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SPATIAL PATTERN VISUALLY-EVOKED RESPONSES
RECORDED FROM THE MID-TEMPORAL SCALP REGION OF HUMANS

by

ANTHONY WILLIAM ROBERTSON

A thesis submitted to the Faculty of Graduate Studies
and Research in partial fulfilment of the requirements
for the degree of

Doctor of Philosophy

Department of Psychology

Carleton University

Ottawa, Ontario

February 26, 1985

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ABSTRACT

A series of studies is presented that describe pattern-reversal, visually-evoked responses (VERs) recorded from the mid-temporal scalp region of humans. Theoretical arguments are presented that suggest that the generators of these responses might include cells within the lateral geniculate nucleus of the thalamus.

Data are presented from normally-sighted observers that support the proposition that mid-temporal VERs are independent from responses recorded at either the proximal or distal poles of the visual pathway. This independence was evident in comparisons of latency and of spatial and temporal tuning among simultaneously recorded pattern electroretinograms (PERGs), pattern visually-evoked cortical potentials (PVECPs) and pattern mid-temporal VERs. Although some degree of inter-observer variability was found in some of these comparisons, several reliable differences were noted.

Recordings from two subjects with well-defined visual pathway disruptions are also reported. These results further support the contentions that (1) the mid-temporal VER is an independent measure of electrical brain activity associated with spatial pattern vision and that (2) the likely source of the mid-temporal VER is the lateral geniculate nucleus.

These findings suggest that the pattern-reversal VER recorded from the mid-temporal scalp region could serve as a valuable clinical tool for localizing and monitoring pathology affecting the visual pathway.

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Chapter I: Introduction

A. Background to the Approach

The theoretical and practical possibility of observing in vivo nervous activity by monitoring electrical changes in neural tissue was first demonstrated by 19th century physiologists such as DuBois-Raymond (peripheral nerves), Holmgren (retina), Caton (cerebral cortex) and Beck (cerebral cortex) (reviewed in Brazier, 1961, 1963 and 1980). However, the clinical application of sensory electrophysiology has only been practical since the advent of suitable technology during the first two-thirds of this century (reviewed in Riggs, 1977).

In the case of the human visual system, adequate clinical electrophysiological techniques have only been developed during the past three decades. In addition to technological advances that allow for accurate measurement of visually-evoked retinal activity with the electroretinogram, or ERG (reviewed in Armington, 1974 and 1980) and cortical activity with the visually-evoked cortical potential, or VECF (reviewed in Sokol, 1980) substantial advances have been made in understanding the functional characteristics of the various cell populations that make up the afferent visual pathway (reviewed in Van Essen, 1979).

Neurophysiological studies of cat and primate visual systems have revealed that photic stimuli with increasingly specific physical characteristics are necessary to elicit optimal responses from afferent visual neurons in visual centres central to the retina. Whereas many retinal ganglion cells respond to

diffuse light stimulation within their respective receptive fields, many cells in the lateral geniculate nucleus (LGN) respond most vigorously to achromatic or chromatic spatial and temporal changes. Many cortical neurons only respond when moving spatial contrasts with particular temporal, directional and orientational characteristics enter their receptive fields (reviewed in Van Essen, 1979).

This increasing specificity or "stimulus tuning" does not imply that there are no retinal ganglion cells that respond to spatial patterns or that cortical neurons do not respond to diffuse light flashes. If a particular visual stimulus elicits a response from a class of cortical neurons this stimulus must also have elicited some type of response from the retina and LGN. But the retinal or LGN cells that take part in conveying a signal regarding spatial pattern to cortical neurons may also take part in the conveyance of other, more simple luminance signals to the cortex. What changes at successively higher levels of the afferent visual pathway is the number of representations of the retinal field. Each representation appears to have a population of cells with specific stimulus tuning characteristics as its physical substrate and it is the number of such populations that differentiates one level of visual processing from another.

This model is supported by the fact that retinal receptors project in a one-to-one or many-to-one fashion upon the retinal ganglion cells but retinal ganglion cells project in a one-to-many fashion upon LGN and cortical neurons. Such discoveries have led to a view of the visual pathway as being comprised of many functional subsystems that physically and functionally

overlap (e.g., Blakemore and Campbell, 1969). Within these, certain cell populations that have broad stimulus tuning characteristics overlap in the anatomical substrate with cell populations with narrow tuning characteristics.

In the case of photopic spatial vision, such segregation exists as early as at the level of the retinal photoreceptors. Since the cones are most densely packed in the fovea and make one-to-one connections with retinal ganglion cells, they are the only receptors capable of conveying certain high spatial frequency information to higher visual centres. These retinal ganglion cells with small receptive fields are reported to project in a one-to-many fashion upon LGN and cortical neurons. The ratio of photoreceptors to cortical neurons receiving retinal inputs has been called the 'cortical magnification factor' (Daniel and Whitteridge, 1961).

In contrast to this may be found peripheral rod receptors that map in a many-to-one fashion upon retinal ganglion cells giving rise to large receptive fields. The axons from the peripheral retinal ganglion cells mainly contact LGN and cortical neurons in a one-to-one or one-to-many fashion, thus limiting spatial resolution in the peripheral visual field. Furthermore, due to the apparent existence of only one spectral sensitivity function for all scotopic photoreceptors, the information that can be carried in the "peripheral rod channel" is limited to low spatial frequency patterns of low intensity comprised of achromatic contrasts.

It seems reasonable to conclude that only a subset of the

afferent visual pathway is active with any one stimulus type in the same way that only a part of the visual system is active when only a portion of the full visual field is stimulated. These parts distinguish themselves as "functional channels" within the visual pathway.

Table 1 lists stimulus characteristics that are thought to be significant at various levels of the retinocortical pathway. Figure 1 illustrates, schematically, the retinotopic organization of the retinocortical pathway.

In principle, it should be possible to assess the functional integrity of the visual pathway by presenting photic stimuli that are suitable for eliciting electrical responses from neurons within each functional channel and recording light-evoked electrical responses at appropriate levels of the visual system.

In practice, however, this approach is only possible when recording intracranially. Extracranial recordings of visually-evoked responses are difficult to interpret due to complications from factors such as the proximity, morphology and spatial orientation of underlying tissues supporting visually-evoked activity and the conductivity and electrical isotropy of 'non-visual' tissues that intervene between the recording electrode and the visually driven neurons.

Aspects of the recording technique itself, such as the choice of reference electrode site and signal filtering during recording, can also introduce complexities into the interpretation of such measures. Discussions of the physiological bases of scalp recorded visually-evoked responses and recording techniques can be found in Schlag (1973), Creutzfeldt and Kuhnt (1973), Llinas and

Table I

Effective Light Stimuli and Electrophysiological Measures of Visual System Activity (after Celesia, 1982)

Portion of Visual System	Effective Stimuli	Electrophysiological Measures
RETINA	<ul style="list-style-type: none"> -monocular -diffuse light (temp. mod.) -high contrast spatial patterns (low spatial frequency) 	<ul style="list-style-type: none"> -Electroretinogram (ERG) -Pattern Electroretinogram (PERG)
LATERAL GENICULATE NUCLEUS	<ul style="list-style-type: none"> -monocular or binocular -chromatic and achromatic spatial contrast patterns (high, medium and low spatial frequencies) -high intensity diffuse light 	<p>NONE</p> <ul style="list-style-type: none"> -visually evoked subcortical potential (PVESP)
STRIATE CORTEX AREA 17	<ul style="list-style-type: none"> -monocular or binocular -chromatic and achromatic spatial contrast patterns (high spatial frequencies espec.) -spatial contrasts oriented in particular ways and of particular sizes 	<ul style="list-style-type: none"> -VECP -PVECP

Figure 1 Retinotopic organization of the right half
of the visual pathway (after Duke-Elder, 1961).

Nicholson (1974), Vaughan (1974; 1982) and Nakayama (1982).

Although these complexities are non-trivial and may prevent the clinical assessment of some afferent visual channels using scalp recorded visually-evoked responses (VERs), some of these putative visual channels appear to have been successfully monitored electrophysiologically. The inability to evaluate all visual channels means that the integrity of the total afferent visual pathway cannot be declared as 'normal' based solely upon electrodiagnostic measures. However, it is still believed by many clinicians who use such tests that electrodiagnostic measures of the visual system can detect pathology more quickly, more objectively and/or more accurately than traditional behavioral measures of visual function. As a result, VERs are part of the selection of visual function tests available in clinical ophthalmology and neurology settings. Clinical applications of visual evoked potentials are reviewed in Armington (1974; 1980), Sokol (1980) and Chiappa (1980).

Despite the apparent increase in stimulus tuning specificity at higher levels of the visual pathway it has been found that bright flash stimuli (composed of diffuse white light) produce clear ERGs and VECs as well as responses that have been attributed to the Lateral Geniculate Nucleus. These latter responses have been labelled Visually Evoked Subcortical Potentials or VESPs. The flash ERG and VEC were the most common visual electrodiagnostic measures until the early 1970's. Since then, however, the flash VEC has fallen from favour because of its high inter-observer variability and because spatially

patterned stimuli have been shown to be more appropriate. This may be due, in part, to evidence obtained from cat and primate visual electrophysiological studies that suggest there are a number of functional subclasses of cortical neurons with quite different stimulus tuning characteristics (eg. Hubel and Wiesel, 1968; Hubel Wiesel and Stryker, 1978; Van Essen, 1979; Hubel, 1983). The patternless flash stimulus, for example, likely drives a class of visual pathway neurons associated with the 'brisk luminance channel' which appears to be unaffected by pathological conditions that give rise to obvious functional visual deficits (Duwaer and Spekreijse, 1978).

The bright flash VESP is a new measure that has been reported to show some sensitivity to anterior pathway dysfunction (Harding and Rubinstein, 1982). If this measure reflects the activity of a discrete number of 'brisk luminance' neurons in the LGN (e.g., in the magnocellular layers) then its future clinical utility might be limited by the lack of a stable cortical measure of this same subsystem to assist in differential diagnosis. Other potential limiting factors for the clinical utility of the flash VESP include the inherent difficulties in controlling diffuse light stimuli for hemifield assessments and the small signal-to-noise ratio necessitating the use of special filtering procedures. These problems notwithstanding, the bright flash VESP appears to be the first electrophysiological measure of the functional integrity of the middle portion of the afferent visual pathway.

The other functional channel that has been monitored regularly in clinical settings during the past 10 to 15 years is

that subserving the processing of patterns produced by achromatic spatial contrast stimuli. This subsystem has received much more basic and clinical research attention recently than has the so-called luminance channel because of the importance of spatial pattern vision. Partly because of the apparent importance of spatial contrast to cortical neurons and partly due to favourable morphological characteristics in human striate cortex, clear pattern VECs (PVECs) can be recorded from the occipital scalp. These responses have been found to show good consistency across subjects and to show sensitivity to many subtle and overt visual pathways disruptions such as amblyopia, multiple sclerosis, compressive lesions of the optic nerve and tract and stroke (Sokol, 1980).

The most commonly used stimulus for PVEC recording is a high contrast luminance checkerboard field. The contrast of the checkerboard is periodically inverted to ensure that no net change in the average luminance of the stimulus field occurs during a stimulus trial. This is important to demonstrate that the electrical recording is not "contaminated" by gross changes in the overall luminance--as is found in patternless flash stimulation. Since this procedure affords a high degree of control over the area of the retina being stimulated, it allows for selective stimulation of portions of the visual pathway. Not only is it possible to selectively stimulate one-half or one-quarter of the visual system with this type of stimulus, but by recording a series of PVECs using differently sized checks (i.e., different balances of spatial frequency components within

the stimulus) it is possible to estimate the functional properties of mechanisms involved in spatial vision.

The feature of the PVECP waveform (quarter-field, half-field or full-field) that is considered to be the most similar across individuals is a scalp positivity slightly anterior to the inion that occurs approximately 100 msec. following each pattern reversal. This event is most commonly known as 'P100', although other nomenclatures exist. Although the latency of this component would lead one to believe that it represents cortical events occurring long after the initial arrival of pattern-evoked geniculo-striate afferent volleys (estimated to occur at about 35 msec., based upon the estimated conduction velocity of myelinated axons and the length of the afferent visual pathway), the P100 latency has been found to be increased by subtle visual pathology. As well, the amplitude of the 'P100' varies as a function of overall field size, retinal image sharpness, fundamental spatial frequency, temporal frequency, adaptation level, luminance contrast and orientation of the stimulus pattern and the relative imbalance of spatial responses from the different classes of photoreceptors (e.g., chromatic contrasts) (Regan, 1972).

The same pattern-reversal stimulus has been used to record pattern electroretinograms (PERGs) that are much smaller in amplitude but relatively standard across emmetropic observers. The PERG waveform is simpler than that recorded with a diffuse flash and typically consists of a monophasic corneal positivity that begins at approximately 30-35 msec., peaks at 55-70 msec. and ends about 100 msec. following pattern reversal. The

amplitude and morphology of the PERG waveform are degraded by some forms of retinal pathology and its amplitude and latency vary as a function of spatial frequency, temporal frequency and visual acuity (Trick and Wintermeyer, 1982). Although the pattern reversal stimulus was first introduced in an ERG study (Riggs, Johnson and Schick, 1964) the clinical application of the PERG has a much shorter history than that of the PVECP. This has probably been due to the very low amplitude of the PERG ($< 1 - 4$ microvolts depending upon technique) and the belief that the human retina may not contain enough neural elements sensitive to spatial contrast to produce a response that can be recorded extra-ocularly. This belief appears to be unfounded, even though it is probably the case that most retinal cells are not as narrowly tuned to specific stimulus characteristics as are some cells in the LGN and visual cortex (Kaneko, 1979).

Simultaneous recordings of a PERG and a PVECP should, in theory, provide some measure of the beginning and end of the afferent spatial contrast channel in the retinocortical pathway. Although there have been no reports of half-field stimulation PERGs, it is possible to estimate retinocortical conduction times in each half of a patient's visual field by comparing the latency of a full-field PERG and half-field PVECP at a variety of spatial frequencies. In addition, the integrity of the prechiasmal section of the visual pathway (the optic nerve) might be assessed by repeating the PVECP monocularly and comparing it with binocular measurements. This information can be combined with behavioural measures of visual field function to detect and

approximately localize the level of a visual pathway disruption.

