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THE TRANSMISSION OF VISUAL INFORMATION TO THE BRAIN VIA DIRECT AND INTERHEMISPHERIC PATHWAYS

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THE TRANSMISSION OF VISUAL INFORMATION TO THE BRAIN VIA DIRECT AND INTERHEMISPHERIC PATHWAYS

by

BARBARA LADENHEIM

A dissertation submitted to the Graduate Faculty
in Psychology in partial fulfillment of the
requirements for the degree of Doctor of
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1983

This manuscript has been read and accepted for the Graduate Faculty in Psychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

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Chairman of Examining Committee
Prof. James Gordon

August 15, 1983
date

Herbert J. Saltzstein
Executive Officer

Dr. Gerald Turkewitz

Dr. Stanley Novak

Dr. Vance Zemon

Dr. John Camisa
Supervisory Committee

The City University of New York

Abstract

THE TRANSMISSION OF VISUAL INFORMATION TO THE BRAIN VIA DIRECT AND INTERHEMISPHERIC PATHWAYS

by

Barbara Ladenheim

Adviser: Professor James Gordon

The apparent delay in the transmission of information to the brain as a function of locus of visual stimulation was measured using the visually evoked potential (VEP). Pathways from the left hemiretinas outside of the foveal area lead only to the left cerebral hemisphere and vice versa. Stimuli were presented at .5 degrees of visual angle lateral to the point of central fixation to assure that stimulation of the central area of the fovea (which has projections to both hemispheres) was avoided. Stimuli consisted of sinusoidally modulated checkerboard patterns (1.5 cycles per degree) contrast reversed at eight different temporal frequencies (3.5, 4.25, 5, 5.75, 6.5, 7.25, 8 and 8.75 Hz) which were presented monocularly to either a right or left hemiretina.

Steady state visually evoked cortical potentials were measured bilaterally over five electrode sites. An electrode was located at Oz, two electrodes at 3.5 cm intervals lateral and to the right of Oz and two electrodes at 3.5 cm intervals lateral and to the left of Oz. All electrodes were referenced to Cz and the two electrodes closest to Oz were also referenced to Oz.

Fourier analyses were performed on the data. By examining the phase of the second harmonic response the relative latency of response at different recording sites was determined. Within the frequency range tested, phase changed as a linear function of frequency. The slopes of the phase by frequency functions were used to determine the apparent latency of response.

Response latencies recorded from over the directly stimulated hemisphere were shorter than those from over the non-directly stimulated hemisphere (receiving input via the corpus callosum). This may be interpreted as evidence of a delay in transmission of information to the nondirectly stimulated hemisphere. No differences in response latencies were found as a result of stimulus presentation through the eye ipsilateral or contralateral to the directly stimulated hemisphere. Consistent differences in the pattern of the VER recorded from over the directly compared with the nondirectly stimulated hemispheres were also observed; a simple delay due to either neural transmission time or volume conduction cannot account for these differences.

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INTRODUCTION

The two hemispheres of the brain are somewhat independent structures with two major channels of communication - the corpus callosum and the anterior commissure (Kupferman, 1981; Geshwind, 1980). In order to study the nature of the information transferred from one hemisphere to the other, it is necessary to be able to present information to each hemisphere independently. The structure of the visual system makes this possible. Information from the left visual field goes directly to the right hemisphere while information from the right visual field goes directly to the left hemisphere.

The first three neurons in the direct line of transmission of visual information, the receptors, the bipolar cells and the ganglion cells, are in the retina. Ganglion cell axons exit the eye at the optic disc and form the optic nerve. Fibers from the nasal hemiretinas of each eye cross over to the other side at the optic chiasm, so that fibers making up the left optic tract have their origins in the left hemiretinas of each eye and fibers making up the right optic tract have their origins in the right hemiretinas of each eye. Since images from the left visual field are projected onto the right hemiretina and vice versa, the right optic tract carries information from the left visual field and the left optic tract carries information from the right visual field. The ganglion cells terminate in the lateral geniculate nucleus of the thalamus. The geniculate cells project to the striate cortex, the primary visual projection area

Figure 1

Highly schematic drawing of the visual pathways in the central nervous system of a primate. The figure shows how the image of a banana is projected through the various stages of the system. The image on the retina is inverted; because of the crossing of the nasal retinal fibers, only half the image is represented in each optic tract. Only the major terminations of the optic tract are shown. (From Glickstein, 1969. Copyright 1969 by the American Association for the Advancement of Science).

