lesevre and Joseph (1979) and Drasdo (1980) have also made suggestions regarding cortical origins of the pattern onset response directly from scalp distributions. Drasdo (1980) based his predictions on the arrangement of a schematic map of visual cortical areas, which is described in Chapter 2.

Biersdorf and Nakamura (1973) and Biersdorf (1974) predicted source locations for the patterned flash response by analysing scalp distributions in terms of radial and tangential equivalent dipoles. According to this simplified approach, dipole sources which lie on cortical surfaces which are parallel to the scalp will be oriented radially, and common reference recordings will demonstrate a monopolar scalp distribution, with a single maximum on the scalp over the activie area. Tangential dipoles arise from cortical surfaces orthogonal to the scalp and produce bipolar distributions with positive and negative maxima along a line parallel to the dipole axis. These authors looked at the distributions of response components for field sector stimuli and attempted to deduce the orientation of the dipole generators by judging the degree to which they fitted into the radial and tangential patterns. Such generators have been modelled mathematically by Vaughan (1974).

The most commonly quoted dipole model for VEP generators is that of Jeffreys and Axford (1972a) who considered that the behaviour of CI of the pattern onset response could be explained on the basis of an origin in surface negative dipole sources in the calcarine area of the striate cortex. This "cruciform" arrangement of dipole generators in the striate cortex of the two hemispheres is illustrated in Figure 4.4 and discussed in section 4.4b(iv).

A given scalp distribution can, in fact, result from an infinite number of possible sources

of different depth, location and orientation. Hence a unique solution to the "inverse" or "backward" problem i.e. that of determining VEP source characteristics from scalp distributions, does not exist (e.g. Kavanagh et al. 1978; Nunez 1981). Solutions for the "direct" or "forward" problem i.e. that of determining the scalp potential distribution which arises from a given dipole source, are, however, readily available. If such computations are made for a series of possible "known" dipole sources, the distributions can be compared with actual recordings, allowing some deductions about source characterisitics to be made. This approach is the general basis of mathematical dipole modelling techniques which have been used to locate cortical sources of the VEP, and the principles behind and application of such techniques are discussed by Darcey (1979) and Nunez (1981).

Darcey and co-workers (Kavanagh et al. 1978; Darcey 1979; Darcey et al. 1980a and b; Lehmann et al. 1982) have developed a method for the localisation of single and multiple dipole sources and applied it to data on the scalp topography of luminance and pattern responses. Kavanagh, Darcey, Lehmann and Fender (1978) produced equations for the determination of scalp potentials arising as a result of a source or sources of known location and orientation for both homogeneous and inhomogeneous (three sphere) volume conductors. They then took actual recorded data on the scalp distribution of major flash VEP components in the form of equipotential contour maps and compared these with a series of maps computed from the model for different source configurations. Finding the model distribution which best matched that observed, the fine details were then manipulated using a computer program to give the optimum match using a least-squares estimation i.e. the sum of the squared deviations of the actual scalp potentials from those computed by the model was minimised.

This method predicted similar source configurations for both homogeneous and inhomogenous models but the latter were slightly more eccentric (further from the centre of the head) and also stronger, presumably due to the attenuating and smearing effects of the skull and scalp. Although the resolution of this method was found to be good, particularly for the homogeneous model, the equivalent dipoles computed for the flash response were felt to have little relevance physiologically since it was likely that the sources could be widespread across the cortex. Application to pattern onset respones (Darcey 1979; Darcey et al. 1980a and b) was much more satisfactory and predicted an origin for the CI component in calcarine cortex with visual field octant generators arranged in a similar manner to that suggested by Jeffreys and Axford (1972a). Application to pattern reversal respones (Lehmann et al. 1982) also yielded meaningful results. Henderson, Butler and Glass (1975) tested their own dipole localisation method using a model head in which current sources were embedded. They found that their method was valid both for homogeneous and inhomogeneous conditions.

4.3b Source derivation

An alternative approach to the localisation of cortical generators has been to detect the position of current sources and sinks on the scalp by means of "source derivation". The principles behind this method have been described by Katznelson (1981). A "source" can be defined as a region in which net current flows out through the skull, and corresponds to a region of relatively high cortical neurone activity. Regions of lower cortical activity accept this excess current which flows back into the skull at a "sink". Sources and sinks, then, represent areas of high current density. Source derivation involves the detection of areas of high and low current density and hence the technique can also be termed "current source density analysis" (although this description seems to be applied more commonly to intracortical source localisation using microelectrodes).

In order to determine the current source density on the scalp, the second spatial or Laplacian derivative of the scalp potential distribution is calculated using the expression

$$\nabla^2 V = \frac{d^2V}{dx^2} + \frac{d^2V}{dy^2}$$

where V is electrical potential and x and y are Cartesian co-ordinates. This essentially gives a measure of the rate of change i.e. gradient of potential. The points at which the value for the Laplacian derivation or "operator" is highest correspond to regions of maximum current flow out of or into the scalp i.e. sources and sinks.

The above equation can be shown to be approximately proportional to

$$V_1 + V_2 + V_3 + V_4 - 4V_o$$

Where 0 to 4 apply to electrodes and electrode "0" is at the centre of an equally spaced array of the four others. This arrangement can be used in the calculation of a "5-point" operator which would give the source density at electrode "0". The expression can be extended to include extra electrodes (at uniform intervals) and so, for example, 7- or 9-point operators can be used. If these arrangements are repeated across the scalp, the points of maximum source density i.e. sources and sinks can be estimated (within the limits of resolution imposed by electrode separation).

Hjorth (1975) has illustrated the application of the Laplacian operator to analysis of the EEG. He pointed out that the solution of a 5-point operator was equivalent to the superposition of the bipolar derivations in all four radial directions. So, for example, for an electrode at C3 the source density could be expressed as

$$C_3 \text{ (source)} = (C_3\text{-}Cz)+(C_3\text{-}F_3)+(C_3\text{-}T_3)+(C_3\text{-}P_3)$$

A simplified method of source derivation has been described by Clement, Flanagan and

Harding (1985) in which lines of electrodes were used. The source derivation was calculated by repeated application of a difference operator, first to common reference and then to the resulting bipolar derivations, so that source derivation can be seen to be essentially the "bipolar of a bipolar" derivation. One problem which this arrangement clearly demonstrates is the lack of information regarding source density at the edge of the electrode array. In effect, the electrodes at the two ends of the line are "lost". Hjorth (1975) overcomes this problem by using a 3-point operator on the edges of his electrode array i.e. the superposition of two bipolar derivations, and applying a correction factor which is calculated from the values at surrounding electrodes.

One obvious advantage of source derivation is that it is reference-free. It also produces a higher degree of response localisation than common reference or bipolar recording, which is particularly useful in the study of lateralistion of responses. Katznelson (1981) considers that a study of current source activity gives more meaningful results than the measurement of scalp potential differences alone.

Several groups of workers have applied source derivation in various forms to the study of EEG (Hjorth 1975; Wallin and Stalberg 1980) and VEP (MacKay 1984; Clement et al. 1985; Flanagan and Harding 1986; Thickbroom et al 1984a; Srebro 1985, 1987) with reports of improved localisation over common reference recording. As already commented, Flanagan and co-workers (Clement et al. 1985; Flanagan and Harding 1986) have used transverse and sagittal lines of electrodes. This cuts down on the number of channels and the amount of computation required but at the expense of more accurate two-dimensional resolution. MacKay (1984) used a method in which the source density at a point was calculated using three surrounding electrodes arranged as an equilateral triangle. Thickbroom and co-workers (1984a) used the average potential gradient for all electrode sites in their scalp montage. They calculated the "source derivation" for each electrode in turn by taking the weighted (according to distance) average of the waveforms at all other electrode positions and subtracting it from the waveform at the electrode being considered. This method has similarities to the average reference method of recording but gives values which are less affected by activity at more remote electrodes, because of the distance weighting.

4.4 Studies on VEP topography and dependence on stimulus visual field location.

4.4a The effect of stimulus size and eccentricity on response amplitude and waveform.

Early workers using both flash and pattern VEPs found that increasing stimulus size beyond the foveal area has little effect on the amplitude of the signals recorded. They concluded, therefore, that the VEP arises predominantly from stimulation of the central 2-4° of the retina (Rietveld et al. 1967; DeVoe et al. 1968; Padmos et al. 1973). This finding is not surprising in view of the disproportionately large foveal representation in the visual cortex and its proximity to scalp recording electrodes (DeVoe et al. 1968). Vaughan (1969) pointed out that more peripheral stimuli might be expected to activate (striate) generator areas on the mesial cortical surfaces, where signals from the two hemispheres would tend to cancel. It would appear, however, that stimulus element size has a bearing on the effectivity of stimuli at different eccentricities in the visual field. Harter (1970) investigated the effect of check size on the patterned flash VEP. He found that whereas relatively small checks (7.5-30') elicited maximal responses at the fovea (0-1.5° eccentricity), large checks (30-60') were optimum for more peripheral stimulation (4.5-7.5° eccentricity). Harter (1970) commented that the reason why Rietveld and co-workers (1967) had found no change in VEP amplitude beyond 3° eccentricity was that only one check size (20.5') had been used. Michael and Halliday (1971) recorded pattern reversal responses between 4 and 8° eccentricity using large (50') checks.

Several other groups of workers have studied the effect of pattern spatial frequency on the amplitude of the VEP at different retinal eccentricities. Meredith and Celesia (1982), using transient pattern reversal of checkerboard patterns and both Tyler and Apkarian (1982) and Cannon (1983), using steady-state grating reversal found that optimum spatial frequency decreases as targets occupy more peripheral areas in the visual field. Plant, Zimmern and Durden (1983) looked at spatial tuning and effects of field size on transient pattern reversal and pattern onset of sinusoidal gratings. They found that for a given spatial frequency, response amplitudes for both types of stimulus increased as field size was made larger, up to a saturation level, the size of which was smaller at higher spatial frequencies. Spatial tuning curves showed maximal amplitudes for both responses at lower spatial frequencies for larger field sizes. Both Harter (1970) and Ermolaev and Kleinman (1984) have stated, however, that check size has less influence at greater eccentricities.

Drasdo (1973) suggested that a target might be designed to take into account the variation in optimal spatial frequency across the visual field. This target would take the form of a "dartboard" (Barber and Galloway 1976; Ermolaev and Kleinman 1984) pattern in which

individual segments grew larger at increasing eccentricities. Such a pattern ought to stimulate cortical neurones uniformly from the centre of the visual field to the periphery. Barber and Galloway (1976) designed such a stimulus using the VEP data of Harter (1970) to calculate the appropriate segment sizes. In this target the individual elements subtended 5' at an eccentricity of 0.5° increasing to 140' at the 30° extreme. These authors used this stimulus to elicit pattern onset VEPs and compared the responses with those to checkerboard patterns of different spatial frequencies. VEP amplitude was found to vary with check size, being maximal at about 35' for the CI-CII transient. In all cases however, the amplitude was substantially larger when the dartboard pattern was used. Ermolaev and Kleinman (1984) based their dartboard pattern on the visual acuity data of Anstis (1974). Their element size ranged from 2' centrally to 30' at the largest eccentricity of 8°. They found that the VEPs elicited by dartboard stimuli were much more stable in terms of reproducibility than those for checkerboard patterns.

The spatial frequency selectivity of the VEP at different eccentricities in the visual field has been related to the receptive field properties of neurones in the visual system. Armington, Corwin and Marsetia (1971) suggested that ganglion cells might act as bandpass filters by virtue of their receptive field properties. Receptive field centre sizes and consequently spatial selectivity appear to change with visual field position both in the retina and in the cortex, with optimal spatial frequency decreasing as eccentricity increases (see Chapter 2).

Wright and Johnston (1982) studied the effect of grating length on the amplitude of the steady-state pattern reversal VEP. They found that response amplitude showed an initial linear increase from threshold as gratings were made longer up to a certain length, after which there was no net increase or even a slight decrease. This critical length appeared to be related to spatial frequency, being shorter for finer gratings. These authors considered that this behaviour might be related to the variation of optimal spatial frequency with retinal eccentricity, so that if for example, a target of moderate to high spatial frequency is applied to the foveal area, as its length is increased it will start to activate more peripheral areas which are less sensitive to that spatial frequency, and eventually a point will be reached where an increase in length will no longer produce an increase in response. This increase will obviously be able to continue for longer with lower spatial frequencies since more peripheral retinal areas will still be responsive.

Tyler and Apkarian (1982) found that selected localised regions in the visual field often gave two peaks in their spatial frequency tuning curves. These peaks were commonly separated by a factor of two. They related the peaks to the operation of distinct populations of cortical neurones which, they considered, might be located in separate cortical areas, for which the most likely candidates were V1 and V2. Such an effect

would be consistent with the findings of Movshon, Thompson and Tolhurst (1978) who showed that the optimal spatial frequencies for cells related to similar retinal eccentricities in these two areas in cat visual cortex were separated by a factor of three.

Meredith and Celesia (1982) conducted detailed studies on the effects of target size on the pattern reversal VEP at different retinal eccentricities. They found that a 2°18' stimulus elicited little or no response beyond the central 4° of the visual field. Increasing the size of the stimulus (with a corresponding increase in check size), however, produced a response outside this area. These authors found, in fact, that the minimum stimulus size required to elicit a response increased with retinal eccentricity. They considered that this effect might be related to the amount of cortical representation of areas at different eccentricities in the visual field, and so designed a further experiment in which the sizes of targets at three different eccentricities were adjusted in line with cortical magnification, using the data of Cowey and Rolls (1974). Based on a central stimulus of 2°18' they found that field sizes of 16°32' and 29°56' were required for targets outside the 8° and 14° meridians respectively. These "M-scaled" targets were thus expected to activate similar (34.73mm^2) areas of striate cortex. Meredith and Celesia (1982) found that such cortically equivalent targets centred at 8° and 14° eccentricity gave similar amplitude responses, whilst a target centred on fixation elicited signals of approximately twice the amplitude. They attributed this latter fact to the activation of both hemispheres of the visual cortex. They considered, therefore, that their data were consistent with the invariance principle of Rovamo and Virsu (1979) (see Chapter 2). The effect of making stimuli cortically equivalent was also studied by Tyler and Apkarian (1982) using steady-state pattern reversal responses. These authors found that roughly equivalent signals were elicited for stimulation of areas out to 32° eccentricity.

Flanagan (1985) conducted an experiment in which he used full and half-field stimuli calculated to activate a particular proportion of striate cortex using the cortical magnification equations of Drasdo (Drasdo 1977; Drasdo and Peaston 1980). He used field sizes of 3°, 10° and 30° diameter which, it was estimated, should stimulate cortical areas and hence elicit response amplitudes in the ratio of 1: 3 : 6 (if depth and orientation were neglected). Check size was also scaled accordingly, being 7'12" for the 3° stimulus. He then measured the amplitude of the pattern reversal response to these targets and compared the theoretical ratio with that actually obtained. Amplitudes were measured at an Oz electrode and also by integrating values over a transverse (in the case of lateral hemifields) and/or a midline sagittal (in the case of altitudinal hemifields) row of electrodes. Neither measure produced a ratio even approaching that expected. Values were variable but a ratio of approximately 1 : 1.5 : 2 was common. Flanagan (1985) considered, therefore, that a linear summation between responses from different sectors of cortex at scalp electrodes was unrealistic and that a complex relationship must exist,

due to the attenuation effects of generator depth and orientation and signal asynchrony (see also Chapter 2).

The position which a patterned stimulus occupies in the visual field with respect to fixation can also have a bearing on the morphology of the signal which is elicited. Several studies have reported an early negative component in the pattern onset response. This negativity commonly has a latency of around 75 msecs and is associated particularly with stimuli containing high spatial frequencies (Kulikowski 1977; Lesevre and Joseph 1979; Drasdo 1980; Parker et al 1982b; Ermolaev and Kleinman 1984; Russell et al 1986). This component seems to be mainly related to stimulation of the central 5° of the retina, and is reduced in amplitude or eliminated when the macular area is occluded (Lesevre and Joseph 1979; Ermolaev and Kleinman 1984). Drasdo (1980) termed this component "C0".

Ermolaev and Kleinman (1983) showed that the main negativity of the pattern onset VEP is composed of two peaks. The first, N100, is prominent in photopic conditions whereas in mesopic conditions the later peak, N130, dominates. The authors also showed (Ermolaev and Kleinman 1983, 1984) that N100 is associated particularly with central retinal stimulation and shows a marked reduction in amplitude when paracentral stimuli are applied. N130, however, is clearly seen with paracentral stimulation and in fact is slightly (although not significantly) larger than with central targets.

Halliday and associates (Blumhardt et al. 1978, Halliday et al. 1979) have looked at the effects of central and paracentral stimulation on the half-field pattern reversal response to large (50') checks. They found that masking the central 5-10° of a 16° radius stimulus reduced or eliminated the major ipsilateral positive component P100, whereas, it tended to enhance the contralateral N105 (see section 4). Reducing field size down to 10° or even 5°, however, had little effect on P100 but markedly attenuated N105. These authors concluded, therefore, that P100 and N105 must be mainly related to "macular" and "paramacular" stimulation respectively (Halliday et al 1979). Haimovic and Pedley (1982a) similarly related their contralateral N100 to peripheral stimulation, but considered that P100 was associated with macular and peripheral areas.

4.4b The relationship of the VEP scalp distribution to the stimulated part of the visual field and its implications with regard to generator sites

4.4b(i) The flash response

Allison and co-workers (1977) investigated the distribution of the flash VEP across the whole head. Among the many components which they defined was a positivity at a latency of about 130 msecs. This positivity appeared to consist of two overlapping

components, an anterior myogenic portion and a smaller occipital neurogenic portion, which were difficult to separate. The occipital portion is probably equivalent to Harding's P2 component (Harding 1974). Spehlmann (1965) found an anterior positivity at around 120 msecs in two of his subjects, which he suggested might be related to eye movements. He found maximum amplitudes for other components of the flash response just above the inion around the midline. Other workers have found maxima for the flash P2 component in a similar area (Nakamura and Biersdorf 1972; Whittaker and Siegfried 1983) although Kooi and Bagchi (1964) stated that their equivalent component was maximal in central regions.

Bourne, Perry and Childers (1971) divided their responses into two major features, the first of which (latency 10-120 msecs) was largest in the anterior part of their electrode array (parietal region) whereas the second (190-310 msecs) had a maximum around Oz. Nakamura and Biersdorf (1972) reported a similar phenomenon. These authors identified five components in the VEP elicited by red flashes. Components I, II, and III (N1, P1 and N2 in Harding's terminology) were maximal in the parietal area whereas IV and V (P2 and N3) were larger over the occipital region.

There seems to be little agreement on the lateralising behaviour of the flash response to half-field stimulation. Lehmann, Kavanagh and Fender (1969) were unable to localise the hemi-field flash response in normal subjects. They attributed this to the effects of light scatter, causing stimulation of the opposite half-field. Harding, Smith and Smith (1980) had similar difficulties. With low intensity light flashes these latter authors demonstrated maximum P2 amplitude over the cerebral hemisphere ipsilateral to the half-field stimulated, but as intensity was increased the peak response tended to shift contralaterally. They therefore repeated the experiment with continuous illumination of the other half of the target i.e. that not being used as a stimulus by means of an external light source, so reducing the effects of stray light. Under these conditions, Harding, Smith and Smith (1980) found distinct ipsilateral localisation of the P2 component at all flash intensities. Hoeppner, Bargen and Morrell (1984) also found that the flash VEP was larger over the ipsilateral hemisphere when recording with a midfrontal reference. Eason and White (1967) and Schreinmachers and Henkes (1968), both using eccentric stimuli, found that amplitudes of the flash response were larger over the contralateral hemisphere. Workers recording in patients with bitemporal hemianopic field defects associated with lesions of the optic chiasma found that the response was maximal on the side of the head ipsilateral to the stimulated eye i.e. over the hemisphere contralateral to the intact (nasal) hemi-field (Lehmann et al. 1969; Kooi et al. 1973).

Nakamura and Biersdorf (1972) found that their early components (I-III) lateralised consistently to the contralateral side of the head, often showing a polarity reversal below

the inion ipsilaterally. The later components (IV and V) however, showed no consistent lateralisation, tending to remain over the midline. These authors suggested two alternative dipole models to represent the sources of the early components, particularly the second (P1). The first of these models was a single dipole below the occipital pole, tangential to the surface of the brain, in the striate area. The second comprised two radial dipoles, one of which was surface positive in the parietal region of the contralateral hemisphere, the other surface negative opposite the inion in the ipsilateral hemisphere.

Spekreijse, Estevez and Reits (1977) studied various aspects of the luminance or homogeneous field VEP. They considered that the VEP elicited by flash or sine wave modulated blank fields can be divided in three sections on the basis of latency and temporal stimulus frequency. Such a classification was suggested by Ciganek (1961) (cited by Spekreijse et al. 1977). These three subsystems were thought to have different cortical origins. The primary response or high frequency subsystem (latency around 30 msecs) was thought to be generated in the primary visual cortex i.e. the striate area. Stimulation of each visual octant in turn using a small eccentric target caused reversals in polarity of the signal which are consistent with the cruciform model of striate cortex within the calcarine fissure (as discussed in section 4.4b(iv)). A striate origin was also supported by the fact that lower field targets produced higher amplitude signals than those in the upper field. Later work using PCA and dipole localisation estimations confirmed this suggestion (Maier et al. 1987). The medium frequency subsystem or secondary response (latency 100-120 msecs) showed maximal signal amplitude in occipital areas above the inion to either side of the midline. It was thought that this component might originate in the secondary visual cortex i.e. areas 18 and 19. This would fit in with the observed larger and more anterior response to lower half-field stimulation. Lateral half-fields produced a maximum over the ipsilateral scalp. It was suggested that the resultant dipole may be localised in the contralateral hemisphere but pointing towards ipsilateral electrodes. The sources of the late response or low-frequency subsystem (120-200 msecs latency) were thought to be widespread throughout the cortex and not specific to visual areas. Under Ciganek's (1961) classification, component P2 is part of the secondary response. Halliday (1982) stated that responses to full field flash stimulation show a maximum on the midline about 6 cm above the inion i.e. towards the upper part of the occipital area. Halliday's (1982) results also suggest that the flash P2 is larger over the hemisphere ipsilateral to the stimulated hemifield, although this asymmetry is not pronounced as in the case of the pattern reversal response (see section 4.4b(iii)).

Some authors have suggested that components which are recorded on the ipsilateral side of the head might arise as a result of callosal transmission of signals from the directly stimulated (contralateral) hemisphere. Lines, Rugg and Milner (1984) defined a major negative component which they termed "N160". This component (which may be

equivalent to Harding's N3) was recorded with flash stimulation confined to one visual hemifield over both contralateral and ipsilateral sides of the head. On ipsilateral channels however, the latency was longer and the amplitude smaller than on contralateral channels. The latency delay was more pronounced for occipital electrodes (around 13 msecs) than central electrodes (around 3 msecs) and was assumed to represent the interhemispheric transmission time. One possible criticism of these findings was that stray light from the stimulus may have spread across the midline, weakly activating the supposedly unstimulated half-field, producing a smaller, delayed signal. Later work (Rugg et al. 1985) showed that the latency delays were virtually unaffected by a change in stimulus eccentricity, suggesting that stray light was unlikely to be the cause. This later paper also demonstrated an effect on P120 (P2) which also peaked earlier over the contralateral hemisphere. The authors suggested that the ipsilateral VEP recorded in occipital electrodes might arise as a result of interhemispheric transmission of information to temporal visual areas. Kooi, Yamada and Marshall (1973) demonstrated an early contralateral negativity in the responses of patients with bitemporal hemianopia. These authors suggested that this component could be the result of commissural transmission between extrastriate areas.

Important information relating to the cortical origin of the flash VEP has come from patients suffering from pre-senile dementia of the Alzheimer type. The pathology of this disease affects the occipital cortical areas but spares the striate area. Recordings of flash and pattern reversal VEPs in such patients show that whereas the pattern reversal P100 is unaffected, the flash P2 component shows an increase in latency (Wright, Harding and Orwin 1984). It was suggested therefore that P100 might reflect the integrity of the striate area whereas the flash P2 relates to the condition of the visual association areas. The results of Kraut and co-workers (1985), as discussed in section 2.6a, suggest that their components N70, P100 and N130 all arise as a result of activity of neurones in the striate cortex.

4.4b(ii) <u>The patterned flash response</u>

Spehlmann (1965) found that the patterned flash VEP had a similar distribution to the blank flash response i.e. maximum just anterior to the inion with little obvious response beyond about 5 cm from it. Eason, White and Bartlett (1970) studied upper and lower half-field responses using single channel recordings. They found that lower field stimulation produced larger signal amplitudes and shorter latencies. The lower field response was also maximally sensitive to a larger check size than that for the upper field. These authors considered that a lower field target must be a more effective stimulus than one in the upper field, except for fine details. They commented that this asymmetry might relate to man's greater reliance on the lower half of his visual field. They also

suggested, however, that the differences in amplitude may relate to the location of the generators in the visual cortex.

Biersdorf and Nakamura (1973) and Biersdorf (1974) studied the scalp topography of the patterned flash response using equipotential contour maps in an attempt to elucidate its cortical origins. Stimulation of lateral halves of a 15^{o} (diameter) field with 15' checks elicited a contralateral occipital positivity at 84msecs which inverted across the midline. Similar behaviour was observed for a contralateral negativity at 150msecs. A 1^{o} radius half-field elicited much smaller respones with distributions which were fairly similar to the above, although the axis of the voltage distribution (the line joining positive and negative maxima) was tilted from the horizontal. Displacing the target away from fixation caused a reduction in signal amplitude and also in the difference between signals on the two sides of the head. These authors attempted to localize the cortical sources of these responses by interpreting the scalp distributions on the basis of tangential and radial dipoles (see also section 4.3a). They considered that their results were consistent with an origin for both components in dipole sources located on the contralateral striate cortex, oriented fairly tangentially to the scalp, and tilted slightly towards it. It was thought tht there could be little contribution from within the calcarine sulcus, because of cancellation effects between upper and lower field generators. This would suggest that the medial cortical surface was the prime contibutor to the response, since the equivalent dipole generator in this region is oriented tangential to the scalp.

Further studies by Biersdorf (1974) showed that the earlier component took the form of an occipital and parietal positivity for lower field stimulation, with a negativity in the same region for the upper field. Stimulation of lower quadrants led to a contralateral positivity and ipsilateral negativity and vice versa for upper quadrants. The quadrant dipoles tended to be variable but in general lateral half-fields appeared to be associated with tangential dipoles whereas altitudinal hemifield respones were more related to dipoles radial to the scalp. Biersdorf (1974) considered that these results were consistent with a striate cortical origin (this fits in with Jeffreys' "cruciform" model, as described in section 4.4b(iv)). The early component was compared by Biersdorf and Nakamura (1973) to a component at around 74msecs in the blank flash response (Nakamura and Biersdorf 1971), which also showed lateralising tendencies, as compared with later flash components which did not.

4.4b(iii) The pattern reversal response

The scalp distribution of the pattern reversal VEP has been studied extensively by Halliday's group using high contrast large (50') checks. Halliday and Michael (1970) stimulated 45° sectors i.e. octants of the central 8° of the visual field. They found a prominent wave at a latency of about 100 msecs which was common to all subjects tested. This component, which later became known as "P100" (e.g. Blumhardt et al. 1978), underwent an inversion in polarity from positive for lower field stimulation to negative when stimulating the upper field. Both upper and lower field stimuli produced a maximum signal amplitude at 5-7.5 cm above the inion. These authors (Halliday and Michael 1970) also discovered that stimulation of octants adjacent to the vertical meridian elicited signals of larger amplitude than those adjacent to the horizontal meridian. Responses to octants in the left or right half of the visual field were larger over the hemisphere contralateral to the stimulated half-field. Halliday and Michael (1970) felt that a polarity reversal for upper and lower vertical octants was not consistent with a P100 origin in calcarine (striate) cortex. Such an origin would predict more prominent responses and a clearer polarity inversion for the horizontal octants, since these have a representation on the cortical surface inside the sulcus itself, where the neurones related to upper and lower halves of the visual field are inverted with respect to each other. For the vertical octants, which are represented on the medial cortical surface, upper and lower field neurones lie parallel to each other and one might expect small amplitude signals and a less clear polarity reversal. In addition, the most prominent signals were recorded several centimetres above the area of striate cortex which would be expected to contain the foveal representation of the visual field.

The above findings prompted the authors to suggest an origin for P100 in extrastriate cortex, so that the generator for the lower field response would be on the upper surface of the occipital lobe, whereas that for the upper field response would be on the undersurface. The similarity in amplitude between lower and upper field signals did, however, cast some doubt on this theory. An alternative explanation was therefore put forward that the signals might be produced by two distinct sets of neurones in the same cortical region, possibly at different depths, activation of which would lead to surface potentials of opposing polarity. These authors investigated further using "double octant" stimuli which straddled the vertical meridian in the lower or upper half-field. The targets occupied the central 8° of the visual field, the central 2° or an eccentric annular area from 4-8°. For the lower field, all targets gave a maximum positivity at 2.5-5 cm above the inion, with a steep rate of fall-off in a posterior direction and a more gradual reduction anteriorly although the 0-2° stimulus did show a tendency to produce a slightly more posterior maximum. Amplitudes were largest for the 8° target and smallest for the central 2°. For upper field responses the signal waveform was affected by the position

expected to be larger in the ipsilateral channels, with the PNP complex seen contralaterally. With a posteriorly or postero-laterally oriented generator area, however, the largest P100 would be picked up on the midline or even, especially with stimuli confined to the foveal area, on the contralateral electrodes. In this latter situation the contralateral PNP complex would be obscured, appearing only at extreme contralateral electrodes if at all.

Beauchamp, Matthew, Small and Stein (1976) and Wildberger and co-workers (1976) suggested that the ipsilateral response might arise in the ipsilateral hemisphere as a result of interhemispheric transmission from the contralateral cortex via the carpus callosum. Recordings made in patients having undergone complete hemispherectomy, however, which demonstrate the presence of all components of both ipsilateral and contralateral complexes, show that the responses must arise in the hemisphere contralateral to the stimulated hemi-field (Blumhardt et al. 1977; Blumhardt and Halliday 1979). Blumhardt and Halliday (1979) found that the response to a full field stimulus of 16° radius shows a maximum P100 on the midline, 5 cm above the inion, falling off rapidly to either side. Computation of the predicted full field response by summation of responses from the two lateral hemi-fields shows that this corresponds fairly well with the activity actually recorded. It can be seen that the midline maximum of the full field response is a result of the summation of the ipsilateral NPN complexes from each half-field. The lateral attenuation of the response is due to cancellation by the phase-reversed contralateral PNP complexes occurring at the same latency (Halliday 1982). The principle of summation of partial field responses can be extended to quadrants and even octants.

Blumhardt and Halliday (1979) also discovered that stimulation of upper field quadrants tends to lead to a more prominent contralateral N105 than is seen for the half-field response, whereas lower quadrant stimulation is associated with greater spread of P100 across the midline. The enhancement of the contralateral complex with upper quadrant stimulation often results in distortion of the midline signal, causing an apparent increase in P100 latency. At lateral channels, where the individual components could be seen clearly, no latency change was evident. These authors considered that the contralateral PNP might result from the recording of activity from the opposite side of the posteromedial dipoles which give rise to the ipsilateral NPN. The widespread NPN associated with lower quadrant stimulation might be expected if the signal is arising from the lower field projections towards the upper surface of the occipital lobe. The increased prominence of the contralateral components with upper quadrant targets is consistent with the extension of the associated projection area onto the under-surface of the hemisphere. Here, the generator area is tilted obliquely so that the negative side of the dipole would point towards the contralateral electrodes. In keeping with this idea, the longitudinal distribution of altitudinal half-field responses suggests that the upper field response

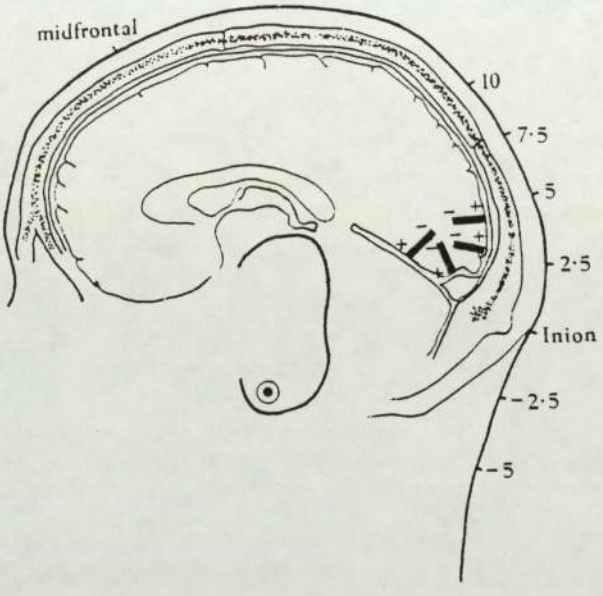


Figure 4.1

Diagrammatic representation of the relative positions and orientations of the hypothetical dipoles representing the central and peripheral parts of the upper and lower field. Peripheral and central lower field dipoles are at 3 and 4 o'clock, central and peripheral upper field dipoles are at 5 and 8 o'clock, respectively.

(After Michael and Halliday 1971)

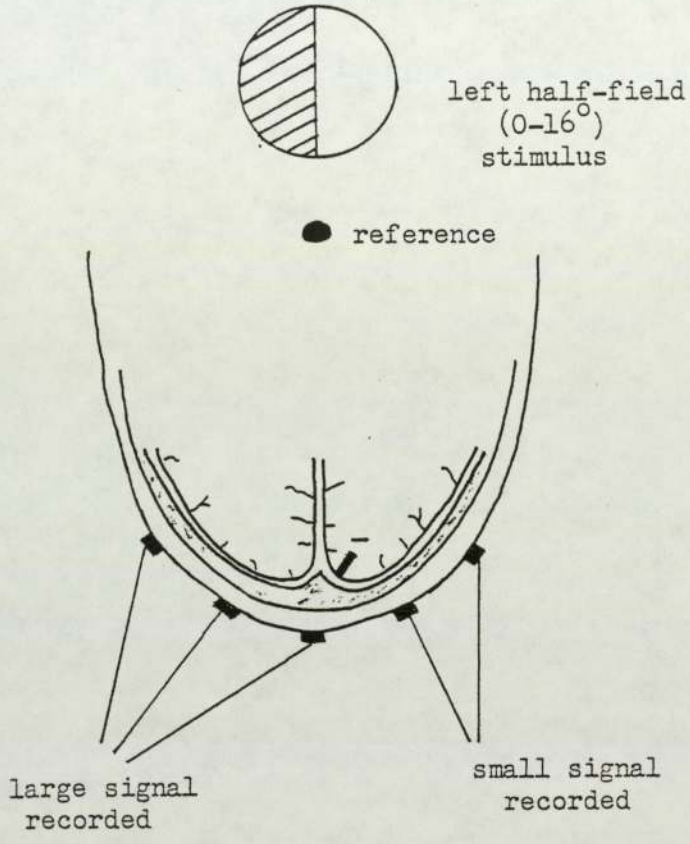


Figure 4.2

Schematic representation of the relationship between the cortical generater area for the left half-field pattern reversal response and the scalp electrodes. The electrodes at midline and ipsilateral to the stimulated half-field are best placed to record the response from the posteromedial surface of the contralateral visual cortex.

(After Barrett et al. 1976)

hemisphere. An ipsilateral P100 maximum for common reference recordings has been found by other workers (Shagass et al. 1976; Harding et al. 1980; Haimovic and Pedley 1982a; Hoeppner et al. 1984). This "paradoxical lateralisation" (Barrett et al. 1976a and b) did not occur with bipolar recordings, with a maximal amplitude being recorded on the contralateral side (see also Shagass et al. 1976; Harding et al. 1980; Hoeppner et al. 1984). Comparison of monopolar and bipolar recordings, however, showed that the reason for contralateral maximum with bipolar leads is that the maximum voltage gradient occurs between the electrode on the midline and that adjacent to it on the contralateral side. The largest amplitude is actually recorded at the midline, with little activity contralaterally and a larger but fairly even response ipsilaterally.

Barrett and co-workers (1976a and b) suggested that the cortical generators of the response might be located on the medial and postero-medial surfaces of the occipital lobe. Figure 4.2 shows a schematic representation of a dipole generator in this region. As can be seen, due to the orientation of this generator, which is perpendicular to the cortical surface, electrodes on the midline and ipsilateral side of the head are more optimally placed to record the signal than those on the contralateral side. Reducing the size of the stimulating half-field down to 0-4° had little effect on the distribution of the response. Using a 0-2° stimulus, however, resulted in a less well lateralised or even contralateral maximum. This effect was explained by the authors in terms of the more posterior location of the foveal projection. At the tip of the occipital lobe, the cortical neurones and therefore the dipole generator would face in a posterior direction, so reducing or removing the ipsilateral bias. This change in lateralisation with a decreased field size has also been demonstrated by other authors (Harding et al. 1980; Meredith and Celesia 1982; Brecelj and Cunningham 1985; Kakisu 1985).

Harding, Smith and Smith (1980) found that reducing field size caused a shift of maximum P100 amplitude from ipsilateral to slightly contralateral. In addition, these authors investigated the effect of check size. Decreasing check size in a 0-14° radius half-field stimulus from 56' down to 11' had no effect on lateralisation, even though smaller checks might be expected to preferentially activate foveal areas. An effect of check size has, however, been found by other authors. Brecelj and Cunningham (1985) used 0-2° and 0-16° hemifield stimuli and 20' as well as 50' checks and found that the more contralateral spread of the major positive component with foveal stimulation was enhanced when using the smaller check size. A similar effect has been demonstrated for the steady-state pattern reversal response (Kakisu 1985).

Halliday, Barrett, Halliday and Michael (1977) stimulated octants of the central 8° of the visual field as did Halliday and Michael (1970), using a more extensive electrode array referred to a midfrontal position. Their results with vertical octants confirmed the

findings of Michael and Halliday (1971) with respect to upper and lower field stimulation i.e. lower field targets elicit a positivity above the inion, upper field targets produce a positivity below the inion with a negativity anteriorly. Upper vertical octants were also found to produce a contralateral negativity, sometimes accompanied by an ipsilateral positivity. Upper horizontal octants tended to produce a more pronounced but less well lateralised positivity. This became even less well lateralised for the lower horizontal octant, and with the lower vertical octant it was maximal on the midline or even contralaterally. It appeared, therefore, that an ipsilateral positivity as found by Barrett and colleagues (1976a and b) is associated with stimulation around the horizontal meridian.

Halliday and associates have investigated the more detailed form of the ipsilateral and contralateral half-field responses and their relation to stimulation at different retinal eccentricities (Blumhardt et al 1978; Blumhardt and Halliday 1979; Halliday et al. 1979) (See also section 4.4a). Blumhardt, Barrett, Halliday and Kriss (1978) found that a 16° radius hemifield elicited a P100 component which was maximal at midline and ipsilateral channels. This component was preceded and followed by negative deflections at around 75 and 145 msecs, forming a negative-positive-negative (NPN) complex. Over the contralateral hemisphere the response was usually smaller and consisted of a negativity, N105, flanked by positive deflections at 75 and 135 msecs, forming a positive-negative-positive (PNP) complex. Channels on the midline and slightly contralateral often showed a mixed or "transitional" response representing the interaction between the two complexes. There was considerable variation in position of the P100 maximum between subjects, so that in some cases the contralateral components were difficult to distinguish. These authors (Blumhardt et al. 1978; Halliday et al. 1979) found that occluding the central portion of the half-field target altered both the amplitude and the scalp distribution of the two complexes. Increasing the occluded portion up to 10° gradually reduced and then eliminated the P100, whereas the contralateral N105 first increased to a maximum amplitude before decreasing slightly. Consequently, with paramacular stimulation the contralateral complex often became larger and tended to spread further towards the midline. Blumhardt et al (1979) considered that the P100 was largely associated with stimulation of the central 0-8° of the visual field and that this was consistent with an origin around the occipital pole, as suggested earlier (Barrett et al 1976a and b). This theory is supported by the findings of Spalding (1952b) who suggested that the portion of striate cortex lying posterior to the calcarine fissure contains the representation of the central 8° of the visual field. The variability in amplitude and distribution of response components between individuals might be a result of the anatomical variability in the visual cortex, depending on how much of the central and paracentral visual field projections lie on the medial and lateral surfaces of the occipital pole. When the area of projection faces medially or postero-medially the P100 would be

expected to be larger in the ipsilateral channels, with the PNP complex seen contralaterally. With a posteriorly or postero-laterally oriented generator area, however, the largest P100 would be picked up on the midline or even, especially with stimuli confined to the foveal area, on the contralateral electrodes. In this latter situation the contralateral PNP complex would be obscured, appearing only at extreme contralateral electrodes if at all.

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response originates predominantly from projection areas on the inferior surface of the occipital lobe, whereas the lower field response arises from generators much closer to the scalp electrodes (Halliday 1982).

Kriss and Halliday (1980) found that lower half-field stimulation produced a generalised P100 at 5 cm above the inion. Upper field stimulation, however, elicited a negativity at 80 msecs at a similar position and a broad positivity at 120 msecs, with only a suggestion of polarity inversion below the inion. This effect was thought to be possibly related to the midline distortion associated with prominent contralateral components as suggested by quadrant responses (Blumhardt and Halliday 1978; Halliday 1982).

Haimovic and Pedley (1982b) studied pattern reversal responses in patients with different types of visual field defects in whom the areas of damage to the visual system had been fairly well defined. They found that patients who had cortical lesions associated with similar homonymous hemianopic defects had VEPs which were affected differently according to the location of the affected area. They suggested that the effects on their ipsilateral P100 and contralateral N100 might related to the involvement of the geniculo-calcarine pathway or parastriate and association areas of the cortex and proposed a model of cortical generators to explain these effects. In this model P100 is associated with activation of neurones in area 17, possibly as a result of synchronous EPSPs in cells deep in the cortex, which would result in a surface positive potential over this area. Independent but fairly synchronous activity spreading into parastriate cortex could lead to the surface negativity recorded contralaterally as N100. This negativity could be a result of either excitatory activity in superficial cortex or IPSPs in deeper layers. The orientation of the neurones in the striate area would lead to a maximum P100 on the midline or ipsilaterally. This fits in with the model of Halliday and associates (Barrett et al. 1976a). Lesions affecting the geniculo-striate pathway or area 17 itself would be expected to alternate or eliminate the VEP as a whole, since the parastriate response depends on activation of the striate area. In patients with lesions afffecting only the parastriate areas, loss of the contralateral N100 might be expected. P100 would remain intact resulting in a distorted response. These predictions fitted in with clinical findings.

The results and interpretations of Haimovic and Pedley (1982a and b) therefore, suggest that P100 arises from generators in the striate cortex. This does not agree with the earlier suggestion of Halliday and Michael (1970) and Michael and Halliday (1971) which indicated an extrastriate origin for this component. The results of later work by Halliday and associates (Barrett et al 1976a; Blumhardt et al. 1978; Halliday et al.1979), however, implicated the exposed part of area 17 around the occipital pole as the generator area. Although these authors have not stated outright that P100 has a striate

origin, Halliday (1982) does relate the behaviour of this component directly to visual field projections in this area.

Lehmann and co-workers have also studied the scalp topography of the pattern reversal response to half-field stimulation, with particular emphasis on the interpretation of equipotential contour maps derived from recordings using extensive electrode arrays (up to 48 channels). Lehmann, Meles and Mir (1977) compared the distribution of responses to upper and lower hemiretinal stimulation (i.e. lower and upper half-fields) using a large field (16^{o} radius) and large (50') high contrast checks in a single subject. Examination of the response waveform at occipital recording sites showed a major positive component peaking at 103 msecs (P100). Comparison of the waveform of upper field responses revealed a negativity of smaller amplitude at a similar latency, creating an apparent polarity reversal. An inspection of a series of maps at different points in time showed, however, that the most prominent component in the upper field response was a positivity which was maximal near the inion at a latency of 146 msecs. The study of the change in distribution of lower and upper field responses with time led these authors to suggest that the major positivities were related and that the results should be interpreted as demonstrating a delay in latency of the upper field response compared with the lower rather than as a polarity inversion. The maps of these two components at their times of peak amplitude showed similar scalp distributions. Lehmann, Meles amd Mir (1977) proposed that such a latency difference might be related to various anatomical and behavioural findings which suggest that upper and lower halves of the retina might have slightly different properties. For example, receptor density and visual acuity are both higher in the upper hemiretina, suggesting a higher level of visual performance in the lower half of the visual field. This, in turn, might reflect the greater importance to man of the inferior aspect of his visual environment. Later work on larger subject groups has confirmed this latency difference (Lehmann and Skrandies 1979a, 1979b; 1980a, 1980c; Skrandies 1984), as have the results of other workers (Flanagan and Harding 1986). Lehmann and Skrandies (1979a) found a delay of 11 msecs in the upper field response. Lehmann's group have also noticed that the maximum positivity is often slightly more anterior for lower field stimulation than for the upper field (Lehmann and Skrandies 1979a; 1980a; Skrandies et al 1980).

Lehmann and Skrandies (1979b) defined two major components in the lower half-field response. The major positive component, as previously described, had an occipital maximum near the midline at 102msecs. This was followed by an occipital negativity which again was often maximal near the midline, at 135msecs. In both cases, anterior electrodes tended to show a fairly flat distribution with a slight polarity inversion. These authors also studied the effect of lateral half-field stimulation using large (26^{o} radius) and "small" (13^{o} radius) targets on these components, (see also Lehmann and Skrandies

1980a). The large targets tended to elicit a maximum P100 on midline and ipsilateral channels. For the small target there was a tendency for slight movement of the peak response towards the contralateral hemisphere. These findings are in keeping with those of Barrett and co-workers (1976a and b). For both large and small targets the occipital positivity was accompanied by an anterior negativity contralateral to the stimulated hemifield. At a latency of about 140msecs, both large and small targets showed a contralateral occipital positivity and a negativity at more anterior electrodes on the ipsilateral side. Hence, the response at 100msecs was maximal occipitally for both lower and lateral half-field stimuli whereas the response at 140msecs shows an occipital negativity for the lower half-field target but an occipital positivity for lateral half-field stimuli. This difference in behaviour led these authors to suggest that the response at the two latencies might have separate neural generators. Lehmann and Skrandies (1980b) did consider, however, the possibility that the positive and negative components in the lower field response might arise as a result of excitatory and inhibitory activity in the same population of neurones.

Lehmann, Darcey and Skrandies (1982) recorded pattern reversal responses from scalp and intracerebral electrodes, and applied a dipole modelling procedure to locate the position of the VEP generator areas. These authors developed a computer program derived from data on potential distribution which was collected from recordings made from a model head with embedded current generators. They applied this program first to responses from a group of normal subjects and predicted equivalent dipoles for the generators of the half-field major positive component. Upper and lower field dipoles lie on the midline with their positive pole directed towards the occipital area, the lower field dipole being slightly more anterior. For right and left half-field stimulation, dipoles for both large and small targets are situated in the hemisphere contralateral to the stimulated hemifield, with their positive side pointing towards the electrodes on the ipsilateral scalp. The dipoles for the small target are oriented less ipsilaterally i.e. more towards the midline. These proposals are consistent with those of Barrett and co-workers (1976a and b). Intracerebral recordings in patients (Lehmann et al. 1982) indicated that for lower and upper half-field responses the generators were above and below the level of the calcarine fissure respectively. For 26^{o} lateral half-field stimulation intracerebral recordings showed symmetrical distributions across the midline, with ipsilateral positive and contralateral negative maxima. The authors considered that such a distribution could arise from an ipsilaterally oriented surface positive generator near the midline. A voltage profile from a parasagittal row of electrodes in one hemisphere showed that stimulation of the contralateral hemifield elicited a prominent negative occipital distribution, which is consistent with the above interpretation. Lehmann, Darcey and Skrandies (1982) considered that the estimated position and orientation of the dipole generators might be compatible with origins in extrastriate visual cortical areas. These authors felt that the

results were not consistent with a surface positive striate generator since this would be expected to produce a field maximum which was more posterior for lower field stimulation than for upper.

Adachi-Usami and Lehmann (1983) and Adachi-Usami (1984) compared the scalp distribution of upper and lower half-field responses to monocular and binocular stimulation. As found previously (e.g. Lehmann and Skrandies 1979a) the P100 elicited by lower field stimulation reached a maximum at a more anterior point on the scalp than that for the upper field. In addition, it was found that, for lower field stimulation the maximum for monocular stimulation was more posterior than that for binocular stimuli, whereas for upper field stimulation the reverse was true. Adachi-Usami and Lehmann (1983) related this finding to the proportions of monocularly and binocularly driven cortical neurones which might be expected to be greater in striate and extrastriate visual areas respectively. This interpretation would fit in with the anatomical organisation of cortical areas, since for regions above the calcarine fissure areas 18 and 19 lie more anteriorly than area 17, whereas below the fissure areas 18 and 19 are more posteriorly placed. Skrandies (1984) looked at the effect of grating spatial frequency on the scalp distribution of the response to a lower half-field target of 7^{o} subtense. He found that changing spatial frequency had no consistent effect on the location of the maximum response. Skrandies (1984) commented that this finding may be related to the anatomical representation of spatial frequency channels in the cortex, which may well be such that differential activation does not produce spatially separable responses on the scalp.

Flanagan and co-workers (Clement et al.1985; Flanagan and Harding 1986) have looked at the distribution of the pattern reversal response to large (14^{o} radius) fields and checks (56') using source derivation. They demonstrated a source near Oz for altitudinal hemifield stimulation which was slightly but not significantly more anteriorly distributed for the lower field target than with the upper. Full and lateral half-fields also produced a source at Oz; this was accompanied by a contralateral sink with right and left hemifield stimuli. Thickbroom, Mastaglia, Carroll and Davies (1984) found a midline and ipsilateral source and a contralateral sink at 96msecs for their pattern reversal responses.