Figure 2 illustrates schematically the retinocortical visual pathway and the areas of visual field disturbance that typically accompany disruptions at various levels. These relationships (after Wray, 1980) between visual field deficits and disruptions at particular levels of the visual pathway follow the retinotopic organization of the visual system that was shown in Figure 1. It can be seen from this figure that different disturbances at different levels of the visual system can result in quite similar visual field deficits due to retinotopic organization in the pathway. Although subtle behavioural differences do exist between some of these disruptions, the field perimetry necessary to make these distinctions is labour intensive and not always definitive (Bynke, 1984).

The electrodiagnostic measures mentioned here are not likely to be more definitive in such cases. The PERG and PVECP can only provide information about spatial contrast processing between the retina and optic chiasm and between the chiasm and each occipital lobe. Although the flash ERG, VESP and PVECP can provide measures of luminance processing between the retina and the LGN and between the LGN and visual cortex, they also have drawbacks. The flash VESP and VECF are not as reliably sensitive to visual pathology as is the PVECP and the flash VECF is not considered to be a reliable measure in normal individuals. Since half-field stimulation is not possible with diffuse bright flash stimuli, it is not possible to differentiate pre-chiasmal activity from chiasmal-geniculate activity. Perhaps the most serious drawback

Visual Fields

left eye right eye

Figure 2 Disruptions in the visual pathways. The right side of the figure shows the visual field defects associated with pathology in the regions indicated (A - G).

when using the flash VER methods is that they are likely to contain large contributions from the portion of the visual pathway subserving peripheral vision due to intraocular light scatter. They do not likely contain much information from populations of cells with narrow stimulus tuning characteristics. As such, flash VERs might best be characterized as a gross measure of a relatively unimportant visual channel.

There are four purposes to the present study: 1. To investigate the possibility of recording a pattern-reversal VER that monitors the spatial contrast channels at anatomical location(s) intermediate to the retina (PERG) and striate cortex (PVECP); 2. to determine whether such scalp recorded VERs are correlated with PERG and PVECP records over a range of temporal and spatial frequencies; 3. to determine whether such VERs can be attributed to cells of the LGN on the basis of latency, stimulus tuning characteristics and findings in patients with known anterior or posterior visual pathway pathology, and; 4. to evaluate the possibility of recording this VER simultaneously with the PERG and PVECP measures to more definitively evaluate the spatial contrast subsystem of the retinocortical pathway.

Since the attainment of any of these objectives depends upon the ability to stimulate cells of the LGN such that their responses can be recorded at the scalp, a review of the anatomy, physiology and functional characteristics of the LGN will follow.

" B. The Lateral Geniculate Nucleus

Retinal ganglion cell axons exit the posterior pole of the eye as the optic nerve and retain the relative spatiotopic organization of their retinal receptive fields (shown in Figure 1.). The nerve fibers arising from the nasal hemiretina of each eye (about 60% of each optic nerve) decussate at the optic chiasm near the base of the brain, superior to the pituitary, and combine with the uncrossed fibers from the temporal hemiretina of the other eye to form the two optic tracts. Beyond the chiasm, each optic tract contains the fibers that subserve the entire contralateral visual half field of binocular vision.

In humans (and macaque monkeys) the LGN appears superficially as a small eminence on the posterolateral aspect of the pulvinar of the thalamus, near the termination of each optic tract. This small eminence is actually only the ventral convex surface of the lateral horn of the LGN. Its gross anatomy has typically been studied from reconstruction models based upon tissue slices (Duke-Elder, 1961). Such studies show the LGN to be a laminated structure with 6 layers. These layers have been numbered '1' through '6' starting with the most ventral layer. The term 'geniculate' refers to its overall appearance as being 'bent upon itself' or 'knee-like'. Figure 3 illustrates, schematically, the general shape of the LGN and its laminations.

FIGURE 3. Cross sections of the Human Lateral Geniculate Nucleus.

The optic tract fibers from the upper quadrant of the ipsilateral retina (lower visual field quadrant) terminate in layers 2, 3, and 5 of the medial portion of each LGN. Those fibers from the homologous quadrant of the contralateral retina terminate in layers 1, 4 and 6 of the medial LGN. The fibers from the lower retinal quadrants (upper visual field quadrants) terminate in the lateral half of each LGN with the same retinal laterality-to-layer relationship. Thus, the spatiotopic organization of the retinas and their laterality are preserved at the LGN. This mapping of retinal areas upon the LGN is considered to be "point to sector" rather than "point to point" (Duke-Elder, 1961). This is illustrated in Figure 4.

Morphologically, the principal neurons of the LGN are of two main classes: large multipolar cells in the ventral magnocellular layers (1 and 2) and medium or small multipolar cells that are mainly found in the four dorsal parvocellular layers (3, 4, 5 and 6). In addition, in all layers there are to be found small intrinsic neurons with short axon processes whose function is not well understood.

The medium cells of the parvocellular laminae are all contacted (directly or via interneurons) by smaller diameter, slower-conducting axons from "sustained" or "X-type" retinal ganglion cells whereas the large parvocellular neurons receive inputs from the larger diameter, faster-conducting, "transient" or "Y-type" retinal ganglion cells. In the medial and lateral portions of the LGN, where a majority of the peripheral (mainly rod-driven) retinal fibers project and the number of laminae is

FIGURE 4. Schematic representation of the "Point-to-Sector" projection of retinal afferents upon the lateral geniculate nucleus. (after Duke-Elder, 1961).

reduced (through a fusion of layers 4+6 with 1 and 3+5 with 2), the ratio of large principal neurons to smaller (medium) principal neurons is greatly increased (Brodal, 1981).

The afferent fibers entering the LGN constitute 80% of the optic tract fibers. The other 20% are all "Y-type" retinal ganglion cell axons that project to the superior colliculus and pretectal region of the brainstem. The superior colliculus projects to the pulvinar of the thalamus, which in turn projects to extrastriate visual cortex in the parietal and temporal lobes, whereas the pretectal area projects via the posterior commissure to the Edinger-Wesphal nucleus of the oculomotor nerve (cranial nerve III).

All geniculostriate fibers from both classes of principal LGN neurons pass ipsilaterally through the posterior portion of the internal capsule and then form the optic radiations. These fibers travel along the lateral aspect of the lateral ventricles and terminate upon stellate neurons in layer IV of the primary visual cortex on the superior and inferior banks of the calcarine fissure.

Within each geniculostriate projection, retinotopic organization is preserved with the macular fibers from each half-field of vision projecting to the posterior region of the contralateral calcarine fissure and the peripheral field fibers projecting to a smaller cortical region in and around the anterior portion of the calcarine fissure. There are approximately twice as many fibers projecting from the LGN to striate cortex as there are from the retina to the thalamus and each geniculostriate fiber contacts many cortical cells. The

ratio of principal LGN neurons to striate cortical neurons has been estimated to be 1:1350. The ratio is higher for macular vision and lower for peripheral vision (Hecanen and Alibert, 1978). For this reason it is believed that there are even more representations of the visual field in striate cortex than there are in the LGN.

Earlier studies of the stimulus-response characteristics of LGN neurons in monkey showed these cells to have center/surround receptive fields similar to retinal ganglion cells (Wiesel and Hubel, 1963) and to be involved in: spectrally-opponent spatial contrast (DeValois, Abramov and Jacobs, 1966; DeValois, 1971, 1973); brightness information processing (DeValois et al., 1966); temporal and spatial averaging of luminance (Hughes and Maffei, 1966; Maffei, 1968) and contrast enhancement (Weisel and Hubel, 1963; DeValois, 1971). Previous to these reports, the LGN in higher primates and humans was considered to be merely a relay station for retinocortical afferents where spatiotopic and binocular organization of these fibers took place prior to their contact with striate neurons.

Neurophysiological studies of macaque LGN function are not numerous and even recent results show inconsistencies between laboratories (presumably due to methodological differences and small samples sizes). However, it is probably best to restrict the current discussion to these results due to the strong anatomical similarity between human and macaque LGN and their strong similarities on behavioural visual measures. These comparative findings are of interest here in connection with

present attempts to record spatial contrast responses from the human LGN.

Questions of interest related to the physiological basis of scalp-recorded VEPs include: 1. Are there populations of LGN neurons in macaques (and presumably humans) that show stimulus tuning characteristics that are suitable for stimulation with conventional spatial stimuli such as checkerboards? 2. Can these LGN neurons be differentiated from cortical cells on the basis of spatial frequency or temporal frequency tuning? 3. Are these cells physically distributed within the LGN such that a net imbalance of current 'sinks' (voltage negativities) and 'sources' (voltage positivities) might be evoked across the LGN laminae by one stimulus type -- permitting scalp recordings? 4. Are there features of the responses of such cells that might assist in detecting those responses at the scalp surface (e.g., response morphology as monophasic or biphasic; relative response latency differences, etc.)?

There is increasing neurophysiological evidence that there is some measure of physical segregation of LGN cell populations with particular stimulus tuning characteristics similar to those listed earlier. Dreher, Fukada and Rodieck (1976) and Schiller and Malpeli (1978) have suggested that all cells in the parvocellular layers (PCL) of macaque LGN resemble 'X-like' cells of the cat LGN and that cells in the magnocellular layers (MCL) of macaque LGN are like cat "Y-like" LGN cells. However, Kaplan and Shapley (1982) propose that such conceptions of primate LGN neurons as being "X-like" and "Y-like", by analogy to retinal ganglion cells and cat LGN cells, are probably

oversimplifications resulting from methodological practices and particular classification criteria. Shapley, Kaplan and Soodak (1981) and Kaplan and Shapley (1982) report that they did not find such a total segregation of cells between the two sets of laminae (MCL and PCL) and that they found this homology to be most similar between x- and y-type cells of the cat LGN and two classes of cells found within the MCL of the macaque LGN.

Large multipolar neurons of the MCL receive inputs from both macular and peripheral "y-type" retinal ganglion cells. Such cells respond transiently to a light stimulus presented steadily to their receptive fields and do not show linear spatial summation within their receptive fields. All of the MCL cells in macaque LGN were considered to be "y-like" on the basis of their short latency responses (Dreher et al., 1976; Schiller et al., 1978) but Kaplan and his co-workers (1981, 1982) found MCL cells of two types; those that showed linear spatial summation and those that did not. Kaplan et al. found MCL cells that were "x-like" in their spatial summation but these cells showed short response latencies to electrical and photic stimulation, high contrast sensitivity and monophasic responses to medium spatial frequencies (mean sensitivity peak at 6 cycles/degree). The "y-like" MCL cells reported by these authors showed non-linear spatial summation of receptive field inputs in that they only responded to spatial discontinuities (i.e. edges) between high and low luminances within the stimulus field. These cells also showed short response latencies and high contrast sensitivity (i.e., they were apparently more sensitive to low contrast).

However, these showed low spatial resolution at the fundamental of the temporal stimulation frequency (monophasic responses with a mean spatial frequency sensitivity peak at 2.2 cycles/degree) and medium spatial resolution at the second harmonic of the temporal stimulation frequency (biphasic responses with a mean spatial frequency sensitivity peak at 5 cycles/ degree).

The PCL of the macaque and human LGN make up the majority of its mass and are almost entirely composed of smaller (medium) multipolar neurons that receive "x-type" retinal afferents. The retinal ganglion cells, projecting to the PCL are morphologically different from "y-type" retinal ganglion cells and respond tonically relative to spatial summation within their receptive fields. As noted in Figure 1, these afferents are mainly macular in origin and might, therefore, be expected to play an important role in spatial pattern vision. Kaplan et al. (1982) reported that the PCL neurons in their sample mostly showed linear spatial summations, long response latencies to both electrical and photic stimulation, to have high spatial resolution (bandpass characteristics with a mean sensitivity peak at 8 cycles/degree), to be chromatically tuned and to have low contrast sensitivity. In addition, these authors found that PCL cells showed greater sensitivity to the phase of moving spatial contrast stimuli than did MCL cells. They report that the PCL cells respond monophasically in a sustained fashion when appropriately-sized stimuli are entirely within their receptive fields.

There is some evidence that the PCL cells themselves are segregated on the basis of their centre/surround receptive field

organization. Schiller et al. (1978) found that the dorsal pair of parvocellular layers contained cells with predominantly on-center/off-surround organizations whereas the cells in the ventral pair of PCL showed off-center/on-surround organization. Although these authors did not suggest any anatomical reason for this segregation they do propose that the dorsal and ventral parvocellular layer pairs are functionally like two channels that carry different types of visual information.

The outputs of LGN neurons all project to layer IV of striate cortex but Hubel and Weisel (1972) reported that PCL neurons project to a different level of layer IV than do MCL neurons. In addition, Schiller et al. (1978) reported that the two groups of LGN projections can also be distinguished on the basis of their conduction velocity to striate cortex. When applying antidromic electrical stimulation at striate cortex these authors found the response latency in PCL cells was approximately 2 msec. longer than in MCL cells.

In summary, it could be concluded that there appear to be at least three physically segregated functional channels in the primate LGN. The cells of the two dorsal PCL are apparently opposite to those of the ventral PCL in their centre/surround receptive field organization and the cells of the four PCL are apparently different from those of the MCL in terms of chromatic tuning, response latency, response type, spatial tuning, contrast sensitivity and temporal phase sensitivity.

For the purposes of the present investigation, it is proposed that the stimulus tuning characteristics of populations

of LGN cells and the apparent physical segregation of those cell populations in the various layers of the LGN are favourable for eliciting pattern-reversal VERS from this structure. In view of the prominence of the PCL and their approximate position relative to the scalp surface, it seems most feasible that their responses can be scalp-recorded. Although there does not appear to be adequate information to suggest differential stimulus tuning between LGN cells and cortical cells, the responses from the two areas should differ in scalp distribution and latency. It can be expected though, on the basis of tissue volume, that the magnitude of pattern VERS from the LGN will be very much smaller than the magnitude of those from visual cortex. In terms of the physical suitability of the LGN and of its functional organization for the existence of current dipoles across the laminae, the situation seems quite favourable. The dorsal PCL cells are likely to be stimulated by high spatial frequency patterns while the ventral PCL cells are not likely to be stimulated by these same stimuli due to differences in centre/surround organization. The MCL cells are not likely to be stimulated to the same extent as the dorsal PCL cells due to stimulus tuning differences and the MCL cell responses should have much shorter latencies. Last, it is anticipated that pattern VERS from the LGN might have longer latencies than would be predicted on the basis of conduction velocity and retinogeniculate fiber length alone. This is because spatial pattern is apparently carried in the "x-like" channel where x-type retinal ganglion cells summate responses within their receptive fields (tonic responses) and project to striate cortex via

neurons with slower conducting axons. . It may be recalled that the primary positivity in the PERG occurs after 50 msec. and that the 'P100' response of the PVECP occurs at approximately 100 msec. It is therefore expected that any tonic positivity from the LGN that can be recorded at the scalp during spatial pattern stimulation might occur at some intermediate latency (50 - 100 msec.). Furthermore, if such a response is from PCL neurons, it might be expected to follow the fundamental of the temporal stimulation frequency (PCL "x-like" cells as described by Kaplan et al., 1982) whereas if such a response is due to MCL activity it might follow the second harmonic of the temporal stimulation frequency at medium spatial frequencies (MCL "y-like" cells as described by Kaplan et al., 1982). This distinction would not be definitive though if the scalp response arose from a current dipole due to differences in the responses of the two areas (PCL and MCL).