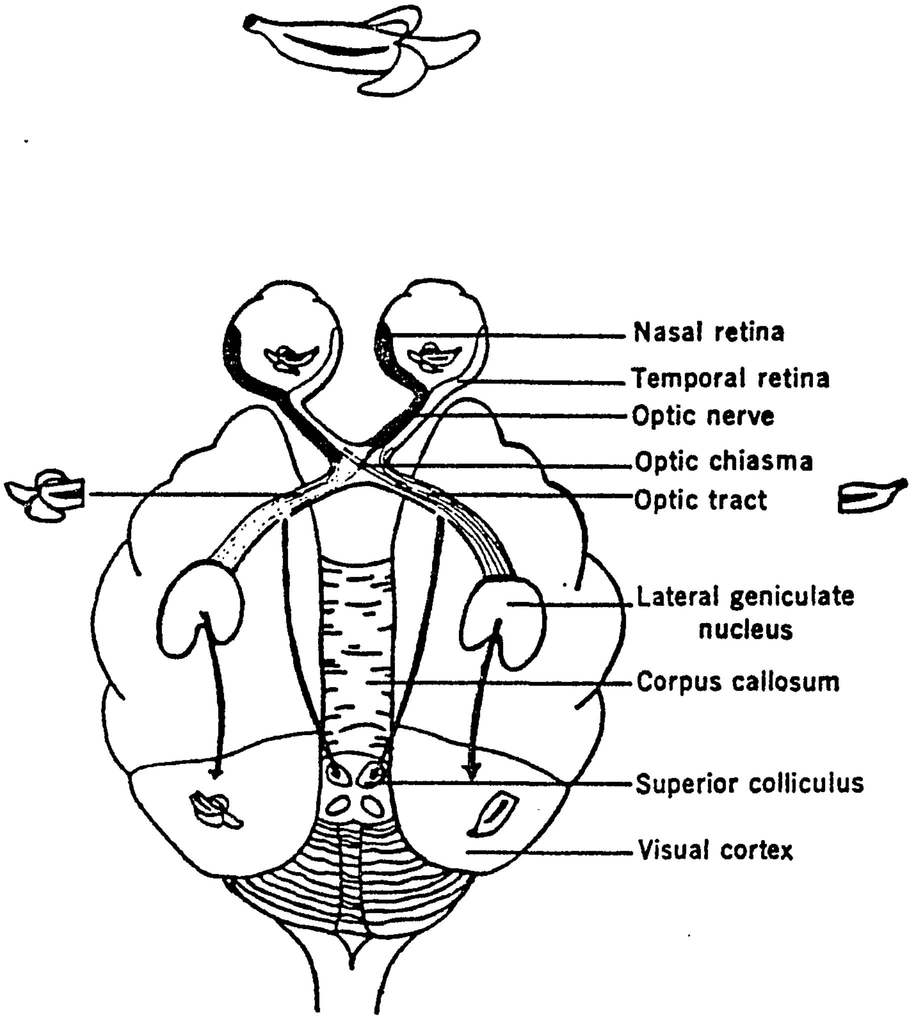

Nasal retina
Temporal retina
Optic nerve
Optic chiasma
Optic tract
Lateral geniculate nucleus
Corpus callosum
Superior colliculus
Visual cortex

Figure 1

(figure 1).

The topographic representation of the visual field remains intact throughout the visual pathway. The representation of the visual field on striate cortex is topographic with foveal (central retina) projections wrapped around the occipital pole and peripheral projections buried deeper in the the calcarine and other cortical fissures (Poggio, 1980).

In the macaque monkey, and probably in man, callosal fibers carry information between the extrastriate cortical areas of the two hemispheres. Both the origins and terminations of the fibers of the corpus callosum are in extrastriatal areas with none in the striate area (Van Essen et al, 1982). It can therefore be assumed that visual information is transmitted interhemispherically from the striate cortex of one hemisphere, to its extrastriate cortex and then to the extrastriate cortex of the other hemisphere. The pattern of distribution of the callosal cells are highly complex and show a high degree of individual variability with respect to their structure and relationship to the cortical landmarks leaving specific properties and functional significances of the callosal pathways poorly understood (Van Essen et al, 1982).

Electrical signals generated in the retina reach cortical areas 17 and 18, the primary visual areas of the brain. Activity in these areas can be used as an indication of the encoding and transmission properties of the visual system. Measures of this activity have played a major role in the exploration of the localization and development of human visual processing and can be used in the diagnosis and prognosis of ophthalmic and neurological disorders.