4.4b(iv) The pattern onset response

The first detailed studies on pattern onset response topography were conducted by Jeffreys (1971) and Jeffreys and Axford (1972a and b), using up to 12° diameter fields and 14' high contrast isolated squares. These authors demonstrated that for a lower half-field stimulus the pattern onset CI was positive in polarity with a latency of 65-80 msecs whereas CII was negative, peaking at 90-110 msecs. The later peak CIII at around 180 msecs was also positive. Upper field stimulation resulted in a reversal of these polarities so that CI and CIII became negative and CII positive at similar latencies. Jeffreys (1971) looked at the antero-posterior distribution of the onset VEP with altitudinal half-field stimulation. Lower field responses showed a fairly symmetrical distribution with a maximum 2.5-5 cm above the inion. Upper field responses, however, showed a less well-defined maximum at 5-10 cm above the inion and a steeper fall-off towards the posterior aspect than the anterior. CII distribution for the lower field target varied according to stimulus eccentricity, becoming wider and more anterior as regions further from fixation were stimulated. Increasing eccentricity did not affect upper field CII distribution although the amplitude of this component was reduced. Jeffreys (1971) considered that the behaviour of CII with lower and upper field stimulation was consistent with an origin in extrastriate cortical regions on the upper and lower surfaces of the occipital lobe respectively. Stimulation of more eccentric regions of the visual field would then activate more anterior generator areas for lower field and more posterior (deeper) areas for upper field targets. Component distributions predicted from a dipole model based on this assumption showed reasonable agreement with recorded data (see Figure 4.4).

Jeffreys and Axford (1972a and b) studied the distribution of CI and CII for half-field, quadrant and octant stimulation using transverse and sagittal rows of electrodes. These authors found that, for left and right half-field stimulation a horizontal row of electrodes showed a polarity reversal across the midline for CI, which was positive contralaterally and negative on the ipsilateral side. CII, however, did not demonstrate this inversion. Upper quadrant stimulation produced a negative CI ipsilaterally whereas for the lower quadrant this component was positive contralaterally, reversing polarity across the midline. Both horizontal and vertical lower octants produced a contralateral positive CI, as did the upper vertical octant. The upper horizontal octant, however, produced a negative CI which was maximal on the midline. CII distributions appeared to vary little in relation to the field sector stimulated, showing a broad contralateral maximum in most cases.

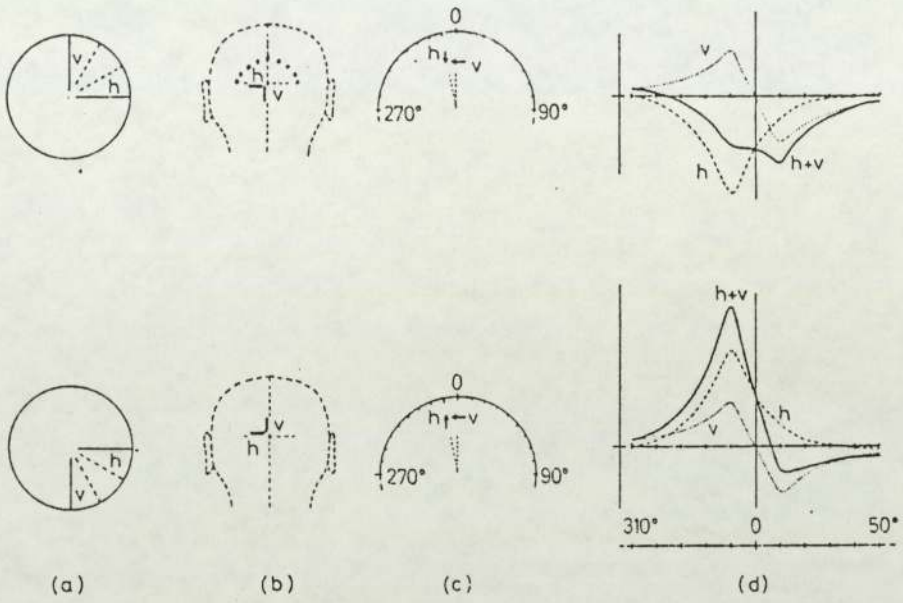


Figure 4.3

Schematic arrangement and simple dipole model of the regions of striate cortex representing upper and lower quadrants of the visual field. The right upper and lower quadrants (a) are represented in transverse cross-section, by right-angled sheets of cortex (b), whose horizontal and vertical arms represent, respectively, the horizontal and vertical octants of the visual field. In (c) these cortical sections are representded by pairs of perpendicular dipoles of appropriate location and orientation. The surface potential distributions associated with these dipoles are shown in (d). The basic forms of these potential fields are similar to the distributions of CI for stimulation of the corresponding regions of the visual field.

(After Jeffreys and Axford 1972a)

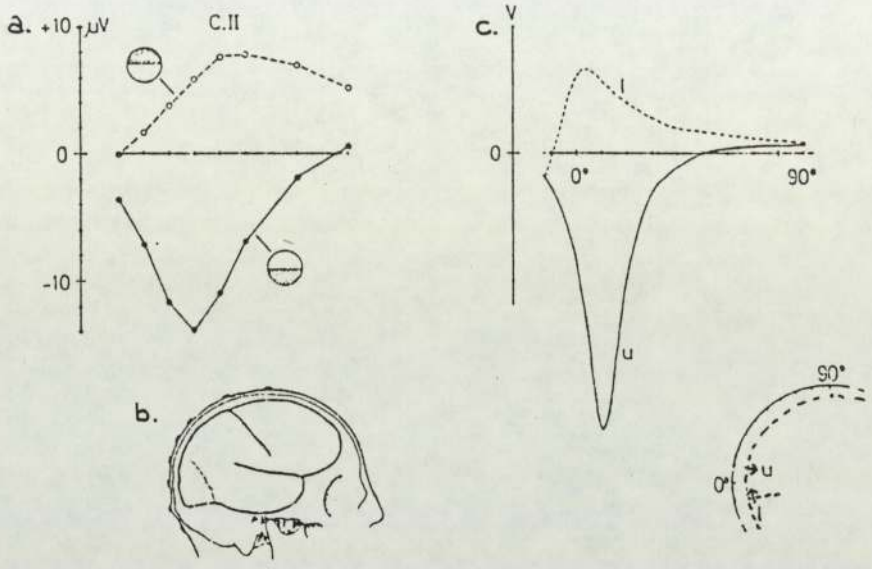


Figure 4.4

Comparison of the upper and lower half-field distributions of CII with those of the dipole model of the extrastriate cortical regions representing the upper and lower field. a. The longitudinal distribution of CII for upper and lower half-field stimulation. b. A simple schematic longitudinal section of the head indicating the approximate position and form of the visual cortex on the occipital lobe. c. Potential fields at the surface of a homogeneous sphere produced by single surface negative dipoles of corresponding direction and location to the upper surface (u) and to the under-surface (1) of the occipital lobe.

(After Jeffreys and Axford 1972b)

The distributions of CI showed a good relationship between those for half-field stimulation and the sum of those for individual quadrants, and also to a certain extent between those for quadrants and individual octants. Stimulation of annular regions showed that whereas CII was elicited by central field stimulation, CI was related mainly to the region outside the central 1^{o}.

Jeffreys and Axford (1972a) considered that the modifications of polarity and distribution of CI in relation to the stimulated portion of the visual field could be explained in terms of a simple dipole model based on surface negative activity in the striate area, in and around the calcarine fissure.

Studies of visual field projections in area 17 have demonstrated an orderly, retinotopic arrangement (as described in Chapter 2). Lower and upper quadrants are represented above and below the calcarine fissure, respectively, whilst regions adjacent to the vertical meridian project to the medial cortical surface and the horizontal meridian is represented deep in the calcarine fissure. Foveal projections occupy the most posterior aspect of the striate area, around the occipital pole, and visual field regions at increasing eccentricities are represented more and more anteriorly. If a simple symmetric schematic arrangement, as illustrated in Figure 4.3, were assumed, equivalent dipoles for vertical octants would lie in a horizontal plane pointing towards the ipsilateral hemisphere. This would explain the ipsilateral negativity recorded at scalp electrodes with vertical octant stimulation. Dipoles for the horizontal octants would, however, lie in a vertical plane with the negative pole pointing towards the opposing aspect of the calcarine fissures. Cortical activity on the opposing surfaces of the floor and roof of the calcarine fissure or on the medial surfaces of the two hemispheres might be expected to cancel. For upper and lower field stimulation therefore, activity recorded at the scalp might be expected to arise largely from projection areas within the calcarine fissure i.e. those associated with the horizontal octants. For lateral half-fields the medial cortical surfaces should be the more effective generators i.e. the projection areas associated with the vertical field octants. These factors would predict that, assuming surface negative cortical activity, the CI produced by lateral half-field stimulation would have a "bipolar" distribution, being positive contralaterally and inverting across the midline. For upper and lower field stimulation the (transverse) distribution might be expected to be "monopolar" being negative and positive respectively. These predictions fit in quite well with the observed distributions. Quantitative predictions of the expected scalp distribution of potentials arising from such an arrangement of generators also showed good agreement with recorded data.

Jeffreys (1977) stated that CIII topography is generally more similar to that of CII than

CI. Both James and Jeffreys (1975) and Jeffreys (1977) suggested that CIII originates in extrastriate cortex, but in a different region from CII. The double polarity reversal of CI associated with half-field and quadrant stimulation has been demonstrated by other authors who also interpret this behaviour on the basis of the "cruciform" arrangement of striate cortical generators in the calcarine fissure (Darcey et al 1980a and b; Parker et al. 1982b; Butler et al. 1987). Darcey, Ary and Fender (1980b) and Butler and colleagues (1987) used dipole modelling techniques which gave a reasonable prediction of such an origin. There were, however, important differences in the results of these authors from those of Jeffreys. Darcey, Ary and Fender (1980a and b) suggested that some modification of Jeffreys and Axford's (1972a) model was required to take account of projections related to the central 2^{o} of the visual field, on the posterolateral cortical surface. They also found that in some subjects their second peak (CII) appeared to show the same type of polarity reversal across the midline for lateral field stimulation as did CI (but with negativity recorded over the contralateral hemisphere) even to the extent that the two distributions were mirror images of each other. These authors considered therefore that the two components (CI and CII) might have one source which reverses in polarity with time or, more likely, that there might be two sources of opposing polarity situated close to each other.

Butler and co-workers (1987) considered that Jeffreys and Axford's (1972a) model provided a good fit for the distributions of CI observed for peripheral (in this case from about 5-17^{o} eccentricity) stimulation but could not be applied to the results for foveal targets. Application of a dipole modelling technique to the data acquired using foveal (up to 2^{o} radius) full field and sector stimulation predicted a source lateral to the midline and deep to the surface, with its positive pole facing posterolaterally. There was little change between quadrants although the upper field source showed a tendency to be slightly lower down than that for the lower field. These authors considered that their results could not be interpreted on the basis of an extrastriate cortical origin for CI. Such an origin would predict spatially separated sources for upper and lower quadrants and no such separation was found. Nor, they felt, could a diffuse origin in multiple areas of cortex explain the polarity reversals of the equivalent dipoles for different sectors of the peripheral visual field.

One suggestion put forward was that stimulation of foveal and extrafoveal areas of striate cortex might give rise to sources of opposite polarity. An alternative, more favourable proposal was that the organisation of foveal visual field projections was not as predicted. These authors conducted anatomical studies in which they found that the striate area often does not wrap directly around the medial surface of the occipital pole but instead folds in onto the posterior surface of the lateral calcarine sulcus (LCS) where the

orientation of the generator is reversed compared to that on the posterolateral surface of the occipital pole. A surface negative foveal generator in such a position would in fact give rise to positivity at scalp electrodes. Foveal projections on the LCS and on the posterior surface of the occipital pole would tend to cancel each other. This might explain Jeffreys and Axford's (1972b) finding of little contribution to CI from the central 1^{o} of the visual field.

As found by Jeffreys and Axford (1972a), most studies have shown that for lateral hemifields CI is maximal contralateral to the stimulated half of the field although it may or may not show a polarity reversal across the midline (Shagass et al. 1976; Lesevre and Joseph 1979; Drasdo 1982; Parker et al. 1982b; Ermolaev and Kleinman 1983). Kriss and Halliday (1980) showed, however, that their P90 component was larger over the midline and ipsilateral scalp. It was suggested that this might be a result of the comparatively large field and check size (16^{o} radius field and 50' checks) used in their study which would tend to activate generators on the medial cortical surface, by the same logic as that used to explain the paradoxical lateralisation of the pattern reversal P100 (see section 4.4b(iii)) (Barrett et al. 1976a). Over the contralateral scalp a broad positivity at 105 msecs was observed which, Kriss and Halliday (1980) suggested, might be related to foveal projections. These authors found a polarity reversal for P90 between upper and lower half-fields which suggested a relation with Jeffreys' CI.

Other authors consider that an alternative explanation of a CI origin in surface positive extrastriate generators fits in better with their data (Lesevre and Joseph 1979; Drasdo 1980; Maier et al. 1987). Lesevre and Joseph (1979) conducted a detailed chronotopographical analysis on responses to full field and sector stimulation using a 20^{o} diameter field and high contrast 20' checks. These authors distinguished several components in the responses to full field stimulation. P90 (probably equivalent to CI) in most subjects had bilateral maxima 4 cm from the midline in both hemispheres; in the other subjects it was maximal on the midline. Components N140 (CII) and P200 (possibly equivalent to CIII) and also an early negativity N60 (Drasdo's "C0") peaked on the midline. In addition to these components these authors also distinguished two negative components which both peaked laterally, at about 12 cm away from the midline. LN150 was maximal about 12 cm above the inion, whereas LN210 peaked on or below it. P90 demonstrated a polarity reversal for altitudinal half-fields, becoming negative with upper field stimulation, although in some cases a delayed positivity could be seen in the most posterior electrodes. Although N140 was replaced by an anterior midline positivity for upper field stimulation these two peaks did not have a constant relationship in time, suggesting that this was not a dipole orientation effect.

For lateral half-field stimulation, N60, N140 and P200 remained on or near the midline. P90 appeared contralaterally, and on the ipsilateral hemisphere either a weak positivity or a negativity at a different latency were observed. Lower left and right quadrants produced purely contralateral P90 distributions and for lower half-field and quadrants the lateral negative components often appeared bilaterally but were always larger on the contralateral side. Upper quadrants produced a contralateral positivity in place of N140. P200 showed marked attenuation for upper field stimuli. Stimulation confined to the foveal area led to a reduction in amplitude of most midline components especially P200 and a more posterior location of P90 and N140. Lower amplitudes were also observed with extra-macular stimulation although P200 was only slightly affected. Component N60, however, showed no reduction in amplitude or change in distribution with the foveal target but tended to disappear when stimulation was confined to the extra-macular area. The LN components were affected little in either condition.

Lesevre and Joseph (1979) considered that they could use these results to make reasonable deductions regarding the cortical sources of these components. The preference for foveal stimulation and the absence of polarity reversal and topography change of N60 suggested an origin in area 17 at the foveal projection on the tip of the occipital pole. The failure of P90 to demonstrate a polarity reversal across the midline with lateral half-field stimulation, coupled with the change in location between the maxima of the lower field P90 and upper field N90 suggested that this component did not originate in area 17 as Jeffreys suggested (Jeffreys and Axford 1972a). Rather, these authors considered area 19 as a more likely alternative. The relatively constant midline topography of N140 and P200, the absence of polarity reversals and the small differences between foveal and extrafoveal stimulation appeared to rule out areas 17 and 19. (The authors could not suggest from where the anterior positivity replacing N140 in upper field stimulation might originate). They considered, therefore, that an origin in area 18 was more likely. These authors considered that their montage was not adequate for the detailed study of LN150 and therefore did not draw any conclusions as to its origin. The behaviour of LN210, however, with its constant far lateral distribution and its failure to reverse in polarity was suggestive of an origin in infero-temporal cortex.

Drasdo (1980) has also expressed the opinion that CI has its origin mainly in extrastriate cortex. His results with small (2-2.5^{o}) foveal fields showed that for medium to large checks CI was often absent on the midline over striate projections, whereas it was substantially larger at lateral positions which, according to Drasdo's schematic map overlay areas 18 and 19. Drasdo (1982) also, as did Lesevre and Joseph (1979) failed to demonstrate a polarity reversal of CI across the midline for lateral half-field stimulation. For small checks, however, CI appeared to be more evenly distributed over all three

areas suggesting that its origin became "more striate" (Drasdo 1980) CII appeared largest on the midline over the striate projections. Drasdo (1980) suggested that CI and CII arise from separate neural generators and perhaps represent the activity of deep transient and superficial sustained detectors.

Maier, Dagnelie, Spekreijse and Dijk (1987) applied principle component analysis to data on flash and pattern VEP distribution. For pattern stimulation they used half-field foveal (2^{o} radius) and extrafoveal ($2\text{-}4^{o}$ eccentricity) targets containing 12' and 32' checks respectively. For pattern onset VEPs they defined two principle components. PC1 comprised of a positive peak (CI) followed by a negativity peaking 30 msecs after PC2 which itself consisted of a single negative deflection. These authors considered Jeffreys' "CII" to be a composite of these two negativities. In conventional waveforms the negative "CII" appeared to be distributed bilaterally although the ipsilateral peak was actually delayed in comparison by about 30 msecs. PC1 was maximal contralaterally around 4.5 cm up from and lateral to the inion, and shifted about 3 cm anteriorly when changing from foveal to extra-foveal stimulation. PC2 peaked about 2 cm up from the inion on the midline but shifted ipsilaterally with more eccentric stimulation. Equivalent dipole localisation computations suggested that PC2 and PC1 arise mainly from striate and extrastriate cortex respectively. The authors suggested that CI appears to originate in area 18 or 19 whereas CII probably arises from area 17 and also from area 18. The more anterior distribution of PCI with extrafoveal stimulation was explained on the basis of the position of the extrastriate generator areas on the upper and lower surfaces of the occipital lobe. On both these areas visual field regions at greater eccentricities are thought to be represented further from the occipital pole. The upper field generators on the under surface of the occipital lobe are less accessible to recording electrodes than those related to the lower field. Consequently the overall change in response distribution with increased eccentricity is more affected by the anterior shift in lower field generator position, which results in the apparent forward displacement of the maximum response.

Srebro (1985,1987) used Laplacian derivation to identify the current sources of the pattern onset responses to foveal ($0\text{-}2^{o}$) and peripheral ($2\text{-}6^{o}$) field sector stimulation. Srebro (1987) distinquished two major components at latencies of around 90 and 130 msecs. He associated these with separate regions of cortical activation which he termed R1 and R2. R1 was situated on or near the midline in the occipital area, and showed little lateral spread, although its topography was sensitive to visual field target position. R2 was more laterally placed on the contralateral hemisphere and showed much less sensitivity to stimulus locations. R2 also showed a response to stimuli in the ipsilateral hemifield, at its lateral border and also near its border with R1. Its latency, however, was delayed by 26 msecs as compared with that for contralateral stimulation. Srebro

(1987) also demonstrated that regions near the vertical meridian were much more strongly represented than those near the horizontal for R1. He considered that the topography of R1 and its sensitivity to stimulus location were suggestive of a striate origin. It was thought, however, that the laterally placed R2 probably contained more than one representation of the visual field, suggesting origins in more than one extrastriate visual area. The author suggested that the responses to ipsilateral stimulation might arise as a result of trans-callosal connections, which project to V2 and V4 from the opposite hemisphere. This would explain the latency delay. Srebro (1987) considered, therefore, that R2 must extend from V2 to V4 and therefore includes V3 and V3A. He suggested that these findings supported Jeffreys' conclusions as to the striate and extrastriate origins of CI and CII respectively.

As discussed in section 4.4b(iii), Lehmann's group has conducted extensive studies on the scalp distribution of the responses to upper and lower field stimulation. As was the case for the pattern reversal P100, the latency of the major positive component (CI) appeared to be longer for upper hemifield stimulation. Lehmann and Skrandies (1980a) found a mean value of 11 msecs for this latency difference. Skrandies, Richter and Lehmann (1980) also looked at the positions of the peak response on a midline electrode row and found a maximum for the upper field response at around inion level compared with 5 cm above it for the lower field.

Jeffreys and Smith (1979) disagreed with the interpretations of Lehmann's group, considering Jeffreys' earlier findings of a polarity reversal in the first two components for lower and upper field stimulation (Jeffreys and Axford 1972a and b; Jeffreys 1977). Jeffreys and Smith (1979) demonstrated that CI and CII both inverted in polarity between lower and upper field stimulation at similar but not always constant latencies. These authors used selective adaptation of CII to check the identity of the two components. Jeffreys and Smith (1979) commented that the isolated CI and CII "components" did not bear a consistent relationship to the peaks evident in the recordings.

Barber and Galloway (1981) used localised pattern onset stimuli to study further the differences between upper and lower halves of the visual system. They commented that the responses to a 2^{o}stimulus field with 15' checks centred at 1^{o} above and below fixation produced responses which appeared to show polarity reversal of CI and CII but not at constant latency. Responses from upper and lower peripheral areas appeared to resemble each other more closely than those from central areas. The largest responses were elicited with a stimulus centred on the vertical meridian and about 1^{o} below the horizontal meridian. The authors termed this position the "epicentre". If the responses

were considered as not changing in polarity there was an abrupt change in CI latency between central and peripheral areas from about 90msecs to 100-120msecs. This central area did not coincide with the physical centre of the visual field but formed a "plateau" which was displaced into the lower half of the field. Barber and Galloway (1981) considered that for large fields a lower field stimulus would elicit a mainly "epicentral" type of response whilst an upper field stimulus would elicit a more peripheral responses, and that the asymmetries shown in VEPs from upper and lower fields are more related to a distinction between foveal and peripheral responses.

Parker, Salzen and Lishman (1982a) studied the effect of spatial frequency on the topography of the pattern onset response. They found that for a 6^{o} field a change in spatial frequency of a sine wave grating from 1 to 6 c/^{o} caused little change in distribution of the early positive component (probably equivalent to CI). They concluded that responses for low and high spatial frequencies probably originated in the same cortical area.

As commented in section 4.4a, several groups of workers have observed an early negative component in the pattern onset VEP which is particularly prominent with fine pattern details and shows a predilection for foveal stimulation. It appears to be maximal on the midline several centimetres above the inion (Lesevre and Joseph 1979; Drasdo 1980; Ermolaev and Kleinman 1984). Drasdo (1980) has termed this component "C0". Kulikowski's group (e.g. Russell et al.1986) believe that this negativity which is the only component distinguishable in pattern onset responses to fine (15-30 c/^{o}) sine wave gratings reflects activity in area 17 at the tip of the occipital pole. Lesevre and Joseph (1979), as mentioned above, hold a similar opinion.

Ermolaev and Kleinman (1984) demonstrated a negative peak (N75) with a centrally fixated target using small (8') checks, usually on the midline. This peak followed the first positive component recorded by these authors at around 50 msecs latency. An increase in check size, however, led to a decrease in amplitude of both P50 and N75 and the emergence of a positivity at 70-100msecs (P75). P75 was maximal with large checks and at lateral electrode positions. It would therefore appear from these results that N75-P75 might represent Jeffreys' CI. Russell and co-workers (1986) found that their negativity, which had a latency of around 130 msecs, was followed by a positive component for gratings below 10-15 c/^{o}. They observed that both the positive and negative components showed polarity reversal for upper field stimulation.

As commented by Butler and co-workers (1987), one objection to an origin for the CI component in surface negative striate generators is the apparent inability to record a

negative CI for foveal stimulation. Parker, Salzen and Lishman (1982b) found, however, that for a 6^{o} (diameter) central target CI sometimes appeared as a midline negativity with high spatial frequency gratings. Lower spatial frequencies elicited a positive CI at electrodes slightly lateral to the midline. Recently, both Jeffreys (Jeffreys et al. 1988) and Butler (Butler et al. 1988) have demonstrated a negative CI to foveal stimuli. Jeffreys, Musselwhite and Murphy (1988) found that for a 3 x 1.5^{o} stimulus in the lower foveal area check sizes of less than around 0.15^{o} (9') elicited a midline negativity in the occipital area. Butler and colleagues (1988) found that CI became negative with pattern spatial frequencies greater than 3 $c/^{o}$ for the central 1^{o} of the visual field.

Drasdo (1980) considered that this early negative component might be an artifact caused by the superimposition of CI on the descending slope of CII. On one of his subjects it appeared that CI changed its position relative to CII depending upon the electrode position and the spatial frequency of the pattern. With large pattern elements and on more lateral electrodes CI appeared before CII and with increasing spatial frequency or moving towards midline electrode positions CI appeared to move across CII, producing the apparent early negative C0.

The composite nature of the negativity following CI has been demonstrated and studied by several groups of workers. As detailed above, Lesevre and Joseph (1979) demonstrated an anterior lateral negative (LN150) component. This was distinct from the midline N140 which is probably the equivalent of Jeffreys' CII. Ermolaev and Kleinman (1983, 1984) described negative peaks at 100 and 130 msecs which appeared to be related to photopic and mesopic luminance levels. N100 was largest on the midline in the occipital area to full field (8^{o} radius) stimulation whereas N130 was of greater amplitude laterally (Ermolaev and Kleinman 1983). N130 was also clearly evident at parietal electrode placements whereas N100 was reduced. Right and left hemifield stimulation caused an overall decrease of N100 amplitude whereas N130 increased. Unlike N100, N130 failed to demonstrate a polarity inversion between upper and lower fields. As commented earlier (section 4.4a) N130 was affected little by check size and stimulus eccentricity. Jeffreys (1982) distinguished a "non-pattern-specific" component "N150" which was larger at lateral electrodes and showed no polarity changes on partial field stimulation. Using PCA, Maier and co-workers (1987) demonstrated that two Principle Components contributed to the "CII" observed in conventional recordings.

4.5 The physiological significance of the VEP: implications of findings in topographic studies.

4.5a Comparison of responses to pattern onset, offset and reversal.

The majority of studies on the scalp distribution of the pattern reversal response have shown that for lateral hemifield stimulation a maximal P100 component is elicited on the midline and ipsilateral side of the scalp. Those on the distribution of CI, however, normally show its maximum positivity over the contralateral hemisphere. These two respones are generally thought to result from surface positive and surface negative cortical activity respectively. Both are often described as reversing in polarity across the midline although the ipsilateral components, particularly for pattern reversal, may not arise as a result of the activity of the same generator areas as those recorded on the contralateral scalp.

Kriss and Halliday (1980) conducted a systematic comparison of the responses to pattern reversal, onset and offset for large (16^{o} radius) fields and large (50') checks. These authors found that reversal and offset respones, but not onset responses, had similar waveforms, latencies and distributions. Unlike the majority of workers, however, Kriss and Halliday found that P90 of the onset response was largest ipsilaterally for right and left half-field stimulation (as commented in section 4.4b(iv)). These authors considered that the contralateral maximum found by other investigators was possibly a result of their relatively small stimulus fields and check sizes which would tend to activate the macular representation at the tip of the occipital pole. More recently Clement, Flanagan and Harding (1985) have also demonstrated a maximum positivity for CI over the ipsilateral hemisphere using large fields and checks. In addition, these authors also found similar distributions for pattern reversal and offset responses.

Shagass, Amadeo and Roemer (1976) showed that for a 9^{o} radius field and 33' checks, their major positive onset component (P125) was positive contralaterally, becoming slightly negative over the ipsilateral hemisphere, whereas the pattern reversal P125 was largest ipsilaterally and showed no inversion (the increased latencies found by these authors were thought to be related to the relatively low stimulus luminance levels used). Van Lith and co-workers (1981) found a similar distinction between the major positive components of their onset and reversal responses.

Other workers, however, have found similarities between onset and reversal responses. A change in latency as well as distribution between upper and lower hemifield respones has been demonstrated by Lehmann and co-workers for onset, offset and reversal responses (Lehmann and Skrandies 1980a; Skrandies et al. 1980). It was found,

however, that although the major reversal and onset components showed maximal positivity more anteriorly for lower half-field stimulation, that for the offset response peaked more posteriorly. Parker, Salzen and Lishman (1982a) reported similar longitudinal distributions for early onset and offset components in the full field respones to sine wave gratings.

Clarke (1973) found similarities between the distributions of motion-reversal, motion-offset and pattern onset responses, all of which were seen to invert in polarity between lower and upper half-field stimuli. Motion-onset and pattern offset responses also showed similar distributions which differed from those of the preceding group. These responses did not demonstrate polarity reversal between lower and upper hemifields. These results implied that the two sets of respones arose from the activity of different neural mechanisms. Jeffreys (1977, 1980) suggested that the pattern reversal P100 was made up of two components with different scalp distributions, resembling those of CI and the major positive offset component. The study of Maier, Spekreijse and Dijk (1987) using dipole localisation of Principle Components demonstrated a striate origin for the major part of both pattern reversal and motion responses as compared with an extrastriate origin for CI.

Dagnelie, De Vries, Maier and Spekreijse (1986) also studied the relationship between pattern contrast and motion responses, using intracranial recordings from area 17 in the macaque monkey. These authors found that although the pattern onset responses from foveal and parafoveal projection areas were similar, this was not the case for the pattern reversal response. In fact, the pattern reversal response from foveal projections was similar to the pattern onset response but smaller in amplitude. Motion onset responses for foveal and peripheral projections resembled the pattern offset response, and likewise for motion offset and pattern onset. The combination of motion onset and motion offset responses resembled the pattern reversal responses. It appeared from these results that only a contrast response could be generated in foveal projections whereas parafoveal and peripheral areas were responsive to both contrast and motion. For foveal stimulation, both motion and pattern reversal stimuli seemed to elicit contrast responses. These results support the presence of contrast and motion contributions in the pattern reversal response, as suggested in section 3.4d.

4.5b <u>The cortical origins of the VEP.</u>

In spite of the many studies reported there still seems to be no concensus opinion as to where the cortical origins of the principle VEP components might be. With regard to the pattern onset VEP, the orthodox view is that of Jeffreys and Axford (1972a and b). The behaviour of the CI component in relation to stimulus visual field location was related by

these authors to the "cruciform" arrangement of surface negative dipole sources in the calcarine region of the striate cortex. Several groups of workers, however, have disagreed with this interpretation, suggesting that this component might originate in surface positive activity in extrastriate cortex (e.g. Lesevre and Joseph 1979; Drasdo 1980). The apparent failure to record an occipital negative foveal response, commented on by Butler and colleagues (1987) is perhaps resolved by reference to the early negativity described by many authors for foveal stimuli and/or high spatial frequencies. There is, however, some doubt about the relationship between this early negativity and CI, and as to whether it should be treated as a separate component. Jeffreys (1971) and Jeffreys and Axford (1972b) suggested that component CII has its origin in surface negative activity in extrastriate cortex. Other investigators have tended to agree that CII originates, at least partially, in extrastriate visual cortex. The earliest suggestion for the origin of the pattern reversal P100 component came from Halliday and Michael (1970) who considered that it might arise from surface positive extrastriate cortical activity. Although Lehmann, Darcey and Skrandies (1982) agreed with this interpretation, later work by Halliday and associates (e.g. Barrett et al. 1976a) and also Haimovic and Pedley (1982b) suggested that this component may be related to activity on the mesial surface of the cortex near the occipital pole, a region which is occupied predominantly by the striate area.

Based on the idea that his assumptions about the cortical origins of CI and CII are correct, Jeffreys has used the stimulus related properties of these components to draw conclusions as to the possible characteristics of cortical neurones in striate and extrastriate areas. The fact that the CI elicited by gratings shows both spatial frequency and orientation specific adaptation effects which transfer interocularly (Smith and Jeffreys 1978) suggested that this component was related to the activity of striate neurones themselves rather than to the neural input to this area. The inter-ocular transfer of adaptation effects on CI and CII were studied in more detail by Smith and Jeffreys (1979). They found that transfer was almost complete for CII whereas it was only partial for CI. They concluded that since CI was considered to have a striate origin, and CII was thought to originate in a specific area of extrastriate cortex, the results could be interpreted as a demonstration of the higher proportion of binocularly driven neurones (and consequently lower proportion of monocular neurones) in extrastriate as compared with striate cortex. The finding of more anterior lower field and more posterior upper field maxima for binocular than monocular pattern reversal stimulation caused Adachi-Usami and Lehmann (1983) and Adachi-Usami (1984) to draw similar conclusions. Contrast- and contour-specific mechanisms as discussed in section 3.4b are also thought by Jeffreys (1977) to originate largely in striate and extrastriate cortical regions respectively, although these contour related mechanisms are present to a lesser degree in the striate area.

CHAPTER 5

Pilot study: Investigation of the scalp topography and cortical origins of the major positive components in the visual evoked potentials elicited by foveal pattern and flash stimulation.

5.1 Introduction

There is general agreement in the literature that the waveform and scalp distribution of the visual evoked potential (VEP) and the way in which these are modified according to the position of the stimulus in the visual field is related to the manner in which visual space is mapped onto the surface of the cerebral cortex. In man, each visual hemifield is represented as a single, complete retinotopic ("first order") map on the surface of the striate area in the contralateral hemisphere (e.g. Holmes 1945; Spalding 1952). Evidence from primates shows orderly mapping of all or part of the visual field in some extrastriate areas (Zeki 1978a; Allman et al. 1981). Single cell recordings suggest that different areas may be biased towards the processing of different types of visual information, for example colour in V4 and motion in MT (Zeki 1978a). Cortical phosphene studies have suggested that multiple representations of the visual field may exist in human visual cortex (Dobelle et al. 1979). Studies of the cortico-cortical connections between areas indicate that there may be two parallel systems in macaque visual cortex, one concerned with colour and form and the other with visual motion, involving different groups of cortical areas (Van Essen and Maunsell 1983). Within these systems, levels of sequential processing appear to exist. Evidence for sub-cortical "sustained" and "transient" pathways in cats and primates is extensive (see section 2.3b). There is also psychophysical and electrophysiological evidence for the operation of parallel channels in the human visual system (see Chapters 2 and 3). It seems reasonable to assume, therefore, that the different stimulus-related properties of the VEPs elicited by different types of stimulation and their constituent components (see sections 3.3, 3.4 and 4.4b) might be indicative of origins in separate visual cortical areas.

Many workers have, as discussed in Chapter 4, attempted to deduce the areas of origin, within the visual cortex, of particular VEP components, from data on scalp distribution and on the way in which this changes according to the stimulated part of the visual field (e.g. Halliday and Michael 1970; Jeffreys and Axford 1972a and b; Spekreijse et al. 1977; Lesevre and Joseph 1979; Drasdo 1980; Darcey et al. 1980a; Lehmann et al. 1982; Srebro 1987; Butler et al. 1987; Maier et al. 1987). The results and interpretations of different groups of authors looking at corresponding components, however, have been contradictory (see section 4.5b). This is almost certainly due at least in part to differing experimental condtions, particularly field size and in the case of pattern stimulation,

stimulus element size. Methods of recording and analysis have also varied, some authors relying on direct interpretation of scalp distribution of components and others employing dipole localisation or source derivation methods, and even, in one case, intracerebral recordings.

The components which have been investigated most extensively are the major (early) positive components in the responses to pattern reversal and pattern onset stimulation. These have been termed "P100" (e.g. Blumhardt et al. 1978) and "CI" (Jeffreys 1970) respectively and are illustrated in Figures 3.2 and 3.3. Jeffreys (Jeffreys 1971; Jeffreys and Axford 1972a) put forward the orthodox view regarding the origin of CI, which is that this component arises from surface negative cortical activity in the striate area. This theory has been upheld by some workers, at least with regard to peripheral field generators (e.g. Darcey et al. 1980a; Parker et al. 1982b; Butler et al. 1987), but disputed by others, who believe that an origin in surface positive extrastriate generators is more likely (Lesevre and Joseph 1979; Drasdo 1980; Maier et al. 1987).

The early studies of Halliday (Halliday and Michael 1970; Michael and Halliday 1971) suggested that P100 might originate as surface positive activity in extrastriate areas and the intracerebral recordings of Lehmann, Darcey and Skrandies (1982) led these authors to a similar conclusion. Later work by Halliday's group (Barrett et al. 1976a; Halliday et al. 1979; Halliday 1982) and also by Haimovic and Pedley (1982a and b), however, indicated a source around the tip of the occipital pole, possibly in striate cortex. The first large positive component in the flash response, here termed "P2" after Harding (1974), has received less attention in the literature. P2 would, according to Spekreijse, Estevez and Reits (1977), be part of the medium frequency subsystem or "secondary" response and as such might originate in area 18 or 19. The results from work on Alzheimer's disease also suggest an extrastriate origin (see section 4.4b(i)). Intracortical recordings in the macaque, however, have demonstrated activity in the striate cortex which is related to a response component which may be the equivalent of P2 in the human (Kraut et al. 1985). It has also been suggested that the flash response has a more diffuse cortical origin than the pattern response, arising from simultaneous activity in multiple cortical areas (Drasdo 1981).

The cortical sources of the VEP have, as discussed in sections 2.6, 4.3a and 4.4b, often been approximated as dipole field generators. Drasdo (1986) demonstrated, using simplified electric field theory, that the major "dipole" generators of the scalp-recorded VEP must be the surfaces of the visual cortical gyri, particularly those which lie on the proximal (posterior and postero-lateral) aspects of the occipital lobe. In man, these regions are thought to contain at least the striate and possibly also further, extrastriate projections of the central few degrees of the visual field (see section 2.4). More

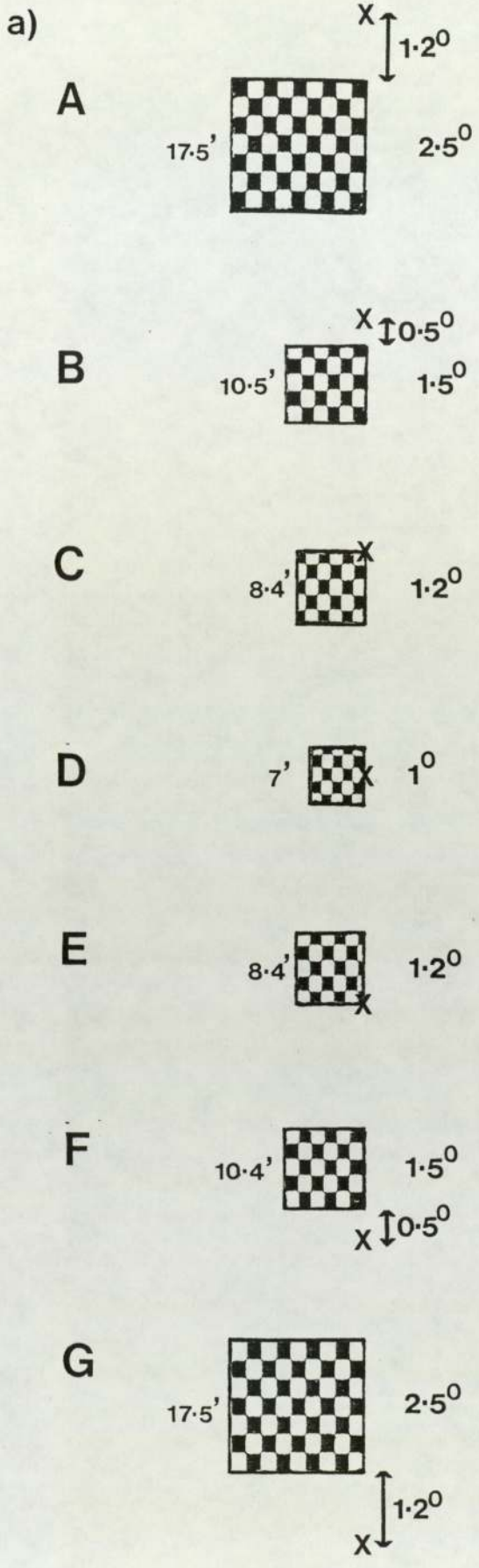
peripheral portions of the field are represented in the striate cortex on the mesial surface of the occipital lobe and within the calcarine fissure, and possibly have extrastriate representations on the postero-lateral and tentorial cortical aspects as well as the mesial surface. Clearly, stimulation of large portions of the visual field might be expected to lead to activation of regions on more than one cortical surface. The mixing of signals from such differently oriented generator areas must complicate the interpretation of scalp distribution data in terms of dipole generators considerably. The majority of workers investigating the cortical sources of VEP components have therefore stimulated limited sectors of the central and/or peripheral field at one time. In the present study we have employed stimuli confined to the foveal and parafoveal area, with the expectation that mainly the posterior and postero-lateral aspects of the visual cortex would be involved in the generation of signals.

Drasdo (1986) compared the strength of signals which might be expected to be recorded at scalp electrodes from a gyral generator on the proximal surface with that from cortex within a fissure and also from a portion of cortex on the mesial surface of the occipital lobe. He found that generator areas within a fissure and on the mesial surface should be less effective as a result of depth, orientation and cancellation effects. He suggested that very small targets could be designed which stimulated portions of cortex of comparable extent to individual gyri, at different positions within the foveal area of the visual field. If a target were correctly positioned to activate the surface of a single gyrus in the striate area it should elicit a relatively large signal over a fairly localised region of the scalp. A target whose projection fell in a fissure would give rise to a much smaller response. The cortical gyri are relatively constant in size, being around 1cm in width (Polyak 1957), but the pattern of gyri and fissures varies between individuals. Consequently, it may be that a target in a particular visual field location would stimulate a portion of cortex which is on the surface of a gyrus in one person but buried in a fissure in another, thereby giving rise to large and small signals respectively. A different target might be projected onto a fissure in the first person and a gyrus in the second. It is conceivable that some subjects could be found in whom a series of targets close together in the visual field might project first onto a gyrus, then in a fissure and then onto another gyrus, with an associated decrease and then increase in signal amplitude. This issue is complicated by the likely existence of repeated visual field projections in extrastriate areas. Simultaneous activity from multiple sources, particularly if spatially separated, might lead to a confusing picture of scalp activity. Although it is possible that each component in a particular response is associated with activity from a single cortical area, evidence reviewed in sections 3.4 and 4.4b suggests that a single peak or component may contain contributions from more than one type of visual physiological process and/or cortical area (Jeffreys 1977; Maier et al. 1987; Srebro 1987). Nevertheless, one would still expect to see some modifications in signal amplitude and/or scalp distribution with

Figure 5.1

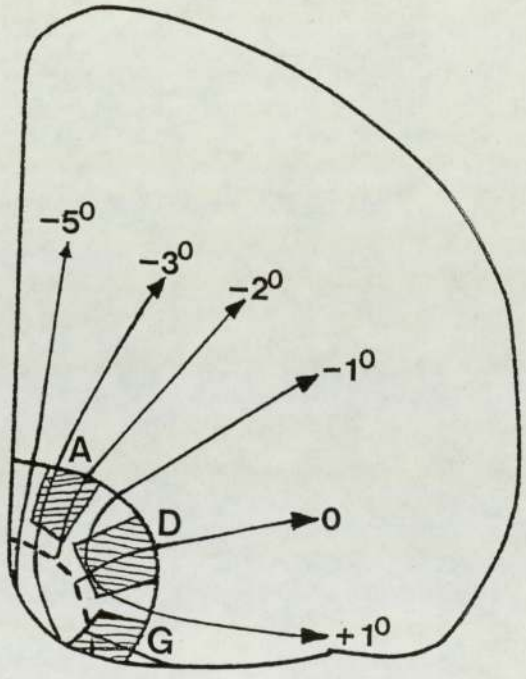
(a) The M-scaled target series. Reference letters are shown on the left, as are the check sizes for each target. The position of the fixation point with respect to the stimulus is shown by the cross. The numbers on the right give the target dimensions and, where appropriate, the distance of the fixation target from the edge of the stimulus.
(b) This rear view of the right hemisphere shows the predicted position of the striate cortical projection of targets A, D and G, according to a schematic model.

a)



CHECK SIZE

b)



TARGET SIZE
& FIXATION

change in visual field position and also between individuals.

In order to investigate these ideas a series of targets was designed to activate $1cm^2$ patches of striate cortex and associated extrastriate re-projections, at different eccentricities in the central visual field. These are illustrated in Figure 5.1a. The extent of striate cortex devoted to each degree of the visual field is, as discussed in section 2.4, not constant at different eccentricities. Consequently it was necessary to scale target size in accordance with the decrease in cortical magnification associated with increasing eccentricity. The calculations were based on the cortical magnification equations of Drasdo (1977). In addition to changing target size it was considered appropriate to vary pattern spatial frequency with eccentricity. Optimum stimulus element size, as commented in section 4.4a, appears to increase between central and peripheral visual field locations, an effect which is possibly related to the increase in size of retinal and/or cortical receptive field sampling areas with eccentricity. The stimuli, which in this study were all confined to the left half-field, comprised a column of six (termed A to G) in apposition to the vertical meridian, each target designed so that it should stimulate an area overlapping that of the next by 0.5cm. These targets could, of course, be reversed so that the right hemifield was stimulated. Figure 5.1b shows the approximate projection of three of the targets onto the the striate cortex of the right cerebral hemisphere, as predicted from a schematic map of the average cortical projection of the visual field in humans (Drasdo 1983; see Figure 2.6).

Initial explorations were made using these M-scaled targets in both left and right hemifields on some 15 normal subjects, using pattern onset-offset stimulation. These were made using a Nicolet Pathfinder II system which had a maximum of 8 channels. Due to the limited number of channels and the restricted amount of information obtained on each subject, these results have not been presented here. They did, however, give some indication of the following:-

a) The feasibility of recording using such small targets, which seemed reasonable providing the subject maintained fixation as accurately as possible and repeat recordings were made to check consistency.

b) The appropriate check size for use in the central target (D), which appeared to be approximately 7' of arc.

c) The necessity for a greater number of recording channels to cover the area of interest on the scalp without having to repeat recordings with electrodes in different positions. Attempts to carry out such repeat recordings revealed that a great degree of duplication and cross-checking was required in order to confirm

the accuracy of data acquired. This resulted in lengthy sessions and subject fatigue.

d) The need for some manner of displaying signals such that their scalp distribution is easily visualised. The use of a "brain mapping" system, with 16 recording channels and a colour equipotential contour display provided a solution to this problem and also that in c).

The choice of a midfrontal reference position (Fz) was made partly on the basis of previous experience in our laboratory, where such a reference location has been employed in the majority of monopolar recordings. The problems of reference location have been discussed in section 4.2. Brief attempts at recording with non-cephalic reference positions on the knee and wrist and also with a chin reference showed that responses were badly affected by myogenic movement artifacts. Linked ear or mastoid references were rejected because of their ambiguity and the possible effects on lateralisation of responses. It was considered that for these very small stimulus fields a single cephalic reference electrode on the midline, positioned as equidistant from the active electrodes as possible, was the most suitable alternative for investigation of distribution of responses. The midfrontal position therefore seemed to be the most appropriate.

The use of monocular and binocular stimulation has varied between authors. In studies with a clinical basis or in which a clinical technique is being developed, the use of monocular stimulation is obviously necessary since both eyes of a patient need to be assessed separately. In the investigation of the anatomical and physiological organisation of the visual cortex, however, it is perhaps more appropriate to use binocular stimulation, since this is better related to "normal" viewing conditions. Questioning of experienced subjects reveals that they feel much more comfortable without an occluder covering one eye and also that they consider that they are able to maintain their fixation more accurately when viewing binocularly.

The purpose of the initial study presented here was two-fold. On the one hand, we wished to study the scalp distribution of responses to central stimulation, in the hope of gaining further information about the cortical sources of VEPs elicited by pattern and luminance stimulation. In the first part of this experiment therefore, we studied the scalp distribution of the major positive components of the pattern reversal, pattern onset and flash VEPs using four degree central full and lateral half-field stimuli. The other aim of this study was, as described above, to investigate the local nature of VEP generator areas and their relationship to cortical gyri and fissures, using the small "M-scaled" target series. In this section of the study only pattern reversal and pattern onset-offset

stimulation were used.

5.2 Materials and methods

Nine normal volunteer subjects were employed in the larger field study, four of whom were female. Their age range was 21-28 years, and they had visual acuity of 6/6 or better, wearing optical correction where necessary. All had previously participated in electrophysiological and/or psychophysical investigations. Only five of these subjects were used in the more detailed study, and for only three of these were recordings obtained using both pattern onset and pattern reversal stimulation.

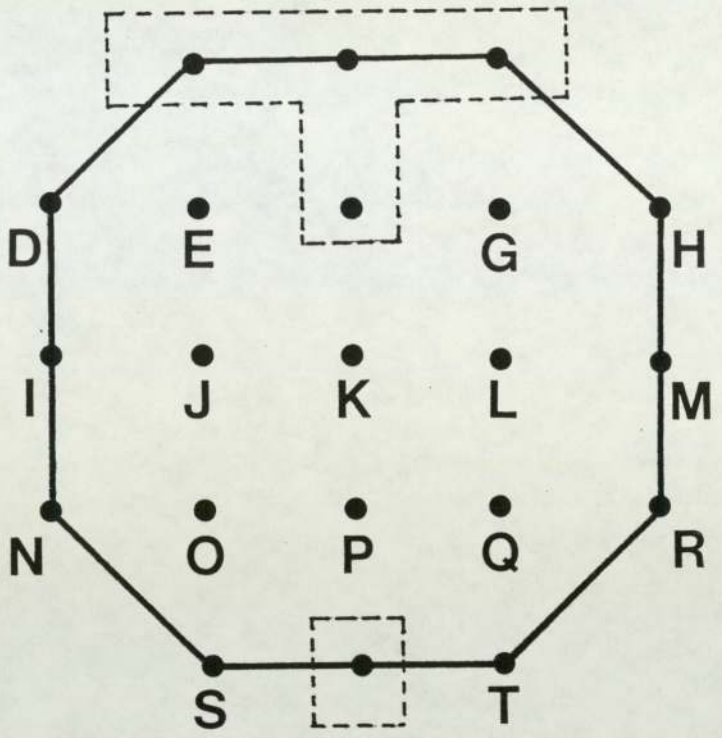
The larger stimuli used in the first part of the study were four by four degree square full fields and four by two degree lateral half-fields. The fixation target in each case was a cross with limbs subtending 40 x 5 minutes of arc. The M-scaled target series, as discussed above, is shown in Figure 5.1a. For each target the field size, check size and position of the fixation cross is shown.