It is curious that the one laboratory that reports to have successfully recorded a scalp VER from the human LGN used a bright diffuse light flash stimulus (Harding and Rubinstein, 1980) and that such a stimulus does not fit the narrow tuning characteristics of many of the the LGN cell types reported here. Intra-thalamic recordings from monkey LGN have been reported for such a stimulus by Vaughan and Gross (1969) and Creutzfeldt and Kuhnt (1973). These authors report that such a stimulus does elicit a response in the LGN but that the magnitude of this response appears to decrease drastically as the recording electrode is positioned in more superficial layers. This finding

and the fact that the predominant feature of the triphasic VESP recorded by Harding et al was a negativity with a latency of 23-25 msec. would be consistent with an origin in the magnocellular layers ("y-like" MCL cell of Kaplan et al., 1982).

The intention here was to employ stimuli whose physical characteristics approximated the stimulus tuning characteristics of the PCL cells described earlier. In order that this work might form a useful extension of that done by Harding and Rubenstein (1980), preliminary studies were conducted to examine the following recording variables: active electrode-sites, reference electrode sites and signal filtering. Since Harding et al. used a relatively unique recording protocol, it was considered worthwhile here to examine the effects of such a protocol compared to more conventional methods. The results of these preliminary studies and the general methods for all the research to be presented are described in the following chapter. In addition, an overview of the main studies is provided.

Chapter II: General Methods, Preliminary Studies and Overview of Main Studies

A. General Methods

Subjects: A total of 7 subjects participated in these experiments. Five were healthy young adults (2 males, 3 females, mean age 25 years) associated with the laboratory. Only one was an experienced observer. All had normal or optically corrected vision as measured by Snellen acuity tests and none reported any history of neurological disorders affecting vision. The other two subjects were young adults (females, mean age 27 years) with well-defined visual pathway disruptions and visual symptoms appropriate to their respective pathological conditions. One of these subjects had a history of a pituitary tumor (pituitary adenoma) affecting the anterior, pre-geniculate visual pathway. This subject was found to have a bitemporal hemianopsia. The other of these subjects had a history of a temporal lobe tumor (oligodendroglioma), affecting the left posterior post-geniculate visual pathway. This subject was found to have a homonymous hemianopsia. The specific nature of the lesions and the accompanying functional losses in these two subjects were verified through neuro-ophthalmological assessment.

Stimuli: All stimuli were viewed on a square translucent back-projection screen subtending a visual angle of 30 degrees with a 25', transparent red fixation spot at its center. Diffuse flash stimuli were produced with a Grass PS2 photostimulator or an Ansco photoflash producing a "bright flash" stimulus of about 200 Watt/seconds. Both flash systems produced a transient flash of approximately 10 μ sec. duration.

Spatially patterned stimuli were produced with an optical system designed and calibrated by the author. This system was powered by a 450 Watt Xenon arc lamp source, with the images being produced with the use of 35mm photographic negatives placed in image-forming portions of the optical path. Figure 5 shows a schematic diagram of this system. Pattern reversal was accomplished by rotating a first-surface mirror mounted on an optical scanner. The scanner was driven with a square wave signal of appropriate amplitude at each check size. The checkerboard field was circular (subtending 10° degrees) and had a mean luminance of 90 cd/m^2 . The Michelson contrast between adjacent checks was $>85\%$ and each check subtended a visual angle of $11'$, $16'$, $27'$, $40'$ or $62'$ on a side. These patterns were spatially reversed (i.e., the bright checks and dark checks exchanged with one another) at 1.7, 3, 7, 12 or 15 Hz. and during full-field pattern reversal. The fixation spot on the viewing screen was bisected by the vertical edge between two checks. During half-field pattern reversal, one half of the circular stimulus field was occluded at the final aperture such that the vertical edge of the resulting semicircular stimulus field was positioned off of the central fixation point by approximately $30'$. This was done to avoid bilateral stimulation of the visual pathway due to the overlap that exists through the central foveal region.

Response recordings: Recordings were made with 1 cm. silver cup electrodes filled with conductive paste. These were attached to the scalp and face with collodion after the skin had been

FIGURE 5. Stimulation apparatus.

cleaned and gently abraded. Electrical impedance was monitored and maintained below 3K ohms for each electrode position. When linked earlobes served as the reference, skin preparation was the same but the electrodes were held in place with spring-loaded clips rather than with collodion. A ground electrode was attached to the neck of the observer with collodion. Care was taken to ensure that the risk of electrical shock from equipment was minimized.

With the exception of the active electrode during ERG recording (lower eyelid), the ground (neck) and on some occasions non-cephalic electrodes, electrode sites were based upon the International 10-20 system sites (Jasper, 1958) or were defined in terms of their relation to 10-20 system sites (see Figure 6). These will be described in each experiment.

The signals from these electrodes were carried by opto-isolated input cables to Grass P5 series pre-amplifiers where they were differentially amplified with a typical gain of 2×10^5 . The bandpass characteristics of the filters at the preamplifiers differed in different experiments and will be described later. These amplified and filtered signals and the sweep trigger were recorded on FM tape and the signals were also averaged on line with a Nicolet model 1170 signal averager. The trigger signal during pattern reversal stimulation was synchronized with the square wave signal used to drive the rotating mirror. The positive-going portion of this wave occurred simultaneously with a pattern shift in one direction and the negative-going portion of the square wave with the pattern shift in the opposite direction. During diffuse flash stimulation a

FIGURE 6. Electrode sites employed.
 a electroretinogram (ERG)
 b visually-evoked cortical potential (VECP)
 c mid-temporal site derived from T4 and T6 = T4.5, T3.5 on left side of head.

photodiode in the visual stimulus path provided the trigger pulse. This ensured that there were no delays between the onset of the trigger and the onset of the light flash stimulus (as can occur when using capacitance discharge systems).

Procedure: The subjects sat on an adjustable chair in an unshielded, sound attenuating chamber and viewed all stimuli with the aid of a chin and forehead rest. The back-projection screen was situated at 95 cm. from the subject's eyes and remained unlit until the beginning of each trial. During monocular trials, a black eye-patch occluded the unused eye. At the beginning of each trial the subject was instructed to relax and fixate the fixation target in the center of the screen. At the completion of each trial a brief rest period was given and the subject was permitted to sit back from the chin/head rest and relax until the next trial was prepared.

During each trial, 256, 512 or 1024 sweeps were averaged in real time. The sweep length was varied depending upon the stimulation frequency. While the trial was in progress, one of the channels (typically that showing the ERG) was monitored for muscle and eye movement artifacts. Otherwise, it was left to the subject to verbally indicate when fixation was lost or when a trial should otherwise be aborted.

At the beginning of each recording session a baseline recording was made using the stimulating and recording parameters of that session but the stimulus was occluded. This provided a control measure of electrical artifact due to the procedure and a measure of the electrical noise level to be expected due to the

procedure, recording environment and physiological state of the observer. When this baseline recording indicated unacceptable noise levels due to muscle artifact, the subject was instructed to contract and relax head and neck muscles prior to recording.

Analysis: The three channels of EEG and the trigger pulse that were recorded on FM tape were played back through the signal averager for presentation purposes and to evaluate the consistency of VERS within each trial by varying the sweep length during averaging. In the case of pattern reversal stimuli, where the trigger was a square-wave, it was possible to average EEG sweeps associated with check movement in one direction separately from or in combination with those associated with check movement in the opposite direction. Averaging both directions in combination averaged out of the records any luminance discontinuity effects to provide a better estimate of the VERS associated with spatial change alone.

The filtered, amplified and signal averaged VER traces from both tape and real-time recordings were initially analyzed as transient waveforms against a 5 microvolts, 20 msec. calibration pulse produced in each recording session. The amplitudes and latencies of consistent major voltage changes in these records were noted and compared to data for similar stimulation and recording conditions that have been published by others. Many of the analyses involved within-subject and between-electrode site comparisons of averaged responses as a function of variables such as stimulus parameters (spatial frequency, temporal frequency) and viewing conditions (monocular, binocular, half field, full field, etc.).

As far as possible, the amplitudes and latencies of major wave peaks were considered in the context of functions across stimulus dimensions within each subject, as opposed to discrete response values associated with one stimulus. It was hoped that this would facilitate the approximate localization of VER generators, comparisons with results presented in the literature and comparisons between subjects.

Due to the large number of measures made here and the small sample sizes employed, it was not considered appropriate to calculate formal statistical measures of between- or within-subject variance. Instead, the individual recordings and the functions relating specific aspects of those recordings to particular stimulus characteristics were compared directly within and between these subjects.

The reliability of these responses was evaluated formally and informally before they were included in such comparisons. This was done by repeating some of the trials on different occasions, and comparing the replications to the originals by visual inspection, or by averaging the two halves of one trial separately and comparing the two resulting waveforms by visual inspection (Perry and Childers, 1969). Since all spatially patterned stimuli involved pattern-reversal, less formal observations of within-trial consistency were made on every recording through the comparison of the VER associated with check movements in each direction. Further details of analyses will be presented with each study.

B. Preliminary Studies

As this was the first study conducted with this apparatus, electrical calibrations were made to ensure equality among the four recording channels (input leads, preamplifiers, signal averager channels and tape channels).

1. Assessment of Apparatus and Methods

After electrical and photometric calibrations of the apparatus were completed, standard VERs were recorded from 3 normal subjects for comparison with accepted norms. These measures included ERGs and VECs elicited with diffuse flash and pattern-reversal stimuli. Samples of the flash and pattern ERGs and VECs are shown in Figure 7. Stimulation and recording parameters and a calibration reference appear with the figure.

With the exception of the PERG, these waveforms are consistent with previously obtained results. The PERG is not typically recorded with this particular electrode derivation due to its small amplitude. There is also a high probability that volume conducted cortical activity might obscure or distort the retinal responses recorded this way. Since the early portion of the PERG waveform is consistent with reports from other labs, it was concluded that this electrode derivation would be adequate at slow stimulation frequencies (transient analysis). The other three response waveforms (ERG, VEC and PVEC) are consistent with previous results and published norms.

2. Active Electrode Sites

Although the measures reported above are consistent with previous reports, it was necessary to establish that the active electrode sites were providing optimal records. Only 4 channels

FIGURE 7. ERG and VECP waveforms. All recorded with (A1 + A2) reference.

could be recorded at any one time so any description of the scalp distribution of visually-evoked activity required successive trials where one channel was kept constant. The intention here was to establish the best active electrode sites in the regions of the occipital pole and the retina rather than the scalp distribution of VEPs per se as this has been described by others (Thickbroom, Mastaglia, Carroll and Davies, 1984).

It has become common practice in some laboratories to record VEPs from an occipital site that is specified as a constant linear distance on the scalp from the inion. In this study it was considered preferable to use electrode sites derived from "10-20" system electrode sites as they are based upon fixed ratios of the distance around the circumference of each subject's skull.

The active electrode sites used for VEP recordings are shown in Figure 6b and some of the results of preliminary recordings are shown in Figure 8. These responses were elicited with full field binocular stimulation. Responses elicited with monocular stimuli showed a similar distribution of electrical activity along the midline in both subjects but were all of lower amplitude. This is consistent with the work of Spekrijse, Estavez and Reits (1977). The recordings from the Oz electrode site (vs. Cz reference) were also equal to or larger than recordings from the other sites for 4 other spatial frequencies. It was concluded that Oz was the optimal site over the range of stimuli employed.

The choice of an active ERG electrode site was governed to some extent by the need for a method that was convenient and

FIGURE 8. VECP waveforms from occipital scalp distribution study. All recorded with Cz reference.

comfortable enough for the subject to allow for 2-3 hour recording sessions. The ERG is often recorded with an active electrode that is in contact with the corneal surface (e.g., gold foil-on-mylar or a contact lens electrode) and a nearby reference such as the ipsilateral canthus, temple or forehead. Since the long-term goal was to record the ERG simultaneously with the VECP and the VER from a mid-temporal location, it was considered desirable to use a physically similar active electrode (1 cm. silver cup electrode) and a reference that would be suitable for the other two sites. By recording ERGs under these conditions it was expected that latency and polarity comparisons among the three responses could be made (ERG, mid-temporal and VECP).

The active ERG electrode locations that were sampled are indicated in Figure 6a and some of the results appear in Figure 9. It can be seen that no PERG responses were recorded at Fpz or Fp2, even though small flash-evoked ERGs were recorded at these sites. Both the flash ERG and the PERG recorded from the lower eyelid are similar to those presented earlier in Figure 7. These results indicate that this electrode derivation (lower eyelid vs. Cz) may not provide an adequate signal-to-noise ratio for all proposed stimulus conditions; especially high spatial frequencies. However, for reasons stated earlier, it was decided that future PERGs would be recorded (at least, initially) with the lower eyelid active electrode.

No preliminary study of VERs in the mid-temporal region was conducted but an attempt was made to replicate the findings of Rubinstein (1981) who recorded simultaneous flash ERGs, VESPs and VECPs and conducted extensive scalp topography studies.

FIGURE 9. ERG waveforms from periocular distribution study. All recorded with Cz reference.

Rubinstein reported that the VESP is best recorded at the electrode sites that lie midway between "10-20 system" sites T3 and T5 ("T3.5") and between T4 and T6 ("T4.5") which are indicated in Figure 6c.