THE RECORDING OF EVOKED POTENTIALS:

There is ongoing electrical activity in the brain (as measured by EEGs) which can be affected by external stimulation. Stimulus bound electrical activity (evoked potentials - EPs or evoked responses - ERs) can be measured as gross potential changes between electrode placements on the scalp. What is actually being measured is the summated response of many neurons. The characteristics of the evoked response depend on the response properties of the individual neurons involved and the electrode placements with respect to those neurons. Characteristics of the visually evoked response (VER) can, with some assumptions, be related to the activity of those groups of cells and be used as an indication of the integrity of the system and its pathways (Sokol,1976), as well as a measure of visual information processing.

The electrical activity of the brain was first measured in the late 19th century with galvanometers that could detect gross electrical potentials. Caton interpreted these as being associated with localized function in the brain (Halliday, 1980a). More efficient galvanometers and amplification techniques were developed during the first quarter of the twentieth century, enabling the recording of the waveforms of action potentials from muscles, the retina and nerves. Relationships between sensory stimulation and brain activity in primary sensory areas were seen, as well as relationships between cognitive functions such as attention and activity in sensory association areas. The development of oscillographs in the 1930's made multichannel recordings possible - several different areas of the brain could be monitored simultaneously. The recording, storage and component analysis of very small electrical signals are now possible through the use of sophisticated oscillographs, film, magnetic tape recorders and computers (Riggs, 1977; Halliday, 1980a).

USE OF THE VER:

Evoked potential studies have played a major role in the exploration of the localization and development of human visual processing. Employing a noninvasive measure of a physiological response makes the collection of comparable data possible from nonverbal, noninstructible subjects such as infants, animals and disabled adults (Riggs, 1977; Kinney, 1977). In fact some aspects of vision have been successfully measured only by the VER. For example, some aspects of stereoscopic vision are obvious only with VER and not other techniques (Regan, 1977).

The VER has also proven to be a valuable tool in clinical areas of ophthamology and neurology. Methods employing VER techniques can be used to test visual functions and determine the suitability of optical refractive corrections and corrections of astigmatism. Due to the variability of 'normative' data, however, corrections can only be comparatively checked. The best correction will be obvious as a function of VEP amplitude. A blurred image will cause attenuation of the response, while the largest amplitude response will indicate the best correction. The techniques generally use an on-line average and are fast, reliable, and especially useful with nonverbal or noninstructable subjects (Riggs, 1977; Kinney, 1977; Regan, 1977). Since infants and children often fall into one or both categories, pediatric ophthamologists and neurologists use the VER in testing visual function. In addition to checking the improvement of refraction, VER component analysis can yield information about amblyopic patients. Using averaging graphs which result in a more refined analysis of the waveform than the running average, differential responding from stimuli presented separately to each eye gives an indication of the severity of the problem. Here again, relative measures are used - the differences between the eyes are the primary measure because of the unreliable nature of absolute amplitude data. The effectiveness and the appropriate course of therapy can be determined by retesting (Sokol, 1976; Regan, 1977). Some defects of color vision can also be diagnosed by measuring the VER to heterochromatic flicker (Regan, 1977).

Visual disorders resulting from diseases of the optic nerves and pathways and of the CNS can be diagnosed and followed using the VER.

Specific waveform distortions and peak amplitude and/or latency abnormalities can all indicate the stage of the disorder even when no other obvious symptoms are present (Kinney, 1977; Sokol, 1976; Regan, 1977). VER studies of patients with visual field defects, although yielding similar information as to the retinal locus of the defect as when traditional field testing methods are used, can also yield information as to the locus and extent of possible cortical involvement (Holder, 1980; Sokol, 1976; Kinney, 1977; Regan, 1977). Finally, VER's can be used as gross measurements of brain function in situations involving the CNS such as the effects of alcohol and nitrogen narcosis (Kinney, 1977).

ANALYSIS OF THE ER:

Since stimulus bound potential changes are not occuring in isolation they must be separated from the "noise" of unrelated potentials and/or spontaneous activity in the brain. Methods developed to isolate signals and reduce the variability often found in the data are based on the superimposition and averaging of repeated responses. Early techniques simply superimposed the signal photographically. In the 1950s and 1960s other non-electronic averaging methods based on electrostatic, photoelectric or electromagnetic storage methods were employed. Records of several hundred responses, time locked to the stimulus, were necessary in order to cancel out the unrelated cortical activity so that the common features making up the evoked potential signal would become visible. These were not techniques that could be used to study the response to occasional, unique or naturally occuring stimuli. Presently, computers have the capability of transforming incoming analog signals to digital information so that the pulse rate is proportional to the EP signal voltage (Halliday, 1980a; van der Tweel et al, 1980; Riggs, 1977). Filtering capabilities and correlational methods have improved the signal-to-noise ratio, preserving the shape of the signal while decreasing the noise (van der Tweel et al, 1980). In addition to more precise detection of the signal, computers can be programmed to perform complex statistical analyses making more precise component analysis of the waveform possible. Averaging techniques are based on the assumption that the signals which are not part of the ER are random, so that they are indeed cancelled out.