High contrast (0.8) black and white checkerboards were used as pattern stimuli, in which the individual checks subtended 19' of arc for the four degree stimuli. For the M-scaled targets, check size was 7' for stimulus D, increasing at the same rate as target size, so that the number of checks within the stimulus field remained constant. Pattern stimulation was provided by an optical projection system in which the mean luminance of the screen was 500 cd/m^2. Pattern stimuli were projected from standard 35mm slides. The screen, onto which patterns were back-projected, was masked down using white card and its position changed with respect to the subject in order to achieve appropriate stimulus dimensions. Fixation distance varied from 80 to 200cm. Reversal of the pattern was carried out by means of a rotating mirror mounted on a pen motor. Onset-offset stimulation was mediated by means of a diffusing shutter placed in the path of the light beam. This was periodically removed, causing the pattern to be projected on the screen. For flash stimulation a Medelec OS5 stroboscope was used. This was set at intensity 2, but attenuated using a 0.5 log unit neutral density filter. This gave a low intensity flash of around 40 nit seconds. A similar method for localising the flash stimulus has been used previously (Drasdo 1982). For both pattern and luminance stimulation, background luminance had a value of 150 cd/m^2, ensuring a medium photopic level of adaptation. Stimulus presentation rate in all cases was 1.3 per second. In pattern onset stimulation, the pattern was exposed for a period of 150 msecs during each stimulus cycle. Timing was controlled by means of a function generator and a Digitimer. All stimulation was binocular, with natural pupils.

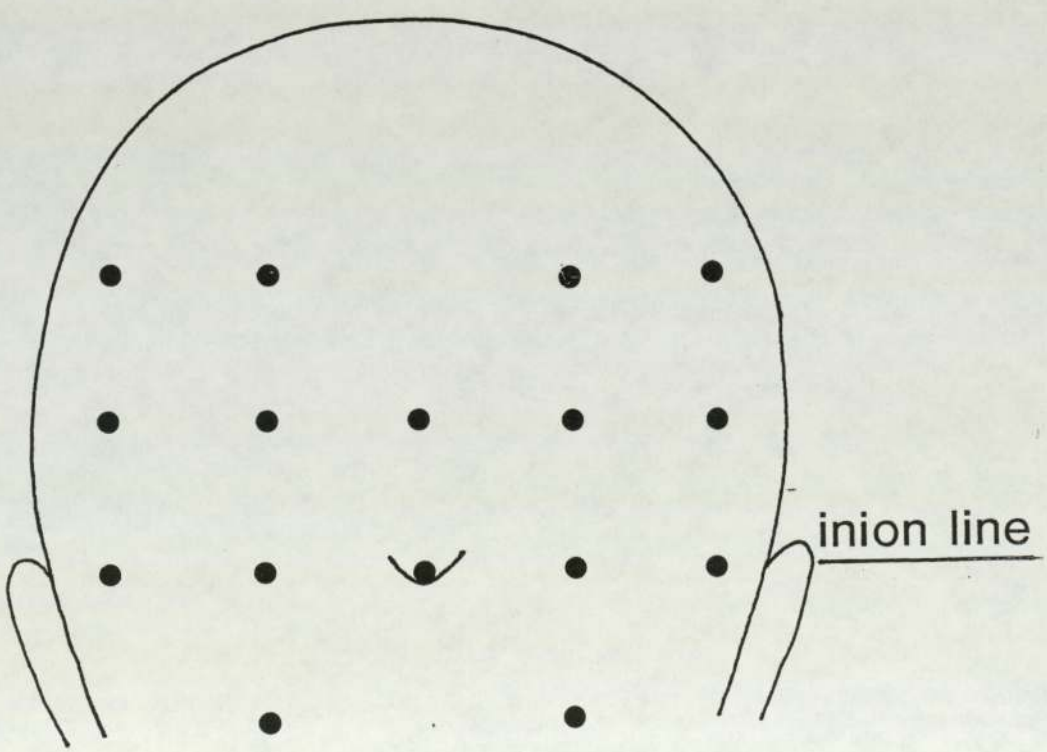
Figure 5.2

a) The brain mapper display, showing relative positions and reference letters of recording channels. This display represents a rear view of the head. The channels outlined were not used for recording; amplitude levels at these points on the map are linearly interpolated from those at surrounding electrodes.
b) The electrode montage, as seen from a rear view of the head. Electrode separation was normally around four centimetres in either direction.

a)



b)



The VEPs recorded from 16 scalp electrodes were simultaneously averaged by a Bio-logic Brain Atlas III mapping system. The montage used, which was confined to the back of the head, is shown in Figure 5.2b. Electrode separation was around 4 centimetres, the exact value being dependent upon transverse and sagittal (along the median plane) percentage head dimensions (inion-nasion distances). This value, on an "average" head, represents a compromise between a 15% transverse spacing and a 10% sagittal spacing, and gives complete coverage of the area of scalp of interest whilst retaining adequate sampling detail. Figure 5.2a shows the corresponding arrangement of the channels on the Brain Atlas display map. These channels have been labelled "D", "E" and "G" to "U" as illustrated. The channels which have been outlined (actually termed "A" to "C", "F" and "T") are not actually recorded from, the amplitude levels at these points on the map being linearly interpolated from those at surrounding electrodes. By spacing the electrodes equidistantly it was considered that the best match between the appearance of the montage on the head and the representation on the monitor display map would be acheived.

Recording was monopolar, to a common midfrontal reference (Fz), with the ground electrode on the forehead (Fpz). Filter settings were 1Hz high pass, 30Hz low pass and the time base was 512 milliseconds. Subjects reclined comfortably in a chair in front of the stimulus and were directed to watch the fixation target closely throughout the actual recording periods. Normally two runs, each of 50 to 100 sweeps, were carried out for each stimulus condition, performed in an "A-B, B-A" manner. If necessary, repeat runs were carried out until at least two similar responses were recorded. On no occasion was it necessary to perform more than four trials to achieve this. Data was recorded on magnetic media for subsequent analysis.

The scalp distributions of the responses are displayed in the form of "equipotential" contour maps, plotted at the latency of the first clear positive peak in the response. This description is not, however, strictly accurate, since the amplitude on each trace was measured in a peak to peak manner i.e. as the voltage difference between the preceding negative peak or inflection and the maximum positivity of the transient.

Table 5.1

Mean amplitudes and latencies of the major positive components in the responses to the four degree full and lateral hemifield stimuli.

		P100	CI
Full Field	LATENCY ± SE MSEC	92.0 ± 1.5	85.6 ± 1.9
	AMPLITUDE ± SE uV	5.4 ± 1.3	7.8 ± 2.3
Left Half-Field	LATENCY ± SE MSEC	92.9 ± 2.1	82.7 ± 2.0
	AMPLITUDE ± SE uV	4.4 ± 0.7	7.7 ± 2.0
Right Half-Field	LATENCY ± SE MSEC	93.9 ± 0.9	86.2 ± 1.1
	AMPLITUDE ± SE uV	5.3 ± 1.4	7.1 ± 2.6

5.3 Results

Figure 5.3 shows the group average distributions of the three components for four degree full and half-field stimulation. The maps show positivity of the active electrodes with respect to reference as an upward deflection on the colour scale. Table 5.1 shows peak to peak amplitudes and peak latencies for each component measured (for each individual) at the point of maximum amplitude on the map. For all stimulus conditions, CI tended to be of larger amplitude than P100 or P2, but was more variable.

On full field stimulation, all three components reached maximum amplitude on the line of electrodes 4 cm above the inion ("I" to "M"). CI, however, showed a tendency to a more anterior distribution than P100 and P2. With regard to lateral distribution, P100 showed a midline maximum, whereas CI had distinct bilateral maxima at 4cm to either side of the midline on row "I" to "M". Analysis of the data on individuals reveals that for two subjects the signal at the midline channel on this row was negative in polarity. For one of these subjects, this negativity reached a peak at the same latency as the contralateral positivity and may therefore represent a polarity inversion of CI. For the other subject, however, this negativity peaked some 10msecs earlier.

For lateral half-field stimulation, P100 and C1 again show maximum amplitudes on the line of electrodes 4cm above the inion. Both components can be seen to have lateralised over the hemisphere contralateral to the half-field stimulated, that is the "correct" hemisphere in terms of visual field projection. This tendency is clearer for CI, which shows a steep gradient and a sharp cut-off near the midline, than for P100, which spreads somewhat over the midline onto the ipsilateral side. In the data on individuals, CI was always found to be maximal contralaterally whereas P100 lateralisation was more variable. Only five subjects showed clear contralateral maxima for P100; for the other four subjects this component was largest on midline and/or ipsilateral channels. Recordings on the individual who demonstrated the possible polarity reversal of CI for full field stimulation showed an ipsilateral negativity for lateral hemifield stimulation at the same latency as the contralateral positivity. P2 shows a much more widespread distribution than the other two components for full field stimulation and did not lateralise clearly on half-field stimulation. Five subjects showed maximal amplitudes on the midline electrode and for the others P2 was of similar magnitude on midline and ipsilateral electrodes.

Figure 5.4 shows examples of the distributions of components P100 and C1 for the M-scaled stimuli in one subject. These small targets elicited responses of varying

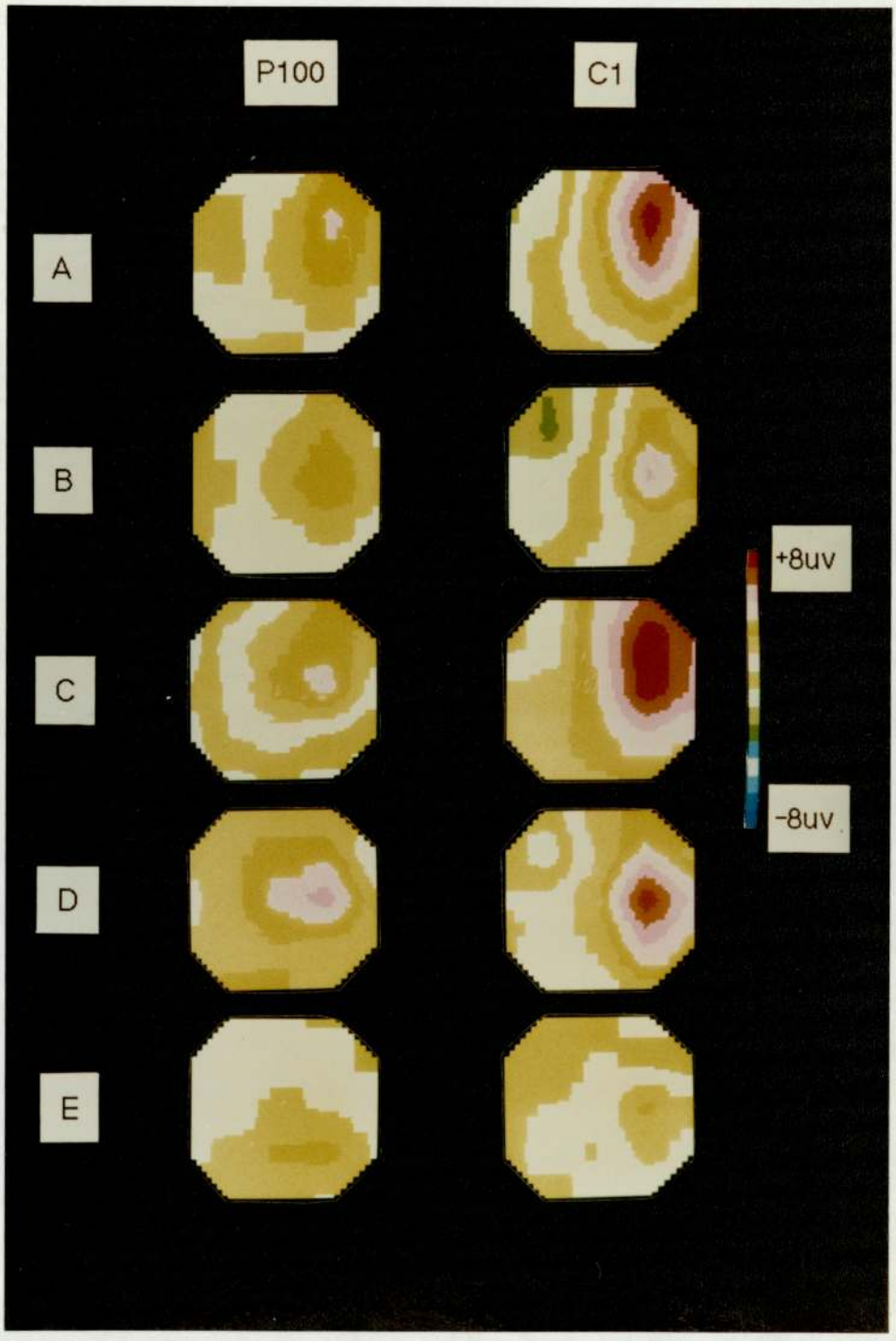
Figure 5.3

Group average distributions of components P100, CI and P2 for the four degree full field and lateral half-field stimuli. Positivity of the active electrodes with respect to the reference is represented as an upward deflection on the colour scale.

P100
C1
P2
+8uv
-8uv
FULL FIELD
LEFT HALF FIELD
RIGHT HALF FIELD

Figure 5.4

Distributions of components "P100" and "CI" elicited by the M-scaled targets A to E in an individual subject.


P100
C1
A
B
C
D
E
+8uv
-8uv

amplitude in different subjects. Also, intra-individual amplitude varied somewhat depending upon type of stimulation and on target position relative to fixation. For example, Figure 5.4 shows P100 to have a maximum amplitude with target D, but for CI the amplitude was highest with target C. As with the four degree stimuli, pattern onset tended to produce larger signals than pattern reversal. Responses were, on the whole, smaller for the more peripheral targets than for the central ones, particularly for the upper field targets F and G, which produced very small signals if at all. Figure 5.4 shows P100 spreading across the midline more than CI. This was not the case for all subjects; the examples shown were recorded on a subject in whom P100 was maximal on the midline for four degree hemifield stimulation. In the other two subjects in whom a comparison was possible the degree of lateralisation appeared similar for the two components. An examination of the latencies of these two components showed an apparent increase between target positions A and E, i.e. going from lower to upper hemifield stimulation. As a result of the very low signal amplitudes with targets F and G, it was difficult to assess peak latencies at these positions.

In all five subjects there was some evidence of movement of both component maxima on the map when target position was changed. In three subjects there was a slight, gradual, downward movement as stimulus position was moved from below fixation to above it. The example shown illustrates this point. This tendency was not, however, seen clearly in all cases. One subject showed a distinct lateral movement of both P100 and CI maxima so that both components appeared largest on electrode "L" for targets A to C but on electrode "M" for targets D and E.

5.4 Discussion

The localisation of cortical sources of VEP components directly from data on scalp distribution is, in some respects, a controversial practice. The attenuation and smearing effects of the skull and scalp, the influence of source depth and orientation and the sometimes unpredictable behaviour of current flow in the head can combine to produce misleading information. In the present study, however, to minimise these effects we attempted to confine stimulation to a fairly restricted region of the striate area, and any associated projections to extrastriate areas, on the proximal cortical surface around and lateral to the occipital pole. We hoped that by doing this we would be able to draw at least some tentative conclusions about the cortical origins of response components without the need for complex dipole localisation methods, which themselves can produce misleading results.

For the larger (four degree) fields, the results for P100 lend themselves to the interpretation of Halliday's group (Barrett et al. 1976a; Halliday 1982), suggesting that this component is the result of surface positive activity in the region of visual cortex around the postero-lateral convexity of the occipital pole, for foveal stimuli. In man, this region is largely occupied by the striate area (see Chapter 2). The results of these authors show that when using a large field size (16°) and large checks (50') the majority of subjects show maximum positivity on midline and ipsilateral channels for half-field stimulation, when electrodes are referred to a midfrontal channel. This behaviour, as explained in section 4.4b(iii), was thought by Barrett and co-workers (1976a) to be possibly related to the predominantly posteromedial orientation of the generators around the convexity at the occipital pole (see Figure 4.2). When using small fields (0-2°), however, there was a tendency for the maximum response to appear on the midline or even over the contralateral hemisphere. It was suggested that this was a result of a change in effective orientation of the generators to a more posterior or even posterolateral direction as stimulation was confined to the foveal area. These findings have been confirmed by other workers (e.g. Harding et al. 1980; Brecelj and Cunningham 1985). Brecelj and Cunningham (1985) showed that this change in localisation may be emphasised by reducing check size for the small fields. The summation of signals from the two hemispheres results in a midline maximum for full field stimulation (Blumhardt and Halliday 1979).

The findings in the present study fit in with those described above. An origin in surface positive activity in the region of striate cortex on the posterior and posterolateral aspects of the occipital pole would explain the contralateral maxima for the P100 elicited by these foveal half-field targets in some subjects. Intra-individual variability in the anatomical arrangement of the visual cortex in this region would account for the midline and

ipsilateral maxima in other subjects in whom the striate cortex might extend very little or not at all beyond the occipital pole. As with the large fields used by other authors, summation of responses from the two foveal hemifields would be expected to result in a maximum P100 amplitude on the midline with full field stimulation. The more posterior and lateral location of the predominant generator area, however, might perhaps produce a more widespread distribution. Examination of Figure 5.3 reveals that although P100 is largest on the midline, the amplitudes at the electrodes 4cm to either side are fairly close to that on the central electrode. The behaviour of this component, in some respects, therefore, appears to be fairly consistent with an origin in surface positive striate cortical generators. Such an interpretation is in agreement with that of Haimovic and Pedley (1982b) and also in part with that of Maier and co-workers (1987).

Component CI shows separate maxima to either side of the midline for full field stimulation. This type of distribution has been noted previously (Lesevre and Joseph 1979; Drasdo 1980). With the hemifield stimuli, this component showed a clear contralateral maximum for all subjects. This behaviour is consistent with that described by the majority of authors for the first major positive component in the onset response (see section 4.4b(iv)). Kriss and Halliday (1980), however, found that CI, like P100, was maximal on midline and ipsilateral channels. These authors considered that this finding might be due to the relatively large stimulus field size (16° radius) and check size (50') used in their sudy, which may have preferentially activated generators on the mesial surface of the hemisphere.

Jeffreys and Axford (1972a) stated that CI reversed in polarity across the midline with lateral half-field stimulation, appearing as an ipsilateral negativity. This behaviour suggested that CI arises as a result of surface negative activity on the mesial surface of the striate cortex. Recording from the opposite end of the dipole would give rise to the contralateral positivity (see section 4.4b(iv)). The group average hemifield distributions in the present study demonstrated no such reversal, with ipsilateral channels showing fairly flat traces. Individual data revealed an apparent polarity reversal in only one subject, who also demonstrated a midline negativity for full field stimulation. In the present study it was our intention to limit the stimulated portions of cortex, as far as possible, to the posterior and posterolateral aspects of the occipital lobe, by using stimuli of small angular extent. It is possible that the majority of subjects did not demonstrate ipsilateral negativity because the portion of cortex on the mesial surface of the hemisphere was not adequately stimulated. One might, however, have perhaps expected at least some subjects to show negativity on midline and contralateral channels as a result of surface negative activity around the occipital pole.

Several groups of workers have, as discussed in sections 4.4a, 4.4b(iv) and 4.5b, found

an early negative onset component on or near the midline when using small fields and/or high spatial frequencies. It is uncertain, however, whether this represents a "negative" CI or whether it is in fact a separate component. The finding of Kriss and Halliday (1980) that for a 16° radius field CI was of maximum positivity on midline and ipsilateral channels confuses the issue further. With such a large stimulus, surface negative striate generators on the mesial surface should certainly have led to negativity on ipsilateral channels if the theory of Jeffreys and Axford (1972a) were correct.

Lesevre and Joseph (1979), working with 10° radius hemifields, did show negative activity on ipsilateral channels in some subjects but this did not peak at the same latency as the contralateral positivity P90. Their early negative component N60 which appeared on the midline and was associated particularly with foveal stimulation was treated as a completely separate entity. These authors considered that the ipsilateral negativity was not related to P90 but to N140 (CII) or in some cases to the lateral negative wave LN150. Lesevre and Joseph (1979) found that their P90 component tended to invert with upper hemifield stimulation, leading to an anterior N90 on the midline. This, they considered, might come about as a result of the summation of signals from deep generators in the two hemispheres. These authors considered that CI might arise as a result of surface positive activity in area 19. Drasdo (1980) and Spekreijse's group (Maier et al. 1987), who both employed foveal stimulation also concluded that CI has a lateral origin in surface positive extrastriate activity.

It is possible that the limited evidence of midline and ipsilateral negative activity found in the present study might be related either to earlier or later negative components, or perhaps even to an inversion of CI associated with upper field extrastriate generators as suggested by Lesevre and Joseph (1979). Analysis of the distributions associated with altitudinal hemifield stimulation and also of the behaviour of early and later negative components would be necessary to explore these ideas further.

The differences observed in the behaviour of components P100 and CI suggest that they have at least partially different origins. If both arise from surface positive activity, the more clearly lateral location of the CI maxima and this component's distinct contralateral lateralisation compared with P100 suggest a more lateral cortical origin, in extrastriate areas. Hypothetical surface positive striate and extrastriate cortical dipole generators which might give rise to the observed distributions have been illustrated in Figures 5.5 and 5.6.

The recording of maximum amplitude for the flash P2 component on the midline above the inion is consistent with the findings of other authors (e.g. Nakamura and Biersdorf 1971; Whittaker and Siegfried 1983). The failure of the flash P2 component to clearly or

Figure 5.5

Schematic representation of a hypothetical foveal striate dipole generator.

(Modified from Barrett et al. 1976a)

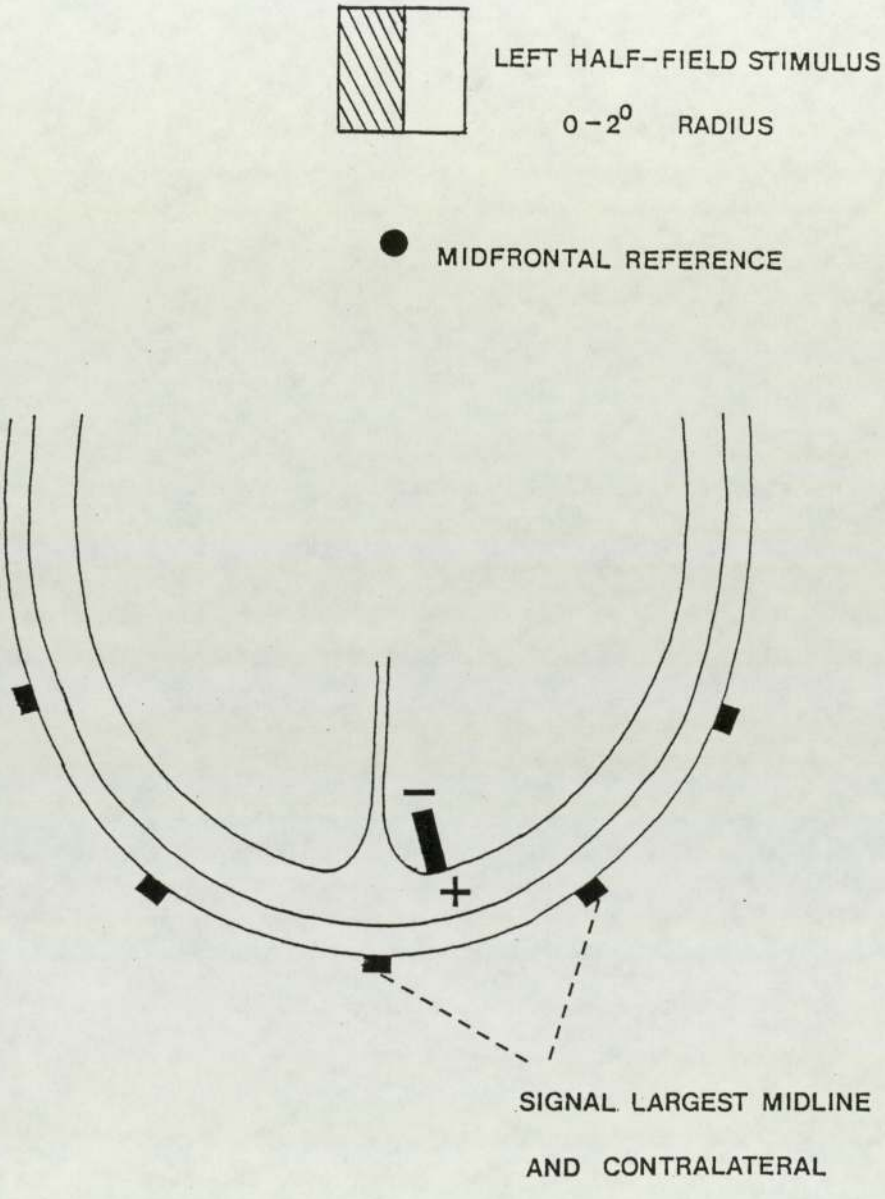
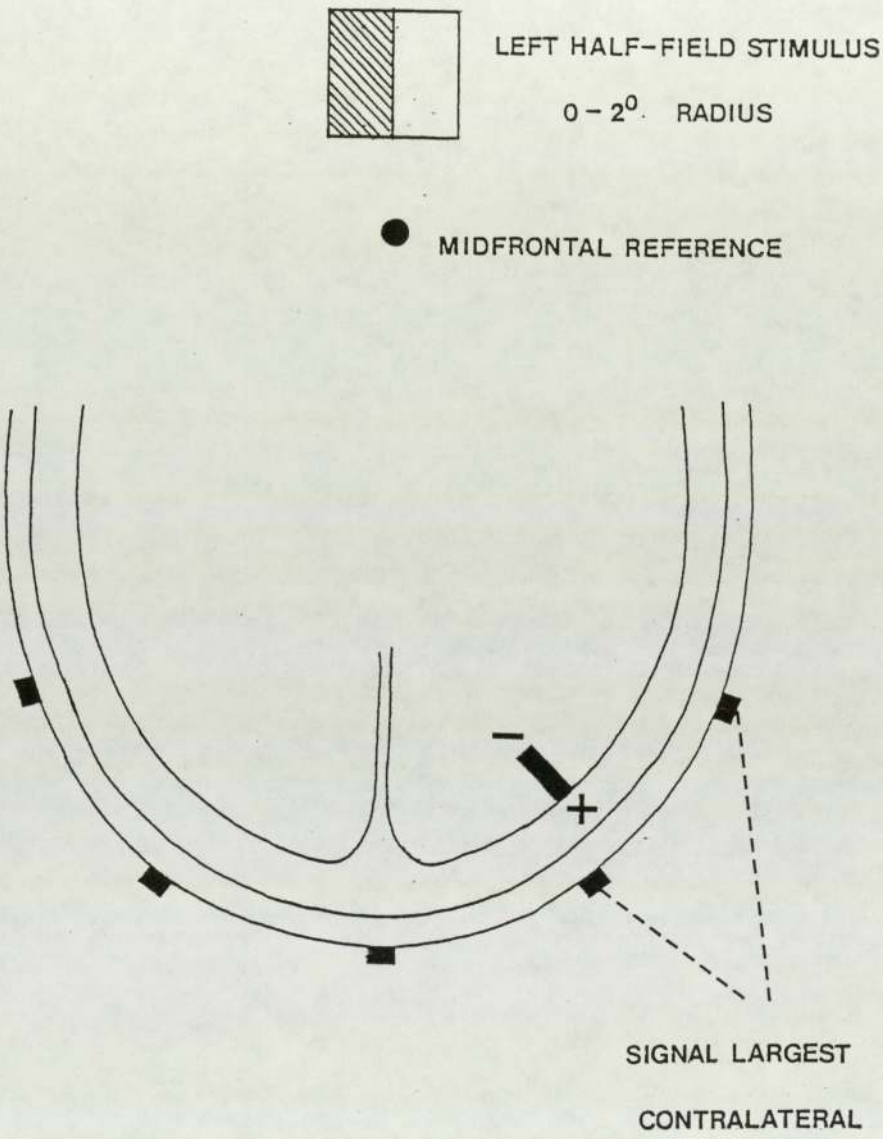

LEFT HALF-FIELD STIMULUS
0-2° RADIUS
MIDFRONTAL REFERENCE
−
+
SIGNAL LARGEST MIDLINE
AND CONTRALATERAL

Figure 5.6

Schematic representation of a hypothetical foveal extrastriate dipole generator.

(Modified from Barrett et al. 1976a)


LEFT HALF-FIELD STIMULUS
0 – 2°. RADIUS
MIDFRONTAL REFERENCE
–
+
SIGNAL LARGEST
CONTRALATERAL

consistently lateralise on half-field stimulation has also been reported by previous workers (see section 4.4b(ii)). This behaviour suggests that perhaps stimulation may not have been confined to one cerebral hemisphere. One explanation is that of stray light (mainly ocular scatter and retinal reflection) causing indirect stimulation of the retina on the other side of the midline. This problem has been discussed by previous workers (Lehmann et al. 1969; Harding et al. 1980). Scattered light has been shown to be important in the generation of the 'b' wave of the electroretinogram (ERG) when using small central stimuli (Boynton 1953). In the present situation, however, it is thought that stray light should have played very little part in eliciting the VEP to the flash stimulus, for several reasons. According to the point spread function for the eye, light spreading from each point on the edge of the stimulus should fall to around half intensity only a few minutes of arc away from the edge (Vos et al.1976) and is virtually negligible at a distance of 10 minutes. Hence, it is unlikely that there would have been much stimulation across the midline of the retina. The retina surrounding the stimulated area was adapted to a photopic luminance level and as such should have been relatively insensitive to the low intensity intra-ocular scatter associated with the low energy light flash. DeVoe et al (1968) showed that even in dark adapted eyes the contribution of scattered light to the VEP was inhibited by the Stiles-Crawford effect. This effect could be expected to be more marked at photopic adapting luminances, as in the present study.

Other potential sources of bilateral stimulation are the imprecise fixation which results from physiological nystagmus, which could be expected to spread stimulation by around 10 minutes of arc (Ditchburn and Fisher 1967) and also the overlapping cortical representation of the vertical meridian of the visual field (Stone et al. 1973). These factors should, however, have also affected the lateralisation of responses to pattern stimulation, had they played a significant role.

Stimulation across the midline may have come about by means of lateral spread of neural excitation within the retina. This is believed to occur over wide areas of the retina with high frequency stimuli (Robson 1986) and could therefore possibly occur with very brief stimuli (i.e. with high rate of change of luminance) such as light flashes. An alternative and more probable explanation for the failure of P2 to demonstrate clear localisation is that it arises in multiple cortical areas. This may relate in part to the finding of a delay in flash P2 but not in pattern reversal P100 in Alzheimer's disease, as discussed in section 4.4b(i). Wright, Harding and Orwin (1984) suggested that the delay in P2 might be indicative of an origin for this component in the visual association areas, which suffer tissue damage in this condition. P100 would, according to this line of reasoning, arise from the striate area, which in histological examination remains unaffected. It may in fact be that both striate and extrastriate areas are involved in the genesis of this component and that the delay in latency comes about as a result of the effects on the

extrastriate portion of the response. This, however, seems a little paradoxical since one might expect a later "portion", if anything, of this component to arise from higher areas.

The results for the M-scaled targets showed some degree of inter- and intra-individual variability in signal amplitude. Inter-subject differences were perhaps not quite as variable as expected with the central targets D and C giving the highest amplitudes in most cases. Barber and Galloway (1981), who used small targets with constant angular subtense and check size, reported that a target just below fixation elicited the largest responses to pattern onset stimulation. In the present study, however, one might have expected a more even distribution. The results may reflect a limited degree of anatomical variability in the arrangement of gyri and fissures with respect to visual field projections. The general tendency for small responses to upper field stimuli might be expected as these targets should stimulate cortical areas towards the lower aspect of the visual cortex, where the generators are less optimally positioned with respect to the scalp electrodes. It may be that the portions of cortex related to the central targets are most optimally placed in most subjects. This would be the case if only a very limited portion of the central visual field were represented on the proximal cortical surface, smaller than that predicted by Drasdo's (1983) schematic map.

An alternative explanation is that we may not have stimulated cortical regions of the required dimensions. Failure to achieve cortical equivalence in these M-scaled stimuli, so that the central targets activated larger regions than the peripheral ones would give rise to such results. The involvement of extrastriate cortical activity may be implicated in such an effect; studies of cortical magnification in mammals show that absolute values of M and also its relation with eccentricity vary between different visual areas (Orban 1984; Gattass et al. 1985). One other factor which may have influenced response amplitude is check size. The relationship between optimal spatial frequency and retinal eccentricity, particularly in the foveal region, may not be the same as that for cortical magnification (see section 2.4). It may be that the check sizes used for the peripheral stimuli in the present study were not appropriate for eliciting a maximal response.

In relation to the projection of these targets onto gyri and fissures, as predicted, one subject did demonstrate the phenomenon of a reduction in signal amplitude followed by recovery as target position was moved out into the lower field. Figure 5.4 shows a larger amplitude for targets A and C than for target B, for both P100 and CI. This effect could be the result of the projection of target B onto an area of cortex which is at least partly within a fissure.

An increase in latency between responses to lower and upper field stimuli is in keeping with the findings of other workers (see sections 4.4b(iii) and 4.4b(iv)). Barber and

Galloway (1981) observed an apparent abrupt latency increase for CI between responses to stimuli just below and just above fixation. These authors, as discussed in section 4.4b(iv), attributed this latency change to a difference between "epicentral" and "peripheral" response properties rather than between upper and lower hemifields. They found that more peripheral upper field stimuli elicited responses of similar properties to those for lower field stimuli. Responses to the more peripheral upper field targets in the present study were too low in amplitude to be able to judge latencies for comparison. Our results differ from those of Barber and Galloway (1981) in that this latency increase appeared to be a gradual one. A latency increase between central and peripheral responses in the present study might be expected purely as a result of the decrease in check size. The increase in component latency which occurs with an increase in pattern spatial frequency is well documented in the literature (see section 3.3b). It may be that both of these factors influenced the results of the present study.

With regard to the sources of these components, it is thought that a diffuse origin in multiple cortical areas might tend to produce a more generalised response distribution than those which were observed, which would vary little with stimulus visual field location. The degree of localisation of these responses and their variability suggests that these two components might originate largely in single cortical areas. The differences in distribution of P100 and CI for the same targets are supportive of the theory of separate cortical origins. On the other hand, these differences are not so marked that one would expect surface positive activity in the case of P100 and surface negative activity for CI from the same (striate) cortical area to be responsible for their production. The more rapid rate of fall-off of P100 amplitude with target eccentricity might be a result of the location and orientation of the striate area which would be less accessible to recording electrodes than extrastriate cortex. A more contralateral location of P100 maxima with these smaller targets might be expected since they are positioned close to the vertical meridian, and would tend to preferentially activate striate regions further away from the midline, towards the striate-extrastriate boundaries.

The apparent gradual migration of component maxima with change in stimulus position could possibly be interpreted as demonstrating a local retinotopic order in VEP generator areas. The variation in amplitude with target position in the visual field also suggests some kind of mapping. This would apply equally for P100 and CI generator areas. If our previous deductions as to component cortical origins are correct, this would suggest that this kind of order exists in extrastriate as well as striate cortex in humans. At this stage however, it is considered that more extensive work on larger subject numbers is required before conclusions can be drawn from any of the findings discussed.

CHAPTER 6

Further investigation of the scalp topography and cortical origins of the visual evoked potentials elicited by foveal pattern stimulation. I. Four degree full and hemifield stimuli.

6.1 Introduction

The previous chapter detailed a study of the major early positive components of the responses to pattern and flash stimulation in the central few degrees of the visual field, using four degree full and half-field targets and also, in the case of pattern stimuli, using very small M-scaled targets placed at different positions in the left visual hemifield. This work produced some interesting results and it was considered that both aspects of the study warranted further investigation to both confirm and extend these findings. In particular, the results for pattern stimulation were thought to be of great interest. In the present chapter a detailed study of the waveform and topography of the responses to four degree full field and four by two degree lateral and altitudinal hemifield targets for pattern reversal and pattern onset stimulation is described. In the next chapter, the findings on a larger group of subjects using the small M-scaled targets are discussed, as in Chapter 5, in relation to the behaviour of the major early positive components in the pattern onset and pattern reversal responses.

In addition to the omission of flash stimulation and the recording of responses to altitudinal hemifield stimulation, this study differs from that described in Chapter 5 in several other aspects. The analysis of responses in the previous study was confined to the major early positive components. Examination of the literature reveals few well documented accounts of constituent components of the pattern reversal and pattern onset responses and their scalp distribution for stimuli in the central few degrees of the visual field. Perhaps the most comprehensive study was that of Lesevre and Joseph (1979), who conducted a chronotopographical analysis of the pattern onset response recorded from longitudinal and sagittal rows of electrodes using 20° diameter fields and 20' checks. Smaller "macular" (5°) and "foveal" (1° 30') targets were used but half-field and quadrant stimulation mainly involved the 20° target. The results, which were discussed in detail (see section 4.4b(iv)), were compared only briefly with those found for pattern reversal stimulation. It was considered, therefore, that the analysis of all major components in the first 250 msecs of the responses recorded in the present study would fulfil a useful role, not least because of the opportunity for visualisation of component scalp distribution in the form of two-dimensional colour maps . Such an analysis is considered particularly important in terms of distinguishing components at latencies of around 70 to 160 msecs. As was discussed in sections 4.4b(iii) and (iv), and also in section 4.5b, there is still some confusion as to the relationship between the

various positive and negative components in full and partial field responses at these latencies.

Another modification from the previous study concerns the location of scalp electrodes. These were placed in an equidistant matrix across the occipital area at about 4cm separation. This method was used as it was considered that equal spacing between electrode positions would result in the best match between the actual electrode positions on the head and the positions of channels on the Brain Atlas display map. In terms of relationship with head and cortex anatomy, however, a percentage spacing is considered to be more appropriate. Consequently, electrode positions in the present study were determined according to percentage head dimensions as described below. This inevitably produces some distortion of the display map as compared with actual potential distribution on the scalp, particularly at the most anterior electrode placements.

As in the previous chapter, scalp distribution of individual components is illustrated in the form of equipotential contour maps. Each map shows the pattern of potential variation across the scalp at a single instant in time. In the present study, however, voltage of each component was measured with respect to the baseline. In the previous study, the voltage transient between the major positive and the previous negative peak was mapped. Such a method of analysis was not considered appropriate for the study of the behaviour of multiple components which overlap in their time course.

One further difference between the two studies is one of check size used. This has been slightly reduced from 19' to 15' of arc in the present study. This change was purely a consequence of the particular slide used in the projection system and was not expected to alter results significantly.

6.2 Materials and methods

Details of methods of pattern stimulation and electrophysiological recording techniques were identical to those in the previous study except where indicated below.

Fourteen normal volunteer subjects were employed in total, four of whom were female. Age range was 21-31 years and all had visual acuity of 6/6 or better, wearing optical correction where necessary. Data analysis was performed only on results for the eleven subjects (two female) for whom full data sets were acquired. Three of these subjects (one female) had taken part in the previous study.

The stimuli used were four by four degree square full fields and four by two degree lateral and altitudinal half-fields. Responses were recorded to pattern reversal and

pattern onset-offset of 15' of arc high (0.8) contrast checkerboard patterns, at a stimulation rate of 1.3 per second (150msecs onset period).

Responses from 16 scalp electrodes were averaged by a Bio-logic Brain Atlas III mapping system. The montage used is represented in Figure 5.2 and was, as in the previous study, confined to the back of the head. Electrode placement was, in this study, however, based on percentage head dimensions. Electrodes were placed at 14% horizontal and 11% vertical (sagittal) distances. On the average head, this resulted in an approximately 4cm separation both horizontally and vertically around the midline occipital region but a somewhat more compressed array anteriorly. All channels were referred to a common midfrontal reference (Fz) with the ground electrode on the forehead (Fpz).

CHAPTER 6
RESULTS

Figure 6.1

Group average traces for pattern onset and pattern reversal four degree full field and lateral half-field stimuli

6.1a Full field responses
6.1b Left half-field responses
6.1c Right half-field responses
6.1d Lower half-field responses
6.1e Upper half-field responses

Reference letters for channels refer to display in Figure 5.2a.