Active electrodes were positioned at the right lower eyelid, T3.5, T4.5 and Oz and all were compared to a linked earlobe (A1 + A2) reference. Due to the reported necessity for a very intense flash stimulus to elicit the VESP (>3900 cd/m.sq.) the ERG electrode was covered with non-reflective black tape to reduce photoelectric artifact. The VER signals were high-pass filtered (30-300 Hz.) and two flash intensities were employed (low = 2500 cd/m. sq. and high = 200 watt seconds).

The simultaneously recorded ERG, VESP and VECF for each stimulus intensity are shown in Figure 10. It can be seen that the lower intensity stimulus was adequate to elicit ERGs and VECFs--but not VESPs. The high intensity data show clear responses at all three levels but the ERG and VECF waveforms from both intensities show evidence of distortion, compared to those shown in Figure 7. This distortion is probably attributable to the unique signal filtering used. The replication of Rubinstein's results was considered successful and the decision was made to employ the T3.5 and T4.5 active electrode sites in the initial attempts to record pattern VERs from the mid-temporal region.

3. Reference Electrodes and Filtering

The VER waveform from a referential recording of the type recorded here is a record of the differences in electrical

FIGURE 10. ERG, VESP and VECP waveforms recorded at two stimulus intensities. At each intensity level the 4 waveforms were recorded simultaneously. A1 + A2 ref. in all cases.

activity between the active and reference electrodes. As such, unique electrical events influencing each electrode are recorded. When a single channel VER is recorded, the best reference is one that is not influenced by visually-driven CNS activity (i.e., visually "silent" brain tissue) but is influenced by non-visually driven electrical activity to the same extent as is the active electrode.

In his study of the flash VESP, Rubinstein (1981) recorded only high frequency EEG activity (30-500 Hz.). This frequency band was probably chosen to reject slow, volume conducted, visually-evoked activity that could obscure the high frequency responses believed to be occurring in the LGN. In view of this consideration and the probability that his bright flash stimulus would drive the "brisk luminance" channel (possibly consisting of "y-like" neurons), the choice of Cz as a reference was appropriate. Rubinstein's interest was in selecting a reference site that was approximately equidistant from the 4 active electrode sites Fpz, T3.5, T4.5 and Oz, so that simultaneous recordings from these could be compared directly. For this reason, too, Cz was a good choice for the reference.

Since it is also the intention here to record simultaneous VERs from similar active electrode sites, similar considerations about the reference electrode were necessary. A major difference between the present study and that conducted by Rubinstein (1981) is in the putative visual channels being stimulated and the response characteristics of cells believed to subserve these channels. It is proposed that the best choices in filtering and referencing for each channel type ("X-like" or "Y-like") are

different. That is, when short latency, phasic responses ("y-like") are to be recorded high-bandpass filtering is appropriate and a reference that is only influenced by slow volume-conducted activity (i.e., below the lower filter setting) is acceptable (e.g. 30-500 Hz. filter setting and a cephalic reference). On the other hand, when slower, tonic responses ("x-like") are to be recorded, it is necessary that slow EEG activity not be filtered out and that the reference electrode be placed out of the influence of such activity (e.g., 0.1-100 Hz. filtering and a non-cephalic reference).

Due to the increased volume of neural tissue devoted to spatial pattern vision in cortex (cortical magnification factor of "x-like" channels from the fovea), compared to that in the retina and LGN, the largest amplitude and possibly most widely distributed visually-evoked activity has a long latency and is relatively sustained (For example, Thickbroom et al., 1984, show significant spread of the PVECP over the scalp 100 msec. following pattern-reversal).

With these considerations in mind, three reference sites (Cz, clavicle and A1+A2) and two signal filtering bands (.3-100 Hz. and 30-300 Hz.) were investigated. Samples of records made under these conditions appear in Figures 11, 12 and 13. In Figure 11 the right lower eyelid was active, in Figure 12 T4.5 was active and in Figure 13 Oz was active.

As might have been expected, the combination of a non-cephalic reference electrode (clavicle) and high-bandpass filtering (30-300 Hz.) resulted in increased high frequency

FIGURE 11. ERG waveforms recorded with different references and filter bandpasses. The stimulus in all cases was a 2500 cd/m² flash (6 fl/sec.).

FIGURE 12. Waveforms recorded at T4.5 with different references and filter bandpasses.

FIGURE 13. PVECP waveforms recorded with different references and filter bandpasses.

noise, mainly muscle artifact and a severely degraded signal-to-noise ratio (SNR). Data recorded with low-pass filtering (.3-100 Hz.) and a clavicle reference also show evidence of extra high frequency noise, apparent waveform distortions and a somewhat degraded SNR (Figures 11a, 12a and 13a). However, these records showed less evidence of what is apparently slow volume conducted activity than did those recorded with a cephalic reference (Cz). While such volume conducted activity can be recognized and taken into account when interpreting data acquired at slow stimulation frequencies (<5 Hz. or 10 reversals/sec), it will overlap inextricably with short latency responses (retinal and LGN) at stimulation frequencies approaching steady-state values for cortex.

It was concluded that these two reference electrode sites (Cz, clavicle) and the high bandpass filter setting (30-300 Hz.) were unsuitable for the present study because the neural activity of interest here is most likely tonic in nature. In addition to the need for an optimal SNR, it was also considered desirable that the PERG and PVECP data here be as similar as possible to those already in the literature. That is, even with a good SNR, the use of a unique referencing or filtering procedure can produce response waveforms with different major peak latencies and other "distortions" (compare Figures 11b and c).

The reference that was chosen for this study is somewhat of a compromise. While the earlobes are connected to the scalp surface, they are removed from the skull ("quasi-cephalic"). In order that any volume conducted activity detected by A1 and A2 is averaged (i.e., such that no left-right difference exists at the

reference), the earlobe leads were linked together electrically before entering the differential amplifiers. The readings made with linked earlobes and low-pass filtering are shown in Figures 11d, 12d and 13d. There is still significant late slow-wave activity in these records but it is somewhat less than that obtained with the Cz reference and the SNR is as good or better. In summary, this recording procedure (lower eyelid, T3.5, T4.5, Oz all referenced to linked earlobes with low-pass filtering) may not be suitable for recording at higher stimulation frequencies but should be adequate for transient analysis and direct comparisons of the pattern-evoked VERS recorded simultaneously at the retina, mid-temporal regions and occipital cortex.

C. Overview of the Main Studies

The following three chapters describe three experiments:

Experiment 1. a limited topographical analysis of the polarity and latency relationships of wavepeaks in VERS recorded simultaneously from three areas: retina, mid-temporal scalp and occipital scalp.

Experiment 2. a comparison between the temporal and spatial tuning characteristics of VERS recorded from the mid-temporal scalp and those recorded from the retina and occipital scalp.

Experiment 3. comparisons between the VERS from the retina, mid-temporal scalp and occipital scalp recorded from one subject with a known pre-geniculate visual system lesion and another with a known post-geniculate visual pathway lesion; comparisons between the three VERS of these two subjects and those recorded from normally-sighted subjects.

The objectives in these experiments were, respectively:

1. to describe the mid-temporal VER and its relationship to the PERG and the PVECP; 2. to determine whether the mid-temporal VER is in any way unique from the PERG or PVECP in its spatial or temporal tuning and 3. to estimate the source of the mid-temporal VER through comparisons in subjects with known visual pathway disruptions.

Chapter III: Limited Topographical Study of Pattern VERS

A. Introduction

This study was conducted to provide an estimate of the scalp distribution of pattern-evoked visual activity. Of particular interest here were the following questions: 1. Do the pattern-reversal VERS recorded at the mid-temporal scalp-sites (T3.5 and T4.5) contain any wave peaks that have different latencies than those in simultaneously recorded PVECPs and PERGs?; 2. How does the mid-temporal VER elicited by half-field stimulation differ from that with full-field stimulation?; 3. Is the PVECP recorded at Oz similar enough to the lateral occipital PVECPs at O1 or O2, during half-field stimulation, to be used in subsequent comparisons with mid-temporal VERS?; 4. Are the PVECPs and the pattern-reversal VERS at T3.5 and T4.5 consistent between subjects for half-field stimuli?; 5. Is there symmetry between the two mid-temporal (T3.5 and T4.5) and between the two occipital (Oz) VERS elicited by left and right half-field stimuli?

As noted in the first chapter, the retinotopic organization of the post-chiasmal visual pathways is such that each half of the visual field is represented in its entirety in the contralateral optic tract, LGN, optic radiations and occipital lobe. Previous studies have demonstrated that half-field pattern-reversal stimulation can be used to selectively stimulate one half or the other of the post-chiasmal visual pathway (Halliday, 1978; Blumhardt, Barrett, Kriss and Halliday, 1982). This procedure has clinical significance because it allows for separate electrophysiological assessment of each half of the

posterior visual pathway. This permits subsequent within subject comparisons as well as comparisons between a patient's VERS and those in a normative data base.

Figure 14 shows a schematic illustration of the portions of the visual system (viewed from above) that are active during binocular, left half-field stimulation (shaded areas). The lower part of this figure shows a magnification of the posterior right quadrant of the head, including a cortical current dipole. In addition, the positions of the active electrodes used in this study are indicated relative to the visual system.

The areas labelled "visual cortex" in this figure refer to Brodmann's Area 17 (striate cortex) that occupies the medial walls of the occipital lobes and includes the upper and lower banks of the calcarine fissures. Each visual half-field is represented at the contralateral occipital lobe with foveal projections near the posterior and peripheral projections in more anterior regions.

When visual stimulation is successfully localized to one half-field (and presumably one occipital lobe), it is not usually the case that the response waveform recorded ipsilateral to the "active" cortical area is the largest or of typical VECF morphology. This phenomenon is referred to as "paradoxical localization" because the largest and best-formed waveforms are recorded over the midline (Oz) and over the "inactive" occipital lobe (O1 in figure 14) (Barrett, Blumhardt, Halliday, Halliday and Kriss, 1976). The usual explanation for this apparent "paradox" is that the primary sources of scalp-recorded VERS are

FIGURE 14. Left half-field stimulation of visual system. The current dipole that would exist at some point in time, in theory, following a pattern reversal is illustrated schematically at the bottom of the figure.

current dipoles that occur between the deep and superficial cortical layers (perpendicular to the laminations) as shown at the bottom of Figure 14.

If occipital scalp electrodes detect visually-evoked current dipoles from the superficial cortical aspect, then VERs recorded from the deep cortical aspect would be expected to have identical peak latencies but opposite polarities. It can be seen in Figure 14 that the end of the current dipole that is in the deep cortical laminae is oriented toward the temporal scalp region. If the magnitude of such a dipole was large enough and the physical conditions suitable for volume conduction, then a VER recorded at a temporal scalp site would contain at least one wave feature that would be the mirror image of that recorded simultaneously over the contralateral occipital pole (i.e., a wave peak with identical latency but of opposite polarity). Such a VECF would obscure visually-evoked LGN activity to temporal scalp electrodes. This theoretical possibility was tested by comparing simultaneously recorded VERs from O1, O2 and Oz with those from T3.5 and T4.5.

The interpretation of half-field VECF waveforms, recorded from active electrode sites lateral to the occipital midline (when using a non-occipital reference), can be very difficult due to variance in occipital pole morphology within (left vs. right) and between normally-sighted individuals (Brindley, 1972; Stansaas, Maddington and Dobelle, 1974). Since the midline electrode site (Oz) is between the two occipital poles and is as close as possible to the two calcarine fissures, it may be the best choice when using half-field stimuli (and a non-occipital

reference) to evaluate each half of the visual pathway independently. However, recordings from Oz may not provide as pure a picture of visually-evoked activity in each occipital lobe as would those from lateral sites such as O1 or O2 because Oz is influenced by current dipoles in both occipital lobes (i.e., it is unlikely that one occipital lobe is actually completely "inactive" during half-field stimulation). So, before further attempts were made to interpret mid-temporally recorded VERS in terms of PVECPs, comparisons were made among the response waveforms from the three occipital sites (O1, O2, Oz) across three stimulation conditions (full-field, left half-field, right half-field).

The next question of interest in this study, relating to the mid-temporal VER during half-field and full-field stimulation, arises from the observation that half-field PVECPs are typically smaller in amplitude than are full-field PVECPs. Furthermore, in a normally-sighted subject, with no history of CNS pathology, it is usually expected that the latencies of wavepeaks in half-field PVECPs will be similar to those from full-field PVECPs. It was hypothesized that if the mid-temporal VER follows this same pattern, then it would seem probable that it monitors the same population of neural generators as the PVECP.

The final two comparisons in this study were aimed at assessing the consistency of half-field, mid-temporal VERS between subjects and within subjects compared to the consistency of PVECPs. If the mid-temporal VER is found to monitor a different aspect of visual activity than the PVECP, it is

necessary that its between-subjects consistency and within-subject (left vs. right) consistency be equally high. Without such consistency, the further analysis and development of the mid-temporal VER as a clinical measure would not seem justified.

B. Method

Since a general method section has already been presented in Chapter II, only details of method that are unique to this study will be described here.

With only a limited number of recording channels available, this limited topographical analysis was carried out in two steps. In the first trial pattern-reversal VERs were recorded simultaneously from the three occipital sites (Oz, O1 and O2) and one mid-temporal site (T4.5). In the second trial, VERs were recorded from both mid-temporal sites (T3.5 and T4.5), one occipital site (Oz) and one retinal site (lower eyelid). The two common electrode sites (Oz, T4.5) were employed to ensure that the recordings in each trial were comparable.

All active electrodes were referred to linked earlobes (A1 and A2) and the signals were filtered with a band pass of .3-100 Hz. The individual checksize in the stimulus fields was 16' and the reversal rate was 3 Hz. (6 reversals per second). The stimuli were presented monocularly and binocularly in full, left half- and right half-fields.

The subjects were three adults (2 males, 1 female, mean age = 28 years) with normal or corrected-to-normal acuity (Snellen Chart) and no history of CNS pathology involving the visual

system. Only one of the subjects (subject 2) had experience as an observer in visual studies.

The recorded VERS were analyzed transiently where the relative amplitudes and latencies of major wave peaks were measured against a 5 microvolt, 20 msec calibration pulse. For the most part, each of the three sets of VERS was analyzed as a case study due to the number of measures made and the small sample size.