The methods described above have been used in the analyses of responses to transient presentation of stimuli - where a stimulus is presented repeatedly with interstimulus intervals of sufficient length to allow recovery of the sensory system between presentations. Analysis of the averaged waveform consists primarily of amplitude measures (the amount of positive or negative deflection from a baseline response level, usually measured in microvolts) and latency measures (the time after the stimulus presentation when response peaks are evident). Component analysis, an analysis based on the latencies of various response peaks has been interpreted in terms of functional subunits in the brain located in primary sensory or other cortical areas (Regan, 1982; Halliday, 1980a). Problems of interpretability arise when components overlap, or "ride" on one another, and when polarity reversals occur (Regan, 1982). Furthermore, even with sophisticated equipment and techniques, there remains inter- and intra-subject variability in the amplitude and latency of the components and of the overall waveform of the response. Methodological factors, such as electrode placement and equipment sensitivity can serve as confounding variables, as can differences in experimental design such as number of subjects, analysis techniques, etc. (Kinney,1977).

Stimuli may also be presented using steady state methods. Interstimulus intervals are shorter (i.e., frequency of presentation is higher) so that the sensory system cannot return to its resting state between stimulus presentations. Rather a steady state of responding occurs after the first few repetitions of the stimulus. Since most stimuli and responses are complex waveforms, methods based on Fourier analysis allow for a direct quantitative measurement of the responses and their relationship to the stimulus. This analysis is based on the fact that any waveform can be broken down or analysed into an appropriate set of sine waves. Thus, response records can be broken down into sine wave components and the amplitudes and phases of each component can be measured. In a linear system, the output of the system is at the same frequencies as the input. The visual system however is not linear - the output is distorted and contains Fourier components that are at higher harmonics (2F, 3F, 4F, etc.) of the fundamental frequency (F) of the input. With Fourier analysis it is possible to measure the entire frequency spectrum (Cornsweet, 1970). Since event related responses only occur at the stimulus frequency and its harmonics, it is only necessary to measure the VER amplitudes and phases at those frequencies. These harmonic components, of steady state EPs, contain the same information as the temporal components of transient EPs for a linear system and complementary information for a nonlinear system (Regan, 1982). Thus, one advantage of steady state presentation is that analysis of only a restricted range of frequencies (the input frequency and its harmonics) are necessary, allowing better separation of the signal from the noise than with transient methods (Regan, 1977; 1982).

Other advantages of using steady-state rather than transient presentation include faster analysis so that shorter run periods are possible. Furthermore, less intersubject variability is found in the data. The capacity to perform component analysis of the waveform is lost, but the frequency analysis may produce more information about the sources of the VER than does component analysis. However, to obtain "apparent" latency information from steady state presentation one must measure responses to more than one rate of stimulus presentation (Regan, 1977; 1982). This will be discussed in detail later.

FACTORS AFFECTING THE VER:

The visually evoked response has been studied in great detail. There is much inter- and intra-subject variability in its amplitudes, latencies and waveform. The choice of appropriate placements for the active and reference electrodes are essential to assure as much consistency as possible. Different sensitivities of recording equipment, types of electrodes and their impedences, and analysis techniques have resulted in seemingly contradictory data from different laboratories. More precise manipulation of the stimulus including greater control of retinal locus, intensity, duration and temporal and spatial aspects are now possible with the use of sophisticated equipment. As a result, and despite the variability still present, consistent, measurable influences of stimulus parameters have been well documented.

During the 1960s transient VERs to unpatterned flash stimuli were most often studied (Halliday, 1980a). Response amplitude showed a positive correlation and latency a negative correlation with stimulus intensity, especially at low intensity levels (Kinney, 1977). Manipulating the frequency of presentation resulted in maximum response amplitudes in three temporal frequency regions; 10, 13-25 and 40-60 Hz (Regan, 1968).

Patterned stimuli were first used in the mid 1960s. Riggs et al (1964) developed a phase alternation technique using gratings as stimuli. Differences in the waveform and latencies of the peak amplitudes were seen, along with absolute amplitude changes as a function of spatial frequency of the square wave gratings.