Figure 6.1a Full field responses

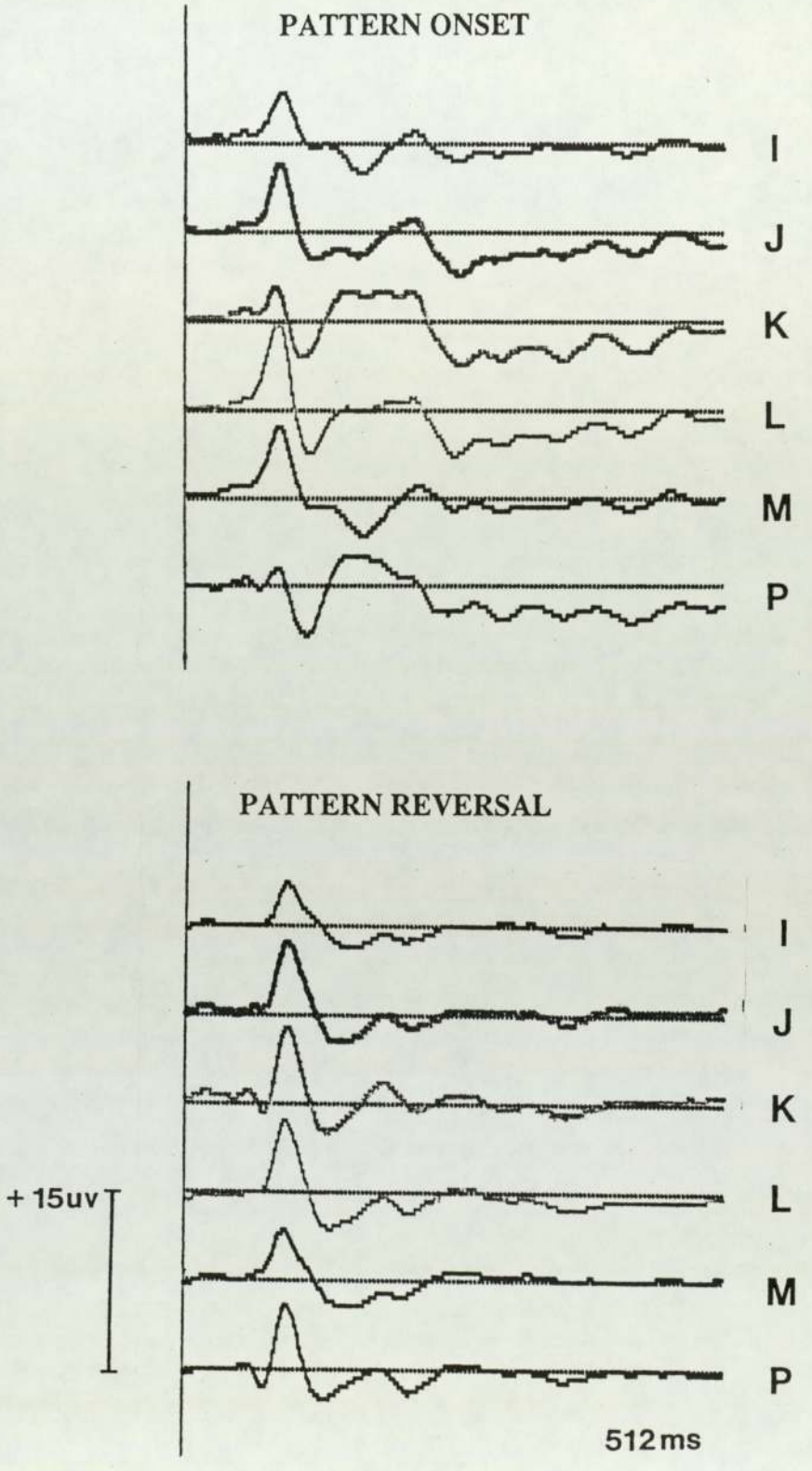


Figure 6.1b Left half-field responses

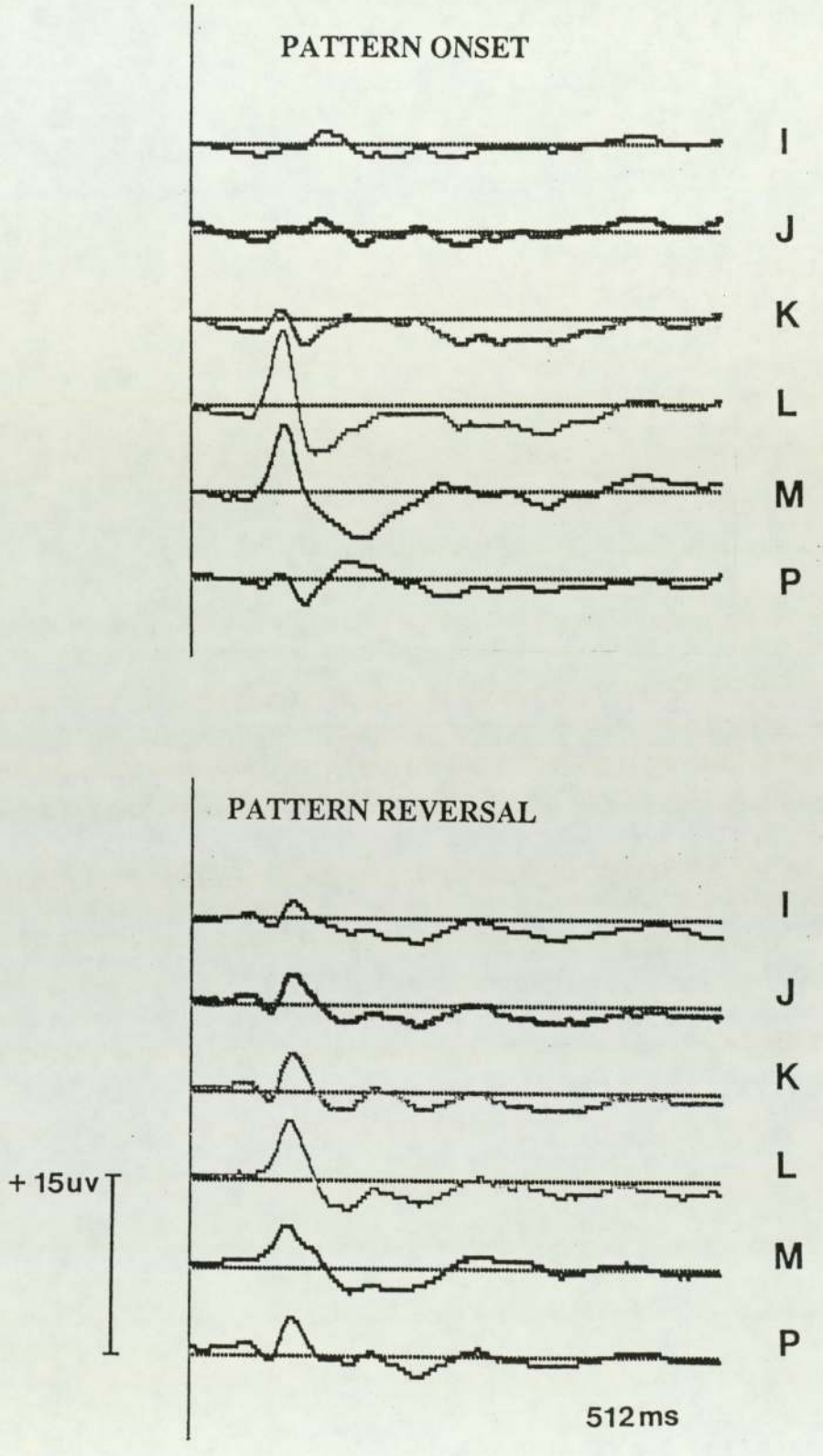


Figure 6.1c Right half-field responses

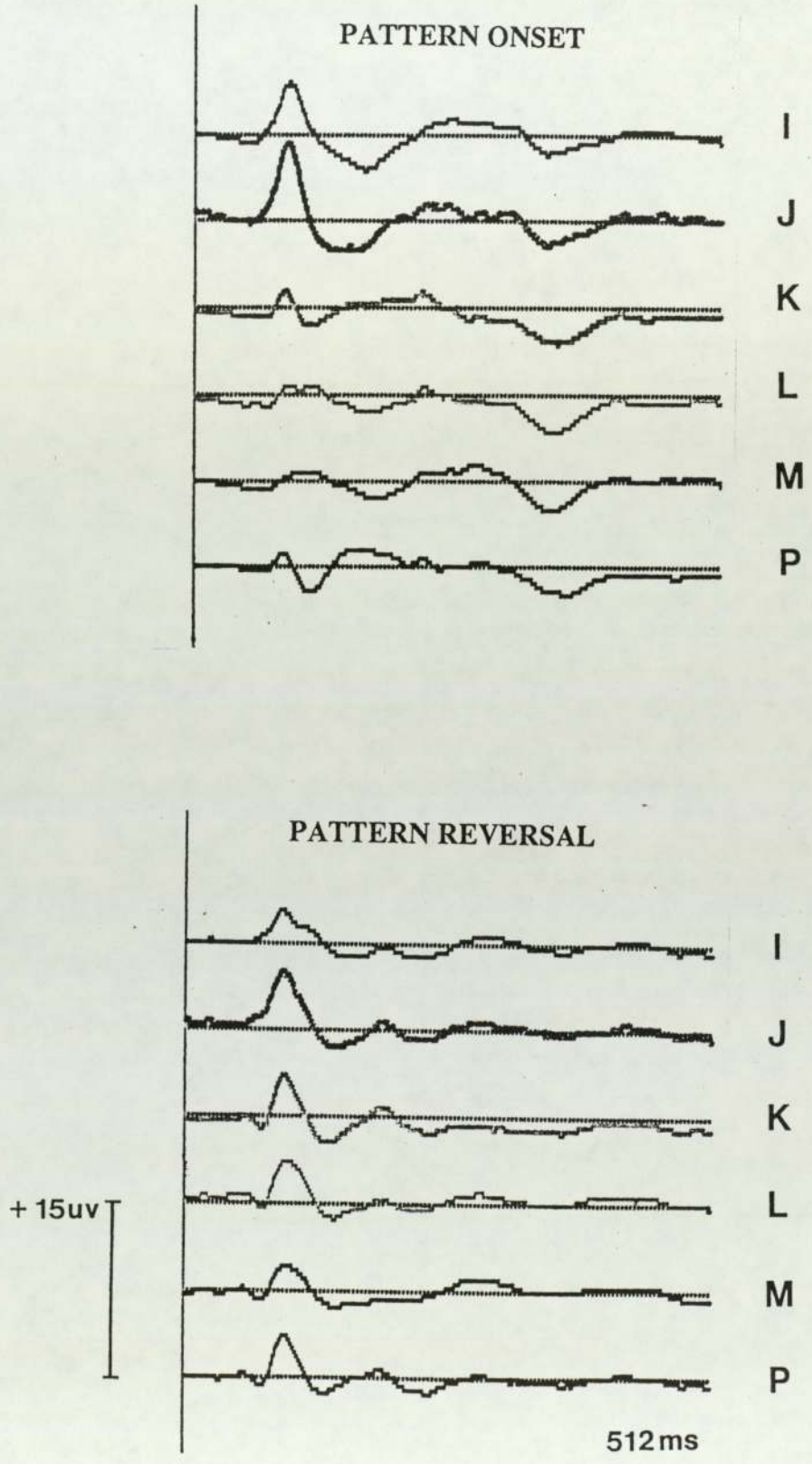


Figure 6.1d Lower half-field responses

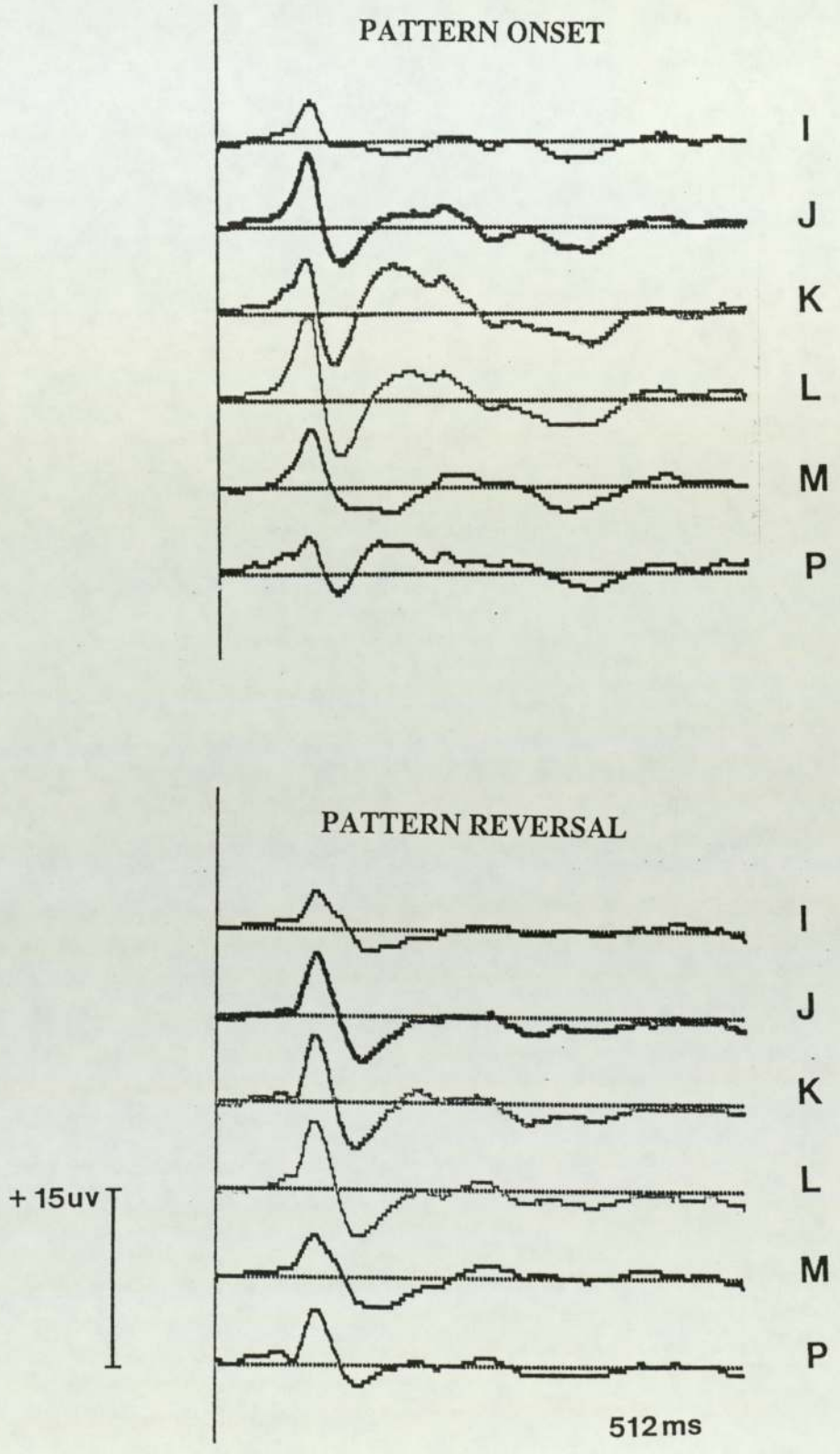


Figure 6.1e Upper half-field responses

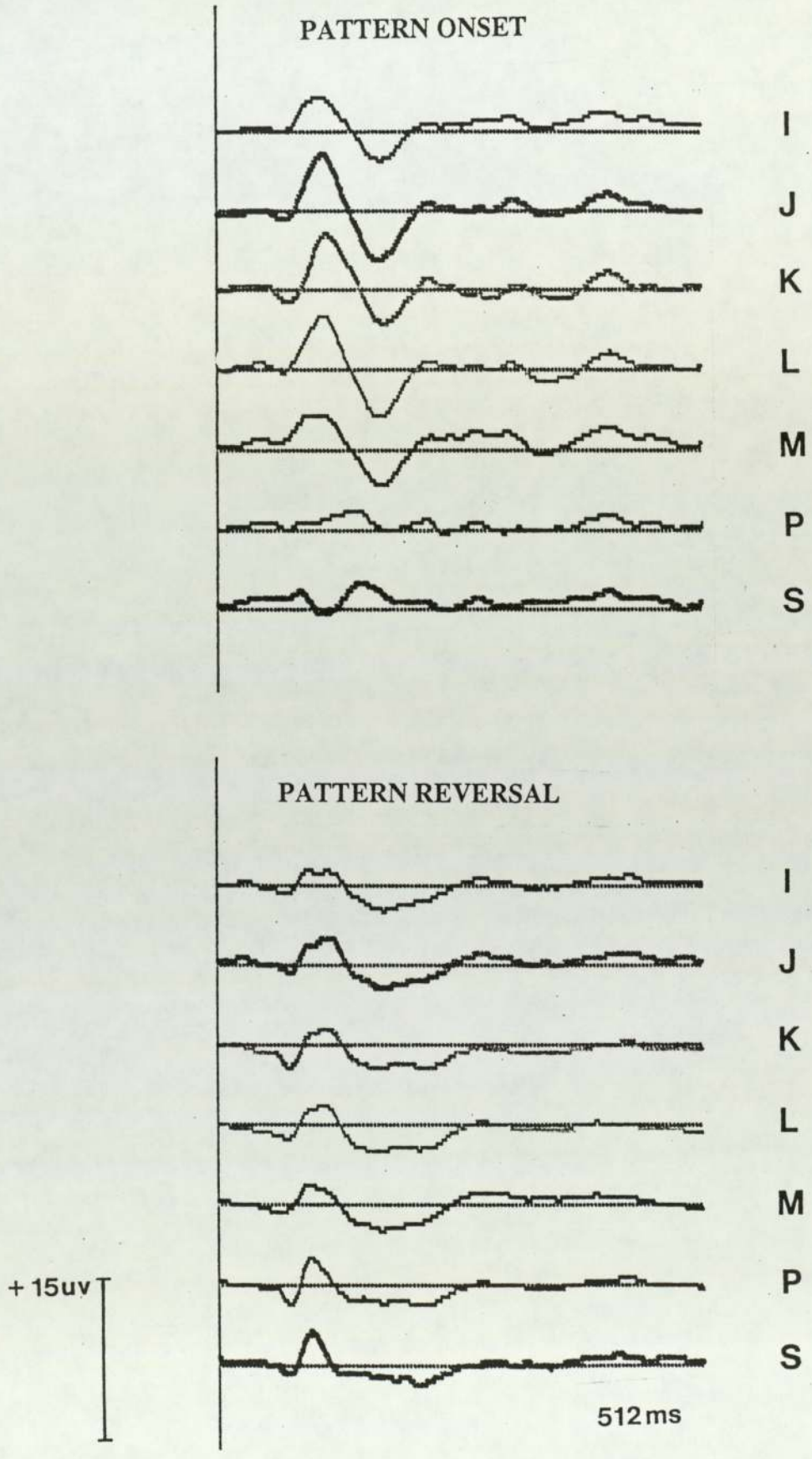


Table 6.1

The peak latencies and maximum amplitudes of the different components in the responses of individual subjects to pattern onset and pattern reversal stimulation with four degree full and half-field stimuli.

6.1a Pattern onset responses
- 6.1a(i) Full field
- 6.1a(ii) Left half-field
- 6.1a(iii) Right half-field
- 6.1a(iv) Lower half-field
- 6.1a(v) Upper half-field

6.1b Pattern reversal responses
- 6.1b(i) Full field
- 6.1b(ii) Left half-field
- 6.1b(iii) Right half-field
- 6.1b(iv) Lower half-field
- 6.1b(v) Upper half-field

6.1c Summary of group means
- 6.1c(i) Pattern onset responses
- 6.1c(ii) Pattern reversal responses

Table 6.1a(i) Pattern onset full field responses

		COMPONENT						
		P55	N70	P90	N110	P155	N170	P220
SUBJECT								
GC	msecs	58	70	88		146	156	184
	μV	+1.6	-0.1	+10.8		+5.1	- 5.8	+6.6
	electrode	P	P	J		P	M	P
DMcV	msecs	56	76	88	108	146	174	220
	μV	+2.8	+0.3	+3.6	-5.3	+7.4	-5.9	+6.4
	electrode	O	J	M	P	U	G	K
JL	msecs	64		92	110	164	166	
	μV	+0.4		+3.8	-24.3	+17.9	+1.2	
	electrode	K		J	L	L	E	
UD	msecs	48	68	84	114	146	188	220
	μV	+1.4	-0.3	+8.7	-7.4	+2.1	-9.7	-0.6
	electrode	S	O	L	L	K	M	K
NH	msecs	56	70	86	100	166	156	196
	μV	+2.7	-1.1	+4.0	-3.2	+11.3	-3.9	+13.1
	electrode	S=U	P	M	P	P	H	K
PB	msecs			88	110	156	200	220
	μV			+8.5	-3.2	+9.1	-3.7	+2.7
	electrode			J	P	Q	I	K
AH	msecs	58	68	90	126	156	174	226
	μV	+1.5	+0.1	+23.3	-11.8	+5.6	-7.1	+6.6
	electrode	K	K	L	L	P	J	E=G
RB	msecs	60	70	90	112		164	242
	μV	+2.0	+0.6	+12.6	-3.4		-6.5	+6.4
	electrode	P	T	L	P		M	L
ARH	msecs			86	106	158	158	220
	μV			+10.0	-13.7	+11.3	-3.7	+12.7
	electrode			J	K	K	I	L
RD	msecs	46	64	90	118		166	220
	μV	+0.9	-1.5	+9.6	-5.5		-9.6	+3.9
	electrode	K	P	J	P		E	E=G
JR	msecs		72	92	114		168	192
	μV		-4.4	+9.3	-2.5		-14.2	-3.7
	electrode		P	L	P		G	P
GROUP MEAN		P55	N70	P90	N110	P155	N170	P220
	N	8	8	11	10	8	11	11
	msecs	**55.8**	**69.8**	**88.6**	**111.8**	**154.8**	**170.0**	**210.5**
	S.E.M.	2.1	1.2	0.8	2.2	2.9	4.1	6.1
	μV	**+1.6**	**-0.8**	**+9.6**	**-8.0**	**+8.7**	**-6.3**	**+6.4**
	S.E.M.	0.3	0.6	1.7	2.2	1.7	1.2	1.8

Table 6.1a(ii) Pattern onset left half-field

		COMPONENT						
		P55	N70	P90	N110	P155	N170	P220
SUBJECT								
GC	msecs		74	88		152	164	220
	μV		-2.1	+7.8		+2.9	-6.1	+3.7
	electrode		N	L		S	M	L
DMcV	msecs			90	110	168	164	218
	μV			+4.7	-4.2	+3.5	-3.6	+3.1
	electrode			M	S	S	H	K
JL	msecs			86	110	172	158	
	μV			+5.9	-17.2	+16.2	-3.2	
	electrode			M	L	L	I	
UD	msecs			86	124	134	162	234
	μV			+11.8	-4.4	+2.9	-10.8	-1.0
	electrode			L	L	J	M	J
NH	msecs	58	70	86		142	164	190
	μV	+1.5	-1.2	+3.8		+5.9	-5.1	+6.5
	electrode	R	J	M		P	M	K
PB	msecs			90	110	160	200	
	μV			+7.0	-5.5	+5.4	-5.0	
	electrode			M	L	L	N	
AH	msecs	44	70	90	126	150	196	250
	μV	+2.9	-2.6	+20.8	-10.9	+4.0	-5.8	+4.8
	electrode	P	J	L	L	P	J	P
RB	msecs			96	144	144	176	246
	μV			+11.9	-4.0	+4.9	-5.6	+8.2
	electrode			L	L	N	M	G
ARH	msecs			86	110	148	156	186
	μV			+7.7	-11.0	+2.2	-1.1	+9.3
	electrode			M	L	S=U	I	K
RD	msecs			90			164	244
	μV			+7.8			-8.1	+3.1
	electrode			L			G=L	K
JR	msecs		70	90	106	130	156	234
	μV		-2.6	+8.2	-2.1	+3.2	-9.6	+2.5
	electrode		U	L	R	S	G	G
GROUP MEAN		P55	N70	P90	N110	P155	N170	P220
	N	2	4	11	8	10	11	9
	msecs	**51.0**	**71.0**	**88.9**	**117.5**	**150.0**	**169.1**	**224.7**
	S.E.M.	7.0	1.0	0.9	4.6	4.3	4.6	7.8
	μV	**+2.2**	**-2.1**	**+8.9**	**-7.4**	**+5.1**	**-5.8**	**+4.5**
	S.E.M.	0.7	0.3	1.4	1.8	1.3	0.9	1.1

Table 6.1a(iii) Pattern onset right half-field responses

			COMPONENT					
		P55	N70	P90	N110	P155	N170	P220
SUBJECT								
GC	msecs		72	90		160	176	202
	μV		-1.0	+10.6		+3.1	-2.3	+5.8
	electrode		U	J		S	H=M	J
DMcV	msecs			96	114	164	174	224
	μV			+4.2	-3.4	+5.4	-4.2	+4.8
	electrode			J	U	U	E	K=L
JL	msecs			94	116	174	160	
	μV			+5.9	-6.6	+6.7	-1.3	
	electrode			J	O	P	I	
UD	msecs		70	86	100	150	168	224
	μV		-1.2	+4.7	-1.3	+3.6	-2.8	+0.9
	electrode		K	J	K	U	I	M
NH	msecs		70	86	122	140	166	196
	μV		-2.4	+5.6	-1.4	+7.5	-3.4	+7.0
	electrode		P	J	J	P	H	K
PB	msecs			90	122	154	200	248
	μV			+6.0	-7.0	+2.8	-7.8	-0.4
	electrode			J	J	O	U	I=J
AH	msecs			90	130	150	168	266
	μV			+12.5	-7.0	+2.1	-12.1	+5.5
	electrode			J	J	M	J	K
RB	msecs			92	106		162	200
	μV			+3.8	-3.0		-6.0	+0.6
	electrode			E	P	U	E	K
ARH	msecs			86	120	156	148	200
	μV			+13.4	-12.9	+1.8	-7.3	+7.1
	electrode			J	J	P	I	K
RD	msecs			92	114		168	244
	μV			+8.1	-1.7		-9.4	+4.2
	electrode			E	K		L	K
JR	msecs		72	94	110		156	200
	μV		-3.9	+5.8	+0.2		-4.5	+6.7
	electrode		L	J	P		E	E=G
GROUP MEAN		P55	N70	P90	N110	P155	N170	P220
	N	0	4	11	10	8	11	10
	msecs		**71.0**	**90.6**	**115.4**	**156.0**	**167.8**	**220.4**
	S.E.M.		0.6	1.1	2.8	3.6	4.0	7.9
	μV		**-2.1**	**+7.3**	**-4.4**	**+4.1**	**-5.6**	**+4.2**
	S.E.M.		0.7	1.0	1.3	0.8	1.0	0.9

Table 6.1a(iv) Pattern onset lower half-field responses

		COMPONENT						
		P55	N70	P90	N110	P155	N170	P220
SUBJECT								
GC	msecs	50		88		158	168	244
	μV	+2.2		+10.4		+4.3	-3.9	+5.4
	electrode	O		J		P	M	J
DMcV	msecs	62	72	86	114	154	160	208
	μV	+1.4	+1.5	+5.5	-5.2	+3.4	-1.3	+4.4
	electrode	P	P	L	L	K	H	K
JL	msecs			84	112	168		
	μV			+3.1	-26.2	+12.3		
	electrode			J	L	K		
UD	msecs	62	72	84	110	146	190	230
	μV	+1.1	-0.1	+7.0	-5.7	+2.2	-6.6	+1.3
	electrode	K	S	L	K	K	I	L
NH	msecs	58	72	86	106	154	166	200
	μV	+2.3	+1.0	+10.8	-3.3	+8.9	-3.4	+8.5
	electrode	P	S=U	J	K	P	M	K
PB	msecs	66		86	108	160	202	254
	μV	+4.2		+8.5	-4.5	+5.6	-6.7	
	electrode	L		J	L	K=L	S	
AH	msecs	54	70	88	122	156	184	246
	μV	+2.7	-0.1	+19.4	-9.7	+2.5	-5.1	+6.4
	electrode	K	P	L	L	K	M	K
RB	msecs	66		90	132	146	158	210
	μV	+2.3		+9.2	-7.0	+2.7	-5.6	+4.9
	electrode	N=S		L	L	N	L=M	K
ARH	msecs			82	104	172	150	218
	μV			+6.4	-13.7	+10.7	-5.6	+5.3
	electrode			E	K	K	I	O
RD	msecs			90	110	146	168	222
	μV			+7.4	-5.8	-1.4	-8.3	+4.9
	electrode			L	K	S	R	K
JR	msecs			90	114	182	158	220
	μV			+11.9	-2.2	+2.8	-5.5	+4.6
	electrode			L	L	P	G	G
GROUP MEAN		P55	N70	P90	N110	P155	N170	P220
	N	7	4	11	10	11	10	9
	msecs	**59.7**	**71.5**	**86.7**	**113.2**	**158.4**	**170.6**	**222.0**
	S.E.M.	2.3	0.5	0.8	2.6	3.5	5.3	5.2
	μV	**+2.3**	**+0.4**	**+9.0**	**-8.3**	**+4.9**	**-5.2**	**+5.1**
	S.E.M.	0.4	0.5	1.3	2.2	1.2	0.6	0.6

Table 6.1a(v) Pattern onset upper half-field responses

		COMPONENT							
		P55	N70	P90	P110	N110	P155	N170	P220
SUBJECT									
GC	msecs		70	80	114		140	172	218
	μV		-1.6	+1.7	+8.9		+3.8	-9.4	+2.1
	electrode		K	U	K		S	M	J=P
DMcV	msecs			86	114	112	152	190	
	μV			+3.3	+5.5	-1.8	+3.6	-5.7	
	electrode			U	G	S	U	G	
JL	msecs			80	108	118	172	150	192
	μV			+1.6	+5.0	-7.5	+2.4	-6.4	+6.6
	electrode			L	E	U	P	J	U
UD	msecs			88	112	118	148	194	246
	μV			+2.9	+5.9	-2.2	+1.2	-8.5	+1.1
	electrode			L	K	U	S	J	J
NH	msecs		80		116		146	164	208
	μV		-2.6		+10.8		+5.1	-4.8	+6.1
	electrode		K		K		P	M	K
PB	msecs			90	104	116	160	198	232
	μV			+6.2	+5.4	-3.6	+6.6	-4.7	+1.7
	electrode			M	E	R	S	E	E
AH	msecs		68	92	112	120	156	166	256
	μV		-2.3	+4.8	+7.6	-2.7	+3.3	-6.4	+5.1
	electrode		K	M	E	S	S	J	K
RB	msecs		80	96	116	110	146	176	244
	μV		-2.0	+3.5	+7.8	-1.0	+1.8	-8.1	+1.3
	electrode		P	N	E	U	U	E	M
ARH	msecs			86	102	102	146	160	210
	μV			+4.0	+7.6	-3.0	+2.9	-12.5	+11.4
	electrode			L=M	E	U	U	J	J
RD	msecs			90	110	120	136	170	224
	μV			+2.6	+7.1	-1.1	+2.3	-8.7	+3.3
	electrode			S	G	S	P	G	K
JR	msecs		74	92	126			172	220
	μV		-2.1	+2.5	+11.4			-4.3	+4.8
	electrode		K	M	K			L	G
GROUP MEAN		P55	N70	P90	P110	N110	P155	N170	P220
	N	0	5	10	11	8	10	11	10
	msecs		**74.4**	**88.0**	**112.2**	**114.8**	**150.2**	**173.8**	**225.0**
	S.E.M.		2.5	1.6	2.0	2.3	3.3	4.5	6.2
	μV		**-2.1**	**+3.3**	**+7.6**	**-2.9**	**+3.3**	**-7.2**	**+4.3**
	S.E.M.		0.2	0.4	0.6	0.7	0.5	0.8	1.0

Table 6.1b(i) Pattern reversal full field responses

		COMPONENT						
		P60	N75	P95	N130	N170	P190	N210
SUBJECT								
GC	msecs	58	74	92		162	220	
	μV	+1.4	-3.0	+7.7		-3.9	+3.3	
	electrode	P	P	J		M	J	
DMcV	msecs	60	72	92	122		184	212
	μV	+0.9	-0.1	+4.4	-8.2		+3.0	-1.2
	electrode	S=U	K	L=Q	P		K	S
JL	msecs		80	98	124	152	190	228
	μV		-3.6	+5.5	-6.1	-3.9	+5.8	-6.8
	electrode		K	S	L	N	K	K
UD	msecs	64	74	92	132	172	186	212
	μV	+0.1	-0.8	+7.5	-1.3	-4.7	+0.6	-3.8
	electrode	P	P	L	L	M	K	S
NH	msecs	54	74	94	134	166		210
	μV	+2.0	-7.2	+7.8	-3.0	-4.6		-8.8
	electrode	K	P	J	E	H		Q
PB	msecs	58	70	94	132		186	208
	μV	+1.2	-1.0	+9.1	-5.6		+2.1	-4.7
	electrode	U	S	L	L		K	N
AH	msecs	54	72	92	130	160	184	208
	μV	2.1	-2.5	+11.4	-5.8	-4.2	+0.4	-4.9
	electrode	P	K	L	K	J	K	L
RB	msecs	60	80	100	144	160	174	200
	μV	+2.2	-2.5	+7.1	-3.9	-4.0	-0.1	-5.1
	electrode	S	N	L	K	L	E=G	N
ARH	msecs			94	124		188	
	μV			+9.6	-11.3		+7.7	
	electrode			J	K		K	
RD	msecs		74	98	148		196	
	μV		-3.3	+11.1	-7.7		+0.4	
	electrode		K	K	K		K	
JR	msecs	62	76	94		160	194	
	μV	+1.3	-1.5	+6.1		-6.0	-0.6	
	electrode	U	P	L		L	E	
GROUP MEAN		P60	N75	P95	N130	N170	P190	N210
	N	8	10	11	9	7	10	7
	msecs	**58.8**	**74.6**	**94.6**	**132.2**	**161.7**	**190.2**	**211.1**
	S.E.M.	1.3	1.0	0.9	3.0	2.3	3.8	3.2
	μV	**+1.4**	**-2.8**	**+7.9**	**-5.9**	**-4.5**	**+2.3**	**-5.0**
	S.E.M.	0.3	0.6	0.7	1.0	0.3	0.9	0.9

Table 6.1b(ii) Pattern reversal left half-field responses

		COMPONENT						
		P60	N75	P95	N130	N170	P190	N21O
SUBJECT								
GC	msecs		74	88	138	150	180	200
	μV		-3.4	+2.6	-2.2	-3.5	0.0	-3.7
	electrode		P	L	P	L	P	R
DMcV	msecs	56	70	94	134		176	230
	μV	+2.6	+0.3	+3.1	-4.6		+0.7	-5.8
	electrode	S	O	L	L		P	U
JL	msecs	56	80	100	128	152	196	
	μV	+2.1	-0.4	+10.5	-4.8	-3.9	+5.5	
	electrode	U	P	L	L	J	L	
UD	msecs	64	80	90	144	186	202	218
	μV	+0.8	-0.5	+4.8	-7.1	-1.3	+0.1	-4.1
	electrode	T	S	L	M	N	K	U
NH	msecs	50	74	92	144	188	204	222
	μV	+1.3	-4.4	+2.9	-3.6	-5.2	+2.0	-2.7
	electrode	O	K	L	G	S	G	I
PB	msecs			94	124	152	178	206
	μV			+7.6	-2.4	-1.7	+2.1	-4.1
	electrode			L	L	M	G	U
AH	msecs	54	74	94	126	156	176	202
	μV	+1.7	-2.2	+8.1	-4.8	-3.2	+2.3	-6.7
	electrode	K=O	J	L	K	L	K	Q
RB	msecs		80	98		170	180	
	μV		-3.7	+4.6		-5.3	-2.0	
	electrode		O	L		L	E	
ARH	msecs	58	76	90	122	188	178	
	μV	+0.5	-1.8	+3.6	-8.4	-3.0	+4.5	
	electrode	P	I	G	L	M	K	
RD	msecs	60	76	98		156	170	192
	μV	+0.3	-1.7	+7.1		-3.1	-1.8	-4.9
	electrode	J	K	K		K	P	Q
JR	msecs		74	92		170	180	
	μV		0.0	+5.9		-7.6	+0.7	
	electrode		P	L		G=H	P	
GROUP MEAN		P60	N75	P95	N130	N170	P190	N21O
	N	7	10	11	8	10	11	7
	msecs	**56.9**	**75.8**	**93.6**	**132.5**	**166.8**	**183.6**	**210.0**
	S.E.M.	1.7	1.1	1.1	3.1	5.0	3.5	5.1
	μV	**+1.3**	**-1.9**	**+5.5**	**-4.7**	**-3.8**	**+1.4**	**-4.6**
	S.E.M.	0.3	0.6	0.8	0.8	0.6	0.7	0.5

Table 6.1b(iii) Right half-field responses

		COMPONENT						
		P60	N75	P95	N130	N170	P190	N210
SUBJECT								
GC	msecs	60	74	90		150	196	214
	μV	+0.5	-1.0	+8.0		-2.8	+2.8	-0.8
	electrode	P	R	J		L	J	R
DMcV	msecs	54	76	96	124	176	190	234
	μV	+1.0	-1.0	+4.0	-3.7	-1.7	+1.1	-2.9
	electrode	Q	G=L	O	R	E	P	S
JL	msecs		78	96	140	158	180	218
	μV		-2.0	+3.2	-4.3	-2.2	+3.2	-2.6
	electrode		L	O	O	N	O	L
UD	msecs		70	94	140	174	198	234
	μV		-0.7	+5.0	-4.1	-0.9	+2.3	0.0
	electrode		K	P	M	I=J	S	N
NH	msecs	46	74	92	128	172	188	204
	μV	+1.9	-2.5	+6.3	-4.0	-2.4	+2.3	-2.9
	electrode	P	P	J	K	M	K	U
PB	msecs		72	100	128	160	178	206
	μV		-1.3	+6.5	-2.8	-0.6	+2.8	-3.1
	electrode		K	J	J	H	Q	I
AH	msecs		70	92	132	164	188	198
	μV		-1.0	+6.8	-2.5	-5.0	+0.2	-1.4
	electrode		L	K	K	J	K	L
RB	msecs	60	78	94	142	196	196	232
	μV	+1.1	-2.5	+3.2	-2.5	-1.7	+0.9	-2.2
	electrode	P	S	J	K	M	K	E
ARH	msecs	54	72	92	136		190	
	μV	+2.7	-1.1	+3.7	-9.4		+3.7	
	electrode	U	M	J	J		K	
RD	msecs	60	74	98	146	168	194	218
	μV	+1.2	-1.2	+9.9	-3.8	-2.9	+1.6	-1.4
	electrode	K	R	K	E	L	K	N
JR	msecs	58	76	100		172		
	μV	+3.4	-0.5	+3.8		-4.0		
	electrode	M=R	L	P		G=L		
GROUP MEAN		P60	N75	P95	N130	N170	P190	N210
	N	7	11	11	9	10	10	9
	msecs	**56.0**	**74.0**	**94.9**	**135.1**	**169.0**	**189.8**	**217.6**
	S.E.M.	2.0	0.9	1.0	2.5	4.0	2.1	4.5
	μV	**+1.7**	**-1.4**	**+5.5**	**-4.1**	**-2.4**	**+2.1**	**-1.8**
	S.E.M.	0.4	0.2	0.7	0.7	0.4	0.4	0.3

Table 6.1b(iv) Pattern reversal lower half-field responses

		COMPONENT						
		P60	N75	P95	N130	N170	P190	N210
SUBJECT								
GC	msecs	62	72	92	144	166	228	200
	μV	+1.0	-0.1	+7.5	-4.5	-2.7	+3.8	-2.4
	electrode	S	P	J	J	M	J	R
DMcV	msecs			96	134		182	
	μV			+5.1	-5.1		+2.8	
	electrode			L	K		K	
JL	msecs			102	132	154	200	
	μV			+8.0	-5.7	-4.4	+5.8	
	electrode			L	L	J	L	
UD	msecs		70	94		160	216	
	μV		-2.5	+4.6		-6.9	+2.1	
	electrode		O	P		M	Q	
NH	msecs	54	74	94	132	168		192
	μV	+3.6	-3.1	+7.5	-5.3	-3.8		-4.0
	electrode	P	K	J	K	M		S=U
PB	msecs			96	126		176	212
	μV			+8.5	-3.4		+2.0	-3.8
	electrode			J	L		G	N
AH	msecs	58	68	92	128	174	186	196
	μV	+1.2	-1.0	+9.4	-7.2	-3.8	-1.0	-3.2
	electrode	S	P	L	K	N	K	U
RB	msecs			98	136	174	198	210
	μV			+8.7	-4.0	-3.4	+3.1	-2.3
	electrode			L	L	M	K	N
ARH	msecs		74	94	128		188	208
	μV		-2.1	+6.5	-12.5		+5.4	-1.8
	electrode		Q	J	K		K	U
RD	msecs	62	76	98	142	178	196	220
	μV	+2.1	-2.3	+9.1	-9.1	-6.0	-0.5	-3.8
	electrode	J	K	K	K	R	P	S
JR	msecs			94		158		
	μV			+5.4		-5.4		
	electrode			L		L		
GROUP MEAN		P60	N75	P95	N130	N170	P190	N210
	N	4	6	11	9	8	9	6
	msecs	**59.5**	**72.3**	**95.5**	**133.6**	**166.5**	**196.7**	**205.4**
	S.E.M.	1.5	1.2	0.9	2.1	3.0	5.5	3.7
	μV	**+2.0**	**-1.9**	**+7.3**	**-6.3**	**-4.6**	**+2.6**	**-3.0**
	S.E.M.	0.6	0.4	0.5	1.0	0.5	0.8	0.3

Table 6.1b(v) Pattern reversal upper field responses

		COMPONENT							
		P60	N75	P95	P120	N130	N170	P190	N210
SUBJECT									
GC	msecs		74		116		180	222	
	μV		-3.5		+4.7		-4.0	+0.9	
	electrode		P		K		M	P	
DMcV	msecs			94	134	124	164	178	224
	μV			+3.2	+3.0	-3.6	-2.1	+0.6	-4.0
	electrode			O	E	U	Q	R	L
JL	msecs		78	102	126	146	162	192	
	μV		-2.8	+3.5	+1.7	-6.4	-5.7	+2.1	
	electrode		K	S	E	S	I	P	
UD	msecs		74	94	116	140	172	198	
	μV		-2.4	-0.2	+1.5	-6.7	-4.0	-0.1	
	electrode		T	U	K	M	J	M	
NH	msecs	54	74	98	110	122	170		206
	μV	+0.7	-5.7	+2.9	+4.4	-0.1	-5.3		-7.9
	electrode	K	P	S	K	S	M		Q
PB	msecs		74	96	106	118	150	174	208
	μV		-1.0	+6.5	+4.2	-1.6	-2.9	+3.1	-4.5
	electrode		K	U	E	U	J	U	J
AH	msecs		72	92	116	126		206	196
	μV		-2.2	+4.6	+2.0	-6.5		+2.4	-2.7
	electrode		K	O=Q	E	P		E	M
RB	msecs		76	102	120		172	226	206
	μV		-3.6	+1.5	+6.4		-4.7	+2.4	-4.8
	electrode		S	T	E		K	E	S
ARH	msecs			98	106	140	184		
	μV			+2.6	+2.4	-8.0	-3.6		
	electrode			K	E	J	M		
RD	msecs	64	76	96	116	150	178	216	214
	μV	+2.5	-0.2	+9.0	+5.5	-4.3	-4.7	+1.7	-1.7
	electrode	J	J	T	G	K	N	E	S
JR	msecs		78	96	128		166	186	
	μV		-2.9	+1.4	+3.7		-2.5	+1.5	
	electrode		P	M	E		H	J	
GROUP MEAN		P60	N75	P95	P120	N130	N170	P190	N210
	N	2	9	10	11	8	10	9	5
	msecs	**59.0**	**75.1**	**96.8**	**117.6**	**133.2**	**169.9**	**199.8**	**209.0**
	S.E.M.	5.0	0.7	1.0	2.7	4.3	3.1	6.3	3.8
	μV	**+1.6**	**-2.7**	**+3.5**	**+3.6**	**-4.6**	**-4.0**	**+1.6**	**-4.3**
	S.E.M.	0.9	0.5	0.8	0.5	1.0	0.4	0.3	0.9

Table 6.1c(i) Summary of group means, pattern onset responses

		COMPONENT							
		P55	N70	P90	P110	N110	P155	N170	P220
CONDITION									
	N	8	8	11		10	8	11	11
FULL	msecs	55.8	69.8	88.6		111.8	154.8	170.0	210.5
FIELD	S.E.M.	2.1	1.2	0.8		2.2	2.9	4.1	6.1
	μV	+1.7	-0.8	+9.6		-8.0	+8.7	-6.3	+6.4
	S.E.M.	0.3	0.6	1.7		2.2	1.7	1.2	1.8
	N	2	4	11		8	10	11	9
LEFT	msecs	51.0	71.0	88.9		117.5	150.0	169.1	224.7
HALF-	S.E.M.	7.0	1.0	0.9		4.6	4.3	4.6	7.8
FIELD	μV	+2.2	-2.1	+8.9		-7.4	+5.1	-5.8	+4.5
	S.E.M.	0.7	0.3	1.4		1.8	1.3	0.9	1.1
	N	0	4	11		10	8	11	10
RIGHT	msecs		71.0	90.6		115.4	156.0	167.8	220.4
HALF-	S.E.M.		0.6	1.1		2.8	3.6	4.0	7.9
FIELD	μV		-2.1	+7.3		-4.4	+4.1	-5.6	+4.2
	S.E.M.		0.7	1.0		1.3	0.8	1.0	0.9
	N	7	4	11		10	11	10	9
LOWER	msecs	59.7	71.5	86.7		113.2	158.4	170.6	222.0
HALF-	S.E.M.	2.3	0.5	0.8		2.6	3.5	5.3	5.2
FIELD	μV	+2.3	+0.4	+9.0		-8.3	+4.9	-5.2	+5.1
	S.E.M.	0.4	0.5	1.3		2.2	1.2	0.6	0.6
	N	0	5	10	11	8	10	11	10
UPPER	msecs		74.4	88.0	112.2	114.8	150.2	173.8	225.0
HALF-	S.E.M.		2.5	1.6	2.0	2.3	3.3	4.5	6.2
FIELD	μV		-2.1	+3.3	+7.6	-2.9	+3.3	-7.2	+4.3
	S.E.M.		0.2	0.4	0.6	0.7	0.5	0.8	1.0

6.1c(ii) Summary of group means, pattern reversal responses

		COMPONENT							
		P60	N75	P95	P120	N130	N170	P200	N210
CONDITION									
	N	8	10	11		9	7	10	6
FULL	msecs	58.8	74.6	94.6		132.2	161.7	190.2	211.1
FIELD	S.E.M.	1.3	1.0	0.9		3.0	2.3	3.8	3.2
	μV	+1.4	-2.8	+7.9		-5.9	-4.5	+2.3	-5.0
	S.E.M.	0.3	0.6	0.7		1.0	0.3	0.9	0.9
	N	7	10	11		8	10	11	7
LEFT	msecs	56.9	75.8	93.6		132.5	166.8	183.6	210.0
HALF-	S.E.M.	1.7	1.1	1.1		3.1	5.0	3.5	5.1
FIELD	μV	+1.3	-1.9	+5.5		-4.7	-3.8	+1.4	-4.6
	S.E.M.	0.3	0.6	0.8		0.8	0.6	0.7	0.5
	N	7	11	11		9	10	10	9
RIGHT	msecs	56.0	74.0	94.9		135.1	169.0	189.8	217.6
HALF-	S.E.M.	2.0	0.9	1.0		2.5	4.0	2.1	4.5
FIELD	μV	+1.7	-1.4	+5.5		-4.1	-2.4	+2.1	-1.8
	S.E.M.	0.4	0.2	0.7		0.7	0.4	0.4	0.3
	N	4	6	11		9	8	9	6
LOWER	msecs	59.5	72.3	95.5		133.6	166.5	196.7	205.4
HALF-	S.E.M.	1.5	1.2	0.9		2.1	3.0	5.5	3.7
FIELD	μV	+2.0	-1.9	+7.3		-6.3	-4.6	+2.6	-3.0
	S.E.M.	0.6	0.4	0.5		1.0	0.5	0.8	0.3
	N	2	9	10	11	8	10	9	6
UPPER	msecs	59.0	75.1	96.8	117.6	133.2	169.8	199.8	209.0
HALF-	S.E.M.	5.0	0.7	1.0	2.7	4.3	3.1	6.3	3.8
FIELD	μV	+1.6	-2.7	+3.5	+3.6	-4.6	-4.0	+1.6	-4.3
	S.E.M.	0.9	0.5	0.8	0.5	1.0	0.4	0.3	0.9

Figure 6.2

Group average maps for components in the responses to pattern onset and pattern reversal four degree full and half-field stimuli.

6.2a Full field responses
6.2b Left half-field responses
6.2c Right half-field responses
6.2d Lower half-field responses
6.2e Upper half-field responses

Colour scale represents voltage gain + 8 to - 8μV, positivity of active electrode with respect to reference is represented by upward deflection. For explanation of component labels, see text.