C. Results and Discussion

The pattern-reversal VERS, elicited with full- and half-field stimuli viewed binocularly, are presented in Figures 15 (subject 1), 16 (subject 2) and 17 (subject 3). Each figure shows baseline records for the three tape-recorded channels where all stimulus and recording parameters were the same as those during VER recording, except that the stimulus signal was occluded at the final aperture. An amplitude reference appears at the lower left of each figure and the latencies of the major wavepeaks (in msec) are noted on the figures to facilitate visual comparisons. The VER waveforms are organized in columns (in the same order: Oz, O1, O2, T4.5 and T3.5) beneath the symbols showing the stimulus conditions (full-field left half- and right half-fields).

The full-field PVECPs from all subjects are consistent with previously published norms (e.g., Starr, Sohmer and Celestia, 1978; Sokol, 1980) as are the PERGs recorded from the lower eyelid (there are no published norms for this particular electrode derivation but the latencies are similar to those found

FIGURE 15. VER waveforms recorded from subject 1 under three different viewing conditions: full field, left half-field and right half-field binocular. (16' checks, 3 Hz reversal, all referenced to A1+A2). Smaller numbers on figure = peak latencies in msec.

FIGURE 17. VER waveforms recorded from subject 3 under three different viewing conditions: full field, left half-field and right half-field binocular. (16' checks, 3 Hz reversal, all referenced to A1+A2). Smaller numbers on figure = peak latencies in msec.

in records made with corneal electrodes, e.g., Trick and Wintermeyer, 1982). The mid-temporal VERs (T3.5 and T4.5) were not well defined in the full-field stimulus condition and were often inconsistent from trial to trial (the signal-to-noise ratio at these sites was often poor).

The half-field PVECPs from all subjects showed evidence of "paradoxical localization" in that the VER recorded over the occipital pole that was ipsilateral to the visual half-field being stimulated (e.g., O1 for left half-field stimulation) was larger and of more "typical" morphology than the VER recorded over the theoretically active occipital pole (i.e., O2). In all cases, the VER recorded at Oz closely resembled the active occipital pole VER (O1 or O2). Although these subjects all had normal acuity and no history of visual system pathology, only subjects 2 and 3 (Figures 16 and 17) had symmetrical half-field VERs. The right half-field PVECPs recorded from Subject 1 (O2 and Oz in Figure 15) were abnormal in general morphology, smaller in amplitude and had a much earlier latency at what is apparently the 'P100' when compared to the left half-field PVECPs (O1 and Oz). This asymmetry in Subject 1's PVECPs appeared to be reliable since it was observed in other recording sessions with various check sizes. The left half-field PVECPs recorded from Subject 1 were also somewhat unusual in that they were equal to or larger than those elicited with the full-field stimulus. The half-field PVECPs recorded from Subjects 2 and 3 were consistently lower in amplitude than their full-field PVECPs. The only explanation that can be proposed for the asymmetry in Subject 1's half-field PVECPs, given the absence of known visual

system pathology, is an asymmetry in occipital pole morphology.

The half-field VERS recorded at T4.5 and T3.5 were well defined and consistent within and between subjects compared to the full-field VERS recorded at these sites.

On the assumption that the mid-temporal response arises from some part of the posterior visual pathway that is closest to it (ipsilateral LGN, optic radiations or occipital lobe), it was expected that during half-field stimulation the contralateral mid-temporal site would best monitor visually-evoked CNS activity (left half: T4.5; right-half: T3.5). It is of interest that both mid-temporal sites showed VERS during half-field stimulation. The two responses were of approximately equal amplitude and contained peaks with similar latencies but opposite polarities (i.e., they are like mirror images of one another). In terms of the current dipole model of scalp-recorded VERS, discussed in the introduction to this study, this finding strongly suggests that the sources of these half-field mid-temporal VERS lie between T3.5 and T4.5 rather than at more posterior intracranial sources (ie.primary visual cortex).

There are no known normative data for making comparisons with these mid-temporal VER waveforms but they are very similar between these subjects (left 1/2: T4.5 = P53 N64 P83; P50 N69 P85; P55 N69 P89; right 1/2: T3.5 = P55 N68 P84; P48 N73 P87; P56 N70 P90). In the sample of monocular data from Subject 2 (shown in Figure 18) it can be seen that the T3.5 response for right half-field stimulation is similar in overall shape and has similar peak latencies to the binocular response for this Subject

FIGURE 18. Examples of monocular VER waveforms recorded, from subject 2 under two viewing conditions: full field and right half-field monocular (left eye). (16' checks, 3 Hz reversal, all referenced to A1+A2). Smaller numbers on figure = latency in msec.

(Figure 16). This was also found to be the case for the other two subjects and in all cases the amplitudes of the monocular responses were reduced compared to the binocular responses.

There are no cases where the PERG coincides in latency with either the PVECP or the mid-temporal VERs evident in these data (Figures 15, 16, 17 and 18) but there are some strong similarities between the mid-temporal VERs and the PVECPs in the half-field stimulation conditions. These waveforms are redrawn together in Figure 19 (left-half: O1 vs. T4.5; right-half: O2 vs. T3.5) and the wavepeaks of similar latency but opposite polarity in these pairs of waveforms are indicated with arrows. In all six pairs, the earlier negative wavepeak indicated in the mid-temporal VER occurs at the same latency as or earlier (mean = 1.4 msec earlier) than the corresponding positivity in the PVECP waveform. The following positivity indicated in the mid-temporal VER follows the corresponding PVECP negativity (mean = 1.9 msec later) in all cases except the right half-field condition for Subject 1 (T3.5 positivity precedes the O2 negativity by 2.1 msec). These close latency correspondences between the half-field PVECPs and mid-temporal VERs were considered to be at least partially in support of the notion that these two responses might have a common source. However, the portions of these two waveforms that precede and follow the two peaks indicated are considerably less similar and evidence of a dipole source for the T3.5 and T4.5 VERs anterior to visual cortex has already been noted. As a result, no final conclusions were drawn about the uniqueness of the mid-temporal VER.

One way in which the mid-temporal VER does appear to differ

FIGURE 19. Within-subject comparison of mid-temporal half-field VERs with those recorded simultaneously from the ipsilateral occipital lobe (recorded over the contralateral occipital pole). Note that the pairs of waveforms have peaks at similar latencies that are of opposite polarity (arrows in figure). Recording details and latencies with Figures 15, 16 & 17.

FIGURE 20. Within-subject comparison of full-field and half-field mid-temporal VERs. In all cases the half-field VER has a larger amplitude and an earlier peak latency than the full field VER. Recording details with Figures 15, 16 and 17.

form the PVECP is in the consistent difference seen in a comparison of the full-field and half-field waveforms. Whereas the half-field PVECPs were typically smaller in amplitude than the full-field PVECPs, the half-field mid-temporal VERs were consistently larger, earlier and better defined than the full-field mid-temporal VERs (see Figure 20). This difference across the two stimulus conditions was considered as evidence in support of the notion that these two responses have different sources.

The next question of interest relates to the suitability of the Oz electrode site for recording half-field PVECPs. The PVECPs recorded at Oz and the appropriate occipital pole (left-half: O1; right-half: O2) are redrawn together in Figure 21 for direct comparison. With the exception of the right half-field condition for Subject 1, the pairs of PVECPs are strikingly similar. For the purpose of the subsequent comparisons to be made here, it was concluded that half-field PVECPs recorded at Oz would be acceptable in most cases (the 'P100' of Subject 1's Oz PVECP is 7 msec. earlier than the O2 PVECP 'P100' with right half-field stimulation).

The degree of consistency between these Subjects on the half-field PVECP and the mid-temporal VER measures is illustrated in Figure 22. Although the left half-field PVECPs are similar in general morphology and peak latencies, they differ in amplitude between individuals to a greater degree than do the left-half field T4.5 VERs. In the right half-field condition the PVECPs are similar in amplitude but differ in morphology and peak latencies across subjects whereas the T3.5 VERs are once again

FIGURE 21. Within-subject comparison of mid-occipital (Oz) VER with occipital pole (O1 or O2) VER during half-field stimulation. Note similarity between the pairs of waveforms (except Subject 1, right half-field). Latencies and recording details with Figures 15, 16 and 17.

FIGURE 22. Between-subjects comparisons of PVECPs (Oz) and mid-temporal VERs (T3.5, T4.5) with half-field stimulation. Recording details with Fig 15,16&17.

FIGURE 23. Within-subject comparisons of left and right half-field PVECPs* (Oz) and left and right half-field mid-temporal VERs. Recording details with Fig. 15, 16 & 17.

relatively similar (especially between 50 to 100 msec). The greater consistency of the mid-temporal VER was also evident in within subject comparisons of left half- versus right half-field stimulation (Figure 23). Regardless of which occipital electrode sites were used, Subject 1's PVECPs are clearly asymmetrical for half-field stimulation when the simultaneously recorded mid-temporal VERs are not (over the latency period of 50 to 100 msec.). This finding was also interpreted as evidence that the mid-temporal VERs may have different sources from the VERs recorded at Oz (or O2) during half-field stimulation. Furthermore, the high degree of consistency in the mid-temporal VER between subjects and within subjects was considered to be good reason for its further study.

Chapter IV: Spatial and Temporal Tuning of the PERG, Mid-Temporal VER and PVECP

A. Introduction

In the preceding study it was shown that a relatively consistent pattern-reversal VER can be recorded at the mid-temporal scalp sites defined as T3.5 and T4.5. This response was found to have a prominent positivity that peaked at approximately 82 msec. ('P82') following pattern-reversal. Although this 'P82' wavepeak did not appear to be correlated with the PERG, it was very similar in latency to the 'N75' wavepeak of the simultaneously recorded PVECP in two of the three subjects tested. Generally speaking, the 'P82' recorded at T3.5 and T4.5 differed from the 'N75' of the PVECP in the following ways: 'P82' was larger, earlier and more consistently recorded when using contralateral half-field stimuli than when using full-field stimuli; 'P82' showed greater 'between-subjects' consistency than the PVECP; 'P82' showed greater 'within-subject' consistency (left versus right) than the PVECP, especially in one subject whose half-field PVECPs were left-right asymmetrical but whose 'P82' peaks were not.

While these findings alone were not considered to be proof of the uniqueness of the mid-temporal VER, they were considered to suggest that this response may have a different intra-cranial source than the PERG or the PVECP. On the basis of the stimulus tuning characteristics of cells within the LGN that were presented earlier, it would not be impossible for the mid-temporal VER to have as its source either the LGN or visual

cortex.

Stimulus tuning functions for the PERG and PVECP have been reported by other researchers and have usually been interpreted in terms of the stimulus tuning characteristics of the visually excited cells that contribute to the extracranially recorded VER. To some extent, these VER tuning functions reveal the prominence of the various functional channels that are being monitored at particular levels of the afferent visual pathway (discussed in Regan, 1972). The spatial tuning function of the PERG has been described as "low-pass", or more sensitive to low spatial frequencies (Armington, 1974; Trick and Wintermeyer, 1982) and its temporal tuning function as "band-pass", favouring intermediate temporal frequencies between 3.75 and 7.5 Hz. (Trick et al., 1982). At slow reversal rates the PVECP ('P100') has been found to exhibit "band-pass" spatial frequency tuning, favouring checks of 10' to 20' angular subtense (Harter and White, 1968; Harter, 1970). At faster reversal rates it has been reported that there is an interaction of spatial and temporal frequency tuning that results in two maxima in the amplitude of the PVECP (at the stimulation fundamental) for large checks (>30') at approximately 7 and 10 Hz. and one for smaller checks (<15') at 7 Hz. (Regan, 1977 and 1978). The explanation that has been offered for the two maxima in the PVECP temporal tuning function is that there may be cells contributing to the PVECP whose receptive fields are sensitive to local luminance changes and cells whose receptive fields are sensitive to pattern changes (Regan, 1977). This interpretation is consistent with findings

reported by Jeffreys (1977) and Harter (1970) who proposed that high spatial frequencies, or small checks, stimulate primarily foveal receptive fields while low spatial frequencies stimulate parafoveal and peripheral retinal receptive fields.

Considering its retinotopic organization, its functional organization and the stimulus tuning characteristics of its PCL cells (discussed in Chapter I) it seems feasible that pattern VERs might be recorded from the LGN. Furthermore, such pattern VERs might exhibit spatial and/or temporal tuning characteristics that resemble those of PVECPs at some spatial and temporal frequencies but not at others. To test this possibility and to further examine the apparently unique aspects of the mid-temporal VER, simultaneous PERGs, mid-temporal VERs and PVECPs were recorded using a variety of spatial and temporal frequencies viewed in full- and half-fields. With these data, tuning functions were estimated and comparisons among the three responses were made within each of the two subjects.

B. Method

Two subjects were tested in this experiment. Both participated in the previous experiment.

The stimuli were checkerboard patterns like those described earlier. In total, 50 different stimuli were employed with each subject: 5 different check sizes (11', 16', 27', 40' and 62') presented at 5 different reversal rates (1.7 Hz., 3 Hz., 7 Hz., 12 Hz. and 15 Hz.) in binocularly-viewed full- and half-fields.

Active electrodes were situated below one eye, at T3.5, T4.5 and at Oz and linked earlobes (A1 + A2) served as the common

reference. The stimulation and recording procedures were the same as in the previous experiment.

All the recorded waveforms were measured against a 5 microvolt, 20 msec. calibration pulse. At 1.7 Hz. and 3 Hz. the amplitudes and latencies of the 45-65 msec. PERG positivity, the 'P82' of the mid-temporal VER and the 'N75' and 'P100' of the PVECP were measured. At 7, 12 and 15 Hz., the low-pass nature of the visual pathway renders a nearly sinusoidal VER. Consequently, the amplitude of the largest response that followed the fundamental stimulation frequency was taken as the dependent measure.

Since half-field stimulation was found to be optimal for eliciting the mid-temporal VER in the last study, an emphasis was placed upon the analysis of these data and the relationships between waveforms recorded with full-field stimuli and those recorded with half-field stimuli. In addition, functions relating the wavepeak amplitudes to spatial and temporal stimulation frequency were estimated for the full-field PERG, the contralateral, half-field, mid-temporal VER and the simultaneously recorded PVECP.

C. Results and Discussion

Examples of the half-field VERs recorded from Subject 1 are presented in Figure 24a and b. At the two slower reversal rates, 1.7 Hz. and 3 Hz., it can be seen that up to approximately 100 msec., the T4.5 response (dotted line) is in approximate antiphase with the PVECP response (solid line) for different checksizes. However, at higher reversal rates (7 Hz., 12 Hz. and

FIGURE 24a. Examples of mid-temporal VERs (dotted) and PVECPs (solid) recorded from Subject 1 using left half-field stimuli viewed binocularly. Reversal frequency is noted above each column and check size at the right of each pair of waves. The time base changes for each column and there are two amplitude calibrations for the 3 Hz. data (only) (ie. all T4.5 waves in this column are drawn at 2X gain).