Checkerboard patterns have been the primary stimuli since the 1970s. Checks of ten to twenty minutes of visual angle have been shown to produce the highest amplitude responses in adult humans. Presentations of smaller checks not only affect the amplitude but also increase the latency of the response peaks. Interactions between spatial and temporal frequencies are evident. Maximally effective temporal frequencies, as measured by increased amplitude of response, tend to be at about 6 to 7 Hz for small checks and about 10 Hz for larger checks. These functions tend to change as a function of subject age. Amplitudes of VEPs from infants are quite small for the first few months of life. Amplitudes from older adult subjects tend to decrease with age. The latency of the response decreases until about 6 or 7 years of age, then levels off and increases after about 50 years of age (Sokol, 1976).

The VEP is also affected by the retinal location of the stimulus. Amplitudes are largest when stimuli are centered on the fovea, in particular on the central 3 degrees of the retina. This may be partially due to the cortical magnification factor. Also, as described earlier, foveal projections are more accessibly located near the surface of the skull than are peripheral projections. These factors may also partially account for the difficulty in obtaining responses to stimuli at intensities near scotopic levels which are generated by rods which are located predominantly in the peripheral retina (Sokol, 1976; Kinney, 1977).

Other factors such as pupil size, refractive correction, dark adaptation levels, relevance or meaningfulness of the stimulus, duration of trials and test sessions, alertness of the subject, erratic fixation, ambient visual and auditory noise and motivation can also interact with response parameters (Rover et al, 1980; Sokol, 1976; Kinney, 1977). All of the above mentioned intervening technical and subjective variables point to the necessity of extremely well controlled conditions during data collection.

INTERPRETATION OF THE VER:

Influences of stimulus parameters and other variables on the VER have been well documented. Regularities in response waveforms, amplitudes and latencies have been shown. There are several ways of approaching an understanding of the underlying mechanisms and sources of the evoked response. For example, component analysis can be correlated with the responses of single units within the system yielding information as to the relative contributions of neurons in the system.

However, there are problems in locating the sources of VERs. For example, there is the possibility of the potential field of the generator neurons spreading across the scalp making interpretation difficult (Kinney, 1977). Furthermore, component amplitude tends to decrease with repeated stimulation. This can be the result of habituation or adaptation, and is more evident in recordings from the central and temporal regions of the cortex than from primary visual cortex. VEPs recorded directly from monkey primary visual cortex with intracerebral electrodes do not show any evidence of a habituated or attenuated response while these recordings from outside the primary visual area do. These data indicate that the components of the response generated in the primary areas are influenced mainly by stimulus parameters, while those from outside the primary visual area are influenced by both physiological and psychological factors. Yet VERs recorded from scalp electrodes over both areas show the influence of both factors (Jackson and Barber, 1980). Thus the sources of scalp recorded VERs reflect activity away from the recording site as well as directly under the recording site.

The analysis of changes in the characteristics of the VER waveform as a result of changes in stimulus parameters indicate that the cortical origins of different components may be different. The CI component has its peak amplitude at 100 msec and can be recorded from bipolar placements between the midline and 5cm lateral to the midline. The CII component has its peak amplitude at 150 msec and can be recorded from bipolar placements between 5 and 10 cm lateral to the midline. CI and CII have a temporal overlap and their amplitudes are differentially affected by locus of stimulation and electrode placements. The fact that the distribution of the components are separable lead to the hypothesis that their origins are in different cortical areas. Further evidence for this includes the fact that CI is not affected by changes in CII, but CII can be enhanced with respect to changes in CI. Jeffreys and Axford (Jeffreys and Axford, 1972a and b; Jeffreys, 1980) have concluded that the CI component probably has its origin in striate cortex while CII does not.

However, other investigators have attributed the different characteristics of the CI and CII components to the relationships between the inhibitory and excitatory properties of the individual neurons making up the neural popoulation contributing to the VER (Creutzfeldt and Kuhnt, 1973).

Changes in amplitude and latency as a function of maturation also points to component dependence on cortical and retinal maturity (Creutzfeldt and Kuhnt, 1973). In humans, sometime after four months of age, when the macula has fully developed (Abramov et al, 1982) and parts of the CNS have become myelinated VER waveforms become adult-like (Sokol, 1976). Even at five months of age the functional significance of the corpus callosum is questionable due to incomplete myelination (Luttenberg, 1966; Yakovlev and Lecours, 1967).