Figure 6.2a Full field responses

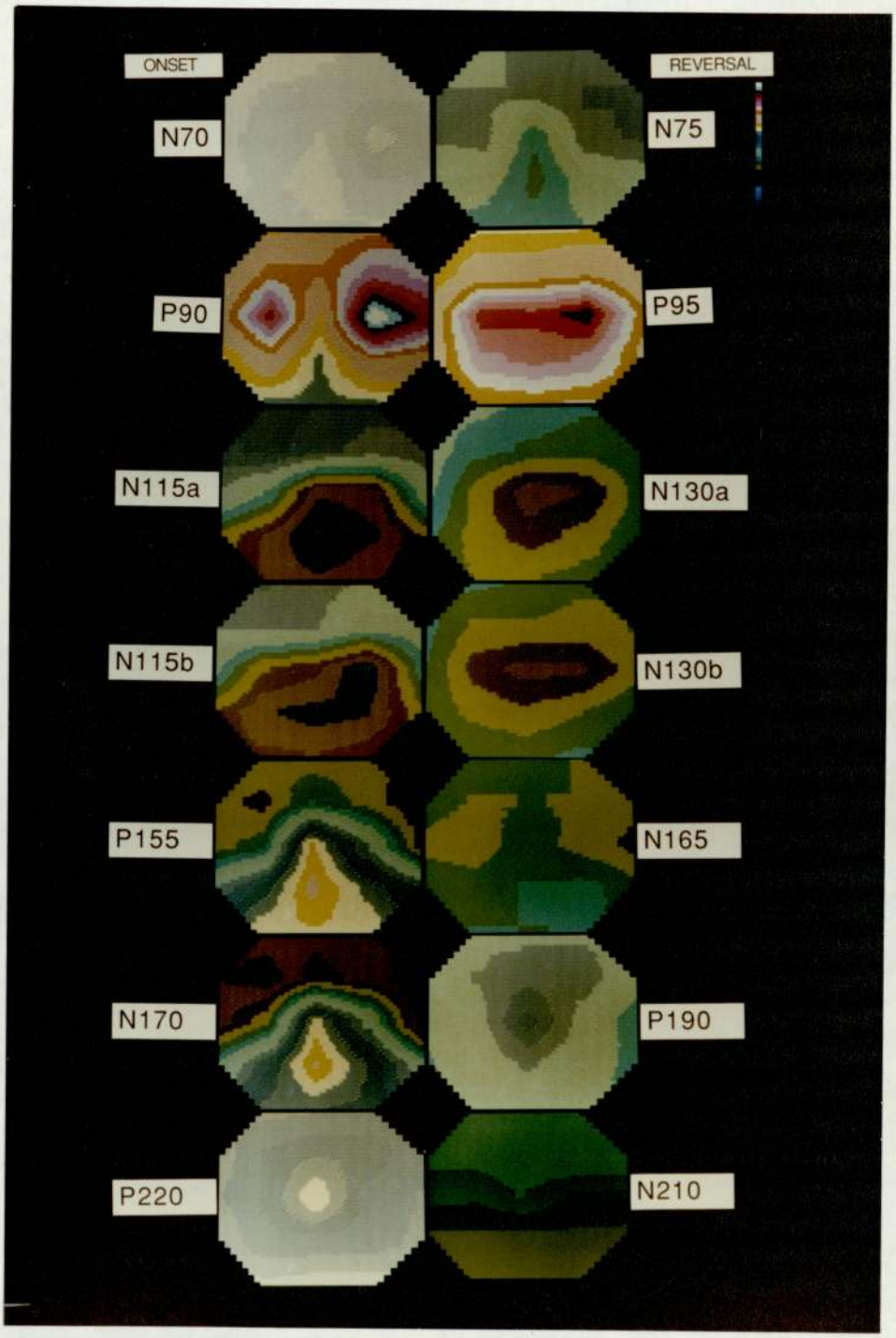


Figure 6.2b Left half-field responses

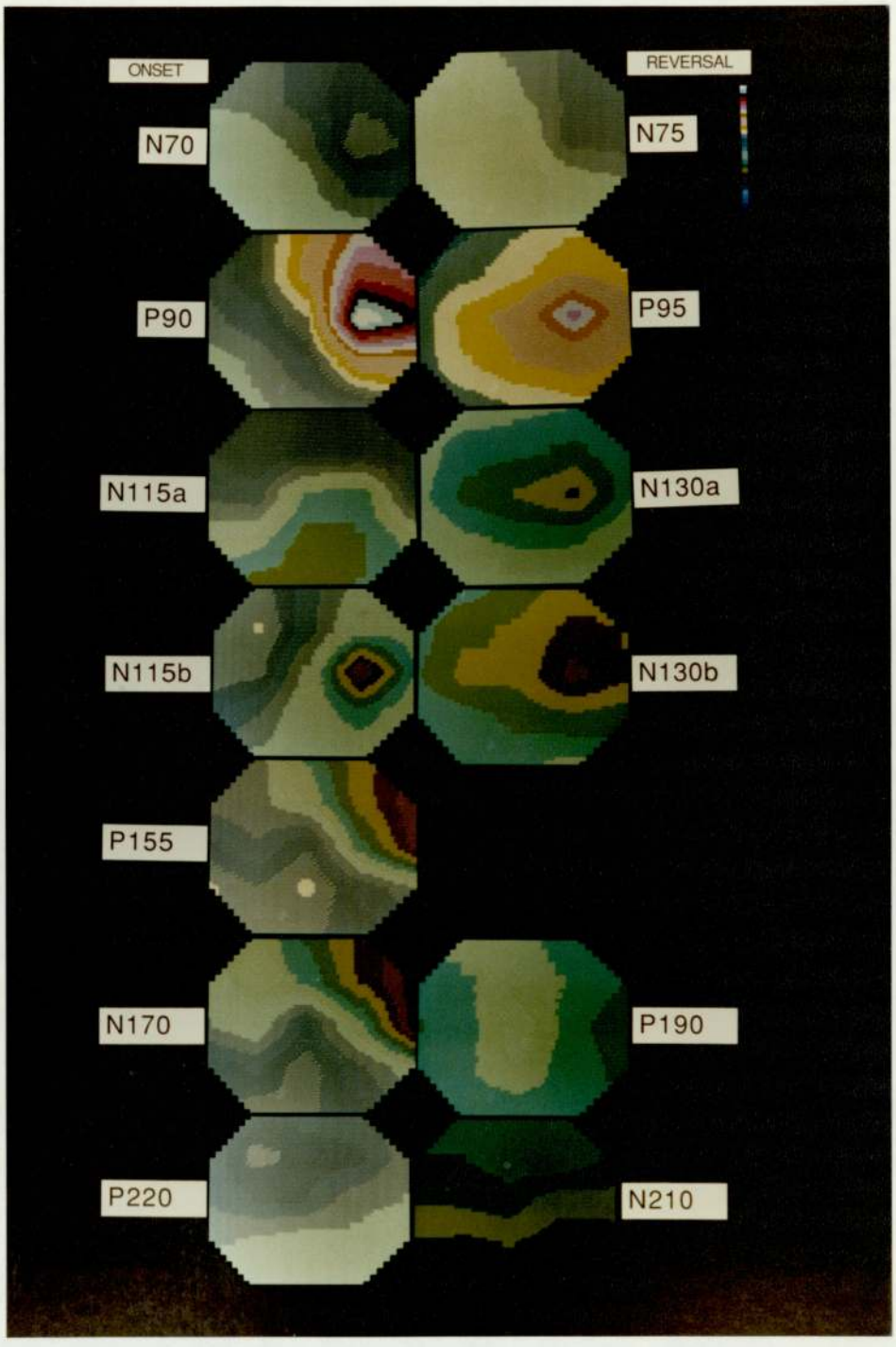


Figure 6.2c Right half-field responses

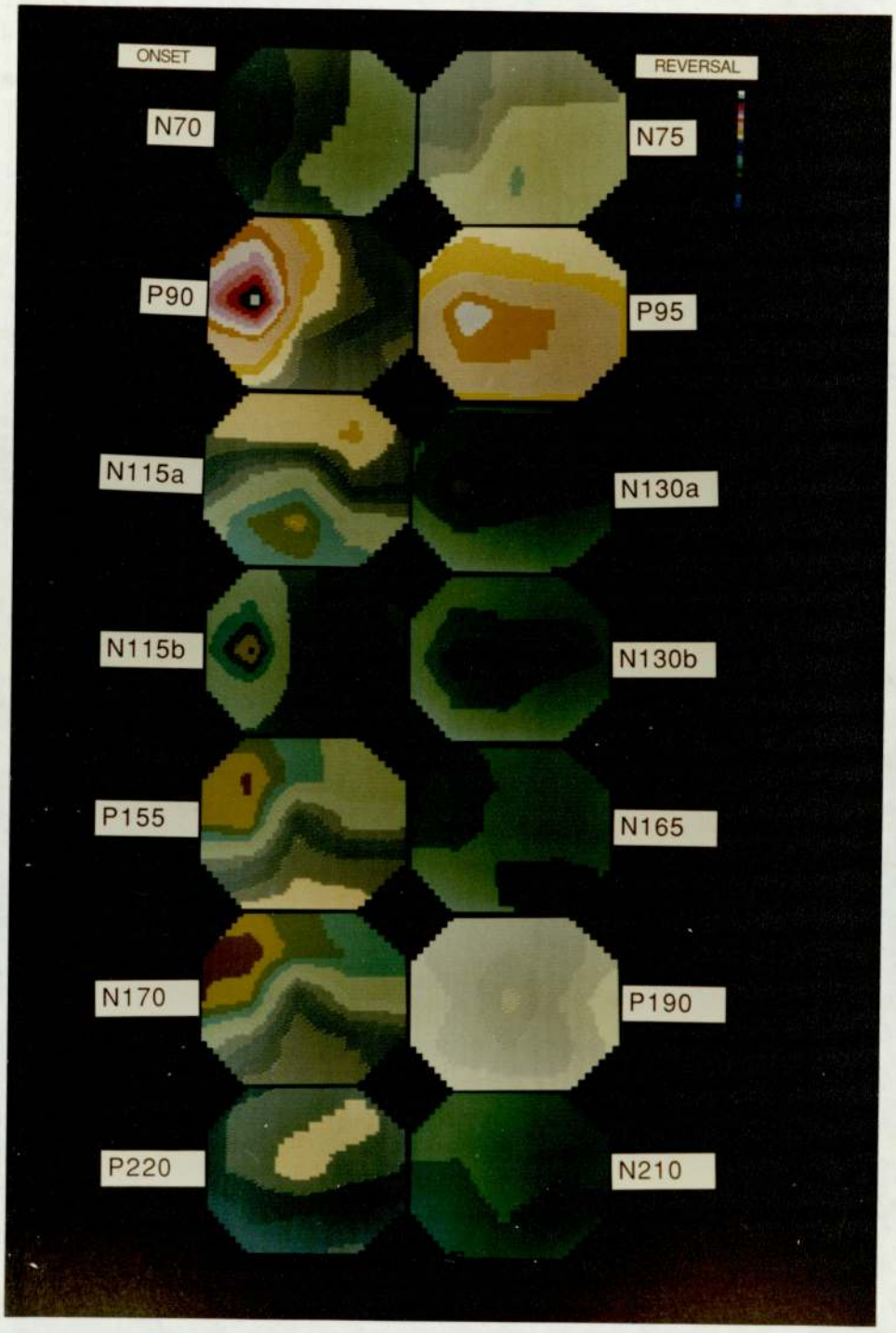


Figure 6.2d Lower half-field responses

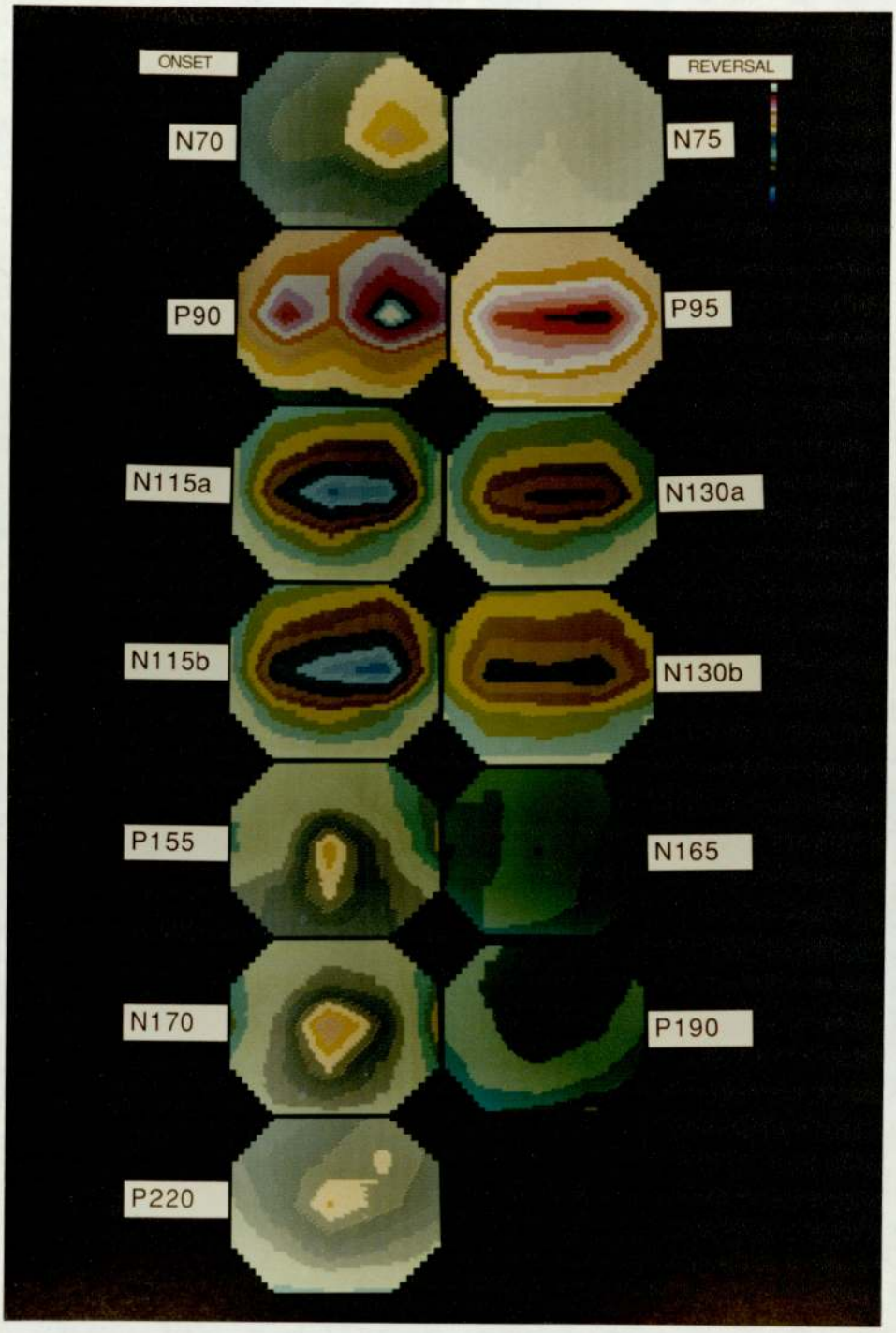
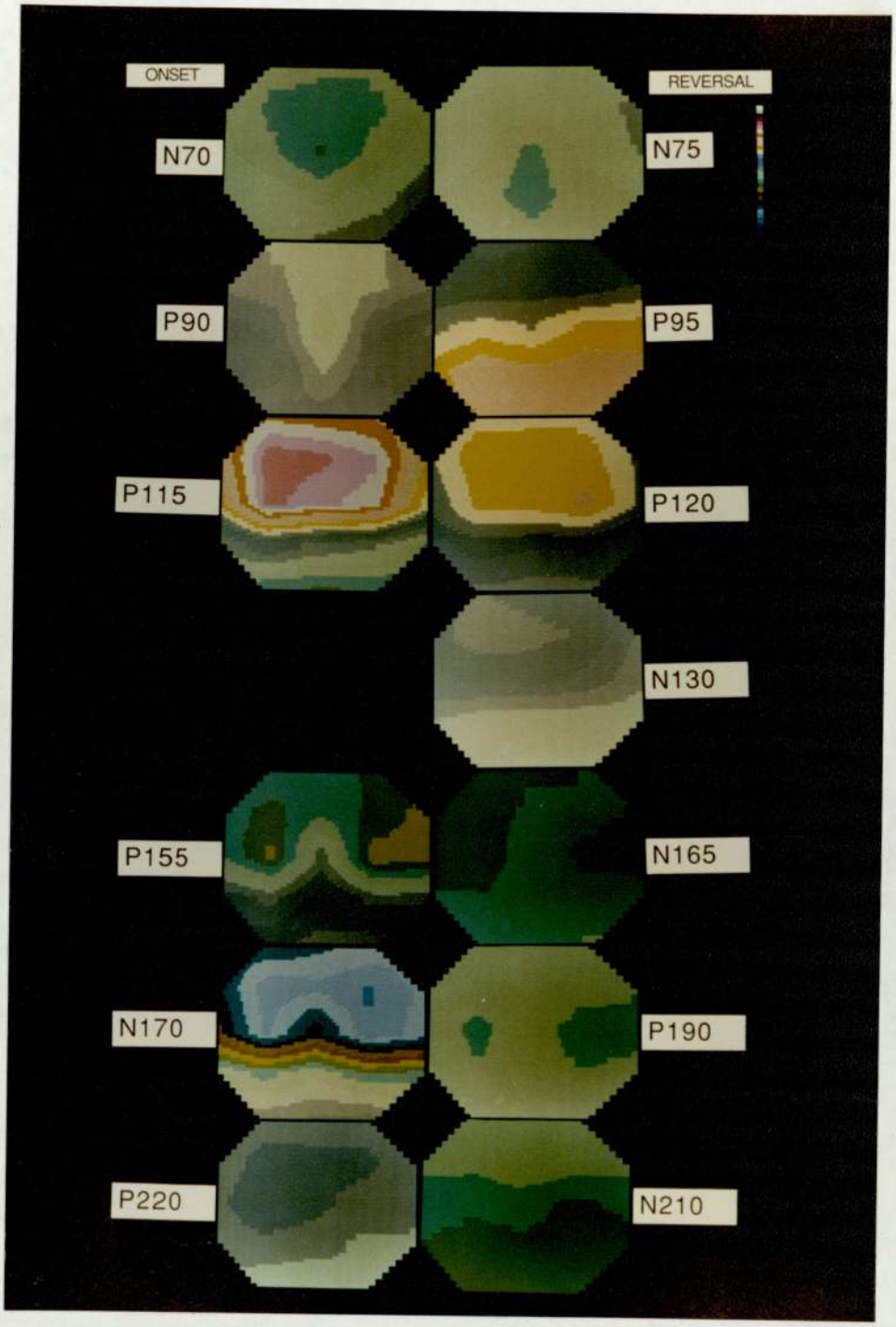


Figure 6.2e Upper half-field responses



6.3 Results

6.3a General

Figures 6.1a to e (pages 154-159) show the group average responses for pattern reversal and pattern onset full and half-field targets from a horizontal row of electrodes approximately 4cm above the inion and from an electrode placed on the inion. These electrodes are labelled as "I" to "M" and "P" as shown in Figure 5.2. For upper hemifield responses the traces from posterior channel "S" have also been displayed. These group responses were determined using standard Brain Atlas software which calculates the average response amplitude at each electrode position at a particular point in time. Consequently the variables of latency and amplitude are, to some extent, confounded and it is difficult to judge the effects of each property separately. It was, therefore, considered necessary to examine the individual responses, to give some idea of the frequency of occurrence of each component as well as the variation in amplitude and latency between subjects. Tables 6.1a(i) to (v) and b(i) to (v) (pages 161 to 170) show the peak latencies of each component, their maximum amplitudes and the electrode(s) at which this maximum response was measured, for each stimulus type and each visual field condition. Group average amplitudes and latencies have been calculated for each component using data from all subjects in whom a particular component could be readily identified. These values are displayed for all stimulus conditions in Tables 6.1c(i) and (ii) (pages 171 and 172) for ease of comparison. The labels applied to all components throughout this discussion were determined by the polarity and mean overall latency of the components identified in the individual results. In keeping with this, the major positive components which were in Chapter 5 termed "P100" and CI" for reversal and onset responses respectively are now referred to as "P95" and "P90". Figures 6.2a to e (pages 154 to 159) show the group average distributions of the components in the responses to pattern reversal and pattern onset stimulation, for all five stimulus conditions, as calculated using Brain Atlas software. The maps relating to the early positive components P55 and P60 have been omitted from this display; due to the low amplitudes of these components, the maps reveal little of interest.

6.3b Full field responses

Examination of the traces in Figure 6.1a reveals seven principle components in the first 250 msecs of both pattern onset and pattern reversal full field responses. There are, however, important differences between the two types of response, particularly in the later parts of their time course. In addition, comparable components in the earlier parts of the responses had a tendency to peak later for pattern reversal than for pattern onset.

The responses to both pattern reversal and pattern onset contain small early positive components which are maximum on the most posterior channels on and near the midline. These have been labelled P55 for pattern onset, P60 for pattern reversal. They can be identified on electrode "P" in Figure 6.1. These positive waves are followed closely in each case by an early negativity, termed N70 and N75 for pattern onset and reversal respectively. Both of these components show a posterior midline maximum, and are seen most clearly on electrode "P". This distribution is well illustrated in the group average map for the pattern reversal N75 but that of the pattern onset N70 seems to be somewhat masked by the earliest effects of the major early positive component which succeeds it (Figure 6.2a). Nevertheless, there is an area of relative negativity around electrode position "P" on this map also. This tendency to be masked by the later positive component was seen in individual responses, to the extent that on some occasions the absolute amplitude measured for this component had a positive value.

The major early positive components P90 and P95 of the onset and reversal responses respectively showed similar distributions to those described in the previous study. The pattern onset P90 showed clear bilateral maxima on electrode positions "J" and "L" in the group average responses. This type of distribution was clearly shown in the individual responses, although two subjects demonstrated maximum amplitude responses on electrode position "M" which is about 8cm from the midline. The group average traces and distributions reveal a tendency for larger responses over the right hemisphere, although individual responses show an almost equal tendency to be larger over the left side (five subjects) as over the right (six subjects). The pattern reversal P95 showed an almost equal amplitude across electrodes "J", "K" and "L", although, as with the pattern onset response, there was a tendency to a higher amplitude response over the right hemisphere. Individual results showed that whilst six subjects had larger amplitudes on the right, the others had their maximum response on the left or on the midline. Statistical comparison of the amplitudes of P90 and P95 as measured on electrodes "J" and "L" for each subject showed that the hemispheric differences which were apparent on the group average maps were not significant (Student's t-test for paired samples). There was no tendency to polarity inversion of either of these waves evident at any electrode position in group average or in individual traces.

Analysis of individual responses showed that in several subjects the pattern reversal P95 had superimposed on it or was closely followed by an additional positive peak with a latency of around 120 msecs. This appeared maximally on different electrodes in different subjects but was most clearly identified on anterior and lateral channels. Only one subject clearly demonstrated a similar phenomenon for the pattern onset response. Group average responses showed no evidence of such a peak for either pattern reversal or pattern onset stimulation.

A major early negative component was found in both onset and reversal VEPs. The overall mean latencies for these components were calculated to be around 115 msecs and 130 msecs for pattern onset and pattern reversal responses respectively, using the values at the position of maximum amplitude for each subject. In fact, however, the absolute latency of this component appeared to depend somewhat on the electrode at which it was measured, being somewhat earlier for midline than for lateral channels The group average maps show that for the pattern onset response, the distribution at a latency of around 112 msecs (map labelled "N115a") shows a clear inferior midline maximum at electrode "P". At midline electrode "K" the peak latency is also 112 msecs. At 118 msecs, however, the maximum has moved to the more anterior and lateral position of electrode "L" (map labelled "N115b"). Inspection of the group average traces shows that this component also peaks at around 118 msecs on electrode "J", although the amplitude at this position is clearly lower than that at electrode "L". The group average traces from lateral electrodes "I" and "M" show a similar peak at a latency of 120 msecs. On these lateral electrodes this major early negative component is followed by a very small positive deflection at about 130 msecs. This peak, which is clearer on the left (channel "I"), appears to separate the major early negative from a subsequent lateral negative component peaking at about 168 msecs (N170).

The effect of electrode position on latency of the major early negative N115 in individual responses was tested using data from electrodes "I" to "M" and "P" (see Table 6.2). Only data from those subjects in which this component could be distinguished from the later component N170 were included. Two-way ANOVA demonstrated that this effect was statistically significant ($p<0.01$).

Examination of the group average pattern reversal traces shows that the major early negative component N130 peaks at about 134 msecs on midline electrode "K", where it has its maximum amplitude, and at around 138 msecs on electrodes "J" and "L". The maps of activity at these two latencies have been labelled N130a and N130b respectively. On lateral electrodes "I" and "M" however, the traces do not reach a peak until a latency of 158 msecs. It is considered that the peak at lateral electrodes might be a manifestation of a similar lateral negative component (N165) to that (N170) found in the pattern onset response (see below). The effect of electrode position on latency of the major early negative peak in individual pattern reversal responses has not been tested statistically, however, due to the difficulty in distinguishing between components.

Inspection of the group average pattern onset traces shows a large midline and posterior positive "plateau" between the latencies of 150 and 220 msecs. This feature, which can be seen clearly on electrode "K", can be considered to be made up of two components.

		ELECTRODE					
		I	J	K	L	M	P
SUBJECT							
DMcV	msecs	108	108	104	110	114	108
JL	msecs	122	118	112	110	112	114
UD	msecs	112	112	106	114	114	112
NH	msecs	118	118	104	126		100
PB	msecs	120	120	112	112	120	110
AH	msecs	128	132	124	126	126	120
RB	msecs	112	112	112			112
ARH	msecs	120	116	106	108	110	108
RD	msecs	124	124	118	118	118	118

GROUP MEAN		I	J	K	L	M	P
	N	9	9	9	8	7	9
	msecs	118.2	117.8	110.9	115.5	116.3	111.3
	S.E.M.	2.1	2.4	2.3	2.5	2.1	2.0

Table 6.2

Latency of the major early negative component in the full field pattern onset response as measured at different electrode positions. Data from subjects GC and JR have been omitted due to the apparent influence of the later negative component N170.

The first of these, which peaks at around 154 msecs, has its maximum amplitude at electrode "P" and has been termed "P155". At lateral channels, this component appears to be manifest in the form of the slight positive deflection which separates the negativities N115 and N170. The responses from some individuals seem to bear this out, with a positivity between 130 and 150 msecs clearly interposed between the two negative peaks.

The second part of this late positive feature appears to have its maximum amplitude on electrode "K" and peaks at about 210 msecs in the group average traces. Anterior channels on row "D" to "H" show only this later peak; P155 is not visible. The maps of these two positive components show that the maximum positivity has indeed migrated from a posterior to a more anterior position between these two points in time. Inspection of individual results shows that the latter part of the positive complex is very variable in latency and that on some occasions it is difficult to distinguish the individual components. In other subjects, however, two clearly separate positive components are visible with a negative component (N170) interposed between them. From the results on individuals the mean latency of the latter positive component has been calculated to be around 220 msecs and so this positivity has been termed "P220".

The group average traces for the pattern reversal responses show a single large midline positive component peaking at 188 msecs on electrode "K". This component has been termed "P190". Although in some individuals there was a vague suggestion of two separate components as found in the pattern onset response, this observation was neither clear nor consistent and so a separate P155 component has not been defined for the reversal response.

For pattern onset responses, as has been commented above, a lateral negative component can be defined. The latency of this component, as calculated from individual data, was about 170 msecs . Hence this component has been termed "N170" . This component tended to be maximal at anterior and lateral positions, most often reaching its highest amplitude on electrode row "D" to "H" or on positions "I" or "M". This distribution can be seen clearly on the group average map in which this negativity is visible at anterior channels against the contrasting positive activity lower down in the picture which is related to the midline posterior complex of P155 and P220. The relationship between the peaks P155 and N170 shows some degree of variation between subjects; in some the midline positivity precedes the lateral negativity, in others it follows it and in two subjects (see Table 6.1a(i), subjects ARH and JL) the peak latencies of the two components virtually coincide .

For the reversal response the group average traces show a negative peak at a latency of

158 msecs on lateral electrodes "I" and "M" and also on anterior electrode row "D" to "H". The map at this latency, which has been labelled as "N165" shows widespread negative activity which reaches its maximum towards the lateral aspects of the picture and unlike the map for pattern onset, there is no posterior positive activity. Isolation of a separate N165 in individual traces was not as easy in the full field pattern reversal responses as in those to pattern onset. In some cases a small interposed positive deflection indicated the possible presence of two components but in others the main negative component merely peaked later on lateral and/or anterior electrodes. As a result of this difficulty, however, it was possible to demonstrate separate components in only five subjects. In a further two subjects (GC and JR) an early major negative N130 could not be distinguished and the main negativity, which peaked at around 160 msecs in both cases, was regarded as representing the later N165 component. The results for these subjects with other stimulus visual field positions, in particular with upper field stimulation, confirmed the accuracy of this assumption.

In the group average response to pattern reversal stimulation, the major late positive component P170 was followed by a late negative peaking at around 214 msecs. This component was maximal on the most posterior and lateral electrodes and can be seen on electrode "P" for the reversal responses in Figure 6.1a. This clear posterior distribution is shown on the group average map. This component, which has been termed "N210" was not detected in the individual responses of all subjects, but where present it could be distinguished from the earlier lateral negative N165 by virtue of its latency - it always followed P170 where this component was present - and its posterior topography. An equivalent component was not demonstrable in the group average responses for pattern onset, and although in some individuals there was the suggestion of such a later component its presence was neither clear nor consistent enough for it to be regarded as a separate entity from the lateral negative N170.

6.3c Lateral half-field stimulation

The group average responses for left and right half-field pattern onset do not show a clear early positive component P55 and the individual results confirmed the complete absence of an identifiable component in the majority of subjects. The pattern reversal P60 was, however, identified in most individuals and its presence can be seen on the group average traces (Figures 6.1b and c). Individual and group average traces show this component in posterior midline and ipsilateral channels.

The subsequent early negative components were identifiable in group average traces in both types of response, like the positive component P60, on posterior midline and ipsilateral channels. The pattern reversal N75 was, however, more clearly defined than

the pattern onset N70 and individual results showed that the latter component was identifiable for only a few subjects. The group average maps (Figure 6.2b and c) of the reversal N75 show a posterior midline and ipsilateral negativity which appears to reach a maximum on electrode"P". The pattern onset N70 is seen as a less clear broad negativity which has a fairly even amplitude over posterior midline and ipsilateral channels. Both negativities are seen against a background of more anterior contralateral positive activity which is presumed to be related to the subsequent major early positive components.

The distributions of the major early positive components in both types of VEP, like those of the full field responses, were very similar to those found in the previous study. Both components showed maximum amplitudes over the contralateral hemisphere on the line of electrodes "I" to"M", which is around 4cm above the inion. As before, the lateralisation was much clearer for the pattern onset P90 than for the pattern reversal P95, with the latter component spreading well over the midline onto the ipsilateral hemisphere. Individual results showed that for all eleven subjects the pattern onset P90 was clearly maximum at an electrode on the contralateral hemisphere. The pattern reversal P95, however, was maximal at midline electrode positions for four subjects in the right hemifield response, and for one subject in the left hemifield response. Statistical comparison of right and left half-field amplitudes as measured at the position of maximum activity showed that there was no significant difference for either of these two components (Student's t-test for paired samples).

Inspection of the group average pattern reversal traces reveals a clear, single, positive component peaking at about 96msecs on contralateral, midline and ipsilateral channels. On the pattern onset traces, however, component P90 is not visible on the far ipsilateral channels "I" for left and "M" for right half-field stimulation. Instead, this component appears to be replaced by a later positivity, peaking at 126msecs and 112msecs for left and right half-field targets respectively. The traces from the electrodes just ipsilateral to the midline ("J" and "L") show a "double" positive peak which appears to be formed by the superimposition of these two low amplitude positive peaks. Individual traces show that a later positive component, either single or superimposed on the major positive peak, is apparent at a latency of 110 to 140msecs on ipsilateral channels for the majority of subjects. Some subjects, however, appear to demonstrate additional positive peaks bilaterally or solely over the contralateral hemisphere. For example, Figure 6.3 shows the responses of subject GC from traces "I" and "M" to pattern onset stimulation of the left half-field. On electrode "M", which is contralateral to the stimulated hemifield, a second, earlier positive peak with a latency of 106msecs is superimposed on the major positive wave. On electrode "I", however, a single small positive peak at a latency of 120msecs is visible. Whilst there appears to be a clear distinction between the ipsilateral single later peak and the contralateral superimposed second peak in this particular

Figure 6.3

Illustration of additional positive peaks at ipsilateral and contralateral electrodes for half-field stimulation. See text for explanation.

Figure 6.4

Illustration of apparent polarity inversion between negative posterior and positive anterior components at at latency of 115msecs. See text for explanation.

Figure 6.3

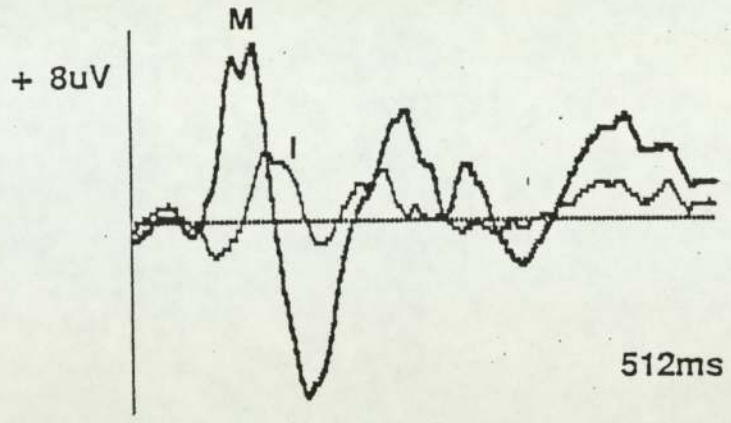
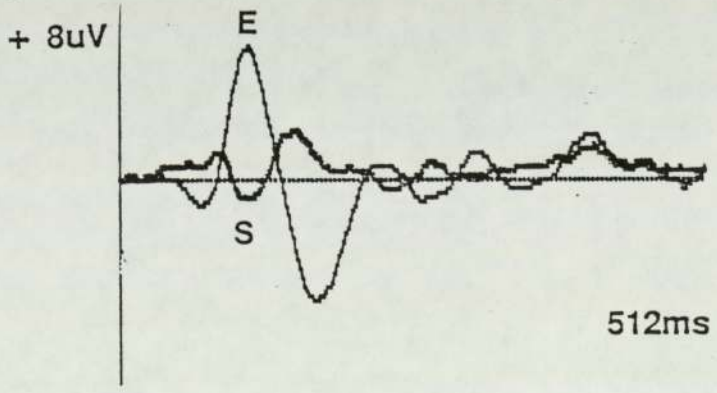


Figure 6.4



situation, such a distinction is not clear in all subjects. For this particular subject, it is of note that a second, superimposed positive peak at a latency of 110msecs is also visible on electrode "M" in the right half-field response. Other subjects demonstrating bilateral or contralateral extra positive peaks also show no consistency in localisation of these peaks.

Although there is no clear evidence in the group average responses, individual pattern reversal traces show the presence of a later positive peak superimposed on or closely following the major positivity in some subjects. As with those in the pattern onset responses, these later peaks - which also have a latency of between 110 and 130msecs - do not show consistent lateralisation with respect to the half-field stimulated.

Although the group average map for the left hemifield pattern onset P90 appears to show low amplitude negative activity at inferior ipsilateral electrode positions, inspection of the traces from electrodes "L" and "N" and also of the traces from electrodes "J" and "R" for the right hemifield response show no evidence for polarity inversion for this component between ipsilateral and contralateral channels. Inspection of individual traces, however, does reveal limited evidence of polarity inversion between the contralateral P90 and a small midline or ipsilateral negative peak at the same or a similar latency. For example, subject NH shows a positivity on electrode "M" and a negativity on electrode "K" which both peak at a latency of 88msecs. This behaviour is by no means clear or consistent, however, and any negative activity appearing on individual maps at the peak latency of the major early positive component appears in the majority of cases to be related to earlier or later negative peaks.

The group average traces show evidence of the major early negative component N115 in the responses to pattern onset stimulation of both lateral hemifields. This component reaches its maximum negativity on electrode "J" at 132msecs and on electrode "L" at the earlier latency of 118msecs for right and left half-field responses respectively, showing clear contralateral localisation. The mean latencies for this component derived from the individual data (Table 6.1c(i)) show that in fact, if anything, the response to <u>right</u> half-field stimulation has a slightly shorter latency (115.4msecs as compared with 117.4msecs). As with full field stimulation, this component peaks earlier at posterior midline electrode "P" than at more anterior lateral electrodes. Both sets of group average traces show a negativity peaking at around 110msecs on this electrode. Maps for both hemifield responses at this latency (maps labelled "N115a", Figures 6.2b and c) show posterior negative activity, which is slightly higher over the contralateral hemisphere, and anterior positive activity. At the peak latency for both of these components (maps labelled "N115b"), as mentioned above, the negative activity is clearly at its highest over the contralateral hemisphere, with positive activity on ipsilateral and anterior channels.

Inspection of the traces for the right half-field response shows an apparent polarity inversion between the negative component peaking at 112msecs on electrode "P" and a positive component peaking at the same latency on electrode "G". This behaviour is apparent from the group average map at this latency. The traces for the left half-field response also show an apparent inversion, this time between N118 on electrode "L" and a positive peak with a latency of 120msecs on electrode"E". Although there are suggestions of polarity inversions between posterior/contralateral negative and anterior/ipsilateral positive components throughout the individual responses, this behaviour is neither clear nor consistent. The electrode position at which component N115 reaches its maximum amplitude varies between individuals, being on the midline for some and at contralateral channels for others (see Tables 6.1a(ii) and (iii)).

The pattern reversal group average traces also show a clear major early negative component which is largest on midline and contralateral electrodes. As in the full field response, this component peaks earlier on midline than on lateral channels. The group average maps (Figures 6.2b and c) show the distribution at 136 ("N130a") and 144msecs ("N130b") for the right half-field response and at 132 ("N130a") and 152msecs ("N130b") for the left half-field response. These latencies apply to the times to peak at electrodes "K" and "M" for the left and electrodes "K" and "I" for the right half-field responses. The maps at both latencies for both hemifield responses shows contralateral maxima at both latencies, although this is clearer for the left than for the right. In the individual responses, as with pattern onset stimulation, the position at which the maximum amplitude was reached varied, being on the midline for some subjects and clearly contralateral for others.

For both pattern reversal and pattern onset stimulation the group average traces show larger amplitude activity for left than for right half-field stimulation. Comparison of the group average data as calculated from the individual traces (Table 6.1c(ii)) shows that this behaviour is not apparent in the results for pattern reversal stimulation. For pattern onset stimulation, however, there is a clear difference between the mean maximum amplitudes, being $-4.4 \pm 2.3\mu V$ and $-7.4 \pm 1.8\mu V$ for right and left half-field targets respectively (Table 6.1c(i)). When tested statistically using Student's t-test for paired observations, however, the difference between maximum response amplitudes for left and right hemifields was found to be not significant ($p>0.05$).

The lateral negative component N170 was clearly visible in the group average traces for the pattern onset response, peaking at a latency of around 160msecs on the anterior lateral channels for both hemifield responses. The group average maps show negative activity at anterior electrode positions on both sides of the head at this latency but this is clearly maximal over the contralateral hemisphere. This lateralising behaviour was not

so clear-cut in the individual responses, with some subjects demonstrating a larger negativity at ipsilateral electrodes.

Component N165 was not clearly distinguished in the group average pattern reversal responses; a negative peak at a latency of 160msecs was visible at lateral electrodes for the right but not the left hemifield responses. The group average map at a latency of 160msecs for the right hemifield response (labelled "N165", Figure 6.2c) shows anterior negative activity which is larger over the contralateral hemisphere. Individual results showed that whilst it was possible to demonstrate an apparent later negativity in the responses of most subjects its topography was variable and it was not necessarily maximal at contralateral or even lateral electrode positions.

The late posterior negative component N210 appears on the more posterior channels in the group average pattern reversal traces and is visible on electrode "P" in Figures 6.1b and c, for both hemifield responses. This component, which could be identified in the majority of individual subjects, showed no tendency to lateralisation. The group average maps show low amplitude negative activity peaking on the most posterior channels on both sides of the midline.

Neither the late midline positive components P155 of the pattern onset response nor P190 of the pattern reversal response showed any marked tendency to lateralisation in group average or in individual responses. Component P190 showed a similar distribution to that found in the full field response but with lower peak amplitudes. The pattern onset P155 became apparently more widespread, with the group average maps showing positive activity extending into more anterior ipsilateral regions, particularly for the left half-field response. For both lateral hemifields, however, this component reached its maximum amplitude at midline and posterior positions. Component P220 of the pattern onset response appeared maximal over the left hemisphere at electrode"E" for the left half-field response, but peaked on the midline at electrode "K" and also, apparently, on anterior electrode "G" for the right half-field response. Individual responses, however, showed no clear tendency for lateralisation of this component for either lateral half-field target.

6.3d Lower half-field responses

Although several subjects demonstrated a pattern onset P55 component at midline and posterior channels in their responses to lower half-field stimulation this is only just evident in the group average traces (Figure 6.1d) as a peak superimposed on the ascending transient of "P90". In the pattern reversal traces component P60 shows as a small positivity maximal at electrode "P". This component is visible in a few

individuals, mostly peaking at inferior electrode positions.

The pattern onset N70 is also not seen clearly in the group average traces; in the few subjects who demonstrate this component it is seen as a negativity superimposed on the ascending transient of the major positive P90. Component N75 in the reversal response was more clearly in evidence in both individual and group average responses, being maximal on or near midline electrodes "K" or "P" in the former and at electrode "P" in the latter. The group average map (Figure 6.2d) shows N75 manifested as a reduction in the amplitude of positive activity at midline and lower electrode positions rather than as a clear area of negative activity.

The group average pattern onset traces show the major early positivity P90 as a clear single peak. In the group average maps this component reaches clear bilateral maxima, as in the full field response, on electrodes "J" and "L". This is larger, also as in the full field response, on the right side of the head. Again, however, of individual responses almost half demonstrate maximum amplitude on the left side of the head. The positive activity in the group average map shows a less prominent reduction on midline and posterior electrodes than for the full field response. In neither group average nor individual traces was there any evidence for polarity reversal of this component at different electrode positions.

For the pattern reversal P95 again a clear single peak was seen on group average traces. This component was maximal at electrodes "J", "K" and "L", with a slightly greater amplitude at position "L" on the group average results although several individuals showed a maximum amplitude on the midline or on the left side of the head. The behaviour of this component was therefore, like the pattern onset P90, similar to that in the full field response. Although not evident in the group average responses, for both pattern reversal and pattern onset, some individuals demonstrated a later positive peak superimposed on the major positivity at 110-120msecs, more commonly at lateral electrode positions.

In the pattern onset group average responses, the major negative component N115 peaks on electrodes "K" and "L". Again this component peaks slightly earlier (112msecs, "N115a" in Figure 6.2d) on the midline than at more lateral electrodes (118msecs, "N115b" in Figure 6.2d). For some subjects this component reached its maximum on the midline and for others at more lateral electrode positions. Similar behaviour is apparent in the pattern reversal responses for which the group average traces show a maximum at electrodes "K" and "L" peaking at 134msecs on electrode "K" ("N130a") and at 140msecs on electrodes "J" and "L" ("N130b"). For both onset and reversal responses the major early negative component appears to show a slightly more anterior

distribution with the lower half-field than with the full field target.

The pattern onset group average traces show a late positive complex on electrodes "P" and "K" with peaks on the former at 154 and at 216msecs, and on the latter at 170 and 216msecs. The map of activity at 154msecs ("P155") shows midline and posterior positive activity which is maximum at electrode "K", demonstrating a similar but slightly more anterior distribution to that in the full field response. The map of activity at 170msecs (labelled as "N170") shows a clear midline maximum at electrode "K" with negative activity at lateral electrode positions. The traces from electrodes "I" and "M" reveal negative peaks at 170 and 164msecs respectively, which in fact appear to represent the lateral negative component N170. The map at 216msecs shows a maximum positivity at "K" ("P220") which appears to spread further anteriorly than that at 170msecs. Individual results show that in most subjects it is possible to distinguish only two components (P155 and P220) in this late positive complex. As was found for full field stimulation, both of these components showed a fair degree of latency variability. In fact, those peaks designated as "P155" have a latency of between 146 and 182msecs (see Table 6.1a(iv)). A distinct "P170" can not be isolated in any responses except for subject JL who has a very prominent peak at 168msecs on channel "K" and no evidence of a later positive peak until a latency of around 270msecs. The later positivity P220 shows a maximum on or near electrode "K" in most subjects. From the group average maps there is an apparently a more anterior distribution of this component as compared with the full field response which is also evident in individual results.

Individual responses show that component N170 varies in latency and does not necessarily coincide in latency with the positivity of P155. The results for some subjects show a more anterior bilateral distribution similar to that found in the full and lateral half-field responses. In the group average traces between the peaks at 170 and 216msecs there is a superimposed negativity with a latency of around 200msecs. Such a component, which may be the equivalent of the pattern reversal N210, is only clearly evident in the responses from one subject and has therefore not been designated as a separate component.

A negative component which is considered to represent N165 can be seen peaking at a latency of about 164msecs in the group average pattern reversal traces. The map at this latency shows bilateral negative activity which is maximum at electrodes "I" and "M"("N165"). As before, there was some difficulty in distinguishing this component in individual traces as compared with the pattern onset N170 but a comparable peak was identified at lateral electrodes in most subjects. The major positive pattern reversal component P190 is clearly evident in both group average and individual traces, tending to peak on or near electrode "K". The group average map for this component which

peaks at a latency of 200msecs (labelled "P190") shows negative activity at the most posterior electrodes which is in fact related to the later posterior negative component N210. Component N210 which, like P190, peaked at 200msecs was identified in several subjects and can be seen on the group average trace for electrode "P". A separate map has not been displayed for this component.

6.3e Upper half-field stimulation

There is no clear evidence of the early posterior positive component P55 of the pattern onset response in individual or group average traces. The early negativity N70, however, is evident in about half of the subjects and can be seen peaking on electrode "K" in the group average traces (Figure 6.1e) and on the map (Figure 6.2e). Component P60 of the reversal response was identified in only two individuals and was not evident in the group average responses. The negativity N75, however, could be distinguished in the majority of subjects on midline and posterior electrodes. Negative activity which is maximal on electrode "K" and "P" can be seen on the group average map.

The major early positive component P90 of the pattern onset response was evident in the most posterior channels of the group average traces. This component is seen as a small peak at about 90msecs on the line of electrodes "N" - "R". The group average map at this latency shows positive activity at inferior and lateral positions. At more anterior electrode positions a later more prominent positivity can be seen which peaks at about 112msecs (termed "P115") and is maximal on electrode row "D" - "H", apparently more prominently on the left. On more posterior electrodes this component is apparently replaced by the negativity N115 which peaks at the same latency, creating a polarity reversal between anterior and posterior channels. N115 can be seen in the group average traces on the most posterior channels "S" and "U". Figure 6.4 (page 187) illustrates the apparent polarity inversion between P115 and N115 on electrodes "E" and "S". In individual results the two positive components P95 and P115 are evident in all but one subject, who only demonstrates the latter. P90 is seen most commonly on posterior and lateral channels; the later P115 is seen at anterior positions, frequently reaching a peak at electrode "E" or on the midline electrode "K". Component N115 is also visible for the majority of subjects on the most posterior channels, although it does not necessarily correspond in latency with the anterior P115.

Component P95 of the pattern reversal response was also evident on posterior channels in both group average and individual traces, and the group average map shows a broad posteror area of positive activity at this latency. As with the pattern onset response, more anterior eletrodes showed a second, overlapping positive component which peaks at a latency of around 116msecs (termed "P120"). This component appears fairly

equally prominently on rows "D" - "H" and "I" - "M" although it reaches an apparent maximum on electrode "L". The majority of individual subjects show this component at its maximum amplitude on electrodes "E" or "K". The most posterior channels "S" and "U" show a negative peak at a latency of 140msecs which probably represents component N130. The map at this latency (labelled "N130") shows very low amplitude negative activity at posterior electrodes, against anterior positive activity which is related to P120. Some individual subjects show a negative component of variable latency at posterior electrodes. This does not bear a consistent relationship with the preceding positive component P120.

The posterior positive onset component P155 is visible on the most posterior channels in group average and individual traces peaking at a latency of about 150msecs. The map of at this latency shows positive activity reaching a maximum at a more posterior position than that for the lower half-field response. The anterior negative activity in this map is related to the subsequent negative component N170. A small but definite P220 component is also visible peaking at or near electrode "J" in group average and in individual pattern onset responses.

The "lateral" negative component N170 peaks on anterior channels in the group average traces and the map of activity at this latency shows a clear area of negative activity spreading across the midline, although it appears to reach a maximum at electrode positions "G" and "E". The behaviour of this component is echoed in individual responses. In the pattern reversal group average traces a prominent negative component N165 at a latency of around 170msecs is visible on the group average traces on anterior channels "D" to "H". On electrodes "I" to "M" a broad negative wave is visible which has no clear peak. On the most posterior electrodes ("S" and "U") a peak at 210 msecs can be seen, which represents component N210. The map at a latency of 170msecs (labelled "N165") shows generalised negative activity which is highest at anterior and lateral electrodes. An equivalent component is demonstrable in all but one individual subject, reaching its maximum at various electrode positions but more commonly at lateral channels. Both the lateral negative components N170 and N165, therefore, appear more clearly in upper than in lower hemifield responses.

The major late positive reversal component P190 appears only as a very low amplitude positive tendency on the group average traces at a latency of 190 msecs. This appears most clearly on electrode "K". The group average map at this latency (labelled "P190") shows only widespread low amplitude negative activity. Most individuals, however, demonstrate such a component peaking at or near this position although its latency is quite variable. The late negative reversal component N210 can be identified only in about half of subjects but, as commented above, can be seen as a posterior negative peak

in the group average traces. On the map of activity at this latency ("N210"), a broad area of negative activity can be seen at posterior electrodes.

6.3f Summary

6.3f(i) Early posterior pattern onset and pattern reversal components

Both types of response contain small early positive and negative components which, where distinguishable, have their maximum amplitudes over posterior parts of the montage, at and around the midline. Both positive and negative components are more prominent in the responses to pattern reversal. This applies particularly to the positive peak which is only clearly evident in full field and lower half-field responses for pattern onset. The early negativities N70 and N75 show a clearer tendency to localisation on the midline itself, tending to appear maximally on electrodes "P" or "K" in all stimulus conditions, than the early positivities P55 and P60 which are slightly more widespread. With lateral half-field stimulation the reversal P60 and both the onset N70 and the reversal N75 can be seen on midline and ipsilateral channels. All components are less clear in lower than in full field responses, and only the negative components N70 and N75 can be distinguished in upper field responses. There is apparently little change in distribution of any of these components, where they can be identified, with change in stimulus visual field position.

6.4f(ii) Major early positive components

Components P90 of the pattern onset response and P95 of the pattern reversal response showed similar behaviour to that described in the previous study. Both components reached their maximum amplitudes about 4cm above the inion for full and lower field stimulation but whereas the onset P90 was maximal to either side of the midline the reversal P95 was fairly evenly distributed across the midline. P90 also appeared to spread further anteriorly than P95. The reduction in amplitude on midline electrodes for the onset P90 was less well emphasised in lower than in full field responses. Lateral hemifield stimulation resulted in contralateral localisation of both components although this was much clearer in the case of the onset P90. There is no clear, consistent evidence for a polarity reversal of P90 at midline or ipsilateral channels although in some individuals there is a suggestion of such behaviour. Group average responses show that P90 is replaced, on ipsilateral channels, by a positivity which peaks some 20msecs later. P95, however, was still seen as a clear, single positive component on ipsilateral channels. A later positive peak, superimposed on or closely following the main positive component, and peaking between 10 and 30msecs later, was evident in individual responses to onset and reversal for full field and lower and lateral half-field targets.

Although more commonly seen at lateral electrode positions, this later peak was not confined to ipsilateral electrodes on lateral half-field stimulation, appearing bilaterally or solely on contralateral electrodes in some cases. In the upper field responses both P90 and P95 are clearly visible on posterior electrodes. The onset P90, however, tends to be maximal at lateral electrode positions whereas the reversal P95 is of highest amplitude at more posterior electrodes across the midline. These components are replaced at more anterior channels by the later positivities P115 in the onset response and P120 in the reversal response, which tend to show their maximal amplitudes about 4 to 8cm above the inion.

6.3f(iii) Major early negative components

Both pattern onset and pattern reversal responses contain a prominent negative component peaking on and/or just lateral to the midline for full field stimulation. The pattern onset N115 shows a tendency to peak several milliseconds later at more lateral electrode positions, for full field and lower and lateral half-field responses. Group average distributions show a tendency for this component to peak on the midline first of all and then at slightly more lateral positions, shortly afterwards. Both lateral hemifield responses show the maximum amplitude for this component at posterior and contralateral electrode positions. At anterior and ipsilateral electrode positions the activity is predominently positive. There is a suggestion of a possible inversion in polarity between the major negative component at posterior and contralateral locations and a positive component appearing at a comparable latency at anterior and ipsilateral locations, although this is not clearly seen in individual responses. The main negative component in the full field group average pattern reversal response peaks later at the far lateral electrode positions than on the midline or near lateral positions. Individual pattern reversal responses suggest the presence of a later negative component peaking at lateral electrode positions. Consequently the main negative peak on lateral channels 4cm above the inion is regarded as probably representing a separate component. The peak which is visible on midline and near lateral channels in the group average responses and sometimes also at lateral channels in individual responses is regarded as the major early negative component N130. This component also appears at a slightly earlier time on midline electrodes than on those just lateral to it for full field and lower and lateral half-field stimuli. For right and left hemifield responses N130 appears maximally on contralateral electrodes. In lower field responses N130 has a similar distribution to that for the full field condition. The lower field pattern onset N115, however, shows a more anterior distribution than for the full field response, being definitely maximal at 4cm above the inion. In the upper field responses both components can be seen on the most posterior channels. In the group average pattern onset response there is a suggestion of a polarity inversion between the posterior N115 and the anterior P115, although such

behaviour was not demonstrated in most individual responses.

6.3f(iv) Major late positive components

In the pattern onset response a major late positive complex can be observed which peaks on the midline. Within this complex two components, P155 and P220, can be distinguished. The fomer is maximal at posterior electrode positions, commonly on electrode "P" whereas the latter has a more anterior distribution normally reaching its maximum amplitude at or near electrode "K". In the pattern reversal response only one comparable component, P190, is observed, peaking on the midline commonly at electrode "K". Components P190 and P220 show little change in their distribution for field sector stimulation, tending to peak around the same positions whatever the half-field target. Both of these components appeared with reduced amplitudes in upper field responses. Component P155 has a more posterior distribution with upper field stimulation, appearing at the most posterior electrodes. With lateral hemifield stimulation this component showed a tendency to spread further onto the ipsilateral hemisphere than the contralateral although it still showed its maximum amplitude on the midline.

6.3f(v) Lateral anterior and posterior negative components

Pattern onset responses showed a clear negative component N170 peaking at anterior and lateral electrode positions for all visual field conditions. In lateral hemifield responses this component tended to have a higher amplitude on the contralateral hemisphere although it was still visible at ipsilateral channels. This component was clearest in upper field responses in which it was visible further towards the midline than in full field conditions. For lower field stimulation N170 was less prominent in the group average distributions where it appeared confined to the most lateral electrode positions. Some individual responses showed a similar distribution to that in the full field condition. In the pattern reversal responses an equivalent lateral negative component N165 could be identified in the individual responses of most subjects. This did not come through clearly as a separate component on group average responses except for upper field stimulation, where it appeared as a broad negativity reaching its maximum amplitude at anterior and lateral electrodes. Full field stimulation showed a broad negativity with a similar lateral distribution at the peak latency of the main negative component in the far lateral electrodes, which may be a manifestation of an N165 component. A posterior and lateral component N210 could be distinguished in the pattern reversal responses to all stimulus conditions, peaking most commonly at the most posterior electrodes on the montage below or at inion level. This component was most prominent and appeared to spread more anteriorly in the upper field response. N210 showed no tendency to lateralisation appearing on both sides of the midline in lateral

hemifield responses. A possible equivalent component was visible in the pattern onset responses of some subjects although this was by no means clear or consistent.

6.4 Discussion

Very early positive components equivalent to the pattern onset P55 and the pattern reversal P60 described in the present study have rarely been discussed in the literature. Ermolaev and Kleinman (1984) found a positive peak at a latency of about 50msecs in their pattern onset response to small (8') checks. This component appeared to be related to foveal stimulation since it was never seen in extrafoveal responses.

Component N70 of the pattern onset response appears analogous to the early midline negative component recorded by several authors (e.g. Lesevre and Joseph 1979; Drasdo 1980; Ermolaev and Kleinman 1984). This negativity, which appears more prominently with foveal targets and fine stimulus details, has been discussed in sections 4.4a and 4.4b(iv). Lesevre and Joseph (1979) found that their N60 component, like N70 in the present study, showed a fair amount of inter-subject amplitude variability, underwent little change in distribution with different visual field conditions and was reduced in amplitude for lower and lateral half-field stimulation. They did not comment upon the effect of upper field stimulation except to say that this wave did not change in polarity, which is again consistent with the behaviour of N70.

Component N75 of the pattern reversal response appears comparable, at least in part, with the N75 component described by Halliday and colleagues as part of their "NPN" complex (see section 4.4b(iii)). This consists of the major positive component "P100" and the negative peaks "N75" and "N145" which precede and follow it (Blumhardt et al. 1978). This NPN complex appears maximally on the midline for full field stimulation and at midline and ipsilateral electrodes for lateral hemifield responses. Component N75 in the present study exhibits a similar pattern of behaviour. As the major positive P95 (and also the major early negative N130) appears maximally on midline and contralateral electrodes in the present study one might have predicted that N75, being part of the "NPN" complex, might have a similar distribution. This suggests that either N75 or P95 in the present study may not represent exactly the same component as that described by Halliday's group. Alternatively, the absence of this component in contralateral responses may merely be a result of being "swamped" by the major early positive, as appears to happen in the lower field response.

Lesevre and Joseph (1979) demonstrated an early midline negative component which was equivalent to the pattern onset N60 in their responses to pattern reversal stimulation. This peak appeared more prominent than that in the pattern onset response; likewise, component N75 in the present study was larger and more clearly and frequently identified than component N70 of the onset response.

The early positive and negative components in the pattern onset and pattern reversal responses might perhaps be considered as representing early activity in the portion of the striate area occupied by foveal projections in the manner proposed by Lesevre and Joseph (1979) for their early negative component N60. This would not, however, explain why these components were not seen on contralateral electrodes more commonly.

As discussed in Chapter 5, other authors have proposed an origin for the early midline negative onset component in surface negative striate cortical activity around the tip of the occipital pole. Jeffreys and co-workers (1987) and Butler and colleagues (1987) considered that the early negative components in their responses to small fields and small checks represented surface negative striate cortical activity which was related to the major early positive component CI. Drasdo (1980) considered that the early negative component C0 in his responses to pattern onset for foveal stimulation was perhaps in fact an early portion of the major early negative component CII, the two portions being separated from each other by the positivity of CI. He considered that the midline localisation of both C0 and CII was suggestive of an origin in striate cortex. Lesevre and Joseph (1979), however, considered that their pattern onset N60 component was a separate entity from their major early negative N140 since the former appeared in responses to pure luminance stimulation whereas the latter did not. The early negative peak N70 recorded in the present study appears to be a separate component although it may be influenced to a varying degree by the positive peaks P55 and P90 which precede and follow it.

As an introduction to the present discussion on the behaviour of the major early positive components P90 and P95 of the responses to pattern onset and pattern reversal, the reader is referred to the corresponding discussion in Chapter 5 section 4. In general, the results of the present study are in agreement with those of the previous study. The group average distributions of the two major early positive components for full and lateral half-field stimulation appear very similar in the two cases.

Both the pattern reversal P95 and the pattern onset P90 components show similar characteristics in lower half-field responses to those for the full field condition. Such behaviour is consistent with that reported in the literature (see sections 4.4b(iii) and (iv)). This is believed to be a result of the more optimal positioning of lower field projection areas on the visual cortex in relation to scalp electrodes than those for the upper field. These are thought, for the striate area at least, to lie predominantly on the upper and lower aspects of the occipital lobe respectively. As a consequence, lower field responses appear to constitute a greater proportion of the full field response than upper field responses.