FIGURE 24b. Further examples of mid-temporal VERs and PVECPs from Subject 1. See caption with Figure 24a for details.

15 Hz.) the T4.5 response no longer appears to be in antiphase with the PVECP and undergoes changes in its harmonic content when the PVECP does not. Such changes in the spectral composition of high frequency mid-temporal VERS were not consistent enough across these two subjects to merit formal analysis but would appear to be worthy of further study.

The latency relationships among the two half-field VERS and the full-field PERG at 1.7 Hz. and 3 Hz. stimulation rates are plotted as functions of checksize in Figures 25a and b and 26a and b. In each of these figures the upper points of the PVECP graphs "(+)" refer to the 'P100' and the lower points "(-)" refer to the 'N75'. The upper points in the T3.5 and T4.5 graphs "(+)" refer to 'P82' and the lower points refer to the preceding negativity. The lower two sets of points show the PERG positivity latencies "(+)" and its approximate starting points "(-)". At 1.7 Hz. (Figure 25a), it can be seen that the positivity in the mid temporal VER recorded at T4.5 from Subject 1 precedes the 'N75' of the PVECP at all checksizes except 40'. Although their latencies are close, this finding is not consistent with the proposition that the T4.5 response is volume conducted from a common cortical source that is shared with the 'N75' of the PVECP. In Figure 25b, the T3.5 positivity recorded from Subject 2 only precedes the 'N75' of his PVECP for 11' checks and 62' checks but the latency difference is more than 5 msec. in both cases. At intermediate checksizes, Subject 2's T3.5 positivity follows the PVECP 'N75' by more than 5 msec. and this is also inconsistent with the above proposition. At 3Hz. (Figures 26a and b) the pattern is similar for Subject 1, but in

FIGURE 25a. Latency relationships among the major positivities(+) and negativities(-) of the PERG and left half-field PVECP and T4.5 responses from Subject 1, recorded with five different checksizes at 1.7Hz.

FIGURE 25b. Latency relationships among the major positivities(+) and negativities(-) of the PERG and right half-field PVECP and T3.5 responses from Subject 2, recorded with five different check sizes at 1.7 Hz.

FIGURE 26a. Latency relationships among the major positivities(+) and negativities(-) of the PERG and left half-field PVECP and T4.5 responses from Subject 1, recorded with five different checksizes at 3 Hz.

FIGURE 26b. Latency relationships among the major positivities(+) and negativities(-) of the PERG and right half-field PVECP and T3.5 responses from Subject 2, recorded with five different checksizes at 3 Hz.

Subject 2's data it can be seen that the T3.5 'P82' follows the PVECP 'N75' at all checksizes by 5 or more msec. in most cases.

If the T3.5 positivity and the PVECP 'N75' at each checksize were due to a common dipole source, it would be expected that the differences in their latencies would only be due to differences in the conductivity of the tissues intervening between that dipole and the two recording electrodes and differences in the distances between each end of the current dipole and each respective recording electrode. Since such factors would be expected to produce a constant delay, it seems unlikely that they alone could account for these findings. Therefore, it is concluded that either these two responses have different sources or that the source is closer to T4.5 than Oz in Subject 1 and closer to Oz than T3.5 in Subject 2.

With few exceptions, the PERG positivity precedes the T3.5/T4.5 negativity; suggesting that they are independent responses. It is of interest that the PERG shows "low-pass" spatial tuning in its latency in both these subjects in that the PERG positivity is earlier for lower spatial frequencies (larger checks). This finding has been reported before by Arden, Vaegan and Hogg (1982) who suggest that it may reflect the duration of the spatial summation within the receptive fields of the cells that give rise to the PERG.

In the previous chapter it was noted that the main positivity in the half-field, mid-temporal VER had a shorter latency and larger amplitude than the comparable positivity in the full-field, mid-temporal VER. Since this relationship was not found in the 'N75' of the PVECP it was proposed that this

difference might indicate some degree of independence between these two responses. Figures 27 and 28 show the latency and amplitude differences for this same comparison (full-field - half-field) at 1.7 Hz. and 3 Hz. as a function of checksize. In Figure 27, it can be seen that the full-field, mid-temporal VER was always later than the half-field VER (solid lines) at both reversal rates and at all checksizes by virtue of the positive latency difference. In contrast, the latency of the 'N75' of the half-field PVECP (broken lines) was often later (negative values) or at the same latency as that of the full-field PVECP.

Comparisons of full-field and half-field VER amplitudes are shown in Figure 28. Half-field VER amplitudes were subtracted from full-field VER amplitudes in this figure. Negative amplitudes indicate that the half-field response was larger for Subject 1 and all T4.5 response amplitudes were larger for half-field stimuli. For Subject 2, most T3.5 responses were the same size or larger for half-fields (solid lines). Although these differences appear to be small, in absolute terms, they represent substantial percentages of the half-field, mid-temporal VER amplitudes which ranged between 1 and 2 microvolts. The 'N75' of the PVECP (broken lines) which was typically twice the size of the simultaneously recorded mid-temporal VER, was always larger for full-field stimuli than for half-field stimuli in Subject 2's data. In Subject 1's data, the PVECP 'N75' was larger for half-field than for full-field stimuli at 1.7 Hz when the checksize was small, and for all but the largest checksize at 3 Hz.

These findings were considered to be consistent with the

FIGURE 27. Comparisons of latency differences between full- and half-field VEPs recorded at Oz (dotted lines) and at one mid-temporal electrode site (solid lines) with two reversal rates and five different checksizes. The mid-temporal electrode site was contralateral to the half-field stimulated for each subject. A positive latency difference indicates that the half-field response was earlier than the full-field response for that particular stimulation frequency and checksize and a negative latency difference indicates that the half-field response was later.

FIGURE 28. Comparisons of amplitude differences between full- and half-field VERs recorded at Oz (dotted lines) and at one mid-temporal electrode site (solid lines) with two reversal rates and five different checksizes. The mid-temporal electrode site was contralateral to the half-field stimulated for both subjects. A negative amplitude difference indicates that the half-field response was larger than the full-field response for that particular stimulation frequency and checksize. A positive difference indicates that the half-field response was smaller than the full-field response for the same stimulus.

earlier proposals that the mid-temporal VER is largest and earliest for contralateral half-field stimulation and that its primary positivity ('P82') differs from the 'N75' of the PVECP in this regard. For the most part, these data show that this relationship holds for checks between 11' and 62' and at two temporal frequencies.

The rationale for making comparisons between full- and half-field VERs stems from the fact that the contralateral half-field of vision is represented in its entirety in the posterior portion of each half of the visual pathway, from the optic tract to striate visual cortex. In view of this, it was expected that half-field VERs that monitor only electrical activity within the CNS that is adjacent to the active electrodes employed, would be equal to, or slightly smaller than, full-field VERs recorded at these same scalp locations. Half-field VERs are always larger at mid-temporal sites than are full-field VERs. They are often larger at Oz as well. This suggests that some type of cancellation occurs when only half of the visual field is stimulated. One explanation that can be offered here is in terms of the current dipole model that would predict dipole cancellation when two symmetrical current dipoles oppose one another in polarity and are oriented end-to-end (Llinas and Nicholson, 1974; Schlag, 1973; Vaughan, 1982). If two such dipoles only co-exist during full-field stimulation, then a situation exists where dipole cancellation would prevent the detection of either dipole from a scalp recording site during full-field stimulation; but not during half-field stimulation

FIGURE 29a. Temporal tuning functions for PERGs recorded with 5 different checksizes from Subject 1. Checksize is indicated on the left of the figure beside the symbols. All points represent amplitude normalized to the largest PERG amplitude obtained from this subject.

FIGURE 29b. Temporal tuning functions for PERGs recorded with 5 different check sizes from Subject 2. Checksize is indicated on the left of the figure beside the symbols. All points represent amplitude normalized to the largest PERG amplitude obtained from this subject.

FIGURE 29c. Temporal tuning functions for the mid-temporal VERs recorded with 5 different checksizes from Subject 1. All stimuli were contralateral 1/2-fields viewed binocularly. Checksize is indicated on the left of the figure beside the symbols. All points represent amplitude normalized to the largest mid-temporal VER obtained from this subject.

FIGURE 29d. Temporal tuning functions for the mid-temporal VERs recorded with 5 different checksizes from Subject 2. All stimuli were contralateral 1/2-fields viewed binocularly. Checksize is indicated on the left of the figure beside the symbols. All points represent amplitude normalized to the largest mid-temporal VER obtained from this subject.

FIGURE 29e. Temporal tuning functions for the binocular half-field PVECPs recorded with 5 different checksizes from Subject 1. Checksize is indicated on the left of the figure beside the symbols. All points represent amplitude normalized to the largest PVECP obtained from this subject.

FIGURE 29f. Temporal tuning functions for the binocular half-field PVECPs recorded with 5 different checksizes from Subject 2. Checksize is indicated on the left of the figure beside the symbols. All points represent amplitude normalized to the largest PVECP obtained from this subject.

1 differ from those of Subject 2. Whereas Subject 2's functions show generally "band-pass" temporal tuning around 7 Hz., Subject 1's functions show "low-pass" temporal tuning below 7 Hz. The functions of both subjects differ from their respective PERG functions in that they show greater relative sensitivity to checksize at 1.7 Hz. and 3 Hz. reversal rates.

The temporal tuning functions for the half-field PVECP are shown in Figures 29e and f. These functions differ from both sets of functions already presented in that they show greater relative sensitivity to checksize at higher temporal frequencies. Neither Subject's functions show two maxima like those described by Regan (1977) for full-field stimulation. Subject 1's data show peaks at 1.7 Hz. and 7 Hz. for all checksizes but '62'. This is similar to the mid-temporal VER functions for this subject except that those had a higher relative amplitude at 3 Hz. Subject 2's PVECP functions generally show "band-pass" tuning characteristics between 3Hz. and 12 Hz. for most checksizes. They show clearly different temporal tuning from the T3.5 VER functions shown for this Subject in Figure 29b.

The temporal tuning differences seen among these three sets of functions from both subjects were considered to be consistent with the proposition that the three responses have different sources within the visual pathway.

The spatial tuning functions at each temporal frequency are shown in Figures 30, 31, 32, 33 and 34. In all cases the amplitudes of the VERs at each electrode site were normalized to unity so that the relative amplitudes of the various responses

FIGURE 30a. Spatial tuning functions for VEPs recorded from Subject 1 using a pattern-reversal rate of 1.7 Hz. The PERG was recorded with a full-field stimulus while the other VEPs were recorded with binocular half-field stimuli as indicated in the figure. The values for each response represent amplitudes normalized to the largest response recorded at that electrode site with this stimulation frequency.

FIGURE 30b. Spatial tuning functions for VERs recorded from Subject 2 using a pattern-reversal rate of 1.7 Hz. The PERG was recorded with a full-field stimulus while the other VERs were recorded with binocular half-field stimuli as indicated in the figure. The values for each response represent amplitudes normalized to the largest response recorded at that electrode site with this stimulation frequency.

FIGURE 31a. Spatial tuning functions for VEPs recorded from Subject 1 using a pattern-reversal rate of 3 Hz. The PERG was recorded with a full-field stimulus while the other VEPs were recorded with binocular half-field stimuli as indicated in the figure. The values for each response represent amplitudes normalized to the largest response recorded at that electrode site with this stimulation frequency.

FIGURE 31b. Spatial tuning functions for VERs recorded from Subject 2 using a pattern-reversal rate of 3 Hz. The PERG was recorded with a full-field stimulus while the other VERs were recorded with binocular half-field stimuli as indicated in the figure. The values for each response represent amplitudes normalized to the largest response recorded at that electrode site with this stimulation frequency.

FIGURE 32a. Spatial tuning functions for VERs recorded from Subject 1 using a pattern-reversal rate of 7 Hz. The PERG was recorded with a full-field stimulus while the other VERs were recorded with binocular half-field stimuli as indicated in the figure. The values for each response represent amplitudes normalized to the largest response recorded at that electrode site with this stimulation frequency.

FIGURE 32b. Spatial tuning functions for VERS recorded from Subject 2 using a pattern-reversal rate of 7 Hz. The PERG was recorded with a full-field stimulus while the other VERS were recorded with binocular half-field stimuli as indicated in the figure. The values for each response represent amplitudes normalized to the largest response recorded at that electrode site with this stimulation frequency.

FIGURE 33a. Spatial tuning functions for VEPs recorded from Subject 1 using a pattern-reversal rate of 12 Hz. The PERG was recorded with a full-field stimulus while the other VEPs were recorded with binocular half-field stimuli as indicated in the figure. The values for each response represent amplitudes normalized to the largest response recorded at that electrode site with this stimulation frequency.

FIGURE 33b. Spatial tuning functions for VERs recorded from Subject 2 using a pattern-reversal rate of 12 Hz. The PERG was recorded with a full-field stimulus while the other VERs were recorded with binocular half-field stimuli as indicated in the figure. The values for each response represent amplitudes normalized to the largest response recorded at that electrode site with this stimulation frequency.

FIGURE 34a. Spatial tuning functions for VERs recorded from Subject 1 using a pattern-reversal rate of 15 Hz. The PERG was recorded with a full-field stimulus while the other VERs were recorded with binocular half-field stimuli as indicated in the figure. The values for each response represent amplitudes normalized to the largest response recorded at that electrode site with this stimulation frequency.

FIGURE 34b. Spatial tuning functions for VEPs recorded from Subject 2 using a pattern-reversal rate of 15 Hz. The PERG was recorded with a full-field stimulus while the other VEPs were recorded with binocular half-field stimuli as indicated in the figure. The values for each response represent amplitudes normalized to the largest response recorded at that electrode site with this stimulation frequency.

could be compared across the range of checksizes. At 1.7 Hz. and 3 Hz. it was possible to plot the spatial tuning function for the 'N75' of the PVECP as well as the 'P100'. At 7 Hz., 12 Hz. and 15 Hz. all responses became sinusoidal. Consequently, only the amplitude of the fundamental was measured. This waveform probably reflects the 'P100' at lower temporal frequencies.