Changes in the temporal frequency of the stimulus also differentially affect VER components. Component amplitudes show different maxima and properties in different ranges of temporal frequencies. The hypothesis that the cortical origins of different components are different is further substantiated by studies of patients with central nervous system diseases where the response to stimuli in the 13-25 hz range may show abnormal peaks while responses to other temporal frequences do not (Sokol, 1976; Regan, 1977).

Specific populations of neurons as measured with VERs seem to be "tuned" to particular spatial frequencies. In the monkey, for example, as the electrode placement moves lateral to midline the system remains tuned to the same spatial frequency but lower spatial frequencies no longer evoke responses, i.e., the system changes from a low pass spatial filter to a band pass filter (Nakayama, 1982). Similar studies with humans also show a relationship between peak spatial frequency and the eccentricity of the stimulus on the retina. This is evident only in some in some regions of the brain. Although there is the possibility that this may be a result of a potential field spread due to differential orientation of generating dipoles, it seems more likely that it is differential responding of populations of neurons in separate cortical representations (Tyler and Apkarian, 1982).

RETINAL LOCUS OF THE STIMULUS AND RECORDING ELECTRODE SITE:

As mentioned above, the VER is differentially affected by changes in the retinal location and size of the stimulus. These aspects have been explored in various ways using transient presentations of stimuli. Foveal stimulation is the most effective in evoking the largest amplitude response (Sokol, 1976; Kinney, 1977). Some investigators have found that even when the cortical magnification factor is taken into account, by making stimuli presented to the periphery proportionally larger, amplitudes are still attenuated (Celesia and Meredith, 1982). Others, however, under similar stimulus conditions, found responses to lower spatial frequencies comparable to those found as a result of foveal stimulation, (Tyler, et al, 1980) but with the peak response at higher spatial frequencies (Tyler and Apkarian, 1982).

As electrode placements are moved lateral to the midline,the VER changes. Recordings from monkeys show a loss of response to low spatial frequencies (Celesia and Meredith, 1982). Human VERs show changes in relative amplitudes and peak latencies (Jeffreys, 1980). In fact, the CI component is most prominent at electrode placements slightly lateral to the midline (Jeffreys and Axford, 1972a and b; Jeffreys, 1980; Drasdo, 1980).

Analysis of the transient VER has shown the extent of foveal contribution to individual components. For example, the CI component is thought to have its origin in the striate cortex as a response to foveal stimulation (Jeffreys, 1980; Drasdo, 1980). Polarity reversals of CI but not of CII (of extra striate origin) are found when stimuli are presented to the left versus the right visual field, and polarity reversals of both components occur when the fields are split horizontally (Jeffreys and Axford, 1972a). The negative-positive-negative (NPN) peaks characteristic of the VER to foveal stimulation as recorded from midline electrode placements seem to be an algebraic-like summation of two asymmetric half-field (right and left) responses. As the stimulus is moved lateral to the fovea, or the center of a full-field is occluded, the NPN response decreases. The contralateral PNP response reaches its peak amplitude when the stimulus does not include the central 5 degrees of the visual field. It appears that the ipsilateral PNP response masks the contralateral NPN response when there is foveal stimulation (Halliday et al, 1979).

Similar polarity reversals of the EP as a result of half field stimulation have been seen by Lehmann and Skrandies (1979). VER components to centrally located stimuli extending beyond the fovea show peaks at latencies of 100 msec (a positive amplitude peak) and 140 msec (a negative amplitude peak). Half-field stimulation using stimuli subtending 13 degrees of visual angle evokes similar maxima as a function of recording site over the hemisphere ipsilateral to the stimulated hemiretina. Fields subtending 26 degrees of visual angle evoke maximal response in recordings from the hemisphere contralateral to the stimulated hemiretina, with the 100 msec component having a negative peak and the 140 msec component a positive peak (Lehmann and Skrandies, 1979). Kriss and Halliday (1980) also found polarity reversals but no consistent amplitude or latency differences between the contralateral and ipsilateral hemispheres with half-field stimulation that included the foveal area. Midline recordings were similiar to the ipsilateral recordings. Harding et al (1980), using a contrast reversing checkerboard pattern as a stimulus, found that normal subjects showed maximal positive component amplitudes (at 100 msec latency) at recording sites ipsilateral to the half field stimulated. When the stimulus was presented 2.5 degrees lateral to central fixation, and the check size was smaller, the 100 msec component was attenuated and the characteristic ipsilateral response was found to move towards the contralateral side. Stimulation with diffuse flashes to each hemiretina in isolation evoked similar responses. As the intensity of the diffuse stimulus was increased the maximal response again moved towards the contralateral hemisphere. However, patients with hemianopic visual field defects showed maximal responses contralateral to the half-field stimulated by the contrast reversing checkerboard.