Component P90 of the pattern onset response in the present study is considered to be the probable equivalent of the P90 recorded by Lesevre and Joseph (1979) and the CI component of Jeffreys. The comments applying to the behaviour of the "CI" component for full and lateral hemifield stimulation made in the previous study (see section 5.4) and the implications with regard to possible cortical sites of origin are are applicable to the P90 component of the present study. The failure to demonstrate clear and consistent polarity reversals between contralateral P90 peaks and ipsilateral negative peaks at the same latency lends some weight to those arguments already put forward against an origin for this major positivity in surface negative striate activity. As found by Lesevre and Joseph (1979), negative activity occurring on the ipsilateral hemisphere, where present, rarely peaked simultaneously with the major positive component. As suggested in the previous study, the lack of a clear ipsilateral negative "CI" component in the present responses might be related to the small field size used. It is still apparent, however, that there is no evidence of negative activity at contralateral electrodes in any individual subject, although one would certainly expect to see this in at least some subjects for foveal fields. The finding that very small checks (less than 10' of arc) led to the appearance of midline negative "CI" components by Jeffreys and colleagues (1988) and Butler and co-workers (1988) may be relevant to this discussion, since the check size of 15' used in the present study would not allow for this effect. The failure to demonstrate this behaviour using the M-scaled targets and very small checks in the previous study, however, sheds some doubt on the relationship between the early negative midline component found by these authors and the contralateral positive CI. As commented above, the early negative component N70 recorded in the present study appears to be a separate component and it is considered unlikely that this represents a polarity inversion of P90.

Both Jeffreys (Jeffreys and Axford 1972a; Jeffreys 1977) and Lesevre and Joseph (1979) demonstrated a polarity inversion of CI between lower and upper hemifield responses, resulting in negative activity at anterior electrode positions. Such a polarity inversion was not demonstrated in the present study. Rather, P90 demonstrated an apparent posterior and lateral movement of its bilateral maxima when changing from lower to upper field stimulation. This was accompanied by a reduction in amplitude. Electrodes at midline and anterior positions tended not to demonstrate a clear P90 component, where this peak, if present, appeared to be masked by the positive-going transient of the more prominent anterior P115 component. There was, therefore, little change in the location of these points of maximum amplitude of the P90 component between different half-field stimuli.

Analysis of the data of Butler and co-workers (1987) shows that the location of the equivalent dipoles for the CI components elicited by foveal quadrant stimulation is

similar to that of the P90 maxima in the present study. These authors reported little change in the location of this dipole, which was deep to the surface and whose positive axis was oriented in a posterolateral direction, for different foveal quadrant stimuli, although a slight downward movement was apparent for the upper field source. These results are, therefore, consistent with the surface distributions demonstrated in the present study. These authors also found, however, that the behaviour of peripheral field dipoles was consistent with an origin in surface negative striate cortical activity. They considered that an origin for CI in extrastriate cortex was unlikely since this ought to lead to more widely separated dipole sources for lower and upper field targets. These authors felt that in fact the most satisfactory explanation for the apparently surface positive foveal dipoles lies in an origin in surface negative activity on the posterior surface of the lateral calcarine sulcus, as explained in section 4.4b(iv). At this stage such an explanation as applied to the behaviour of the P90 component recorded in the present study can not be ignored. The variations in amplitude of this component with the different M-scaled targets described in Chapter 5 (and also in Chapter 7) suggest, however, that this component must be generated by activity on the proximal cortical surface.

The behaviour of the pattern reversal P95 in upper hemifield responses is consistent with that reported by Michael and Halliday (1971). These authors found that their P100 component showed a positivity at electrodes below the inion in the responses to upper field foveal (0-2°) stimulation using a midfrontal reference. Stimulation with a larger (0-8°) target led to the appearance of a negativity at a similar latency at anterior electrodes, which was apparently related to more peripheral stimulation. This is consistent with the results of the present study, in which no polarity reversals for P95 were demonstrated between posterior and anterior electrodes.

Michael and Halliday (1971) considered that the behaviour of the pattern reversal major positive component in upper and lower field responses was consistent with origins in cortical regions on the lower and upper aspects of the occipital lobe respectively (see section 4.4b(iii)). They suggested that such generator locations were more likely to correspond to extrastriate than striate cortical areas. The results of Lehmann, Darcey and Skrandies (1982) led these authors to a similar conclusion. The behaviour of the lateral hemifield responses in the other studies of both of these authors, however, (see section 4.4b(iii) and section 5.4) suggests origins in the region of cortex around the occipital pole, in a position which is normally largely occupied by the striate area. It may be that in fact this component represents responses from more than one visual area. This idea, which is consistent with the findings of Spekreijse's group (Maier et al. 1987) is discussed further in Chapter 7.

The anterior upper field positive components P115 and P120 are considered to be

separate entities from the major positive components P90 and P95. Lehmann (Lehmann and Skrandies 1979a, 1980a) has reported that the latency of the main positivity in pattern reversal and pattern onset VEPs increases (by about 11msecs) between responses to lower and upper field stimulation. Jeffreys (Jeffreys and Smith 1979) considers that the apparent delay in latency of the pattern onset response in Lehmann's studies is in fact the result of an inversion in polarity of the major early positive and negative components between lower and upper field responses. This would mean that the delayed main positive component in the upper field response was in fact an inverted CII component. Jeffreys' (e.g. Jeffreys 1971; Jeffreys and Axford 1972b) results show that the negative CII of the lower field VEP is replaced by a more anterior (maximum 5-10cm above the inion) negativity at a similar latency in upper field responses. Lehmann, however, finds that the position of the point of maximum amplitude tends to be slightly more posterior with upper field stimulation than with lower. In the present study, the position of maximum amplitude for the major positive components P90 and P95 showed similar behaviour, with the maximum, for P95 particularly, moving towards more posterior electrode positions. The later components P115 and P120, however, demonstrated a distinctly more anterior distribution than P90 and P95. It would appear, therefore, that the latency delay found by Lehmann was one involving the major early positive component P100 rather than the appearance of a later component. In the present study, there is a slight but insignificant change in latency between lower and upper field responses for components P90 and P95.

Other authors have, however, reported the appearance of later positive components in responses to upper field stimulation. Kriss and Halliday (1980) demonstrated a "broad" positivity at about 120msecs in the upper field response to pattern reversal stimulation. Blumhardt and Halliday (1979) found that with upper quadrant pattern reversal stimulation their contralateral "PNP" complex became more prominent. This appeared to result in a distortion of the signal at midline electrodes, causing an apparent increase in P100 latency. Lesevre and Joseph (1979) distinguished a positive peak in upper field pattern onset responses which replaced the prominent N140 component. With upper quadrant stimulation, this positive component invariably peaked on the contralateral hemisphere. The authors commented that this positivity, which appeared at anterior electrode positions, did not have a fixed time relationship with N140, and they could not comment on what its origin might be. It would appear that the anterior positive peaks P115 and P120 demonstrated for upper field stimulation in the present study might resresent a polarity inversion of the major early negative components of full and lower field responses, although, as in the study of Lesevre and Joseph (1979) there appears to be no consistent relationship between the latencies of the two peaks in individual subjects.

The significance of the additional positive peaks appearing superimposed on or closely following the major positive peak in the responses to full field and lower and lateral half-field stimulation is not clear. An inspection of individual responses suggests that there may be a distinction between the later positive peak which is visible at ipsilateral electrodes in the group average and individual pattern onset responses to lateral half-field stimulation and a peak which appears at lateral electrodes on either side of the head in responses to pattern onset and pattern reversal stimulation. The pattern onset responses of Shagass, Amadeo and Roemer (1976) exhibited a small positive component appearing on ipsilateral channels shortly after the main positive component peaks on contralateral channels. The authors commented that this might be an artifact related to the superimposition of responses from a group of individuals; it was only identified in three of their subjects. In the present study, however, the majority of subjects demonstrated this phenomenon. The second type of peak appears at lateral electrodes on either side of the head in the responses to pattern onset and pattern reversal stimulation with full field and lower and lateral half-field targets. In some individuals this second type of peak appears to be related to the anterior positive components P115 and P120 of the upper field response. The presence of these extra peaks therefore possibly reflects anterior / ipsilateral - posterior / contralateral inversion of the major early negative component, particularly the N115 of the pattern onset response. It is also possible, however, that in some cases the ipsilateral positive peak in the pattern onset response might be related to the later midline positive component P155, which appears to be visible at lateral electrodes in group average and individual full field responses as a small positivity separating the two negativities N115 and N170.

The general behaviour of the major early negative components described in the responses to pattern onset and pattern reversal in the present study is in agreement with some of the studies reported in the literature but not others. Lesevre and Joseph (1979) found that their major negative component N140, like N60, tended to remain maximal on the midline for lateral hemifield stimulation. Jeffreys (Jeffreys 1971; Jeffreys and Axford 1972a) reports that his major early negative component CII inverts in polarity between lower and upper field stimulation, but remains localised on the midline for lateral hemifield stimulation. Darcey, Ary and Fender (1980a), however, found that in some subjects their major negative peak inverted across the midline in a similar manner to that shown by their major positive component.

The major early negative component of the pattern reversal response has received relatively little attention in the literature. Jeffreys (1977) is of the opinion that a component which corresponds to the contour-related CII onset component can not be found in the reversal response. Certainly, the more marked lateralising behaviour of the pattern onset N115 as compared with the pattern reversal N130 in the present study

suggests a slightly different cortical origin for these two components by a similar logic to that put forward for the behaviour of the major early positive components. Lesevre and Joseph (1979), however, found that their reversal responses contained a midline negativity of larger amplitude than the pattern onset N140, which behaved in a similar manner. Lehmann (Lehmann and Skrandies 1979b) demonstrated an occipital midline negativity at a latency of about 135msecs. The lateral hemifield response at a corresponding latency, however, showed a positivity over the contralateral hemisphere. The N130 recorded in the present study is possibly equivalent to the second negative component (N145) of Halliday's NPN complex. This would predict a midline and contralateral localisation for N130 on lateral hemifield stimulation with foveal targets, which fits in with the findings in the present study.

Several authors have, as discussed in section 4.4b(iv), demonstrated the presence of a negative component in the pattern onset response which peaks after the major early negative component and is most prominent at lateral electrode positions (Lesevre and Joseph 1979; Jeffreys 1982; Ermolaev and Kleinman 1983, 1984; Maier et al. 1987). These later negative components demonstrate no polarity inversions with lateral hemifield stimulation. Lesevre and Joseph (1979) defined a lateral negative component "LN150", which showed behaviour similar to that of the pattern onset N170 in the present study. Both of these components were most prominent at anterior and lateral electrodes and appeared with a higher amplitude over the contralateral hemisphere for lateral hemifield stimulation. There were, however, some differences between the two components: "LN150" was more prominent in lower field compared to full field responses, whereas N170 was larger in upper field responses. Lesevre and Joseph (1979) also found a comparable component in their responses to pattern reversal, but this tended to be less prominent than the "LN150" of the pattern onset response. This behaviour is consistent with that in the present study, where N165 of the pattern reversal response was much more difficult to demonstrate than the onset N170. Jeffreys "N150" component probably represents a similar entity to "LN150".

The significance of the findings of Ermolaev and Kleinman (1983, 1984) and Maier et al. (1987) in relation to those in the present study and those of Lesevre and Joseph (1979) and Jeffreys (1982) is not entirely clear. Ermolaev and Kleinman (1983, 1984) demonstrated a midline "N100" component which appeared to be related to foveal stimulation and photopic visual conditions, and a lateral "N130" component which responded to a wider area of retinal stimulation and was more prominent at mesopic levels of illumination. Component "N100" was noted to invert in polarity between lower and upper field responses whereas "N130" did not. "N130", then, shows similar characteristics to the lateral negative components discussed above. It appears possible, however, that components "N110" and "N130" might both form part of the major early

negative component in the pattern onset response in the present study. It has been demonstrated that the major early negative component N115, as distinct from the lateral negative component N170, peaks slightly but significantly later at lateral electrode positions. This might also explain the apparent discrepancy between the latency of the anterior positive component P115 and the major early negative component in upper field responses for individual subjects; if the "N100" part of the major negativity inverts to produce the anterior P115, the portion left behind will have a later, variable latency depending on the relative prominence of the different constituents.

Maier and co-workers (1987) also suggested that the CII component of the pattern onset response should not be regarded as a single component. These authors demonstrated contributions from two "Principle Components", having apparent origins in separate cortical areas. The first of these consisted of a positive peak, which was considered to represent CI, followed by a negative peak. This complex, termed "PC1" was identified at contralateral electrode sites with half-field foveal stimulation. "PC2" consisted of a single negative peak which appeared maximally on ipsilateral electrode sites. This negative peak appeared at a latency about 30msecs earlier than the contralateral negative peak of PC1. These results are in some respects consistent with the findings of Ermolaev and Kleinman (1983, 1984), and would again explain why the major early negative component peaks earlier on the midline than at contralateral electrodes.

Lesevre and Joseph (1979) also defined a lateral negative component "LN210" which peaked at more posterior electrode positions than "LN150". This component was more prominent in the pattern reversal responses than in those to pattern onset. The pattern reversal N210 component found on posterior electrode positions for all stimulus conditions in the present study appears to be the possible equivalent of this component. The "LN210" onset component of Lesevre and Joseph, however, appeared maximally on contralateral electrodes, whereas the N210 reversal component in the present study showed no tendency to lateralisation. This peak did not appear clearly enough in pattern onset responses in the present study to be studied as a separate component. Lesevre and Joseph (1979) considered that the lateral and inferior topography of this component were suggestive of an origin in inferotemporal cortex.

The presence of major late positive components appearing on midline electrodes has been reported by several other authors for both pattern onset and pattern reversal responses. The pattern onset component P155 in the present study bears some resemblence to the CIII component of Jeffreys (e.g. Jeffreys and Axford 1972b; James and Jeffreys 1975; Jeffreys 1977). Jeffreys reports that CIII appears to behave in a similar way to CII for partial field stimulation, remaining on the midline for lateral hemifield responses and inverting to upper field stimulation. Although P155 remains more or less on the midline

for right and left hemifield responses in the present study, it does not appear to invert in polarity for upper field responses. Instead, it reduces in amplitude and moves to a more posterior position on the map. This difference in behaviour might be a result of the small field size used in the present study. The inversion of components between lower and upper field responses is thought generally to be a result of the location of visual field projections and associated VEP generator areas towards the upper and lower aspects of the occipital lobe for lower and upper field targets respectively. It is likely that, as predicted, the targets used do not extend far enough into the peripheral visual field for VEP generator areas on the under-surface of the visual cortex to be activated, with the result that the maximum response merely moves to a more posterior location. Jeffreys (1977) considers that CIII arises from extrastriate cortex, but from a different area from CII. The idea of a separate origin for N115 and P155 fits in with the behaviour of these two components - whereas N115 appears to invert in polarity between altitudinal half-fields, P155 does not.

Lesevre and Joseph (1979) described a long lasting positive component "P200" in their responses to pattern onset stimulation. This showed very little change in topography between different visual field conditions, remaining localised on the midline, but tended to be reduced in amplitude. These authors showed, however, that P200 appeared with a much reduced amplitude in foveal (2^{o} diameter field) stimulation. In pattern reversal responses an equivalent component of lower amplitude was observed. Lesevre and Joseph (1979) observed that P200 could sometimes be seen to be composed of two parts, with latencies of around180 and 240msecs. The second of these two parts showed a more posterior distribution than the first. This does not fit in with the findings of the present study, in which P220 is found to have a more anterior distribution than P155. Shagass, Amadeo and Roemer (1976) also defined a component at a latency of about 225msecs in their reversal and onset responses which showed no lateralising tendencies and was largest on midline electrodes for lateral hemifield stimulation. Lesevre and Joseph (1979) considered that its constant midline topography and absence of polarity inversions with hemi-field stimulation might reflect an origin for their "P200" component in area 18. In the present study, it is tempting to draw parallels between the behaviour of component P220 of the pattern onset response and P190 of the pattern reversal response, and that of the flash P2 component reported in Chapter 5. This would suggest that these late positive components might have diffuse origins in multiple areas of visual cortex.

The relationship between P155 and the midline and lateral negative components N115 and N170 presents a problem in the present study. Lower field group average pattern onset responses demonstrate an apparent P170 component on midline electrode "K", whilst the lateral negative N170 peaks at a similar latency on electrodes "I" and "M". In

general P155 and N170 do not peak at the same latency and although on average P155 peaks first, its latency can be later than that of the lateral negative component. It is considered unlikely, however, that components P155 and N170 represent midline and lateral manifestations of the same component. It seems possible that the appearance of two separate components in the late major positive complex of the pattern onset response may be an artifact due to the presence of the lateral negative component N170. This might explain why two separate peaks were rarely disinguished in individual responses to pattern reversal stimulation, where the apparent lateral negative component N165 is not so well defined as that in the onset response. A possible source of the earlier latency of N115 in midline electrodes is the greater prominance of P155 at this position. It is conceivable that if this positivity, which is quite large in some cases, commences before the major early negative component reaches its maximum amplitude, it could "cut off" the negative component and create an apparently earlier peak latency at midline positions. Ermolaev and Kleinman (1984) observed that the prominence of their lateral "N130" was influenced by the behaviour of a positivity peaking at about 180msecs in their pattern onset responses.

In view of the probable interactions between the negative and positive peaks occurring after the major early positive components in these responses, it seems somewhat doubtful that their true cortical origins can be predicted from their surface distributions with any degree of certainty. Rather, as commented by several groups of workers (see section 4.1) it appears that some method may be required for isolating distinct events in these responses, and determining which of these peaks are, in fact, related to distinct underlying components.

An apparent amplitude asymmetry of the signals recorded over left and right hemispheres has been noted for the flash response (Vella et al. 1972) and also for the CI component of the pattern onset response to foveal targets (Butler et al. 1987), which appear larger when recorded on electrodes over the right hemisphere than over the left. Drasdo (1982) reported a similar phenomenon. Vella and co-workers (1982) considered that this finding might be related to right and left hemisphere functional specialisation. Although the group average responses in the present study show an apparently larger amplitude of the major early positive components, and also, to an extent, the major early negative components in the responses to full and lateral hemifield stimulation, these effects did not reach statistical significance.

CHAPTER 7

Further investigation of the scalp topography and cortical origins of the visual evoked potentials elicited by foveal pattern stimulation. II. M-scaled hemifield stimuli.

7.1 Introduction

In Chapter 5, the major early positive components in the responses of a small group of subjects to pattern reversal and pattern onset stimulation, using a series of small M-scaled stimuli confined to the left visual hemifield, were studied. The present chapter describes the results of a similar investigation performed on a larger group of subjects. The reader is referred to Chapter 5 for a discussion of the theories behind this investigation and the initial findings. Briefly, we hoped that by stimulating very small areas of foveal and parafoveal visual field we would be able to study the responses from very localised (1 cm^2) patches of striate cortex (and the extrastriate re-projections associated with them), on the proximal surface of the occipital lobe. This would enable us to study the local arrangement of VEP generators as compared with visual field projections. In addition, we expected that we might be able to demonstrate the projection of adjacent small targets onto cortical gyri and fissures in some subjects. One important aspect of the investigations described in Chapters 5 and 6, using 4 degree and M-scaled targets, was an attempt to clarify the locations of the generators of individual components with respect to different visual cortical areas. Of particular interest in this respect are the major early positive components in pattern onset and pattern reversal responses (here termed "P90" and "P95" as in Chapter 6). It was hoped that the results of the present study would be of further aid in this process.

The results of the initial study using M-scaled targets raised several points which warrant further investigation. The majority of subjects demonstrated maximum responses for the pattern onset P90 and the pattern reversal P95 ("CI" and "P100" respectively) for central targets. It was expected that due to the anatomical variability of patterns of gyri and fissures between individuals some subjects ought to show maximum amplitudes with the more peripheral targets. One possible explanation which was put forward for these findings was a failure to stimulate cortical areas of predicted dimensions, or, if the dimensions were correct, to stimulate them equally effectively. In relation to the latter point it was thought that perhaps the check sizes used for more peripheral stimuli were inappropriate. In the present study, it was considered that the examination of responses from more subjects might reveal a greater number of individuals in whom the more peripheral targets would elicit maximum responses. In addition, it was considered appropriate to investigate the effect of check size on the responses to central and more peripheral targets.

One objection which was raised in the previous chapters to a surface negative striate cortical origin for the major early positive component of the pattern onset response was the failure to demonstrate a midline and contralateral negative peak at a comparable latency with these foveal stimuli. Other workers have recently reported the presence of a "negative CI" in responses to lower field foveal stimuli using check sizes of less than 10' of arc (Butler et al. 1987; Jeffreys et al. 1987). Jeffreys and colleagues (1987) reported that this negative peak was localised on the midline and that it was related to stimulation within the central 3 x 1.5 degree area of the lower visual hemifield. Of the five subjects investigated in Chapter 5, none demonstrated such a phenomenon even though the check size for the central stimulus was 7' of arc. The responses of the subjects used in the present study were, therefore, carefully examined for evidence of such a polarity inversion of the P90 component.

It was noted in the initial study that there was a tendency for the major positive component to peak at an increasing latency as stimuli were moved from lower towards central and upper field positions. It was thought that this could be related to the check size used since this increases with target eccentricity. The increase in component latency for pattern onset and pattern reversal responses with patterns of increasing spatial frequency has been well documented in the literature (see section 3.3b). These phenomena have been studied further in the present study.

In the present study there were certain modifications of experimental procedure and in method of analysis compared with those of the initial study in Chapter 5. As in Chapter 6, electrode placement was determined on the basis of percentage head dimensions rather than absolute measurements. Also, component amplitude was measured from baseline rather than from the previous negative peak. In addition to the seven M-scaled targets used in the initial study, a further target was added which was positioned adjacent to the central stimulus and further from fixation, such that it would stimulate a slightly more peripheral area of the visual field. This presumably would tend to activate a patch of striate cortex at a less lateral position on the occipital lobe. This target might consequently be expected to accentuate any tendency for P90 to appear with an inverted polarity at midline electrode positions, although its check size, at 12' of arc, is slightly higher than that stipulated above for demonstration of this effect. It might also be expected to enhance any tendency for the ipsilateral localisation of the pattern reversal P95, particularly if this component does in fact have a striate cortical origin. As in the study reported in the previous chapter, the check sizes used in the present study were slightly smaller than those used in the initial study, starting at 6' for target D and increasing at the same rate as target size. This was again a consequence of the particular slides used in the projection system and was not expected to affect results significantly

Some of the results for this study have been displayed in the form of equipotential maps representing the scalp potential distribution at the peak latency of the major early positive component of the responses to pattern onset and pattern reversal. The maps for each target position in several subjects, wherever this component could be distinguished, are shown. For each subject and stimulus condition the peak latency and maximum amplitude of the major positivity was recorded along with the electrode position at which this was recorded. In order to ensure that any changes were not an artifact resulting from measurements at different electrode positions, it was considered appropriate to also record the latency and amplitude of the major positive component as measured at a constant electrode position.

7.2 Materials and methods

Details of methods of pattern stimulation and electrophysiological recording techniques were identical to those in Chapter 5 except where detailed below. A total number of nine normal subjects (four female) were used in the present study, eight of whom (two female) participated in the 4 degree study described in Chapter 6. None of these subjects took part in the initial investigation using M-scaled targets described in Chapter 5. All subjects had visual acuity of 6/6 or better, wearing optical correction where necessary. Their age range was 21-31 years.

The M-scaled target series is shown in Figure 5.1. In addition to these seven targets, a further target was added which is termed "H". This has an angular subtense of 2 x 2 degrees with a check size of 12' of arc, and is positioned laterally, away from the vertical meridian, adjacent to the central target D.

Responses from 16 scalp electrodes were averaged by a Bio-logic Brain Atlas III system. The montage used is represented in Figure 5.2 and was, as before, confined to the back of the head. Electrode separation was based on percentage head dimensions, as in Chapter 6. All electrodes were again referred to a common midfrontal position (Fz), with the ground electrode on the forehead (Fpz).

In the first part of this study, the responses of each subject to pattern onset-offset and pattern reversal stimulation were recorded for each target position. In the second part of the study, the pattern onset-offset and pattern reversal responses of five subjects were recorded for target positions A or B and D, using several different check sizes. Unfortunately, complete data sets were collected for only two subjects with targets B and D, and for only one subject for targets A and D.

CHAPTER 7
RESULTS

Table 7.1

Amplitudes and peak latencies of the major early positive components in the responses to pattern onset and pattern reversal stimulation for the M-scaled target series for individual subjects

7.1a Amplitudes and peak latencies for pattern onset stimulation as measured at maximum position

7.1b Amplitudes and peak latencies for pattern onset stimulation as measured at constant electrode position

7.1c Amplitudes and peak latencies for pattern reversal stimulation as measured at maximum position

7.1d Amplitudes and peak latencies for pattern reversal stimulation as measured at constant electrode position.

Table 7.1a

		TARGET							
		A	B	C	D	E	F	G	H
SUBJECT									
GC	msecs	82	88	92	92	94	84		92
	μV	+5.3	+2.5	+5.0	+6.0	+6.0	+2.4		+2.5
	electrode	L	L	M	M	L=M	M		L=M
RD	msecs	86	94	92	100	98			92
	μV	+3.8	+6.7	+6.5	+6.7	+2.8			+2.9
	electrode	G	G	L	L	L			G
ARH	msecs	88	88	84	90	84	92	86	92
	μV	+6.3	+7.7	+3.1	+5.0	+1.5	+1.3	+2.2	+6.9
	electrode	G	G	G	G	L	M	L	L
AH	msecs	88	90	94	96	104	92	96	90
	μV	+8.6	+12.1	+11.2	+11.9	+8.5	+2.1	+2.4	+1.8
	electrode	L	L	L	L	L	L	M	L
UD	msecs	84	88	90	90	98	94	96	
	μV	+1.6	+3.7	+3.7	+6.1	+4.3	+2.8	+1.2	
	electrode	M	L	L	L	M	M	G	
KA	msecs	84	86	86	90	90	92	104	90
	μV	+5.3	+3.0	+8.2	+5.0	+4.1	+2.5	+0.8	+3.2
	electrode	G	G	G	G	H	G	M	G
PB	msecs	86	80	78	92	94	92	92	94
	μV	+1.5	+5.0	+2.3	+5.0	+7.0	+2.5	+1.0	+2.3
	electrode	G	L	L	M	M	U	R	M=R
JL	msecs		82	88	92	88	98	94	94
	μV		+6.1	+8.7	+4.9	+2.2	+1.3	+2.1	+2.5
	electrode		L	L	L	R	G=L	L	L
GROUP MEAN		A	B	C	D	E	F	G	H
	N	7	8	8	8	8	7	6	7
	msecs	85.4	87.0	88.0	92.8	93.8	92.0	94.7	92.0
	S.E.M.	0.8	1.6	1.9	1.2	2.2	1.6	2.4	0.6
	μV	+4.6	+5.8	+6.1	+6.3	+4.6	+2.1	+1.6	+3.2
	S.E.M.	1.0	1.1	1.1	0.8	0.9	0.2	0.3	0.6

Table 7.1b

		TARGET							
		A	B	C	D	E	F	G	H
SUBJECT									
GC	msecs	82	88	88	92	94	84		92
	μV	+5.3	+2.5	+4.7	+5.6	+6.0	+1.7		+2.5
RD	msecs	86	94	92	100	98			92
	μV	+2.4	+6.5	+6.5	+6.7	+2.8			+1.8
ARH	msecs	90	88	80	84	84	92	86	92
	μV	+2.5	+5.0	+1.9	+3.8	+1.5	+0.5	+2.2	+6.9
AH	msecs	88	90	94	96	104	92	96	90
	μV	+8.6	+12.1	+11.2	+11.9	+8.5	+2.1	+1.7	+1.8
UD	msecs	84	88	90	90	96	98	96	
	μV	+1.5	+3.7	+3.7	+6.1	+3.3	+2.3	+1.0	
KA	msecs	84	86	86	90	90	92	104	90
	μV	+3.4	+2.0	+5.1	+2.9	+2.4	+1.7	+0.5	+2.0
PB	msecs	78	80	78	88	92			90
	μV	+1.0	+5.0	+2.3	+3.6	+5.7			+1.8
JL	msecs		82	88	92	88	98	94	94
	μV		+6.1	+8.7	+4.9	+1.0	+1.3	+2.1	+2.5
GROUP MEAN		A	B	C	D	E	F	G	H
	N	7	8	8	8	8	6	5	7
	msecs	84.6	87.0	87.0	91.5	93.2	92.7	95.2	91.4
	S.E.M.	1.5	1.6	2.0	1.7	2.2	2.1	2.9	0.6
	μV	+3.5	+5.4	+5.5	+5.7	+3.9	+1.6	+1.5	+2.8
	S.E.M.	1.0	1.1	1.1	1.0	0.9	0.3	0.3	0.7

Table 7.1c

		TARGET							
		A	B	C	D	E	F	G	H
SUBJECT									
GC	msecs	84	90	94	92	92	88	88	80
	μV	+3.4	+1.0	+5.7	+2.6	+2.3	+0.8	+0.6	+2.1
	electrode	L	L	L	L	R	L	U	L
RD	msecs	96	98	106	104	104	102		98
	μV	+3.3	+3.8	+5.4	+4.7	+4.5	+2.8		+3.5
	electrode	G	G	K	Q	S	P		P
ARH	msecs	90	94	92	98	90	94	90	96
	μV	+4.4	+1.9	+6.4	+3.6	+4.3	+0.6	+2.1	+3.2
	electrode	G	G	M	M	M	M	M	M
AH	msecs	92	94	104	98	100	104		94
	μV	+0.4	+4.7	+3.9	+3.0	+2.1	+0.4		+1.7
	electrode	G	L	L	P	S	M		L
KA	msecs	90	94	94	94	98			
	μV	+2.5	+2.1	+5.1	+4.7	+2.6			
	electrode	L	L	L	L	M			
PB	msecs	84	98	92	96	94	94	104	
	μV	+0.7	+2.6	+2.8	+4.7	+4.1	+1.0	+1.7	
	electrode	G	G	M	M	M	U	U	
GROUP MEAN		A	B	C	D	E	F	G	H
	N	6	6	6	6	6	5	3	4
	msecs	89.3	94.7	97.0	97.0	96.3	96.4	94.0	92.0
	S.E.M.	1.9	1.2	2.6	1.7	2.2	2.9	5.0	4.1
	μV	+2.4	+2.7	+4.9	+3.9	+3.3	+1.1	+1.5	+2.6
	S.E.M.	0.7	0.6	0.5	0.4	0.4	0.4	0.4	0.4

Table 7.1d

		TARGET							
		A	B	C	D	E	F	G	H
SUBJECT									
GC	msecs	84	90	94	92	90	88	88	80
	μV	+3.4	+1.0	+5.7	+2.6	+1.0	+0.8	+0.1	+2.1
RD	msecs	96	98	106	104	102	102		98
	μV	+2.6	+2.6	+5.1	+3.9	+1.7	+1.7		+3.2
ARH	msecs	90	94	92	98	90	94	90	90
	μV	+1.9	+1.6	+5.2	+2.5	+2.4	-0.3	+1.1	+2.2
AH	msecs	88	94	104	98	100	104		94
	μV	+0.2	+4.7	+3.9	+2.6	-0.1	+0.3		+1.7
KA	msecs	90	94	94	94	98			
	μV	+2.5	+2.1	+5.1	+4.7	+2.0			
PB	msecs	84	98	92	96	90			
	μV	-0.1	+2.5	+2.1	+4.4	+2.7			
GROUP MEAN		A	B	C	D	E	F	G	H
	N	6	6	6	6	6	4	2	4
	msecs	88.7	94.7	97.0	97.0	95.0	97.0	89.0	90.5
	S.E.M.	1.8	1.2	2.6	1.7	2.3	3.7	1.0	3.9
	μV	+1.8	+2.4	+4.5	+3.5	+1.6	+0.6	+0.6	+2.3
	S.E.M.	0.6	0.5	0.5	0.4	0.4	0.4	0.5	0.3

Table 7.2

Amplitudes and peak latencies of the major early positive components in the responses for central and peripheral targets using different check sizes.

7.2a Pattern onset responses
7.2b Pattern reversal responses

Table 7.2a Responses to pattern onset

(i) Peripheral target

		CHECK SIZE (min. arc)						
TARGET B		4	6	9	15	23	34	46
SUBJECT								
AH	msecs	98	96	90	86	86	86	88
	μV	+7.3	+9.3	+10.0	+12.5	+10.2	+9.1	+8.8
ARH	msecs	96	90	90	84	86	88	94
	μV	+2.4	+3.3	+4.7	+2.1	+3.5	+3.8	+5.0
TARGET A		8	11	15	26	39	56	77
SUBJECT								
RD	msecs	96	92	88	86	82	80	86
	μV	+0.5	+0.2	+3.2	+2.7	+1.0	+2.4	+1.3

(ii) Central target

		CHECK SIZE (min. arc)							
TARGET D		3	4	6	10	15	22	31	44
SUBJECT									
AH	msecs	108	100	98	96	100	94	92	
	μV	+5.8	+8.7	+12.3	+15.4	+11.2	+8.1	+5.6	
ARH	msecs	88	88	86	82	84	82	86	88
	μV	+2.2	+2.4	+6.3	+2.6	+3.5	+1.5	+2.0	+0.8
RD	msecs	106	100	100	96	96	96	96	94
	μV	+6.4	+4.9	+6.9	+5.1	+4.8	+5.0	+3.0	+3.0

Table 7.2b Responses to pattern reversal

(i) Peripheral target

		CHECK SIZE (min. arc)						
TARGET B		4	6	9	15	23	34	46
SUBJECT								
AH	msecs	102	98	92	92	84	88	88
	μV	+1.7	+2.2	+3.5	+5.0	+5.8	+5.8	+4.7
ARH	msecs		98	86	88	88	94	98
	μV		+2.1	+1.2	+1.9	+3.4	+3.4	+2.2
TARGET A		8	11	15	26	39	56	77
RD	msecs	102	98	96	92	90	94	92
	μV	+4.4	+3.2	+3.0	+4.8	+5.3	+5.3	+4.8

(ii) Central target

		CHECK SIZE (min. arc)							
TARGET D		3	4	6	10	15	22	31	44
SUBJECT									
AH	msecs		104	96	94	90	88	86	86
	μV		+2.6	+3.4	+3.5	+3.9	+3.9	+2.4	+3.3
ARH	msecs	110	104	96	92	92	98	98	98
	μV	+2.0	+4.2	+2.5	+2.4	+3.8	+2.5	+2.8	+3.6
RD	msecs		108	106	98	98	94	94	92
	μV		+2.0	+2.5	+2.6	+3.2	+2.8	+2.3	+3.1

Figure 7.1

Distributions of pattern onset P90 and pattern reversal P95 components in the responses elicited by the M-scaled targets in five individual subjects.

7.1a Subject RD
7.1b Subject ARH
7.1c Subject AH
7.1d Subject KA
7.1e Subject PB

Colour scale represents voltage gain + 8 to - 8μV, positivity of active electrode with respect to reference is represented by upward deflection. Letters refer to target positions. All stimuli were presented in the left hemifield.

Figure 7.1a Subject RD

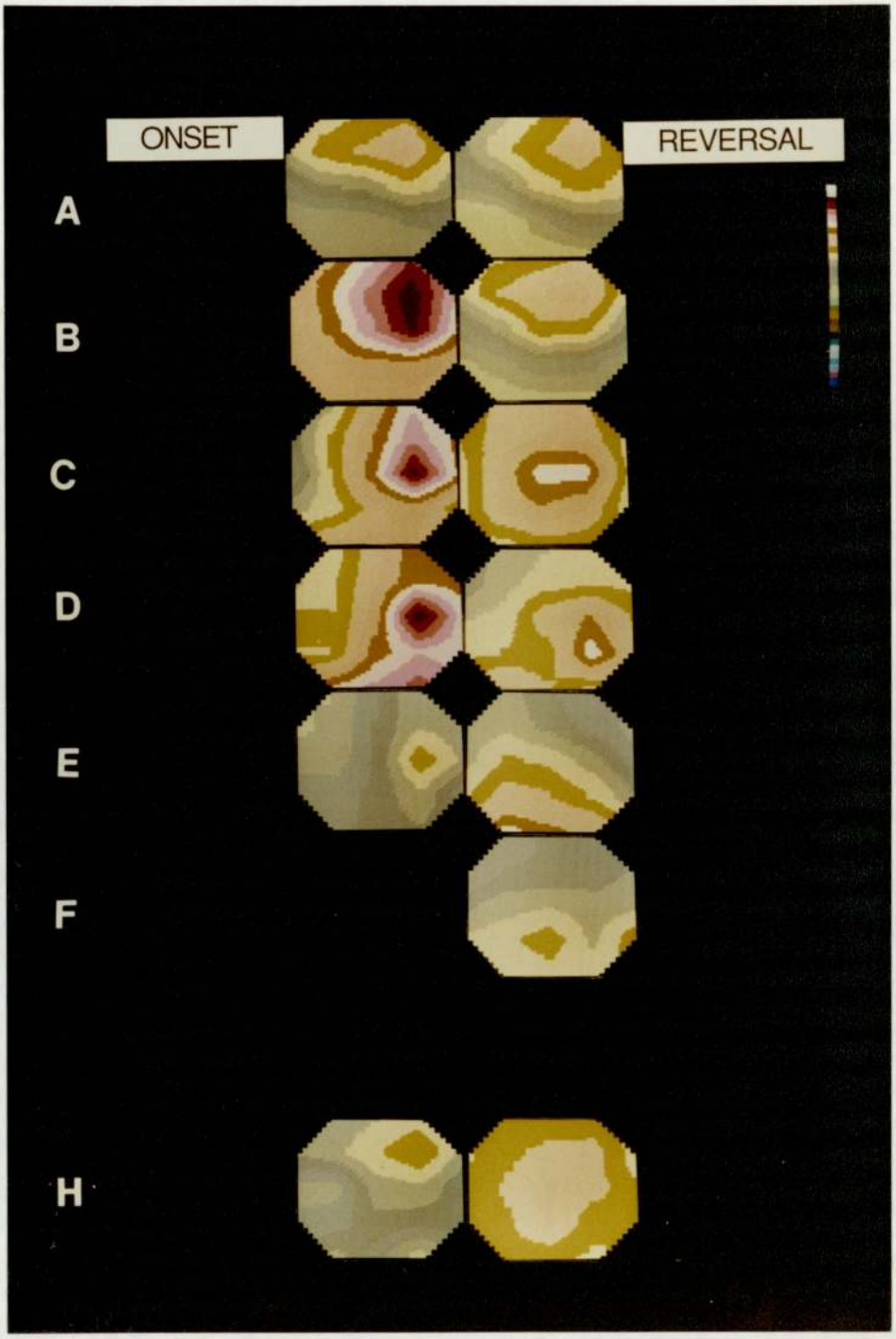


Figure 7.1b Subject ARH

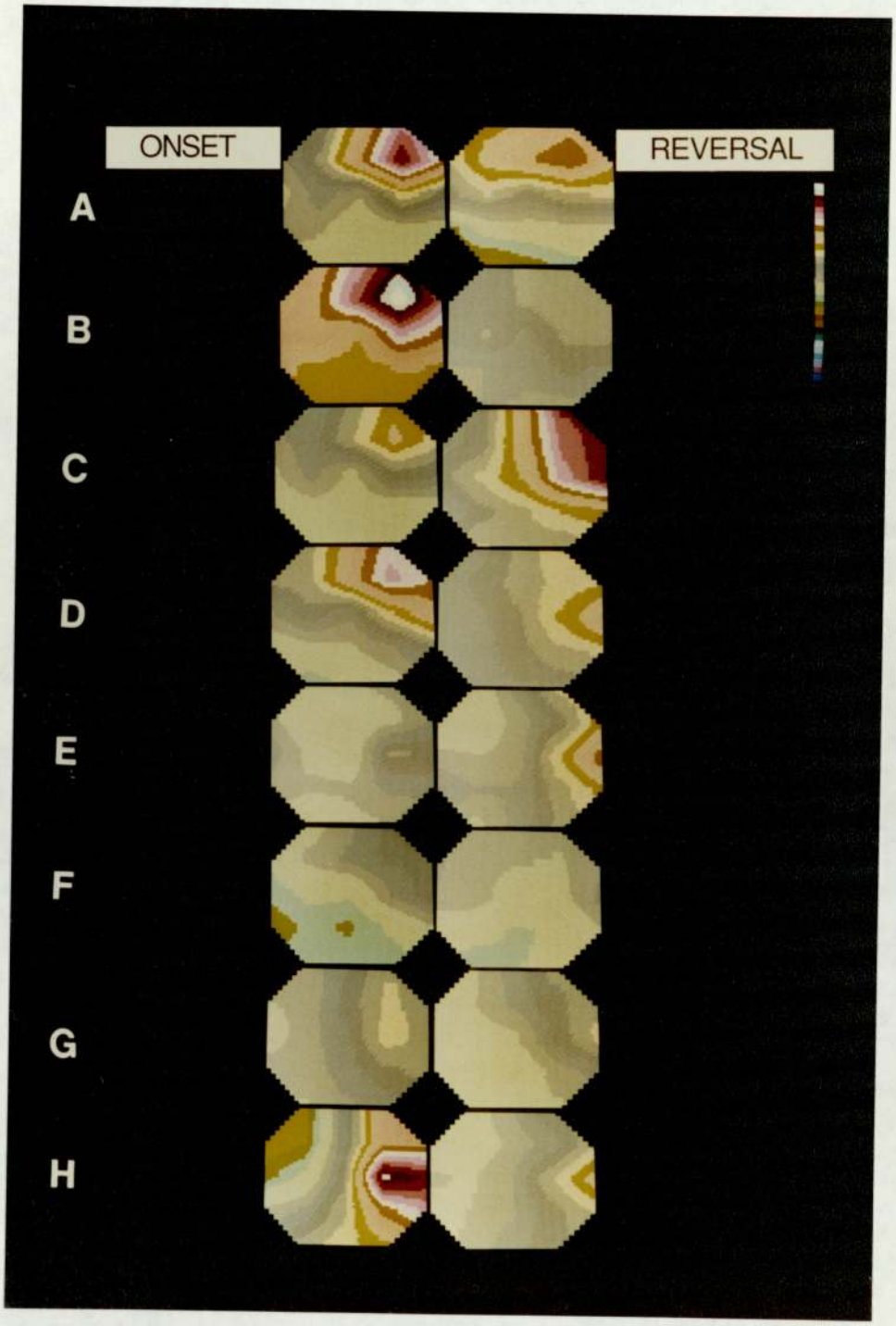


Figure 7.1c Subject AH

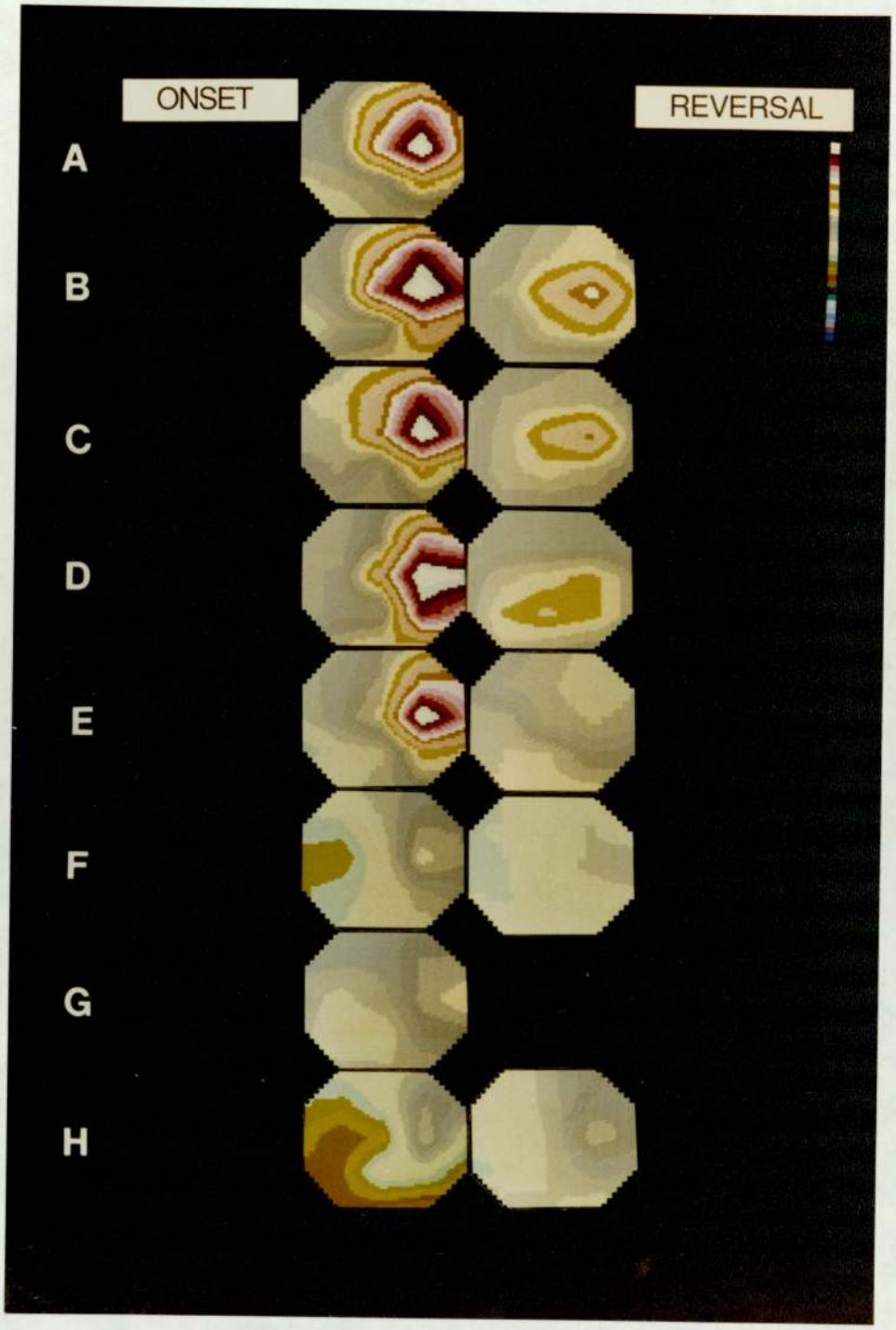


Figure 7.1d Subject KA

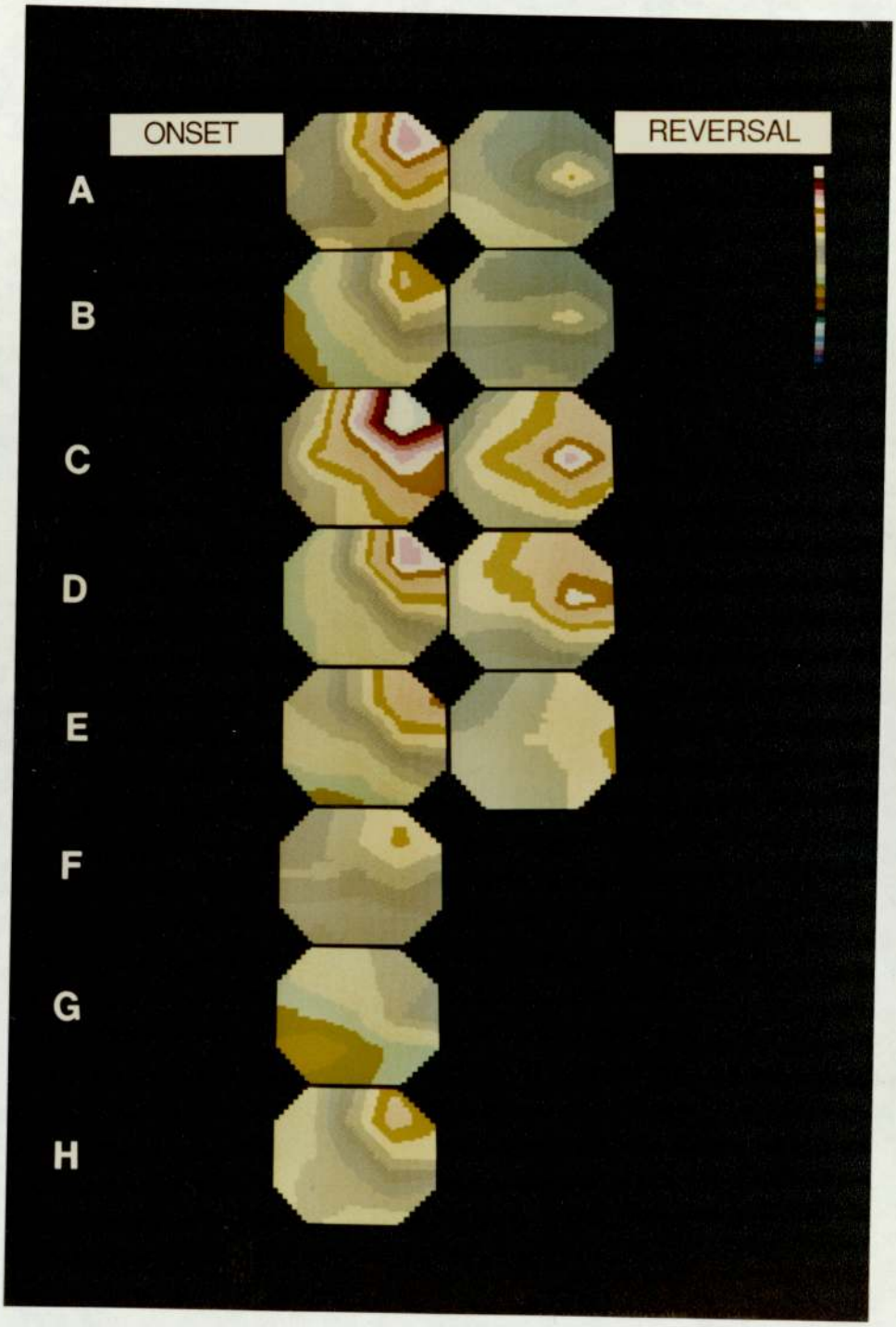
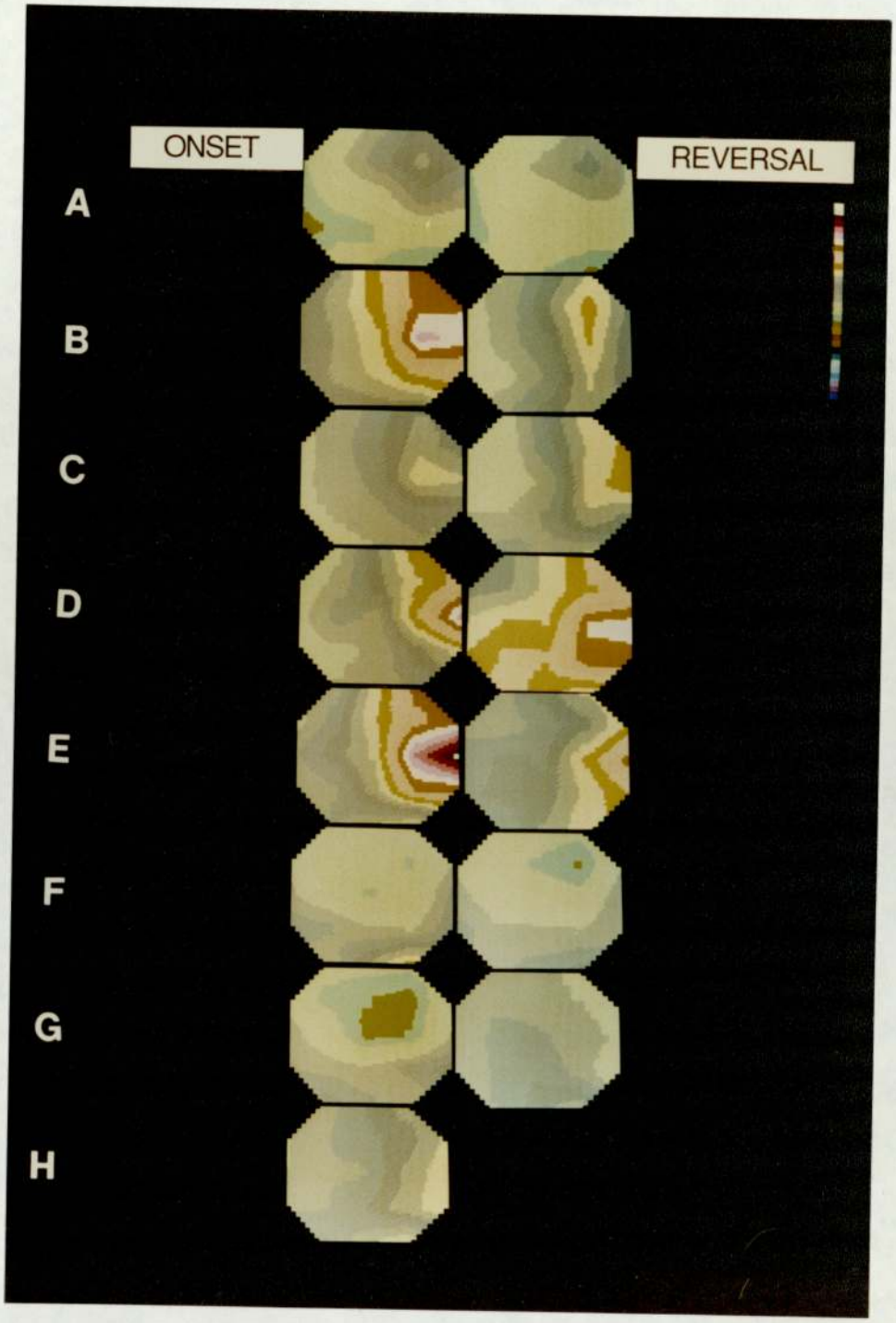


Figure 7.1e Subject PB



7.3 Results

Figures 7.1a to 7.1e (pages 221 to 226) show the individual distributions of the major early positive components P90 of the pattern onset response and P95 of the pattern reversal response for each of the M-scaled targets in five subjects. Maps have not been included in the displays in stimulus conditions where the major positive component could not be defined, or where the responses were of such low amplitude that the map revealed no relevant details. The maps show the voltage distribution across the head at the latency at which the component reaches its maximum amplitude. The relevant latencies are recorded in Tables 7.1a and 7.1c (pages 214 and 216), along with the maximum amplitude and the electrode position at which this was measured, for all subjects and all stimulus conditions.