Consistent with previous reports, the PERG functions for both subjects show "low-pass" spatial tuning at 1.7 Hz. and 3 Hz. However, enhanced sensitivity to high spatial frequencies (small checksizes) was evident at faster reversal rates. Since some of these functions resemble those of the PVECP (Figures 33a and 34b) it is quite possible that the PERGs recorded with this particular electrode derivation may, in fact, be volume conducted from visual cortex at higher temporal frequencies (>7 Hz.). This possibility was recognized in the pilot study (Chapter II) where a variety of reference electrodes and signal filter settings were examined.

The mid-temporal VER functions show some degree of independence from the 'N75' PVECP functions at 1.7 Hz. and 3 Hz. (Figures 30a and b and 31a and b) but are very similar to the PVECP functions at 12 Hz. (Figures 33a and b). Since the shapes of the T3.5/T4.5 functions show considerable variation between these two subjects at all temporal frequencies, the spatial tuning characteristics of the mid-temporal VER cannot be generalized beyond the finding that it differs from both the PERG and the PVECP under the same stimulation and recording conditions.

The PVECP functions also differ for the two subjects but the

difference is consistent across all temporal frequencies. With only one exception (Figure 31a), Subject 1's PVECP functions show peak sensitivity for 11' checks ("high-pass" tuning) and Subject 2's 'Pl00' functions show peak sensitivity for 16' checks ("band-pass" tuning). Subject 2's 'N75' functions strongly differ from the 'Pl00' functions, at 1.7 Hz. and 3 Hz., in that the 'N75' functions show lower sensitivity for 16' checks and peak sensitivity for 11' checks (Figures 30b and 31b).

Since the PVECP data were recorded simultaneously with the T3.5/T4.5 functions, and the PVECP functions are consistent with previously published spatial tuning data (Harter and White, 1968; Harter, 1970), it was concluded that the spatial tuning of the mid-temporal VERs may be more reliable than their inter-subject variability suggests. This supports the conclusion that the spatial tuning of the mid-temporal VER is reliably different from that of the PVECP. It shows no consistent peak sensitivity across this range of temporal rates and may be highly variable between subjects.

In summary, the various comparisons among the mid-temporal VER, PERG and PVECP, over a range of spatial and of temporal stimulation frequencies, suggest that the mid-temporal VER is likely a unique response. Since the methods employed here are not adequate for source localization, it cannot be stated conclusively that the apparently unique spatial and temporal tuning aspects of the mid-temporal VER that were found indicate that it has a different intracranial source from the PVECP. In order that this might be decided, a further experiment was

carried out where the subjects had specific, well defined lesions at different levels of the visual pathway.

Chapter V. The Most Likely Sources of the Mid-Temporal VER and Its Assessment as a Clinical Measure

A. Introduction

The data presented in the last two chapters were interpreted as evidence that a pattern-reversal mid-temporal VER can be recorded from normally-sighted individuals and that this VER : (1) is consistent between and within (left versus right) individuals, even when simultaneously-recorded PVECPs do not show between- or within-subject consistency; (2) shows independence in its spatial and temporal tuning from the PERG and the simultaneously recorded half-field PVECP, and (3) may have a different intra-cranial source than the PVECP.

In order that the apparent independence of the pattern-reversal mid-temporal VER from the PVECP might be further tested and some estimate of its source determined, similar VER recordings were made from two subjects with well described visual system disruptions. One of these subjects had a history of left posterior temporal lobe tumor and had undergone surgery for its excision in 1974. Post-operatively, this young woman was found to have a right homonomous upper-quadrant field defect that was showing signs of deteriorating into a right homonomous hemianopsia in the year previous to this VER assessment. A computed axial tomography (C.T.) scan, completed two months prior to this testing, revealed increased density in the left posterior temporal/occipital region, consistent with re-occurrence of this tumor. All clinical data about this subject indicated a left post-lateral geniculate nucleus disruption of the visual pathway

involving the optic radiations and possibly the left occipital lobe. It was therefore anticipated that half-field pattern-reversal VERs from this subject might provide evidence for the proposition that the mid-temporal VER has its source at, or anterior to, the LGN.

The second subject had undergone a transphenoidal pituitary resection in 1981. Pre-operatively, this young woman had showed evidence of diplopia, reduced acuity in the right eye (20/70) and a bitemporal hemianopic field defect that showed some sparing of function in the left lower quadrant of the left eye. Post-operatively, this subject had a bitemporal hemianopic field defect that split the macula of the right eye and encroached upon the upper nasal macular region of the left eye but the diplopia that had been present pre-operatively had disappeared within 24 hours post-operatively. No C.T. scan was completed for this subject but the nature of the surgical procedure undergone and the bitemporal visual field defect revealed by perimetry provided adequate evidence to conclude that the visual pathway disruption was in the region of the optic chiasm. The nature of the asymmetry in the bitemporal visual field defect suggests that the chiasmal disruption involves the left side of the optic chiasm more than the right and may involve the left optic tract. Since all clinical evidence about this subject indicated that her visual pathway disruption was totally localized anterior to the LGN, she was considered to be an appropriate subject for comparison with the first subject whose visual disturbance was most probably localized posterior to the LGN.

The hypothesis in this comparison was as follows: If the source of the mid-temporal VER, elicited with a contralateral half-field stimulus, is different from that of the simultaneously recorded PVECP, and the T3.5-T4.5 electrode monitors visual activity that occurs earlier than that monitored by the Oz electrode, then the left-right symmetry of the mid-temporal VERs recorded from the first subject (post-LGN disruption) should resemble those reported earlier from normally-sighted subjects (Figure 23 in Chapter III). Mid-temporal VERs recorded from the second subject however should be asymmetrical for monocular and/or binocular stimulation because of the disruption of the pregeniculate pathway. It was reasoned that the assessment of the data, in terms of this experimental hypothesis, would allow for conclusions regarding the identity of the mid-temporal VER source as being the same as, or different from, PVECP sources.

B. Method

The clinical backgrounds of the two subjects in this study have been discussed above. The first subject, 'SC' a young woman 25 years of age, had a history of left posterior temporal lobe tumor (oligodendroglioma). Based upon clinical evidence, (C.T. scan and perimetry) SC was believed to have a post-LGN visual pathway disruption on the left side. SC had visual acuity that was optically corrected to normal in both eyes: right 20/15, left 20/20. The second subject, 'SB', a young woman 28 years of age, had a history of pituitary tumor (pituitary adenoma). Clinical evidence (surgery and perimetry) suggested that SB had a visual pathway disruption in the region of the optic chiasm and

left optic tract. This subject's acuity was optically corrected to near-normal in both eyes: right eye 20/30, left eye 20/25.

The electrophysiological measures included full- and half-field VERS recorded from T3.5, T4.5 and Oz and full-field PERGs. The stimuli were checkerboard patterns like those described earlier and contained checks of 16', 40', or 62' that were reversed in luminance at 3 Hz. The recording methods were the same as those described earlier. In all trials, the four VERS were recorded simultaneously. Three of these were stored on tape with the stimulus trigger pulse for subsequent transient analysis.

Within-subject comparisons of half-field VERS were made for each subject. The results of these comparisons were in turn compared between SC and SB and with the results of similar comparisons made on data from the normally-sighted subjects of Chapter III.

C. Results and Discussion

The full-field binocular VERS recorded from the two subjects are shown in Figures 35 and 36. These figures show the simultaneously recorded PERG, T4.5 VER and PVECP at each of three spatial frequencies and the associated spatial tuning functions.

The PERGs of both subjects are comparable to those recorded earlier and show "low-pass" spatial tuning. The mid-temporal VERS from SC are quite similar to full-field mid-temporal VERS recorded from normally-sighted subjects (Figures 15, 16 and 17). Those of SB however, are earlier, larger in amplitude and better defined. The full-field T4.5 responses recorded from SB are

FIGURE 35. Full-field binocular VERs from Subject SC. Reversal rate = 3Hz, A1+A2 reference, checksize indicated on left of waveforms, smaller numbers on figure = msec.

Spatial Tuning (3 Hz)

FIGURE 36 . Full-field binocular VERs from Subject SB. Reversal rate = 3Hz, A1+A2 reference, checksize indicated on left of waveforms, smaller numbers on-figure = msec.

comparable to contralateral half-field responses from normally-sighted subjects. The PVECPs from SC are all grossly normal in morphology but all show delayed 'Pl00' latencies. The PVECPs recorded from SB are also normal in morphology but show normal 'Pl00' latencies.

The PVECPs from these subjects also differ in 'Pl00' spatial tuning. Whereas SC's data show "high-pass" spatial tuning, SB's PVECPs show little evidence of spatial tuning across this range of checksizes. This apparent lack of spatial tuning in SB's data is consistent with her reduced acuity (Harter and White, 1968) as noted earlier. In spite of a possibly reduced sensitivity to 16' checks in SB, the PVECP elicited from her with this checksize had an amplitude comparable to that of SC and the other subjects, whose data were described earlier. For this reason, it was decided that 16' checks would be employed for recording half-field VERs for comparison with SC and the three subjects discussed in Chapter III.

The full- and half-field VERs recorded with 16' checks reversing at 3 Hz. are presented in Figures 37 and 38. The full-field data for both subjects are comparable to those shown in the previous figures but in this case the T3.5 VERs are shown as well as the T4.5 responses. It can be seen that in SC's data (Figure 37) the T3.5 response appears as the mirror-image the T4.5 response but that this was not the case for SB (Fig. 38). The T3.5 VER recorded from SB differs substantially from that recorded from SC but the T4.5 responses from both subjects are comparable up to approximately 100 msec. As was noted earlier the subjects' T4.5

FIGURE 37 Full- and half-field VEPs from Subject SC. 16' checks, 3 Hz reversal, A1+A2 reference, smaller numbers on figure = msec. Left and right PERGs shown at lower left and control recordings at lower right. All stimuli viewed binocularly.

FIGURE 38. Full- and half-field VERs from Subject SB. 16' checks, 3 Hz reversal, A1+A2 reference, smaller numbers on figure = msec. Control recordings shown at lower right. All stimuli viewed binocularly.

responses differ in that the 'P82' from SB is somewhat earlier and slightly better defined.

The half-field PVECPs, recorded from SC (Figure 37) are consistent with her homonomous hemianopic field defect, as reported earlier, in that the left half-field response is quite similar to the full-field response but the right half-field response is not. The right half-field PVECP is distorted and of low amplitude. In contrast, the mid-temporal VERS recorded with contralateral half-field stimuli are similar up to 83 msec. (left 1/2 field: T4.5; right 1/2 field T3.5). Beyond 83 msec. these responses differ in that the T3.5 response appears to lack the slow negativity that was recorded at T4.5.

The half-field VERS recorded from SB are shown in Figure 38. Unlike SC's half-field PVECPs, neither of SB's half-field PVECPs resemble the full-field response. This is not surprising for binocular stimulation in view of this subject's bitemporal hemianopic field defect as revealed through perimetry. However, the T4.5 response for left half-field stimulation is similar to that recorded from SC and to the contralateral half-field, mid-temporal VERS recorded from normally-sighted subjects. The analogous T3.5 response for right half-field stimulation is not comparable to the T4.5 VER in this subject or to any of the mid-temporal VERS recorded from the other subjects. In SB's T3.5 response, the 'P82' occurs at 97 msec. compared to 82 msec. for the T4.5 response and all other mid-temporal VERS recorded from the other subjects under comparable stimulus conditions. In addition, the late negativity (N126) in SB's right half-field T3.5 response is delayed compared to the left half-field T4.5

response.

Monocular full- and half-field VERS were also recorded from both subjects. These data were of particular interest for SB due to the nature of this subject's bitemporal field defect. Since the monocular data from SC revealed no significant differences between the two eyes and are of less relevance to, the current discussion, only SB's monocular VERS are presented (Figure 39).

For full-field stimulation, only SB's right monocular VERS resemble her binocular full-field VERS at these same electrode sites. The right monocular PVECP has a 'P100' that is larger in amplitude than her binocular PVECP, but it is delayed by approximately 8 msec. In general, all left monocular responses, for all viewing conditions, are lower in amplitude and distorted in morphology compared to the right monocular VERS. This difference is especially pronounced for the left and right half-field PVECPs where the left monocular PVECP for left half-field stimulation is virtually non-existent. The right half-field PVECP from the left eye has peak latencies that are very similar to this subject's full-field binocular PVECP (Figure 38) but is of very low amplitude. The right monocular half-field PVECPs are abnormal as were the binocular half-field PVECPs. They are, however, symmetrical for the two half-fields of the right eye. These PVECP results suggest that both half-fields of both eyes are somewhat abnormal but that the left half-field of the left eye is most abnormal as monitored at Oz.

The only monocular, mid-temporal VER (for half-field stimulation) that resembles those presented earlier is the right

FIGURE 39 . Monocular full- and half-field VERs from Subject SB. 16 checks, 3 Hz reversal, A1+A2 reference, smaller numbers on figure = msec.

monocular response at T4.5 for left-field stimulation (P_{82} latency = 78 msec.). This is consistent with the finding of normality in the nasal hemi-field in the right eye as revealed through perimetry. The analogous T3.5 response for right half-field stimulation of the left eye does show a small positive peak at 79 msec. but the amplitude of this response is very small. If this small positivity is in fact the T3.5 P_{82} that has been reported for the other subjects, then it could be viewed as evidence for right half-field input from the left eye. This would be consistent with the perimetry results that indicate relatively normal function in the nasal hemi-field of the left eye. These monocular results for SB might be summarized as showing some consistency with this subject's perimetry data at both the mid-temporal electrode sites and, to a lesser extent, at Oz. The monocular PVECPs reveal that only the left half-field of the left eye is distinctly abnormal on the basis of within-subject comparisons.

These VERS, recorded from two subjects with well described visual pathway disruptions, were found to be consistent with the proposition that the mid-temporal VER, recorded with contralateral half-field stimulation, is different from simultaneously recorded PVECP and probably has a different source.