Tables 7.1b and 7.1d (pages 215 and 217) show the latency and amplitude of the major positive components as recorded at electrode position "L", for pattern onset and pattern reversal stimulation with each target . For all of these tables, values have been omitted in conditions where a component corresponding to the major early positivity could not be defined. All maps, latencies and amplitudes apply to the average of two or three similar responses for each subject at each stimulus condition.

Pattern reversal responses to these small targets were generally smaller and less well defined than those for pattern onset. Two subjects showed responses to pattern reversal stimulation which were very small and somewhat noisy, so that even after several stimulus repetitions it was difficult to identify any components. The results for these two subjects (JL and UD) have therefore been omitted from the analysis for pattern reversal.

In general, results characteristics were consistent with those of the initial study. Pattern onset stimuli produced larger amplitude responses than pattern reversal stimuli. Response amplitudes showed a degree of variation between subjects, although, as the standard errors show, this was not as large as might have been predicted. For upper field targets F and G responses were smaller, and the reliable identification of the major positive component was more difficult. In cases where this was in doubt, results have been omitted.

The target(s) eliciting the signal of maximum amplitude varied between subjects, moreso for pattern onset where this varied between positions B and E than for pattern reversal where although this varied between positions B and D, most subjects showed maximum amplitude with target C. For both pattern reversal and pattern onset responses there was a significant effect of target position on signal amplitude as measured at maximum

position and at electrode "L" ($p<0.005$). Group averages show that overall, maximum responses were largest with target C for pattern reversal and with target D for pattern onset. Further analysis of data shows, however, that for pattern onset there is no significant difference between the amplitudes recorded between targets A to D (Student's t-test for related samples). For pattern reversal there is a significant difference between amplitudes recorded for targets A and C for both maximum values and those recorded at electrode "L" ($p<0.001$) but there is no significant difference between amplitudes for targets B to E at the maximum position and targets B to D for electrode "L". Target H produced responses which were, in general, of similar latency to those for target D for pattern onset. For pattern reversal, a major positive component could only be distinguished in the responses of four subjects to target H, and in these cases its latency appeared shorter than that for target D. This effect proved not to be significant. For both onset and reversal the maximum signals were of smaller amplitude for target H than for target D. This effect was just significant for pattern reversal ($p=0.04$) but not quite for pattern onset ($p=0.06$).

A tendency for component latency to increase as target position was moved from A towards central field positions was shown for both pattern reversal and pattern onset stimulation (see Tables 7.1a and c, pages 214 and 216). For pattern onset but not pattern reversal stimulation this effect was continued to target position E. At upper field positions F and G, values were more variable. Two-way ANOVA demonstrated a significant effect of target position on latency ($p<0.005$) for pattern onset and pattern reversal responses (values for target position G were omitted from the analysis for pattern reversal due to the lack of data). The effect of target position on latency as measured at electrode position "L" (see Tables 7.b and d, pages 215 and 217) was again significant ($p<0.005$) for the pattern onset P90 and for the pattern reversal P95. Using Student's t-test for related samples the difference between the latencies measured at positions A and D was significant in all four cases, at a level of $p=0.01$ or better.

Inspection of traces shows that in quite a few cases there is a second positive peak visible in the responses to lower field pattern onset targets which closely follows or appears superimposed on the major positive component, peaking at about 10-30 msecs later. This phenomenon, which shows variable prominence and variable lateralisation but tends to be more prominent ipsilaterally, appears to be related to the positive peak seen on ipsilateral electrodes which was described in Chapter 6. In some cases a later positive peak is apparent in the responses to central and upper field stimulation in both pattern onset and pattern reversal responses. For upper field targets this can appear more prominent than the major positivity. This peak, which also shows variable lateralisation, resembles the anterior upper field positivity described in Chapter 6, termed P115 and P120 for pattern onset and pattern reversal respectively. As suggested in Chapter 6, this

Figure 7.2

Illustration of the effect of target position (denoted by letter) on the major positive component and the superimposed positive peak, in the responses of subject GC to pattern onset stimulation. All responses relate to electrode position "M".

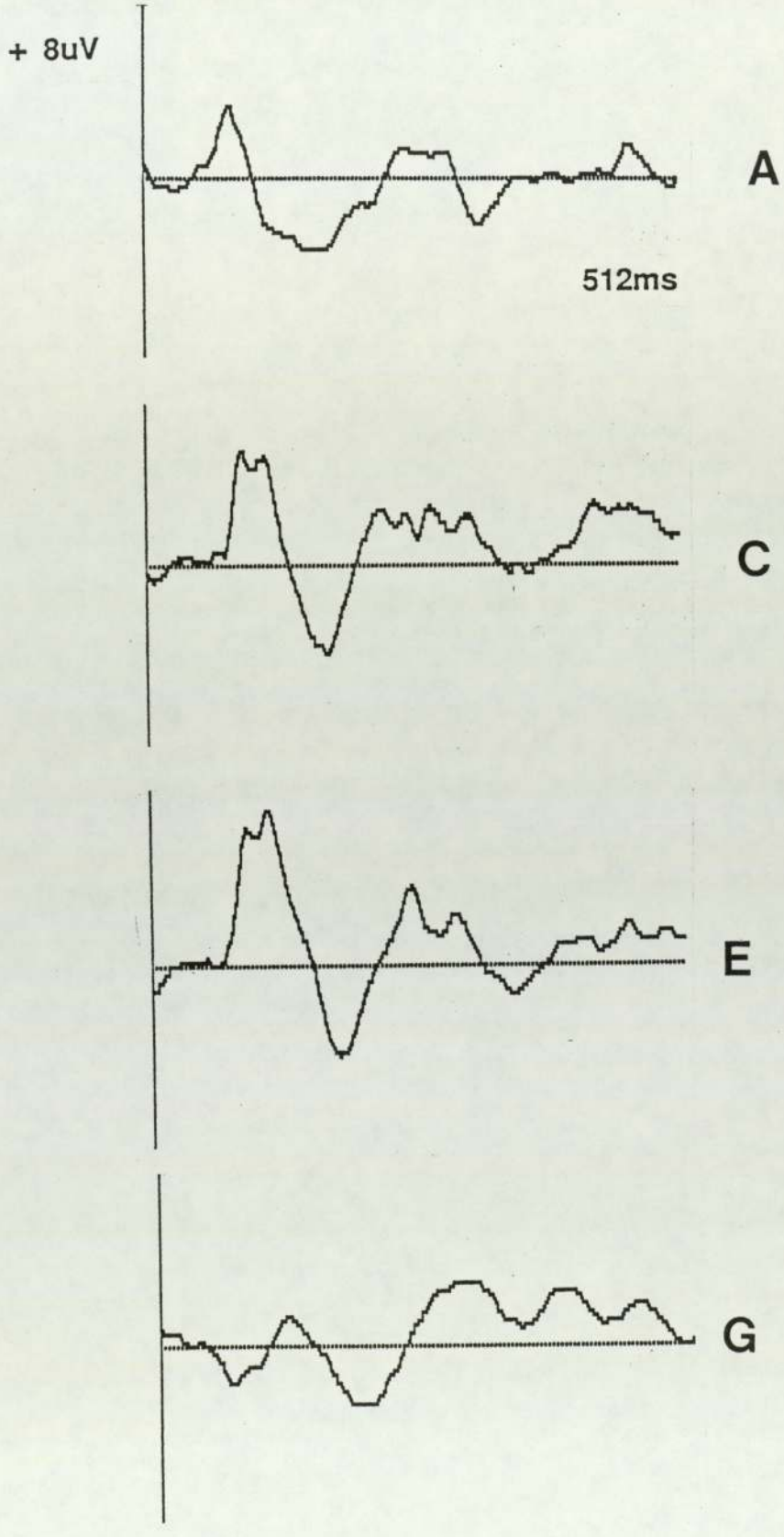
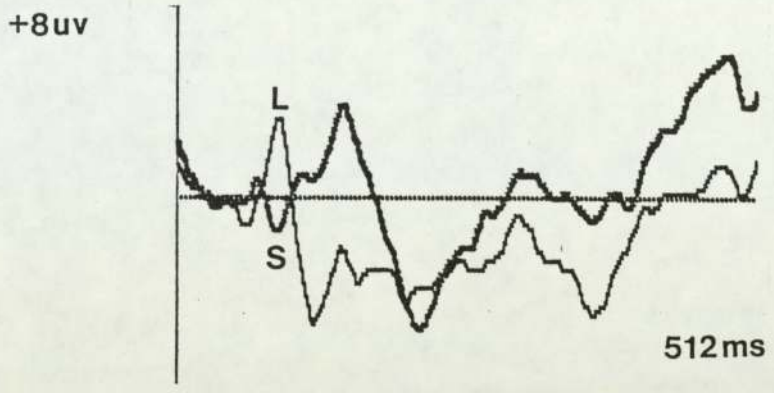

+ 8uV
A
512ms
C
E
G

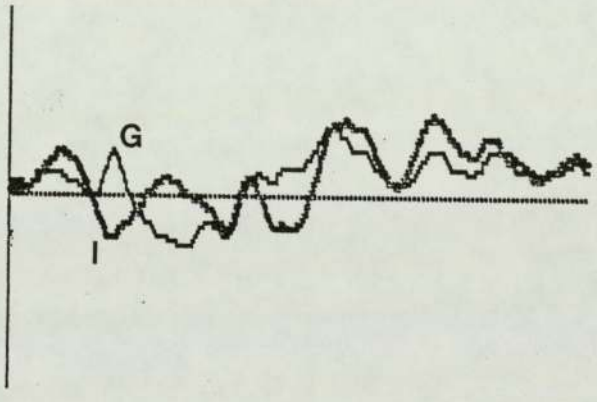
Figure 7.3

Illustration of traces relating to apparent polarity inversions of the major positive pattern onset component between contralateral and ipsilateral electrodes. For explanation, see text.

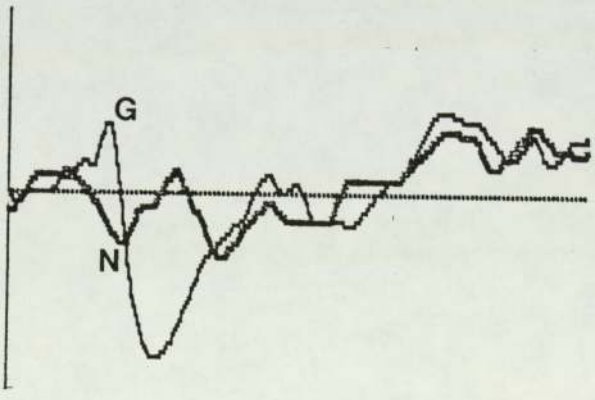
a.



b.



c.



peak probably represents a separate entity from the ipsilateral pattern onset peak described above although the distinction is not clear. These peaks seldom appear to interfere with the identification and measurement of the major positive component although there is a possibility that they may affect the apparent amplitude in some cases. It is also possible that the "P115/P120" peaks mask the presence of the major positive component in the more peripheral upper field target responses (see example below) although this is difficult to ascertain in most cases.

The behaviour of the "P115" peak is clearly demonstrated in the responses of subject GC to pattern onset stimulation. This is illustrated in Figure 7.2, in which the traces from electrode "M" for several target positions are shown. With target A, a single positive peak is visible at a latency of 80msecs. With target C a double positive peak can be observed, with latencies of 90 and 112msecs for the two peaks. The earlier peak appears to be slightly larger. At target position E, however, the later peak is slightly more prominent, and at position G, only a later peak, now at a latency of 120msecs, is clearly visible. The slight deflection at about 90msecs on the upward transient of the later positive peak on the trace for position G may represent a manifestation of the major positive component but due to the prominence of the P115 peak this is not clearly demonstrable.

With regards topography, as shown in Figures 7.1a to e (pages 221 to 226), both the pattern onset P90 and the pattern reversal P95 show a tendency to localise over the contralateral hemisphere. Although in some cases (e.g. subject RD) this tendency is clearer for P90, in others (e.g. subject ARH) P95 actually has a more lateral distribution. Both components tend to have their maximal amplitudes towards the upper part of the map, i.e. on the more anterior electrodes, for the most peripheral lower field target A, and the position of this maximum moves slightly downwards (more posterior) and/or laterally as targets are moved from below fixation to above it. This movement in location, however, is not seen clearly or consistently in all cases. The change in prominence of the major positive component with change in target position can be clearly seen. Few subjects show response distributions which can be clearly distinguished on the maps for upper field targets F and G due to the small amplitudes involved. Consequently, in several cases these have been omitted.

As can be seen from the maps, some subjects demonstrate areas of negative activity on ipsilateral and/or posterior parts of the scalp, or, for upper field stimuli, at anterior positions. Occasionally pattern reversal responses exhibit this behaviour, but it is much clearer and more frequent in the case of pattern onset. Analysis of individual traces shows that in the majority of cases this appears to be related to an earlier or later negative peak. For example, the prominent area of negative activity shown at ipsilateral

electrodes on Figure 7.1d for the onset responses of subject KA to target B is actually related to a negative wave which peaks at about 10msecs later. This is shown on the traces for electrode positions "G" and "N" shown in Figure 7.3c. Similarly, for subject JL, the ipsilateral negative area seen on the map for target D appears to be related to a very prominent negative component which peaks on the midline at a latency of 120msecs. On some occasions, however, such negative activity is related to waves which peak fairly synchronously with the positive component. Figure 7.3a shows an example of apparent polarity reversal between electrode positions. For target B subject UD demonstrates a positive peak at a latency of 88msecs on electrode "L". On electrode "S" a negative peak can be observed at the same latency. In addition, two subjects demonstrated a polarity inversion between positive peaks on contralateral electrodes and negative peaks on ipsilateral electrodes for stimulation with target H. For example subject ARH shows a prominent positive peak at a latency of 90msecs on electrode "M" and a small negative peak at the same latency on electrode "I". Subject AH, as shown in Figure 7.3b, similarly demonstrates a positive peak on electrode "G" peaking at the same latency as a negative peak on electrode "I". A clear tendency for movement of the component maximum in any particular direction between the maps for target positions D and H was not demonstrated for either pattern onset or pattern reversal responses. Of particular interest in these maps is an apparent inversion in polarity between a negative component at a latency of 92msecs on electrode "G" and a very small posterior positive peak at a latency of 92msecs on electrode "R", on the map relating to target G from subject PB. Although the possibility of a polarity inversion for the major positive components between lower and upper field responses was suggested in the results for other subjects this was not clearly demonstrated.

Tables 7.2a and b (pages 219 and 220) show the amplitudes and latencies of the major early positive components in the pattern onset and pattern reversal responses to checks of different sizes, for targets B and D in the case of subjects AH and ARH and for targets A and D in the case of subject RD. The change in check size appeared to have no consistent effect on the topography of either P90 or P95; consequently, amplitudes and latencies recorded in these tables apply to those measured at electrode position "L" in all cases. This avoids the possibility of artifactual latency changes due to measurement at different electrode positions. The results have been represented in graphical form in Figures 7.4a to c (pages 236 to 238). Due to the lack of data sets, it is only possible to make comments about the effects of check size on the individual results.

With regard to amplitude, of the three subjects, only subject AH demonstrated clear spatial tuning functions for onset responses to both targets. The general impression was, however, that the optimum check size for pattern onset responses is towards the lower end of the scale and that it is very slightly larger for the more peripheral targets

Figure 7.4

The effect of check size on amplitude and latency of the major positive component in pattern onset and pattern reversal responses to central and more peripheral stimuli.
7.4a Subject AH
7.4b Subject RD
7.4c Subject ARH

Figure 7.4a Subject AH

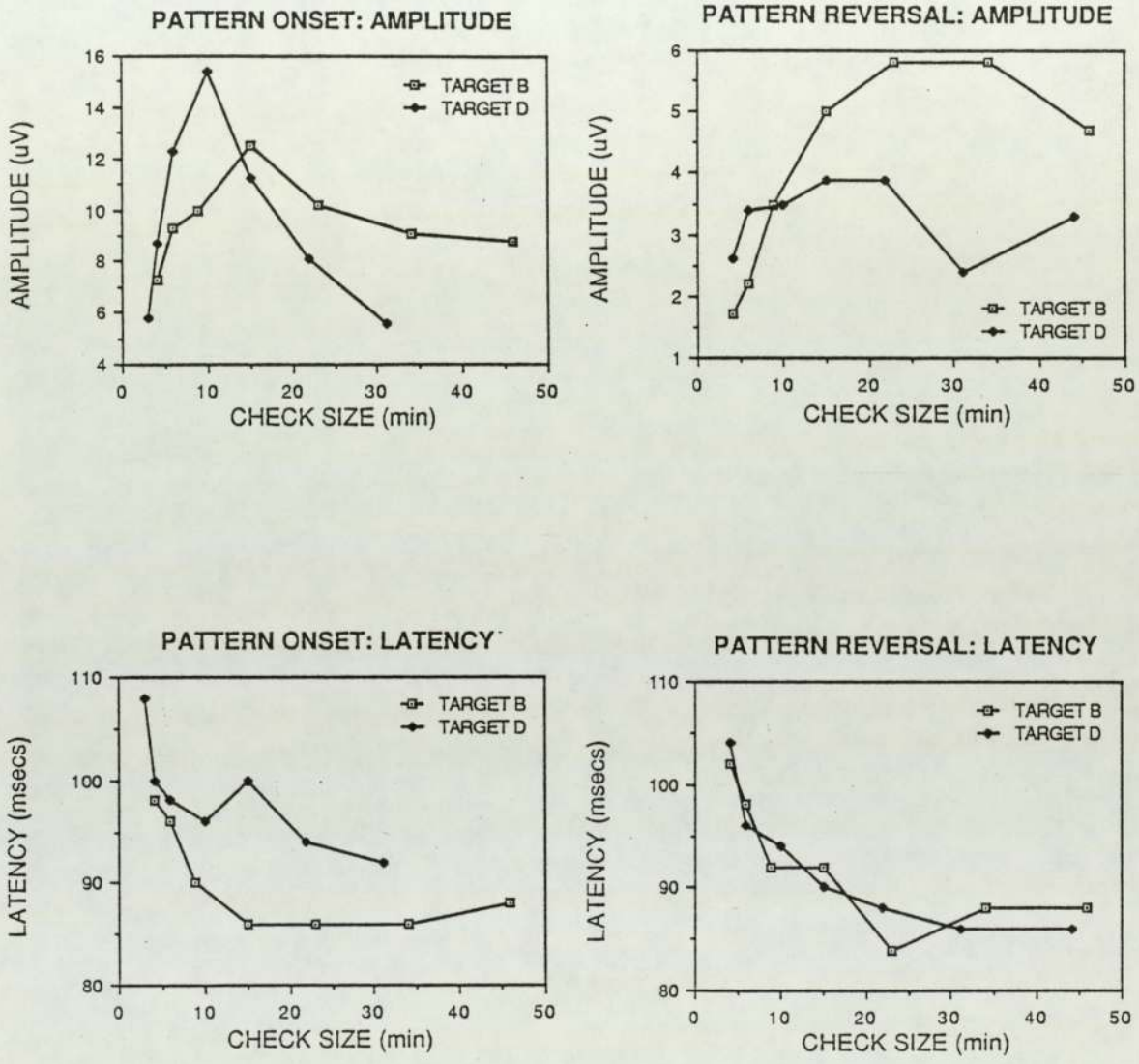


Figure 7.4b Subject RD

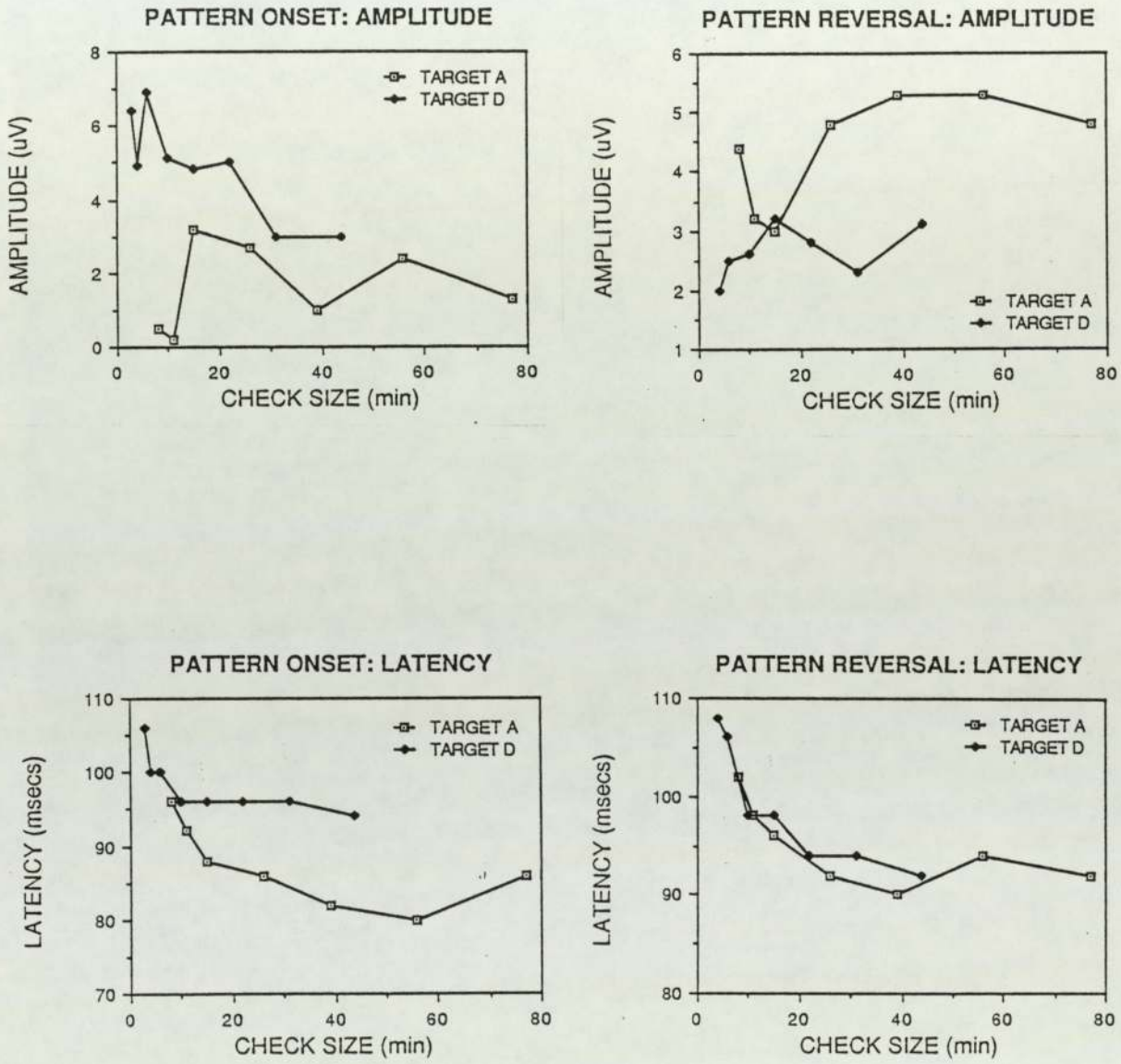


Figure 7.4c Subject ARH

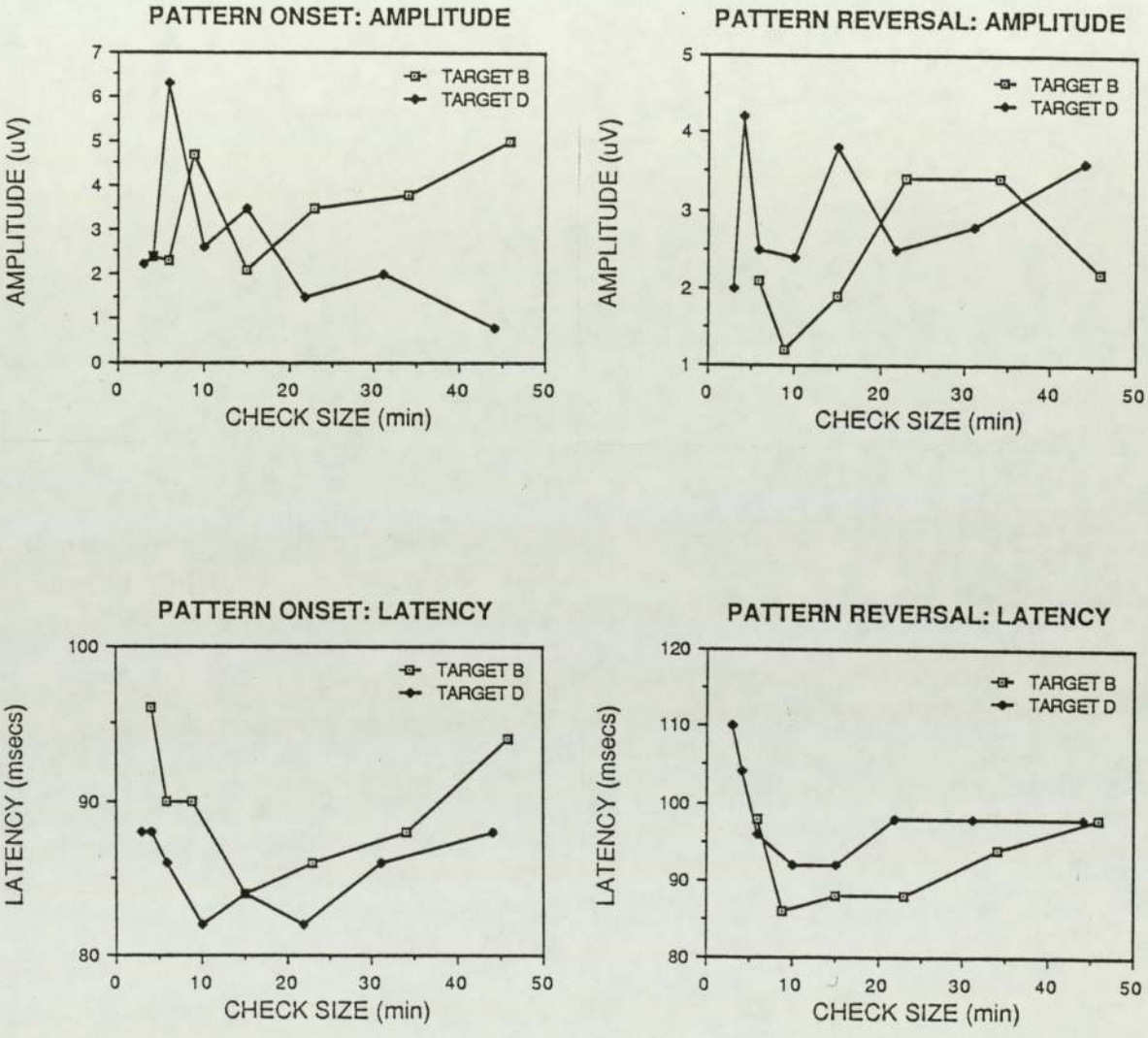
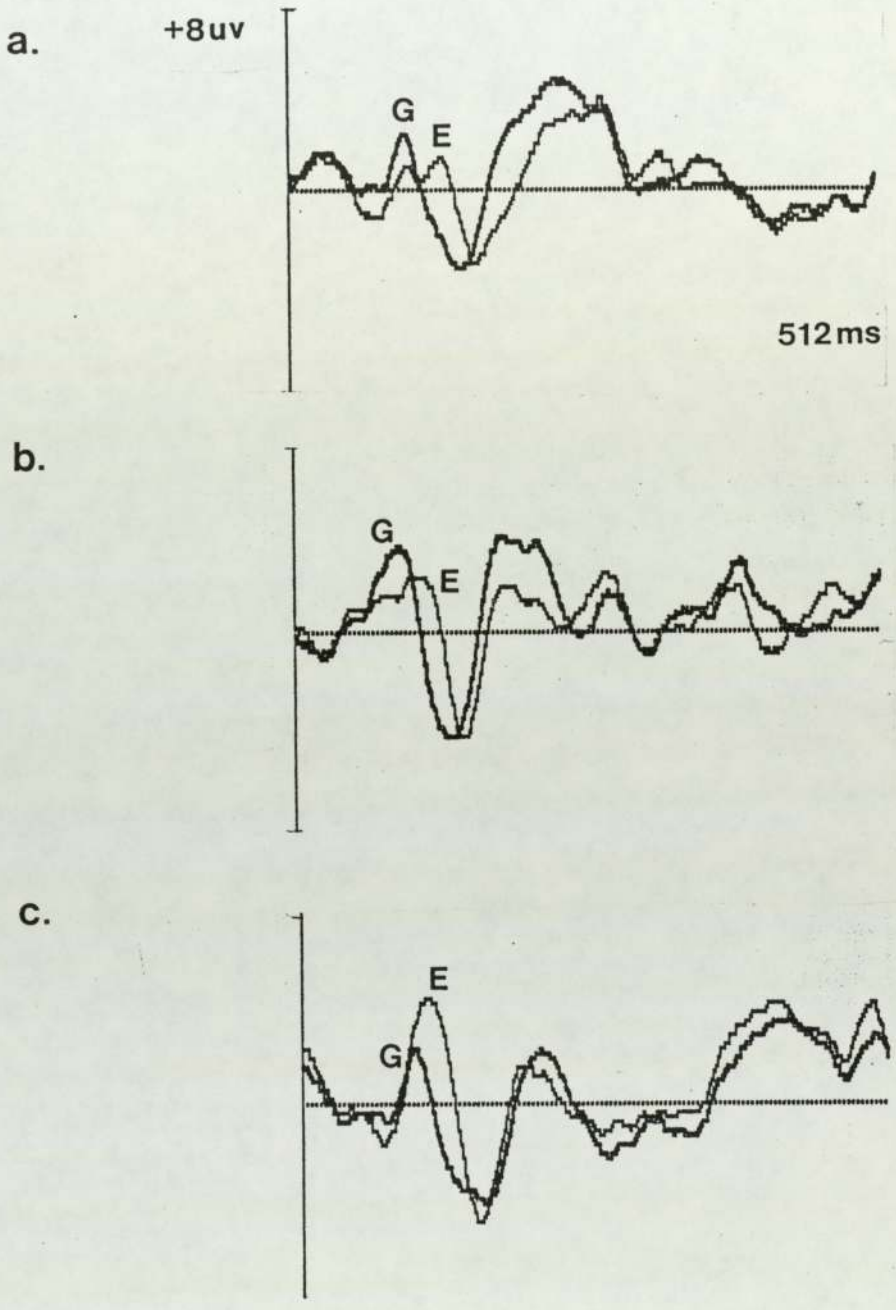


Figure 7.5

Illustration of the effect of check size on the major positive component and the superimposed positive peak in the responses of subject ARH to pattern reversal stimulation with central target D. Letters relate to recording channels "E" and "G".
a. 6 minute check
b. 15 minute check
c. 22 minute check
For explanation, see text.


a.
+8uv
G
E
512ms
b.
G
E
c.
E
G

than for the central target D. The check size which elicits the maximum response in each case appears to be the same as or slightly larger than the check size used in the main part of the study. For pattern reversal peripheral target responses only AH shows a clear relationship between these two variables, with amplitude peaking at a check size of around 30'. For the other two subjects a similar function appears to be present but this is not very clear and breaks down at small check sizes. Optimum check size appears to be around 30' again for ARH (target B) and around 50' for RD (target A). With pattern reversal stimulation at the central target position subjects AH and RD show spatial tuning to a degree, but this breaks down at the largest check size. As with pattern onset, the check size eliciting the maximum response was larger for the peripheral targets. For peripheral targets these optimum check sizes were considerably larger than those check sizes used in the main part of the study. For subjects AH and RD, maximum response amplitudes for pattern reversal were considerably higher for the more peripheral than for the central targets, whereas with pattern onset the responses for these two subjects were more similar for the two targets, with those for the central one being slightly higher. This trend was not apparent in the responses for subject ARH.

With regard to latency, all subjects showed a clear initial decrease in latency with increasing check size for onset and reversal responses. For subjects AH and RD this effect appeared to saturate and the functions levelled out at larger check sizes. For subject ARH, however, latency values reached a minimum or levelled out and then increased again.

Inspection of individual traces reveals that in the responses to medium and large checks both pattern reversal and, to a lesser extent, pattern onset responses sometimes showed peaks closely following or superimposed upon the major positive component. These peaks, which were evident in responses to central and peripheral targets, appeared maximally at ipsilateral electrodes and increased in prominence with increasing check size. The traces in Figure 7.5 (page 240) show the responses for subject ARH to pattern reversal stimulation with target D for three different check sizes on channels "E" (ipsilateral) and "G" (contralateral). Responses for a 6' check show the presence of peaks at latencies of 98 and 130msecs on channel "E" but only at 98msecs for channel "G". With checks of 15' the latencies of both peaks have decreased somewhat, to 94 and 108msecs, and the later peak appears to have increased in prominence. With 22' checks the later peak, at 106msecs, appears larger than the earlier peak at 90msecs. This phenomenon appeared to affect responses to pattern reversal more than pattern onset but showed no clear preference for central or peripheral targets. The effect of this later peak on measurements was not clear; it did not appear to affect the distribution of the major positive component in any clear or consistent manner but it may well have influenced the apparent amplitude and/or latency of this component in some cases. These later positive

peaks showed no clear relationship with those observed in the main part of the study.

7.4 Discussion

As an introduction to this discussion, the reader is referred to the comments relating to results for the M-scaled targets in Chapter 5 section 4. As predicted in this previous discussion, the recording of responses to these targets on a larger subject group resulted in a larger variation in the target eliciting the maximum amplitude response. Inspection of the variation in response amplitudes between the different target positions (see Tables 7.1a and c, pages 214 and 216) shows interindividual differences. For example, subject GC shows a drop in amplitude of the pattern onset P90 between targets A and B and an increase for target C. Subject ARH, however, shows a slight increase between targets A and B followed by a decrease for target C. It appears that over a group of subjects, the responses to a range of targets actually show an insignificant difference in amplitude, for pattern onset (A to D) and for pattern reversal (B to E) stimulation. These results appeared more convincing for pattern onset responses; for pattern reversal, the majority of subjects still showed maximum responses with targets C or D. For neither type of stimulation, however, did any subject demonstrate the largest amplitude responses to the most peripheral lower field target A or to targets F, G or H. Smaller responses to the most peripheral lower field target and to upper field targets might be predicted on the basis of positioning of generator areas with respect to scalp electrodes. If the proximal surface of the visual cortex contains the representations of only a limited portion of the central visual field, smaller than that predicted by Drasdo's (1983) schematic model, it is quite conceivable that targets A, F and G would be projected onto parts of the cortex which are further from the occipital pole and therefore less optimally placed for signal recording at scalp electrodes than the more central targets B to E. The effects of moving target position laterally from D to H appear unconvincing for either reversal or onset stimulation. A reduction in amplitude might be associated with a movement towards a more medial cortical location for more peripheral field striate generator areas. For extrastriate generator areas such a reduction should be less likely since any movement of generator area associated with movement along the horizontal meridian ought to take place across the proximal cortical surface, unless the projection area falls into a fissure.

An increase in component latency between lower and central field target positions has been clearly demonstrated for both pattern onset and pattern reversal major positive components. The fact that component latency as measured at electrode position "L" in all conditions was also significantly affected by target position suggests that this was not an artifact resulting from measurement at different electrode positions. The results shown in Figures 7.2a to c (pages 236 to 238) suggest that for subjects AH and RD, altering the check size would not necessarily produce responses of equal latency for central and lower field stimulation for the pattern onset P90; the functions relating check size to latency appear reasonably separated, so that the latencies for check sizes are longer for

the central target. For the pattern reversal P95, however, the curves for these two subjects appear to overlap to an extent, suggesting that the difference in latency might in fact be solely related to check size. For subject ARH, however, the curves relating latency to check size for the two targets are better separated for P95 than for P90. It appears that more data is required to study this effect properly.

It may be, however, that there are factors other than check size involved. As discussed in Chapter 5, Barber and Galloway (1981) found that an abrupt increase in latency of the pattern onset CI component took place as targets were moved from just below fixation to just above it. They explained this result on the basis of a difference in latency for "epicentral" and "peripheral", rather than for lower and upper field, responses. The phenomenon described in the present study, however, appears different and involves a gradual change from peripheral to central foveal stimulation. The effects of moving the stimuli to upper field positions in the present study are less clear. The increase in latency continues between positions D and E for pattern onset but not pattern reversal stimulation, and both types of response show a variation in effects for the more peripheral upper field stimuli. The results described in Chapter 6 for the four degree hemifields demonstrated, however, that there was no significant difference between the latency of lower and upper field major positive components for pattern reversal or pattern onset with the optical stimulator used in all of these experiments.

The effect of pattern spatial frequency on the latency of the early components of pattern VEPs has been reported by several groups of workers and is discussed in section 3.3b. Plant, Zimmern and Durden (1983) demonstrated an increased latency with increasing spatial frequency above about 2 cycles/degree. For coarse pattern details the relationship appeared less clear, with latencies tending to increase again. The results of the present study are in agreement with these findings. With regard to the effect of check size on response amplitude, it appears that the values used for the targets in the main part of the study were smaller than optimum for both the pattern onset and reversal responses. It is probable, however, that increasing the check size for pattern onset stimulation would affect central and peripheral targets to about the same extent. For pattern reversal, however, the increase in check size appeared to have a much greater influence on the responses to the more peripheral targets compared with that on the central target in two of the subjects. This suggests that perhaps check size should have been increased at a steeper rate than target size with increasing eccentricity for pattern reversal stimulation. It is likely, however, that an increase in check size would have led to greater prominence of the later positive peak found in responses to larger checks. It may be that the apparent preference for larger checks demonstrated by the more peripheral target responses is an artifact resulting from the interference of these two peaks.

The extra positive peaks recorded in the responses to the target series in the main part of this study appear to represent similar phenomena to those reported for the four degree targets in Chapter 6, and may reflect polarity inversions of the major early negative component, for both pattern onset and pattern reversal responses. The later positive peak recorded in the onset responses for subject GC for central and upper field targets particularly appears to resemble the pattern onset component "P115" recorded for upper field targets in the study reported in Chapter 6. A consideration of the results of Barber and Galloway (1981) suggests that the abrupt latency increase of between 10 and 30msecs shown by component CI in their responses when changing from lower to upper field stimulation may be the result of the appearance of a later component similar to the P115 recorded in the present study. Such behaviour would fit in with the observations of Jeffreys (Jeffreys and Smith 1979), who considers that the apparent latency increase in component CI demonstrated by other workers (e.g. Lehmann and Skrandies 1980a) between upper and lower field responses is an artifact due to the polarity inversion of major early negative component CII.

The significance of the extra positive peak recorded in the responses to larger check sizes in the present study is unclear. Other workers have reported the presence of additional early components in responses to low spatial frequencies (Plant et al. 1983; Jones and Keck 1978). This may be related to one or other of the extra peaks demonstrated in the main part of the study, but it seems more likely to represent a separate phenomenon. The possibility exists that this peak actually represents part of the "P100" component recorded in the responses to pattern reversal stimulation by workers using large fields and large check sizes, as discussed below.

In general, the results of this study suggest that for pattern onset responses at least the difference in amplitudes recorded for different targets in a particular individual is likely to be a result of variation of individual projections with respect to the proximal surface of the cortex and/or the positioning of gyri and fissures, rather than a difference in target effectivity. For pattern reversal responses this is less sure. For both types of response, however, there are possible demonstrations of the effects of fissures apparent in the results. For example, subject ARH demonstrates an apparent reduction in amplitude of P90 in the response to target C as compared with targets B and D, and for P95 in the response to target B as compared with A and C. Subjects KA and PB demonstrate a similar phenomenon for P90 but not for P95. In comparison with this behaviour, for subject RD the responses to pattern onset with targets B, C and D are of very similar amplitude. In order to accept the fact that these variations are due to the projection of targets onto gyri in some subjects and fissures in others one first has to accept that both the pattern onset P90 and the pattern reversal P95 originate at least partly in regions of the visual cortex on the proximal surface of the occipital lobe. If the pattern onset P90

originates in surface negative striate cortex on the mesial surface of the occipital lobe then this explanation can not apply. It would seem that a way of demonstrating the presence of generators lying in fissures would help to clarify these points.

The slight, gradual posterior/lateral movement of the component maxima demonstrated by some subjects is, as commented in Chapter 5, suggestive of local retinotopic order in the cortical areas in which these components are generated. This behaviour was not, however, seen clearly or consistently. The fact that a significant effect of target position on response amplitude was demonstrated for measurements at a constant electrode position can, of course, not be considered as proof of a migration of the component maxima, since a significant effect was also demonstrated for measurements at positions of maximal amplitude. Measurements at electrode position "L" do not in fact appear particularly suitable for the investigation of distribution changes, since the maximum activity was recorded on or near this position for many subjects at more than one central or lower field target position. Statistical comparison (Student's t-test for paired samples) of mean amplitudes measured at electrode "L" and at the maximum position, however, reveals a significant difference between the values for targets E and F for pattern onset stimulation ($p<0.05$) and for target E for pattern reversal ($p<0.005$). This demonstrates that there must be some significant change in distribution for both the pattern onset P90 and the pattern reversal P95 with change in target position. A more detailed examination of the scalp distribution of the responses to different targets with a more closely spaced electrode array might yield further evidence for such changes in distribution, although it is possible that the smearing effects of skull and scalp might prevent a clear demonstration of such behaviour.

The determination of precisely which cortical areas these two major positive components originate from poses a problem. As commented in Chapter 5, the lateral position of the P90 maxima suggests an origin in surface positive extrastriate cortical activity. The large, localised positive maxima, often with roughly concentric contours, demonstrated by some subjects for some target positions are suggestive of activity relating to radial dipole generators on the surfaces of cortical gyri on the proximal surface of the visual cortex. From the results of Chapter 6, the theory of an origin for P90 in surface negative striate cortex seemed unconvincing because of the failure to demonstrate the presence of clear negative peaks corresponding in latency to P90 under any stimulus conditions. The results of the present study have, however, demonstrated this phenomenon in some subjects. Notably, for responses to lateral target H, which might be expected to activate the striate cortex at a position further towards the midline than the other targets, there appeared to be clear inversions in polarity between positive contralateral and weak negative ipsilateral peaks at the same latency, in two subjects. For the same subjects, responses to target D demonstrated no such inversion. In spite

of these demonstrations of ipsilateral negativity in some subjects, however, there is still no clear evidence for similar components at contralateral electrodes. It seems possible that weak negative activity at ipsilateral positions on the maps could be the result of a polarity inversion associated with more tangentially oriented equivalent dipole generators in laterally placed extrastriate areas. It also appears strange that a surface negative source in striate cortex should not elicit clear midline and contralateral negative peaks for lower field targets in some individuals. If the pattern reversal P95 does in fact have an origin mainly in surface positive striate cortex it would appear reasonable to expect surface negative striate cortical activity to elicit responses of a similar distribution to P95 but with opposing polarity, behaviour which is clearly not apparent.

A slightly more posterior and lateral location of the P90 maximum on the maps in the present study for stimuli above fixation than for those below it is consistent with the behaviour described in Chapter 6. Butler and co-workers (1987) demonstrated a slight posterior displacement of the laterally placed surface positive equivalent dipole associated with upper foveal quadrant stimulation as compared with other quadrants. These authors considered, however, that responses associated with an origin in lower and upper field extrastriate cortical projections ought to be related to more spatially separated sources. The clear separation of lower and upper field maximum responses might indeed be expected if the extrastriate cortical areas in man were arranged as demonstrated by cytoarchitectonic studies and if visual field projections on these areas were arranged as predicted by direct extrapolation of Drasdo's (1983) schematic map. This might lead to, for example, activation of a region of the cortex near the midline above the occipital pole with target A and a region lateral to and on the same level as the occipital pole with target D. Upper field targets might be expected to activate parts of the cortex at lateral positions on the under surface of the occipital lobe, so leading to relatively small amplitude responses. If targets further and further out in the upper periphery were used, it is conceivable that at some stage a signal of inverted polarity would be observed, possibly peaking at more anterior electrode positions. Inspection of the maps for some subjects reveals that the behaviour of the P90 maximum is in fact not far from that which might be predicted by this theory. One subject (PB) actually demonstrates a possible polarity inversion for this component at anterior electrode positions. It may be that if more peripheral upper field target positions were used, more and clearer polarity inversions of this component would be found. The demonstration of multiple representations of the visual field in occipital and also in temporal parts of the cortex in primates, however, suggests that the situation might not be so simple.

Some subjects demonstrate a posterior migration of the pattern reversal P95, so that where signals can be detected the upper field targets appear to produce the maximum response on the most posterior electrodes. This behaviour is consistent with that

reported in Chapter 6 for the four degree targets. In other subjects, however, the maxima for this component appear at more lateral electrode positions for the central and upper field targets. This behaviour is more consistent with that shown by the pattern onset P90. The more pronounced fall-off in amplitude demonstrated by this component as compared with the onset P90 with targets further from fixation and the generally poorer signals generated by upper field targets could be, as suggested in Chapter 5, consistent with an origin in striate cortical projections around the occipital pole. Displacement of target position from fixation would need to be relatively small in order for activated areas of striate cortex to fall on the mesial or under surface of the occipital lobe.

The differences in the relationship between target position and amplitude for the two components in some subjects points to origins in different regions of cortex. In other subjects, however, there is a more lateral localisation of the P95 maximum than that which might be expected if responses were surface positive striate. Some individuals in fact demonstrate little apparent difference in distribution of P95 from the pattern onset P90. It might be expected, of course, that differences between distribution of responses recorded on the scalp arising from different locations on the cortical surface would might be reduced by the "smearing" effects of the skull and scalp. However, it also seems possible that the pattern onset P95 recorded with the small fields and checks used in the work reported in this thesis might have origins in more than one cortical area.

There has been some suggestion by several groups of workers that the major positive component of both pattern reversal and pattern onset VEPs constitutes responses relating to two different types of visual mechanism (see sections 3.4 and 4.5). Broadly speaking, these components are thought to reflect responses of the visual system to pattern/contrast on the one hand and luminance/motion on the other. The former mechanism is prominent in responses to large and/or peripheral field stimuli, pattern details of low spatial frequency and in responses to pattern reversal. The latter is more prominent with foveal targets, fine stimulus details and in responses to pattern reversal. Some authors consider that the major positive component of the pattern reversal response might be a combination of two different peaks (e.g. Jeffreys 1977; Spekreijse et al. 1973; 1977; 1985; Ochs and Aminoff 1980) or that its characteristics reflect different aspects of visual processing depending upon the stimulus conditions used (Kulikowski 1977b; Dagnelie et al. 1986). Spekreijse's group (Maier et al. 1987) have suggested that it has origins in striate and extrastriate visual cortical areas.

It seems probable that the P95 component demonstrated in the present study in the responses to small fields and relatively small checks at least partially reflects the activity of pattern/contrast mechanisms whereas the "P100" component of Halliday which was

demonstrated most commonly with large fields (16^{o} radius) and checks (56') represents a response better related to luminance/motion mechanisms. It is also possible that the "P100" component recorded with large fields and large checks is of striate cortical origin whereas P95 originates mostly in striate but also in extrastriate visual cortex. Such a joint origin would explain the contralateral localisation of the P95 recorded in Chapter 6, and, in the present study, the apparent similarities in distribution of the P95 and the pattern onset P90 in the responses of some individuals to the M-scaled targets. A closer relationship between the P90 and P95 components with these very small targets might also explain the very short latencies, as low as 84msecs, which were recorded for the P95 component in the present study. It seems possible that the extra positive peaks observed in the responses to larger checks in the present study might be a reflection of a "motion" or "luminance" portion of the major positive component, and that such activity might represent part of the responses of other workers to large fields and large checks.

CHAPTER 8

8.1 Summary of findings and indications

The following conclusions have been drawn from a consideration of the relevant literature and the interpretation of the experimental results:-

1. The VEPs elicited by pattern onset and pattern reversal stimulation of the foveal and parafoveal areas of the visual field consist of a number of components which are in some respects consistent with those recorded by other workers using larger stimulus fields. The differences in behaviour of these components with respect to the position of the stimulus in the visual field are suggestive of origins in different areas of the visual cortex and/or different visual mechanisms.

In particular:

a) The observations on the major early positive component of the pattern reversal response recorded with small fields and small checks, here termed "P95", are consistent with a possible origin which lies mainly in the striate area of the visual cortex, but also partly in extrastriate cortex. This component appears to reflect the operation of both luminance/motion and pattern/contrast mechanisms.

b) The behaviour of the major early positive component of the pattern onset response, here termed "P90", appears largely consistent with a lateral origin in extrastriate cortex. This finding is at variance with the orthodox view which is that this component arises in surface negative striate cortical activity.

2. The behaviour of the major early positive component of the local flash response may be suggestive of a diffuse origin in multiple visual areas.

3. The small M-scaled targets often produced large amplitude, well localised signals, with roughly concentric contours, particularly for the pattern onset P90 but also sometimes for the pattern reversal P95. This suggests that these components are possibly the reflection of surface positive activity from gyral generators positioned on the proximal aspect of the occipital lobe just below the scalp electrodes.

4. The inter- and intra-subject variability in the amplitude and localisation of the pattern onset P90 and pattern reversal P95 components elicited using the very small M-scaled targets appears to be a reflection of the individual variations in relationship of visual field projections with the pattern of gyri and fissures on the proximal surface of the occipital lobe.

8.2 Discussion and suggestions for further study

It seems that in spite of the strategy adopted to simplify matters by confining stimulation to the proximal surface of the visual cortex, the paradox of cortical generators of VEPs is still to some extent unresolved. The waveform of the VEPs elicited by pattern stimulation as discussed in Chapter 6 appears to consist of individual peaks which may interact with each other to such an extent as to make interpretations of component cortical origins difficult. Several authors have, as discussed in section 4.2, used various means of isolating response "components" as compared with "peaks" in the VEP waveform. It appears to this author, however, that such means as employed by Lehmann's group, who use "global field power" to define peak latencies, or by Jeffreys, who places recording electrodes over active sites to "maximise" particular components and minimise others, can result in the loss of valuable information. The answer to this problem may lie in an alternative method of analysis of the scalp distribution data. The technique of "dipole source localisation" discussed in section 4.3a has been used by a number of authors to predict the cortical origins of VEP components. Some recent work, however, has suggested that a more appropriate way of interpreting scalp distribution data is in terms of the rate of change of potential across the scalp. Several groups of workers have, as discussed in section 4.3b, employed a technique known as "source derivation" to interpret the locations of signal generators. Initial explorations with this method as applied to some of the data reported in this thesis have suggested that such an approach might prove useful in terms of greater clarification of the relationship of different peaks in the response to the underlying sources of activity. A careful analysis of the patterns of sources and sinks on the scalp and their changes with time might allow deductions to be made with respect to possible generator locations of the "components" defined in the original monopolar recordings.

It is likely that the electrical signals elicited by visual stimuli which are recorded at scalp electrodes arise largely from radial equivalent dipole generators which lie on the surfaces of the cortical gyri on the proximal aspect of the occipital lobe (Drasdo 1986). The pattern of fissures probably tends to obscure signals from a large proportion of the visual projections. Analysis of the properties of magnetic signals which are elicited from the cortex in response to visual stimulation reveals that these arise largely from tangentially oriented dipole generators (Stok 1986), which lie principally in cortical fissures. It seems, then, that a comparison of the electrical and magnetic responses elicited by the same targets might provide complementary images of the projections on gyri and fissures in particular individuals. Such comparisons are planned for some of the subjects used in the present study in the near future.

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APPENDIX: PUBLICATIONS

Abstract

EDWARDS L. and Drasdo N. (1988) Topography of visual evoked potentials (VEPs) elicited by pattern and luminance stimulation in the foveal region. Electroenceph. clin. Neurophysiol. 69 (2), 43P.

Papers

EDWARDS L. and Drasdo N. (1988) Scalp distribution of VEPs to foveal pattern and luminance stimuli. Doc. Ophthalmol. 66, 301-311.

Drasdo N., Thompson D.A., Thompson C.M. and EDWARDS L. (1987) Complementary components and local variations of the pattern electroretinogram. Invest. Ophthalmol. Vis. Sci. 28, 158-162.

1. Topography of visual evoked potentials (VEPs) elicited by pattern and luminance stimulation in the foveal area. – L. Edwards and N. Drasdo (Dept. of Vision Sciences, Aston University, Aston)

The cortical origins of the major positive components of the pattern reversal, pattern onset and flash VEPs have been studied using foveal stimuli. The scalp distributions of these components in ten normal volunteer subjects were investigated using a 16-channel mapping system (Bio-Logic Brain Atlas III). Responses to 4° full- and lateral half-field stimulation were compared. For component P100 of the reversal response and CI of the onset response, direct analysis of scalp distribution suggests striate and extrastriate visual cortical origins for these components respectively. Data for the flash response were inconclusive.

In 5 of these subjects the foveal pattern VEP generator areas were studied in more detail. 'M-scaled' targets were designed to stimulate 1 cm^2 patches of striate cortex and associated extrastriate re-projections, at different fixation positions in the upper and lower field.

Inter-subject variation in amplitude and to a lesser extent distribution is quite marked. Component amplitude changes with target position relative to fixation, despite the attempt to make the targets cortically equivalent. Scalp distributions of P100 and CI are, in general, much more similar than when 4° targets were used. These and other observations are predictable if the anatomical organisation of the visual cortex is considered.

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Scalp distribution of visual evoked potentials to foveal pattern and luminance stimuli

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Key words: foveal, generators, human, topography, visual evoked potential

Abstract. Scalp potentials elicited by pattern reversal, pattern onset, and flash stimulation have been studied in normal subjects by means of a 16-channel brain mapping system. In two groups of experiments the topography of the major positive component in each response was compared with 4° full- and lateral half-field stimuli and, for more detailed exploration of the pattern components by M-scaled stimuli selected to activate 1 cm^2-patches of striate cortex and associated extrastriate re-projections. The 4° stimuli were found to elicit scalp distributions for the pattern reversal P100 and the pattern onset C1 consistent with striate and extrastriate visual cortical origins respectively. Data on the flash P2 component suggest that stimulation was not localized accurately; this may have been due to lateral spread of neural activity in the retina. Predictably, the M-scaled stimuli showed extensive inter- and intra-individual variations depending on stimulus type and location relative to fixation. The manner in which, in some subjects, the region of maximal activity on the map appears to migrate with change of stimulus position possibly reflects local retinotopic order in visual evoked potential generator areas. However, data are neither extensive nor detailed enough to be conclusive.

Introduction

In this study we have investigated the scalp topography and cortical origins of the major positive components in the visual evoked potentials (VEP) elicted by foveal pattern and flash stimuli, using mapping techniques.

Many workers have attempted to deduce the areas of origin, within the visual cortex, of particular VEP components, from data on scalp distribution and on the way in which this changes according to the stimulated part of the visual field (e.g. Halliday and Michael, 1970; Jeffreys and Axford, 1972; Lesevre and Joseph, 1979; Drasdo, 1980). Their results and interpretations, however, have often been contradictory, owing to widely differing experimental conditions and also possibly to the preferential use of large stimulus field sizes.

In using foveal stimuli we expected that we would activate VEP generators on the proximal visual cortical surface, at and around the occipital pole, with little involvement of the mesial or tentorial surfaces or of cortex within

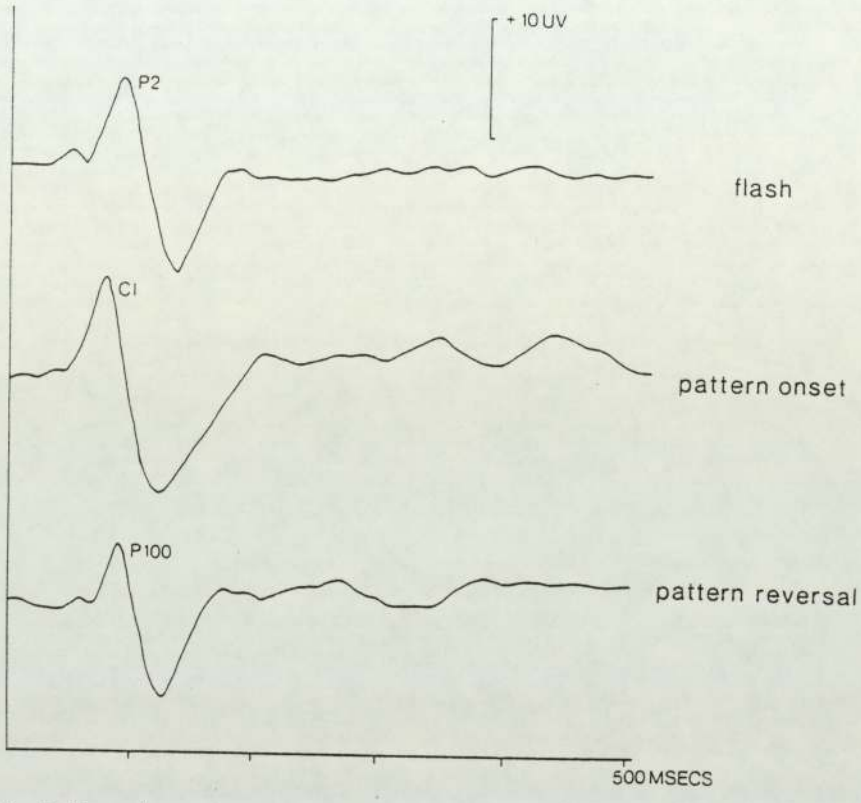

Fig. 1. The major positive components of the visual evoked potentials elicited by foveal stimulation.

the calcarine fissure. We should, therefore, have largely avoided the mixing of signals from these differently oriented generator areas and the confounding of scalp recorded responses, which is inevitable when employing stimuli that subtend large visual angles.

Since we have stimulated the proximal cortical surface, which is closest to the scalp electrodes and the most accessible in recording terms, we feel that we can make some deductions about possible component origins directly from our data on scalp distribution, without the involvement of dipole localization techniques.

In the first part of the study we compared the scalp distribution of the major positive components of the pattern reversal, pattern onset, and flash VEPs using 4° central full- and lateral half-field stimuli. Fig. 1 shows the components of interest, these being the pattern reversal P100, pattern onset C1, and flash P2. We have used the terminology of Halliday and Michael (1970), Jeffreys and Axford (1972) and Harding (1974) respectively.

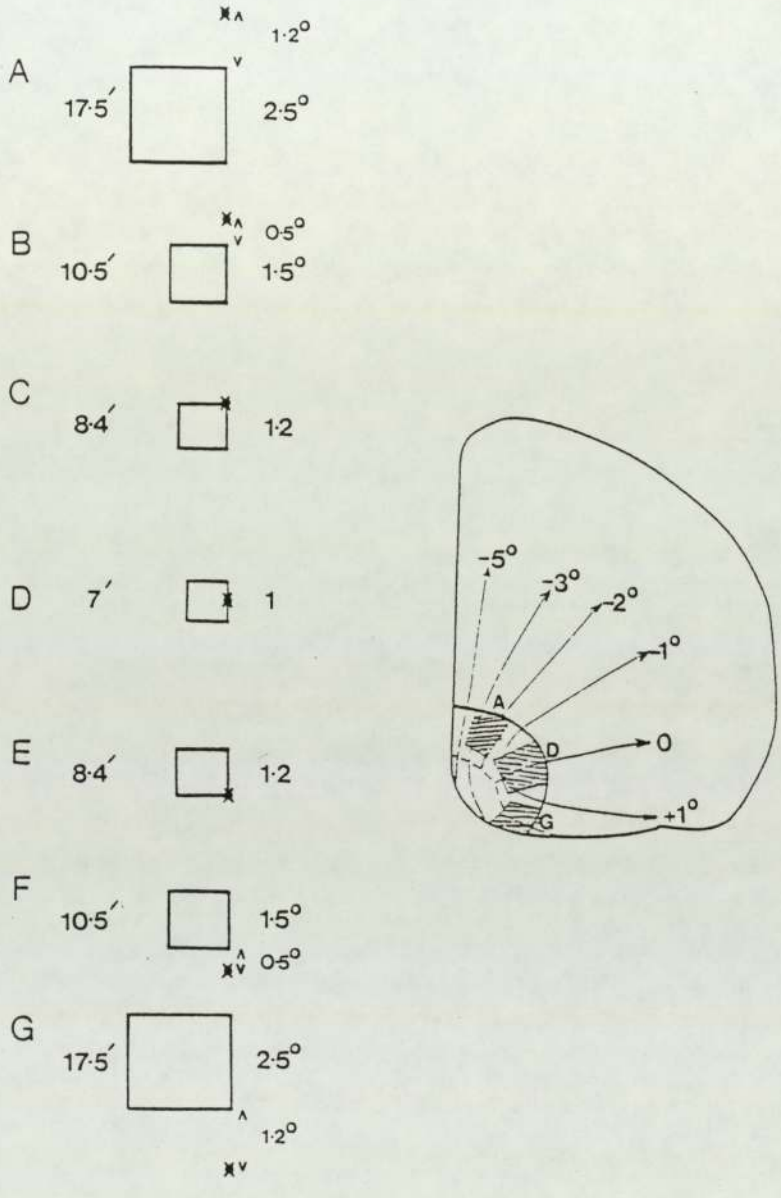

Fig. 2. (a) The M-scaled target series. Reference letters are shown on the left, as are the check sizes for each target. The position of the fixation point with respect to the stimulus is shown by the cross. The numbers on the right are the target dimensions, and, where appropriate, the distance of the fixation target from the edge of the stimulus. (b) This rear view of the right hemisphere shows the predicted position of the striate cortical projection of targets A, D, and G, according to a schematic model (Drasdo, 1983).

The suggestion has previously been put forward (Drasdo, 1986) that, according to dipole theory, the cortical gyri on the proximal surface must be the major generators of the scalp-recorded foveal VEP, with minimal contribution from the related fissures. It was considered that very small targets could be used to stimulate individual gyrus-sized regions of cortex, with pattern stimulation, to investigate the local nature of VEP generator areas and its relationship with the visual field. The gyri are, on average, around 1 cm in width, so cortically equivalent or 'M-scaled' stimuli were designed to activate 1-cm^2 patches of striate cortex and associated extrastriate reprojections at different eccentricities within the foveal region. The calculations were based on the cortical magnification equations of Draso (1977) and on a schematic map of the average cortical projection of the visual field in humans, which was derived from these equations (Drasdo, 1980, 1983).

Materials and methods

Nine normal volunteer subjects were employed in the larger field study. Their age range was 21–28 years, and they had visual acuity of 6/6 or better, wearing optical correction where necessary. Only five of these subjects were used in the more detailed study.

The larger stimuli used in the first part of the study were 4 × 4° square full fields and 4 × 2° lateral half-fields. The fixation target in each case was a cross with limbs subtending 40 × 5 min of arc.

The M-scaled target series is shown in Fig. 2a. The stimuli have been labelled A to G starting with the most peripheral lower field target. They were all confined to the left half of the visual field, in apposition to the vertical meridian, and each one was designed to stimulate a projected area which overlaps that of the next target by half a centimeter. The central stimulus D was the smallest, with angular subtense increasing at greater visual field eccentricity, in line with the decrease in cortical magnification. Figure 2b shows the predicted approximate projection of three of the targets onto the striate cortex of the right hemisphere. The fixation target for these targets had limbs subtending 15 × 2 min of arc.

High contrast (0.8) black and white checkerboards were used as pattern stimuli, in which the individual checks subtended 19 min of arc for the 4° stimuli. For the M-scaled targets, check size was 7 min for stimulus D, increasing at the same rate as target size, so that the number of checks within the stimulus field remained constant.

Pattern stimulation was provided by an optical projection system in which the mean luminance of the screen was 500 cd/m^2. For flash stimulation a

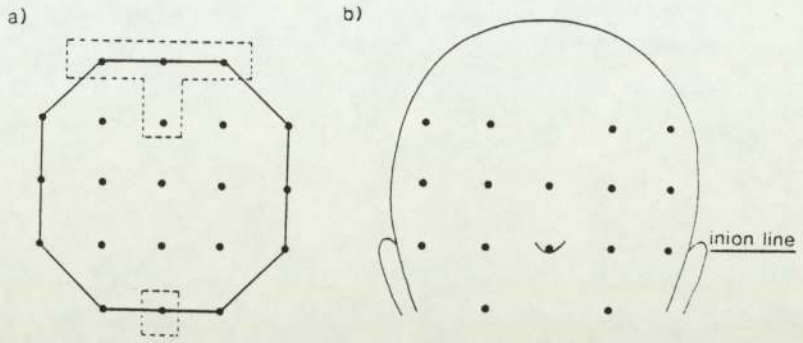

Fig. 3. (a) The brain mapper display, showing relative positions of recording channels. In the present study, this represents a rear view of the head. The channels outlined were not used for recording; amplitude levels at these points on the map are linearly interpolated from those at surrounding electrodes. (b) The electrode montage, as seen from a rear view of the head. Electrode separation was normally around four centimeters in either direction.

Medelec OS5 stroboscope was used. This was set at intensity 2 but attenuated with a 0.5 log unit neutral density filter. This gave a low intensity flash of around 40 nit sec. A similar method for localizing the flash stimulus has been used previously (Drasdo, 1982). For both pattern and luminance stimulation, background luminance had a value of 150 cd/m^2, ensuring a medium photopic level of adaptation.

Stimulus presentation rate in all cases was 1.3 per sec. In pattern onset stimulation, the pattern was exposed for a period of 150 msecs during each stimulus cycle. All stimulation was binocular, with natural pupils.

The VEPs recorded from 16 scalp electrodes were simultaneously averaged by a Bio-logic Brain Atlas III mapping system. The montage used is shown in Fig. 3b. It consisted of four rows of equally spaced electrodes, confined to the back of the head. Electrode separation was around four centimeters, the exact value being dependent on transverse and sagittal (along the median plane) percentage head dimensions (inion-nasion distances). This value, on an 'average' head, represents a compromise between a transverse 15% spacing and a 10% sagittal spacing, and gives complete coverage of the area of scalp of interest while retaining adequate sampling detail. Fig. 3a shows the corresponding arrangement of the channels on the Brain Atlas display map. The channels which have been outlined are not actually recorded from, the amplitude levels at these points on the map being linearly interpolated from those at surrounding electrodes.

Recording was monopolar, to a common midfrontal reference (Fz), with the ground electrode on the forehead (Fpz). Filter settings were 1 Hz high pass, 30 Hz low pass, and the time base was 512 msec. Normally two runs, each of 50 to 100 sweeps, were carried out for each stimulus condition.

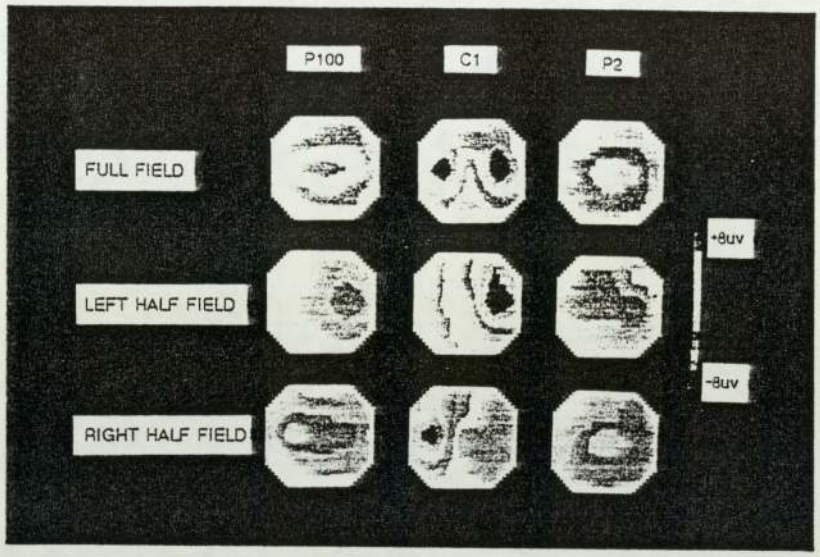

Fig. 4. Group average distributions of components P100, C1, and P2 for the 4° full- and lateral half-field stimuli. Positivity of the active electrode with respect to the reference produces an upward deflection, represented by more red colors on the scale.

Results are displayed in the form of 'equipotential' contour maps, plotted at the latency of the positive peak. This description is not, however, strictly accurate, since the amplitude on each trace was measured in a peak-to-peak manner, i.e. the voltage difference between the preceding negative peak or inflection and the maximum positivity of the transient.

Results

Fig. 4 shows the group average distributions of the three components for 4° full- and half-field stimulation. The maps show positivity of the active electrodes with respect to reference as an upward deflection on the color scale. Table 1 shows peak-to-peak amplitudes and peak latencies for each component measured at the point of maximum amplitude on the map, and standard errors.

Component P100 had a mean latency value which was actually closer to 90 msec, which was probably a result of the high stimulus luminance.

For all stimulus conditions, C1 tended to be of larger amplitude than P100 or P2, but was more variable. This is reflected in the standard errors.

Table 1. Mean amplitudes and latencies of visual evoked potentials with pattern reversal, pattern onset, and flash stimuli.

Stimulus		Component		
		P100	C1	P2
Full-field	Latency (msec)	92.0 ± 1.5*	85.6 ± 1.9	96.2 ± 2.2
	Amplitude (μV)	5.4 ± 1.3	7.8 ± 2.3	5.3 ± 1.4
Left half-field	Latency (msec)	92.9 ± 2.1	82.7 ± 2.0	100.3 ± 1.2
	Amplitude (μV)	4.4 ± 0.7	7.7 ± 2.0	3.8 ± 1.4
Right half-field	Latency (msec)	93.9 ± 0.9	86.2 ± 1.1	102.0 ± 1.3
	Amplitude (μV)	5.3 ± 1.4	7.1 ± 2.6	4.4 ± 1.5

* ± standard error.

On full-field stimulation, all three components show maximum amplitudes on the line of electrodes 4 cm above the inion. C1, however, shows a tendency to a more anterior distribution than P100 and P2. With regard to lateral distribution, P100 shows a midline maximum, whereas C1 shows distinct bilateral maxima at 4 cm to either side of the midline on the line of electrodes 4 cm above the inion, becoming more generalized across the midline 8 cm above the inion.

For lateral half-field stimulation, P100 and C1 again show maximum amplitudes on the line of electrodes 4 cm above the inion. Both components can be seen to have lateralized over the hemisphere contralateral to the half-field stimulated, that is the 'correct' hemisphere in terms of visual field projection. This tendency is clearer for C1, which shows a steep gradient and a sharp cut-off near the midline, than for P100, which spreads somewhat over the midline onto the ipsilateral side. In the data on individuals, C1 was always found to be maximal contralaterally whereas P100 laterization was more variable and was actually found to be slightly ipsilateral for two of the subjects. P2 shows a much more widespread distribution and did not lateralize clearly or consistently on half-field stimulation.

Fig. 5 shows examples of the distributions of components P100 and C1 for the M-scaled stimuli in one subject. These small targets produced vastly different response amlitudes in different subjects. Also, intra-individual amplitude showed high variation depending on type of stimulation and on target position relative to fixation. For example, Fig. 5 shows P100 to have a maximum amplitude with target D, but for C1 the amplitude was highest with target C. As with the 4° stimuli, pattern onset tended to produce larger signals than pattern reversal. Responses were, on the whole, smaller for the more peripheral targets than for the central ones, particularly for the upper field targets F and G, which produced very small signals if at all. Fig. 5 shows P100 spreading across the midline more than C1. In general, this

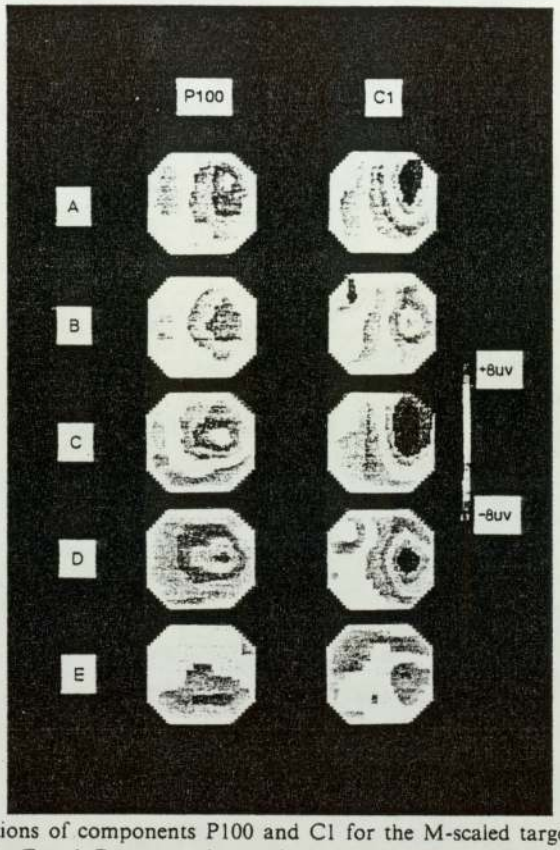

Fig. 5. Distributions of components P100 and C1 for the M-scaled targets A to E in one subject. Maps for F and G are not shown since these targets produced small, inconsistent responses.

tendency was much less marked than for the 4 × 2° half-field stimuli, with both P100 and C1 being distinctly contralaterally localized.

In all five subjects there was some evidence of movement of both component maxima on the map when target position was changed. In three subjects there was a slight, gradual, downward movement as stimulus position was moved from below fixation to above it. The example shown illustrates this point. This tendency was not, however, seen clearly in all cases.

Discussion

For the larger (4°) fields, the results lend themselves to the interpretation of Halliday's group (Barrett et al., 1976; Halliday, 1982), suggesting that this

component is the result of surface positive activity in the striate area, at the occipital pole, for foveal stimuli. This would explain the component's predominantly midline distribution to full-field stimulation and its variable localization with lateral half-field stimulation (see also Harding et al., 1980; Holder, 1980).

C1, however, shows maxima to either side of the midline for full-field stimulation. This type of distribution has been noticed previously (Lesevre and Joseph, 1979; Drasdo, 1980). This factor, combined with the tendency to distinct contralateral localization of the half-field response, suggest that C1 may have a more lateral origin than P100, being the result of surface positive activity in extrastriate visual cortex. This is contrary to the orthodox view that C1 arises from surface negative activity in the striate area (Jeffreys and Axford, 1972), but supports the suggestions of other workers (Drasdo, 1980, 1982; Lesevre and Joseph, 1979).

The failure of the flash P2 component to clearly or consistently lateralize on half-field stimulation precludes a deduction as to its cortical origin. This behavior suggests that stimulation may not have been confined to one cerebral hemisphere.

One explanation is that of stray light (mainly ocular scatter and retinal reflection) causing indirect stimulation of the retina on the other side of the midline. Scattered light has been shown to be important in the generation of the b-wave of the electroretinogram (ERG) when using small central stimuli (Boynton, 1953). In the present situation, however, it is thought that stray light could have played very little part in eliciting the VEP to the flash stimulus, for several reasons. According to the point spread function for the eye, light spreading from each point on the edge of the stimulus should fall to around half intensity only a few minutes of arc away from the edge (Vos et al., 1976) and is virtually negligible at a distance of 10 min. Hence it is unlikely that there would have been much stimulation across the midline of the retina. The retina surrounding the stimulated area was adapted to a photopic luminance level and therefore should have been relatively insensitive to the low intensity intraocular scatter associated with the low-energy light flash. DeVoe et al. (1968) showed that even in dark-adapted eyes the contribution of scattered light to the VEP was inhibited by the Stiles-Crawford effect. This effect could be expected to be more marked at photopic adapting luminances, as in the present study.

Other potential sources of bilateral stimulation are the imprecise fixation which results from physiological nystagmus, which could be expected to spread stimulation by around 10 min of arc (Ditchburn, 1967) and also the overlapping cortical representation of the vertical meridian of the visual field (Stone and Johnston, 1981). These factors however, also would have affec-

ted the lateralization of responses to pattern stimulation, had they played a significant role.

Stimulation across the midline may have come about by means of lateral spread of neural excitation within the retina. This is believed to occur over wide areas of the retina with high frequency stimuli (Robson, 1986) and could therefore possibly occur with very brief stimuli (i.e. with high rate of change of luminance) such as light flashes.

The results for the M-scaled targets showed, predictably, large inter- and intra-individual variability in signal amplitude. This is to be expected because of anatomical differences in the arrangement of gyri and fissures. The general tendency for small responses to upper field stimuli might be expected as these targets should stimulate cortical areas towards the lower aspect of the visual cortex, where the generators are less optimally positioned with respect to the scalp electrodes.

The more contralateral location of P100 maxima with these smaller targets might be expected, since they are positioned close to the vertical meridian and would tend to preferentially activate striate regions further away from the midline, towards the striate-extrastriate boundaries.

The apparent gradual migration of component maxima with change in stimulus position could possibly be interpreted as demonstrating a local retinotopic order in VEP generator areas. This would apply equally for P100 and C1 generator areas. If our previous deductions as to component cortical origins are correct, this would suggest that this kind of order exists in extrastriate as well as striate cortex in humans. Further work needs to be done in this area, with the investigation of more subjects and also using more closely spaced electrode matrices to examine the changes in more detail. In addition, it will be necessary to develop a two-dimensional statistical test, to examine the significance of this movement in the area of maximum response.

Acknowledgement

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Complementary Components and Local Variations of the Pattern Electroretinogram

Neville Drasdo, Dorothy Ann Thompson, Caroline Mary Thompson,* and Lesley Edwards

Pattern electroretinograms have been presumed to arise from a combination of luminance and pattern detection activities. Since the responses at low spatial frequencies are linearly related to contrast and contain negligible pattern specific components, it is proposed that a retinal illuminance response for higher spatial frequencies can be computed from the optical transfer function of the eye. These computed responses are subtracted from pattern electroretinograms to reveal a pattern-specific response with a marked bandpass characteristic. The peak spatial frequency of the bandpass curve declines with increasing peripheral angle. For central vision, the peak amplitude of the pattern-specific response is larger than the retinal illuminance response, but, in the peripheral retina, the two responses are found to be almost equal. The possible origins of these signals are discussed, and it is concluded that the technique provides a method of obtaining separated illuminance and pattern responses from retinal regions having different properties of spatial selectivity. Invest Ophthalmol Vis Sci 28:158–162, 1987

When electroretinograms are elicited by pattern reversal or pattern onset/offset stimulation,[1,2] the signal may include a local luminance response and a pattern-specific response (PSR), which occur in varying proportions depending on the experimental conditions.[2–4] Evidence of the PSR is largely based on spatial tuning characteristics, but this evidence and its interpretation have not been universally accepted.[5] Selective reduction of pattern electroretinograms (PERGs) as compared to focal and flash ERGs in pathology of retinal ganglion cell layers has also been considered as evidence of PSR.[6–8] Such results may be due to differences in the effective locus of retinal stimulation by the two methods or due to lack of sharp focus and fixation.[9] However, despite some controversy in the above reports, studies using low contrast and high spatial frequencies have demonstrated an impressive spatial selectivity, which can probably only be explained by receptive field mechanisms,[4,9] and consideration of existing knowledge has enabled us to propose a simple theoretical model based on complementary components, which, in turn, provides a simple method of separating them (Fig. 1).

The contrast of high spatial frequency bar gratings is greatly reduced in the retinal image due to optical degradation. Stimulation of the retina, therefore, depends on the distribution of retinal illuminance rather than external stimulus luminance, and the term luminance response will be replaced by retinal illuminance response (RIR) in the remainder of this report.

The RIR is the electrical response to local change in retinal illuminance when the stimulus occurs. It is maximal when large areas are stimulated, and is reduced due to optical degradation for the finest stimulus details or high spatial frequency gratings. In the ultimate case of a large white element of a square wave or checkerboard pattern covering the whole stimulus field, the RIR is identical with the classical ERG.

Conversely, the PSR is the sum of responses of spatially selective retinal neurons which, due to their modal receptive field size, must be expected to be inactive at low spatial frequencies. Data on dendritic fields of primate bipolars, which are the most numerous elements, and retinal ganglion cells suggests that most of the receptive field centers would not exceed 10′ angular diameter in the PERG stimulus field.[10] The PSR would, therefore, be expected to have a bandpass characteristic with a peak at a high spatial frequency, but displaced towards lower spatial frequencies with increasing eccentricity from the fovea.

For low spatial frequencies, the amplitude of the PERG, which is virtually a pure RIR, is linearly proportional to contrast.[3,4,11] The RIR contribution for the PERG for higher spatial frequencies might, therefore, be computed from a low spatial frequency PERG attenuated by the amount of contrast reduction due to optical degradation. This reduction will be referred to as the contrast attenuation factor (CAF). In this study, we set out to obtain such RIR signals and to subtract them from the PERG to provide a close approximation

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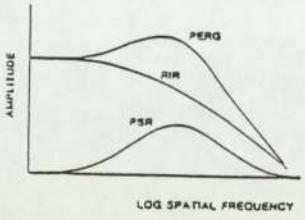

Fig. 1. Hypothetical tuning curve of the PERG resulting from summation of the retinal illuminance response curve (RIR) and the pattern specific response curve (PSR).

to the PSR component expected from stimulation of different zones of the retina.

Materials and Methods

Pattern onset electroretinograms were obtained using an optical projection stimulator, in which a diffusing shutter provided a uniform field of space averaged luminance alternating with a pattern.[12] Vertically oriented square wave gratings presented at three viewing distances (Table 1) with opaque masks and central fixation provided stimulation of three concentric retinal zones. The range of spatial frequencies varied from 0.14–20 cycles per degree (CPD), and the stimulus fields extended from 0–5.1° angular radius for the central zone, 5.6–12.6° for the mid-peripheral zone, and 12.3–26.3° for the peripheral zone. The stimulus contrast was retained at 75% and mean luminance at 250cd/M^2. Room luminance averaged approximately 25cd/M^2. Stimulus patterns were presented for 105 msecs, followed by a uniform field for 106 msecs. This cycle was repeated 100 times, and responses were recorded from both eyes using an electrode as described by Dawson et al in 1979,[13] referred to an Ag/Ag Cl electrode placed temporally on the ipsilateral side. No corneal anaesthetic was used. The subjects experienced no significant discomfort or blurred vision over recording sessions of 1 or 2 hr. Signals averaged on a Nicolet Pathfinder II Computer using a bandpass of 5–70 Hz were stored digitally on magnetic media for subsequent processing. Four informed volunteer subjects who are the authors of this report, with an age of 22–52 yr, wearing refractive corrections where appropriate, participated in the study. The angular zones of the visual field which were stimulated are shown in Table 1, with the spatial frequencies of the square wave gratings and their calculated contrast attenuation factors.

The PERG from the lowest spatial frequency grating used in each zone of the field was treated as a pure RIR for purposes of computation. To determine the RIR for higher spatial frequencies, this signal had to be reduced in its amplitude by the appropriate CAF. To find the CAF for each grating, it was first necessary to determine the retinal illuminance profile which is the spatial distribution of retinal illuminance at right angles to the bars of the degraded image (Fig. 2). This was done by synthesising the waveform from the Fourier components up to the 99th harmonic, filtered by the modulation transfer function (MTF) of the eye. The contrast stimulus was considered to be proportional to the cross-sectional area of a half cycle of this degraded retinal illuminance profile. It had unit value for the perfect image of a square wave. The CAF was, therefore, the ratio between the half cycle of the degraded and perfect waveform.

Table 1. Visual angles, viewing distances, spatial frequencies (CPD) and contrast attenuation factors (CAF) for the pattern stimuli

Angle 0–5.1°, Dist. 126 cm		*Angle 5.6–12.6°, Dist. 50 cm*		*Angle 12.3–26.3°, Dist. 22.5 cm*	
CPD	*CAF*	*CPD*	*CAF*	*CPD*	*CAF*
0.76	0.83	0.30	0.90	0.14	0.97
1.58	0.70	0.63	0.84	0.28	0.92
2.22	0.63	0.88	0.79	0.39	0.89
3.16	0.55	1.25	0.74	0.57	0.86
4.28	0.48	1.76	0.71	0.79	0.81
6.67	0.34	2.50	0.61	1.11	0.77
10.00	0.26	4.00	0.50	1.82	0.66
12.00	0.22	5.00	0.44	2.14	0.64
20.00	0.11	7.50	0.34	3.30	0.54
		12.00	0.22	5.00	0.44

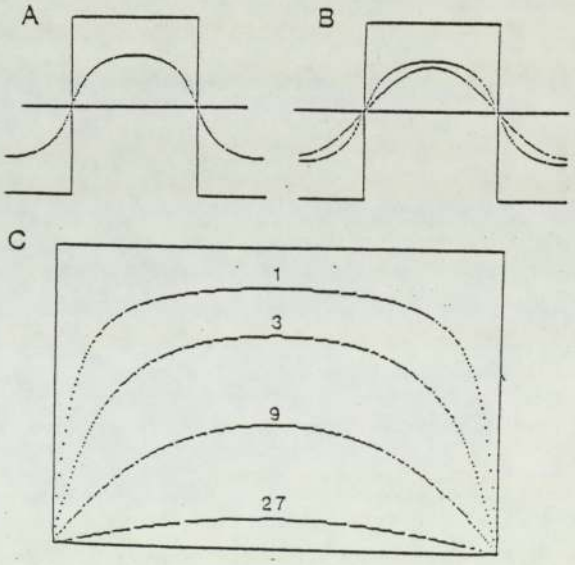

Fig. 2. Retinal illuminance profiles of square wave gratings computed by applying the modulation transfer function to all components up to the 99th harmonic. A, The profile of the retinal image of a 5 cycle/degree square wave grating superimposed on the theoretical image of the perfect square wave. B, The profile for a square wave and a sine wave grating of identical contrast at 5 cycles/degree. A–B, Half cycles of illuminance profiles of the retinal image of a square wave grating for different spatial frequencies normalized for comparison. The contrast attenuation for each grating was calculated by comparing the area beneath the profile with the area of the total rectangle which is the half cycle of a corresponding perfect square wave.

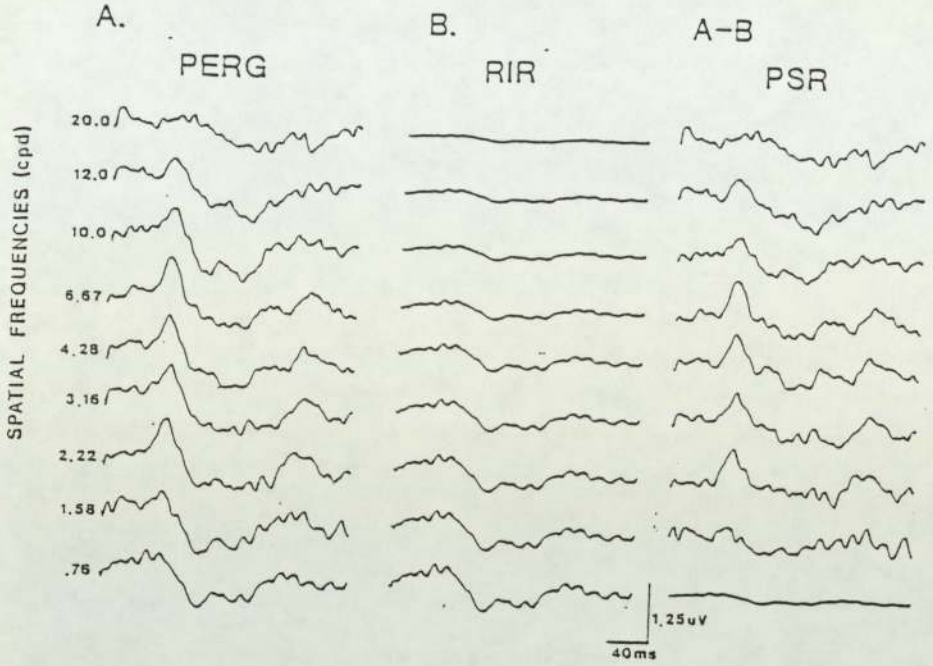

Fig. 3. Group averages of the pattern electroetinograms in the present experiment showing the computed retinal illuminance response and the effects of subtraction to reveal the pattern specific response in the third column. These data relate to the central circular field of 10° angular diameter. Polarity is positive upwards, stimulus delay 4 milliseconds.

The MTF selected was defined by the expression $M = EXP - ((F/8.4)^{0.8})$, where M is the contrast modulation and F the spatial frequency. This expression was based on the work of Campbell and Gubisch on three normal observers with a 4.9 mm pupil.[14] The average pupil size of our subjects was 5 mm. The CAF at each spatial frequency was obtained from the cross-sectional area of a half cycle of the retinal illuminance profile divided by the corresponding area of the perfect image of the square wave (Fig. 2).

Since the electrical waveform of the PERG at the lowest spatial frequency was considered to be a pure luminance response, when it was attenuated by the CAF for each spatial frequency, this produced the computed RIR for that specific spatial frequency. This RIR was subtracted from the corresponding PERG to reveal a residual waveform which was considered to be the PSR. These computations were performed on the group averaged data.

This experiment was approved by the Human Science Ethical Committee of Aston University.

Results

Clearly defined responses to pattern onset were obtained in all subjects. Due to the conditions of experimentation, the offset potentials were small, and are not considered in this report. The onset signals were largest and most clearly defined on stimulation of the most peripheral zone which had the largest retinal area. For the central zone, they were smallest and noisiest, while those in the mid-peripheral annulus had an intermediate amplitude and quality. As a result of the procedure described above, the computed RIR and PSR components of these signals were obtained and separately displayed. Data for the central and most peripheral zones are shown in Figures 3 and 4. Inevitably, the effect of the subtraction process was to reveal a more noticeable bandpass characteristic for each zone (Fig. 5). The peak of this curve was displaced towards lower spatial frequencies with increasing peripheral angle.

The maximal computed PSR trace for each zone was selected and displayed alongside its complementary RIR component (Fig. 6). It was noted that the relative amplitudes change in the different zones. In the central zone, the PSR was larger than the RIR, whereas, in the peripheral zone, they were apparently almost equal.

Discussion

Some previous reports have attributed the spatial tuning properties of the PERG to ganglion cell activity,[4,9] and the results shown in Figures 3–6 might appear to support this conclusion. However, the PSR was not equal in amplitude for the concentric stimulus areas, though they had been calculated to give equal numbers of ganglion cell receptive fields.[15] This could have been due to the fact that the estimated ganglion cell densities declined too sharply with peripheral angle,[16] or that the PSR did not arise purely from ganglion cell activity. It should be remembered, however, that ganglion cells are larger in the peripheral retina, and the signal might reflect this fact; also, the computations we have made

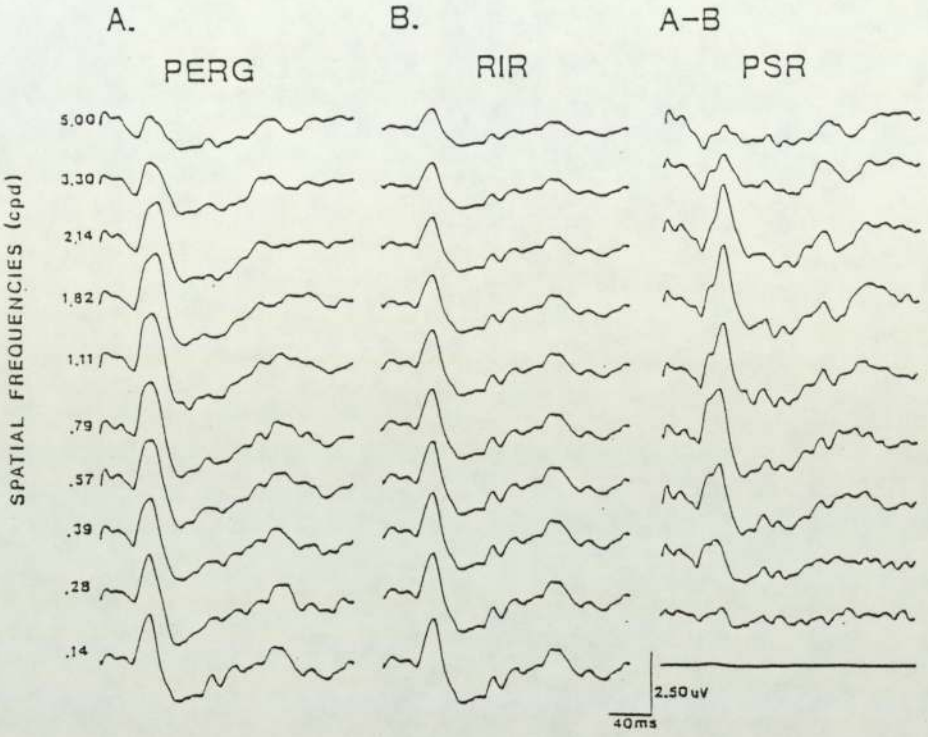

Fig. 4. Data as in Figure 2., for the peripheral zone of 12.6–26.5° angular radius.

on the retinal image relate to an MTF for central vision. Optical degradation may be further increased in the periphery, so that the subtracted signal was too small. These factors could all explain the inequality of the signals if the ganglion cell estimated counts in the zones were, in fact, correct. However, a more important explanation may be that the PSR was not generated solely by ganglion cells, but reflected activity of all the spatially selective elements in the stimulated zone.

The method of computing the retinal illuminance profile had two minor theoretical inadequacies. It was based on consensus data, and not on the MTFs of the individuals: it also took no account of the phase transfer function (PTF) of the eye. No data were available to enable this to be considered for white light, and, even for monochromatic light, the PTF has wide intra-individual variability.[17] It seems probable that the random tendencies of these variations and the effect of chromatic aberration would cancel out any general effect of phase in such an experiment. It has also been reported that the MTF does not change markedly inside a radial visual angle of 25°.[18] It, therefore, appears that the calculations should have provided a reasonable es-

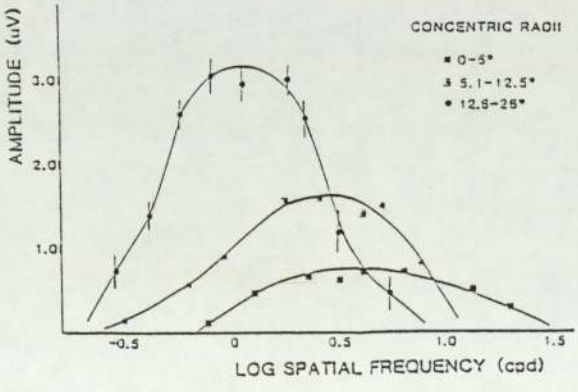

Fig. 5. Bandpass curves of the responses after subtraction. Peaking from left to right are the peripheral, mid-peripheral, and central responses.

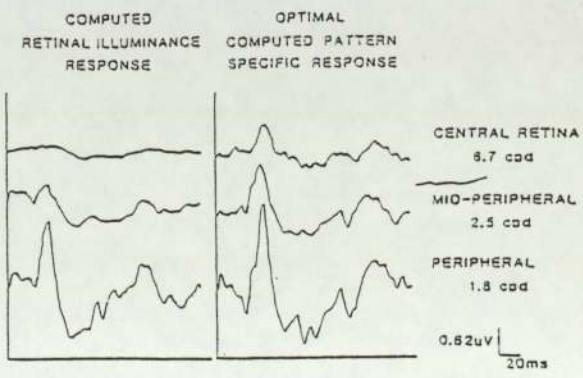

Fig. 6. Computed illuminance and pattern specific responses for the optimal spatial frequency of the pattern response for each zone.

timate of the optical degradation, even taking into account some variation of the MTF in different subjects, and some non-linearity of response to contrast, the shape of the RIR curve would change very little. Since the weight of orthodox opinion supports the view that the PERG consists of a luminance (or retinal illuminance) and pattern response, the form of the complementary PSR must automatically have equal validity.

It is concluded that the strategy adopted provided a method of obtaining separate illuminance and pattern specific responses from the retina. In its present state of refinement, however, although the pattern specific response appeared to be separated from the response to retinal illuminance, its origin could not clearly be identified, because several types of retinal neurone have spatially selective characteristics, which might be expected to change with increasing peripheral angle, as shown in this experiment.

Key words: electroretinogram, luminance, pattern, degradation, spatial-tuning

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