Within-subject comparisons of the subjects' binocular half-field VERS are presented in Figure 40. In SC's data it can be seen that left-right symmetry is present in the mid-temporal VERS at approximately 82 msec., but not in the simultaneously recorded PVECPs. Since this subject was known to have a left posterior

FIGURE 40. Binocular half-field PVECPs and contralateral mid-temporal VERs from Subjects SC and SB showing the degree of left-right symmetry in each. Note the apparent delay in SB's T3.5 response for right half-field stimulus. No such delay is present in SC's mid-temporal responses. Details of recording with Figures 37 and 38.

pathway disruption (post-LGN), the lack of left-right symmetry of the PVECPs and the presence of left-right symmetry in the 'P82' of the mid-temporal VERs is interpreted as revealing the source of the PVECP posterior to this disruption and the source of the 'P82' of the mid-temporal VER anterior to the disruption. The lack of left-right symmetry in SB's mid-temporal VERs is consistent with this interpretation because SB was known to have an anterior pathway disruption involving the optic chiasm and left optic tract (pre-LGN). Considering the other characteristics of the mid-temporal VER, discussed in Chapters II and III, along with these findings, it is proposed that this VER monitors visually-evoked subcortical activity related to spatial pattern vision.

Chapter VI. Summary and Conclusions

The foregoing studies were conducted to describe pattern-reversal VEPs that can be recorded at electrode sites located in the mid-temporal scalp region. In previously published reports, these electrode sites, called 'T3.5' and 'T4.5', have been employed to record diffuse flash VEPs that were attributed to the lateral geniculate nucleus (Harding and Rubenstein, 1980; 1982). Since the LGN represents an intermediate stage in the retinocortical pathway, the possibility of monitoring its function extra-cranially has significant clinical utility for localizing disruptions of the visual pathway.

It was pointed out earlier that the high intensity flash of diffuse light, employed as a stimulus by Harding and Rubenstein, limited the clinical utility of the visually-evoked subcortical potential (VEEP) because diffuse light is difficult to control as a stimulus and because diffuse flash-evoked visual responses are not known to be consistent in detecting retinocortical pathway disruptions. Since spatially-patterned visual stimuli are easy to control and have been found to show consistency in detecting various types of visual system pathology, they are the preferred stimuli for clinical investigations. However, no reports of pattern VEPs have appeared in the literature. The spatial pattern visual channel has historically been monitored from electrodes only near retina and visual cortex.

Prior to reporting on the present attempts to record pattern VEPs, comparative neurophysiological research findings regarding the stimulus tuning characteristics of LGN neurons

were discussed. In addition, theoretical arguments were presented in support of the proposal that pattern evoked LGN activity might be detected at the scalp surface.

As T3.5 and T4.5 were reported to be the best electrode sites for recording the VESP using diffuse light stimuli, these same sites were chosen for the present studies of the pattern VESP. In the first study reported here it was established that a pattern-reversal VER can be recorded at these scalp locations and relationships between this VER and the simultaneously recorded PERG and PVECP were described. The pattern-reversal VER amplitudes from T3.5 and T4.5 were found to be optimal with contralateral half-field stimuli and showed left-right symmetry in all subjects.

The prominent feature of this mid-temporal VER was found to be a positivity at approximately 82 msec. following each stimulus event. Although this 'P82' wavepeak appeared to be highly correlated with the 'N75' wave of the simultaneously recorded PVECP in two of the subjects, it showed some differences from the cortical response which suggested that it might be a unique VER. In one of the subjects, the mid-temporal VERs were found to show left-right symmetry for contralateral half-field stimulation when the corresponding PVECPs did not. In addition, the mid-temporal VER showed independence from the PVECP in that the 'P82' recorded at T3.5 and T4.5 was clearer, earlier and larger in amplitude for half-field stimulation than for full-field stimulation. This same phenomenon was not consistently observed in the 'N75' of the PVECP.

In all three of these subjects, it was found that a negativity recorded at the mid-temporal scalp site ipsilateral to the half-field stimulated, appeared as the "mirror image" of the "P82" recorded contralateral to the stimulus half-field. This was interpreted as evidence for an intracranial current dipole source between T3.5 and T4.5, anterior to visual cortex.

These suggestions of independence between the mid-temporal VER and the PVECP were further investigated in the second study where spatial and temporal tuning functions were estimated for them and for the PERG. As in the first study, it was found that the enhancement of half-field mid-temporal VERs, was evident in the data of both subjects, with virtually all checksizes, when the rate of pattern-reversal was slow (1.7 Hz. and 3 Hz.). This same phenomenon was only observed on a few occasions for the 'N75' of the PVECP. The relationship between the latency of the mid-temporal 'P82' and that of the PVECP 'N75' was also found to vary as a function of spatial frequency, providing further evidence for the independence of these two responses.

Independence of the mid-temporal VER from the PERG and the PVECP was also indicated in the spatial and temporal tuning functions but the spatial tuning of this response was found to be very complex and showed a high degree of inter-subject variability. However, since the mid-temporal VERs were recorded simultaneously with the PVECPs, it was concluded that the two responses were reliably different in spatial tuning in spite of this apparent complexity and high between-subjects variability.

In the final study, two patients with known pathology at different levels of the visual pathway were tested in order to

further investigate the independence of the mid-temporal VER from the PVECP and to gain some estimate of its most probable source. Since the mid-temporal VERs, elicited with contralateral half-field stimuli, were found to be left-right asymmetrical when the subjects' disruption was anterior to the LGN and left-right symmetrical when the disruption was unilateral and immediately posterior to the LGN, it was proposed that the source of the mid-temporal VER was probably not cortical. This proposition was supported by the finding that the half-field PVECPs, from the subject with unilateral posterior pathology, were asymmetrical.

The mid-temporal VERs from the patient whose visual disruption was posterior to the LGN were found to be very similar to the mid-temporal VER recorded from the unaffected side of the other patient and to the responses recorded from 3 normally-sighted subjects using the same stimuli.

On the basis of these findings it is proposed that the mid-temporal VER recorded at T3.5 and T4.5, with contralateral half-field stimuli, composed of high contrast pattern-reversal checkerboards, is a unique response whose source is likely subcortical. This response can be characterized as a 1-2 microvolt positivity that begins at 65-70 msec. and peaks at approximately 80-85 msec. following pattern-reversal of a pattern whose checksize is 16' and whose reversal rate is 3 Hz. Since the generator of this source is not likely to be cortical and its stimulus tuning is consistent with that of neurons in the parvocellular layers of the LGN, it is proposed that the LGN is a likely source for this response. However, this

cannot be decided conclusively on the basis of the data presented here. For example, further studies that might test this proposition could employ stimulus dimensions such as achromatic and chromatic spatial contrasts of magnitudes that correspond closely to those reported for primate LGN neurons (see Chapter I).

The latency of this putative pattern VESP is very late for its source to be the LGN. However, as noted earlier, this latency is intermediate to the latencies of the PERG (50-65 msec.) and the 'P100' of the PVECP. It is quite likely that, as in the cases of the PERG and the 'P100' of the PVECP, the mid-temporal VER does not monitor the initial arrival of afferent volleys initiated by the retinal photoreceptors. It is possible that all of these extra-cranially recorded VERs contain unknown combinations of responses from glial cells and neurons (Dowling, 1970; Somjen, 1981). This possibility complicates the precise identification of intra-cranial sources. These complications do not rule out their clinical utility though (Regan, 1972; Halliday, McDonald and Mushin, 1973a and b; Armington, 1974). If specific changes in features of VER waveforms, consistent between normally-sighted subjects, can be correlated with particular disturbances of the visual system, then VERs can provide valuable information to supplement that available from other clinical tests. As such, the mid-temporal VER seems quite promising.

Although the mid-temporal VER was only applied in two clinical cases here it provided valuable information not available from PVECP recordings. In the case of the patient with an anterior visual disturbance, the left and right half-field

"mid-temporal responses were clearly visible whereas the half-field PVECPs were not. In this patient's data, the mid-temporal VERS revealed a left-right asymmetry in visual function at a latency earlier than the 'P100' of the PVECP. In the data recorded from the second patient, who had unilateral posterior pathology, the mid-temporal VERS were symmetrical at 82 msec. while the PVECPs were asymmetrical at 100 msec. On the basis of the half-field PVECPs alone, it would not have been possible to localize this patient's visual pathway disruption beyond saying that it was post-chiasmal.

Although the latency of the 'P82' in the mid-temporal VER was remarkably similar between the subjects tested here, its main utility as a clinical tool will probably be for making within-subject comparisons. Since its spatial tuning appears to be very complex, it seems likely that between-subjects comparisons of tuning functions will not be feasible until the tuning functions of many more normally-sighted subjects have been calculated. The main technical drawback in making between-subjects comparisons of discrete waveforms is the small amplitude of this response. Although the amplitudes of the mid-temporal VERS reported here were quite similar, the sample size was small. In most cases, at least 512 sweeps were necessary for the recording of binocular responses and 1024 sweeps for monocular responses.

In summary, it is suggested that the mid-temporal pattern-evoked VER shows promise as a clinical measure for localizing visual pathway disruptions. For this application it should be recorded simultaneously at both T3.5 and T4.5 and from at least

one occipital scalp site, such as Oz, using half-field pattern-reversal stimuli of medium to high spatial frequency. The resulting waveforms appear to be useful when compared within the same subject (i.e., T3.5 for right half-field stimulation versus T4.5 for left half-field stimulation and T3.5 and T4.5 versus the occipital records for half-field stimulation).

Now that the existence, uniqueness and possible clinical utility of the mid-temporal VER have been shown here with a small number of subjects and a large number of measures, parametric studies involving larger sample sizes appear to be justified. Other studies that could prove useful in further defining the limits of this response and in further distinguishing it from the PVECP include: 1. multichannel scalp distribution studies; 2. studies involving stimulus characteristics believed to differ in their effectiveness in stimulating cortical and LGN neurons (e.g., chromatic and achromatic spatial contrast, spatial orientation of pattern elements); 3. studies using pattern-onset and pattern-offset stimuli; 4. studies involving a variety of clinical material with well described retinocortical pathology.

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APPENDIX I
Experiment 2 Raw Data : Wavepeak Amplitudes (microvolts)

Subject 1

	1.7 Hz	PERG	3 Hz
11'	.44		.47
16'	.53		.50
27'	.59		.56
40'	.75		1.19
62'	.75		1.16
	7 Hz	12 Hz	15 Hz
11'	1.88	.94	.81
16'	2.00	.38	.50
27'	2.06	.50	.56
40'	1.44	.31	.31
62'	1.25	.25	.63

Subject 2

	1.7 Hz	PERG	3 Hz
	.28		.13
	.30		.19
	.30		.25
	.33		.28
	.38		.28
	7 Hz	12 Hz	15 Hz
	1.25	.31	.19
	1.19	.56	.44
	1.19	.63	.44
	1.56	.50	.25
	1.56	.38	.19

Full-Field Binocular

T4.5

	1.7 Hz	3 Hz
11'	.69	.94
16'	.63	.81
27'	.31	.69
40'	.63	.44
62'	.38	.19

	7 Hz	12 Hz	15 Hz
11'	.63	1.38	.81
16'	.81	1.38	.50
27'	.81	1.38	.50
40'	1.25	1.06	.44
62'	.63	1.00	.63

T3.5

1.7 Hz	3 Hz
.56	1.44
.47	.47
.94	.44
.69	1.16
.50	1.03

7 Hz	12 Hz	15 Hz
.81	.25	.25
.75	.22	.50
.56	.13	.22
.31	.16	.16
.44	.22	.16

Oz ('N75'/'P100')

	1.7 Hz	3 Hz
11'	3.31/7.63	1.56/4.63
16'	2.73/7.50	1.31/4.69
27'	2.88/8.75	.81/4.00
40'	3.06/7.50	.81/5.75
62'	2.50/7.19	1.00/6.00

	7 Hz	12 Hz	15 Hz
11'	.13/5.94	5.63	3.50
16'	.44/5.06	5.88	2.44
27'	1.50/5.50	3.94	1.81
40'	1.13/2.81	2.06	1.75
62'	.13/3.94	1.63	.81

-Oz ('N75'/'P100')

1.7 Hz	3 Hz
3.44/6.13	1.94/5.19
1.88/4.13	1.06/3.94
3.06/2.69	.81/3.56
1.81/3.50	.44/2.88
1.63/3.69	.44/4.88

7 Hz	12 Hz	15 Hz
.56/5.75	1.81	1.44
1.38/5.25	4.38	2.94
1.25/2.69	2.50	1.88
.81/3.38	3.44	2.44
.19/3.75	1.25	1.13

APPENDIX I (continued)
Wavepeak Amplitudes (microvolts)

Subject 1

Subject 2

Contralateral Half-Field Binocular

T4.5

T3.5

	1.7 Hz	3 Hz
11'	1.69	1.75
16'	1.50	1.25
27'	1.00	.88
40'	1.25	1.38
62'	1.13	1.06

	1.7 Hz	3 Hz
	.41	.44
	.70	.81
	.56	.94
	.34	.47
	.19	.47

	7 Hz	12 Hz	15 Hz
11'	1.69/1.25	.94/1.13	.63/.25
16'	1.38/.75	.81/1.13	.75/.25
27'	1.56/1.19	.88/.56	.56/.10
40'	1.75/.63	.50/.38	.50/.13
62'	1.19/.81	.44/.50	.56/.10

	7 Hz	12 Hz	15 Hz
	1.69	.19/.19	.19/.13
	2.81	.69/.6	.25/.13
	1.13	.22/.13	.19/.13
	1.06	.19/.19	.28/.13
	.63	.13/.10	.22/.10

	Oz ('N75'/'P100')	
	1.7 Hz	3 Hz
11'	4.63/7.88	3.00/5.19
16'	3.00/7.75	2.13/4.81
27'	2.88/7.50	1.38/3.50
40'	3.00/6.75	1.19/4.38
62'	2.00/6.25	.69/5.56

	Oz ('N75'/'P100')	
	1.7 Hz	3 Hz
	1.63/.94	.69/1.81
	.31/1.94	.25/3.13
	1.06/1.53	.50/1.94
	.59/1.31	.38/2.00
	.69/.75	.13/1.31

	7 Hz	12 Hz	15 Hz
11'	.13/8.25	5.31	2.75
16'	.31/6.63	3.69	2.00
27'	.75/5.94	2.50	1.50
40'	.75/5.31	1.56	1.25
62'	.13/3.61	1.25	.94

	7 Hz	12 Hz	15 Hz
	1.50/2.56	1.50	.81
	1.75/2.50	2.31	1.25
	1.56/2.19	1.44	.38
	.63/1.13	.81	.38
	.19/.63	.25	.31

END

2	8	H	I	0	H	8	5
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FIN