Other studies of the lateralization of the VER of patients with visual field defects have yielded seemingly conflicting data. Abnormal VERs, with attenuated amplitudes and altered waveforms have been recorded from over the hemisphere contralateral to the affected field (i.e., the hemisphere with projections from the affected visual field, the one affected by lesions or injury). When there were defects in both left and right visual fields, the maximally abnormal response was found over the hemisphere contralateral to the field with the maximal defect (Holder, 1980). Halliday had previously found the opposite results, but attributes them to the different stimulus and recording parameters of the two studies (Halliday, 1980b). These different techniques are thought to result in differential recording of potentials being generated in the same areas of cortex as a result of the distribution of the response on the scalp.

THE PURPOSE OF THE PRESENT STUDY:

Although the studies cited above have explored various aspects of lateralization of the stimulus and recording sites and their effects on the VEP, no one has separated the inputs to each hemisphere via direct visual pathways from the inputs via indirect pathways (commissural fibers, etc.) in terms of the amplitude and phase of Fourier components and apparent delay times. Measures of apparent latency of the VER to steady state stimulation can be derived from phase measurements obtained by Fourier analysis.

Investigators have used steady state stimulus presentations instead of transient presentations to study amplitude as a function of spatial frequency, to obtain temporal tuning curves, to compare EPs from multiple recording sites in the visual field in patients with cortical damage and migraine, to study spectral sensitivity and to develop theoretical models of the generation of EPs and their relationship to neuroanatomy. The analysis of VERs to steady state presentations of stimuli provides more objective information than when stimuli are presented in a transient manner. Transient VER components may be distorted and misinterpreted in terms of which component is actually being measured when the waveform changes in ways previously described. Fourier analysis of steady state VERs, yielding apparent latency measures as described below, leaves less room for error in this respect. Limited use has been made of apparent latency measures (Regan, 1982) but they have been particularly useful in the assessment and diagnosis of Multiple Sclerosis patients (Spekreijse et al, 1979).

In the experiments described below the transmission time of visual information to the cortex via direct or indirect pathways was explored. Steady state VERs recorded over the directly and indirectly stimulated hemispheres were studied with respect to the amplitudes and latencies of the response. Comparisons of amplitudes, phases and apparent delays should give an indication of a) interhemispheric transmission time, b) additional filtering or other restrictions on the flow of information occuring during interhemispheric transmission, and c) differences when stimulating the each hemisphere through the ipsilateral or contralateral eye.

METHODS

SUBJECTS:

Three adult subjects, two right handed females and one left handed male with normal or corrected vision were used Experiments I and II. A right handed adult male with corrected vision was the subject in Experiment III. All subjects were between the ages of 23 and 33 years.

APPARATUS:

The VEP was amplified and filtered (bandwidth: 0.03-100 Hz), and then digitized by computer (270 samples per second). Each two minute trial was sampled and averaged. Averaged responses were displayed on a CRT screen to monitor the progress of the experiment. All data were stored on a disc for later analysis. Fourier analysis yielding the amplitude and phase of the second harmonic response was performed on an LSI 11 computer.

Checkerboard patterns having a mean luminance of 45 footlamberts were generated on the screen of a Tektronix 608 Monitor oscilloscope (P31 phosphor) by means of a computer controlled visual stimulator described in detail in Milkman, et al, 1980.

All stimulus and recording equipment was located in an experimental chamber. The room lights remained on during each test session and the average luminance of the test chamber was about five footlamberts.

PROCEDURE:

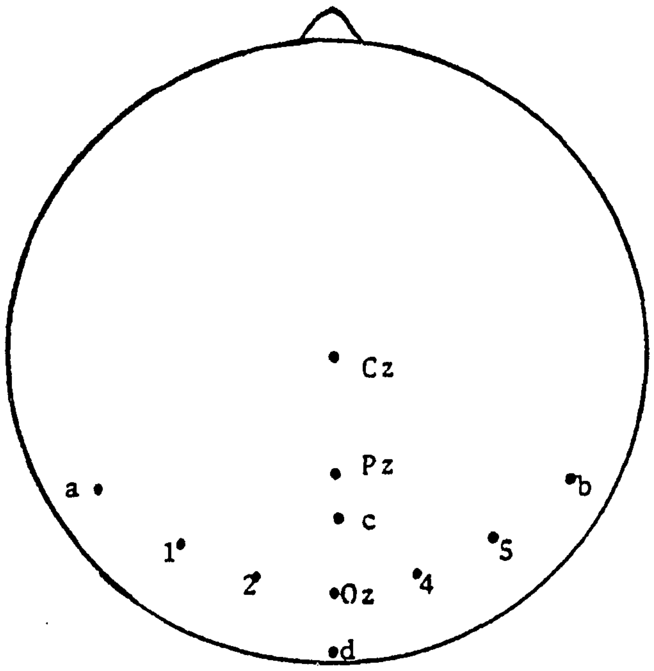
Gold cup EEG electrodes were attached to the scalp with Grass Electrode Paste using the following electrode configuration (figure 2). For Experiments II and III, electrode 3 was located at Oz (according to the 10-20 Electrode System of the International Federation (Jasper, 1958)), electrodes 2 and 1 at 3.5 cm intervals lateral and to the left of Oz and electrodes 5 and 4 at 3.5 cm intervals lateral and to the right of Oz. Two additional electrodes were placed at Cz and Pz. Unipolar recordings were taken from all five lateral placements (electrodes 1 through 5) referenced to Cz. These recordings were considered to be unipolar as Cz is far enough from the occipital area to assume little or no event related activity occuring there (Jasper, 1958). Bipolar recordings were also taken between Oz and the placement immediately to its left (electrode 2) and Oz and the placement immediately to its right (electrode 4).

The same electrode configuration and recording parameters were used in Experiment I, with additional electrodes placed 4 cm above and below Oz and 3.5 cm to the left of electrode 1 and to the right of electrode 5. Additional bipolar recordings were taken from each adjacent pair of electrodes in the lateral array and between Oz and

Figure 2

Electrode configuration:

Nasion to inion measurements were taken for each subject. According to the 10-20 Electrode System of the International Federation (Jasper, 1958) Oz was 10% of that distance above the inion, Cz was halfway between the nasion and the inion, and Pz was halfway between Oz and Cz. Placements a, 1, 2, 4, 5 and b were 3.5 cm apart lateral to Oz and c and d were 4 cm above and below Oz respectively.



ELECTRODE CONFIGURATION

Figure 2

the placements above and below Oz.

Subjects were seated comfortably in the experimental chamber. Stimuli were presented monocularly - the eye not receiving stimulation was covered with an eye patch. Subjects were instructed to fixate on a small, black, visible mark next to the stimulus display set in a position such that that the image of the stimulus would fall a specified distance lateral to central fixation. The distance between the subject's eye and the stimulus display was measured before and after each set of trials.

Experiment I:

In an attempt to determine the stimulus and recording parameters which would yield the most reliable VERs several variables were manipulated. Test trials were two minutes long with one minute intertrial intervals. It was possible to test 32 to 40 conditions during one session lasting between 1 1/2 and 2 hours.

a) Steady state VERs to unidimensional sinusoidally modulated gratings were obtained from all subjects.

b) Steady state VERs to contrast reversing checkerboard patterns were obtained from all three subjects for all combinations of the following conditions. The temporal frequency used was 6.27 Hz (a frequency known to evoke reliable responses in a steady state paradigm) and the checkerboard was sinusoidally contrast reversed around the mean luminance of 45 footlamberts with a contrast of 40%. Checks of either .75, 1.5 or 3.0 cycles per degree made up circular stimulus fields subtending either 8.8, 17.6 or 35.2 degrees of visual angle. All stimulus fields were presented at central fixation and at visual angles of .5, 1, and 5 degrees between central fixation and the boundary of the stimulus nearest to central fixation.

c) Steady state VERs to contrast reversing checkerboard patterns made up of checks of 1.5 cycles per degree and subtending 17.6 degrees of visual angle were obtained from all three subjects at stimulus frequencies ranging from 3.5 Hz to 14 Hz. Contrast remained at 40%.

Experiment II:

The purpose of this experiment was to measure in detail the transmission of information to each visual cortex from each hemiretina. Steady state VERs to contrast reversing checkerboard patterns made up of checks of 1.5 cycles per degree and with the entire circular stimulus subtending 17.6 degrees of visual angle were obtained from all three subjects. Contrast was 40%. Stimuli were presented separately to the right and left visual fields of each eye making up four runs per session. Fixation was .5 degrees lateral to the nearest boundary of the stimulus field. Order of presentation regarding eye and field stimulated were counterbalanced over sessions for each of the three subjects. Each session consisted of four blocks of eight two-minute runs with one-minute interrun intervals. During each run the contrast of the checkerboard pattern was sinusoidally reversed at either 3.5, 4.25, 5, 5.75, 6.5, 7.25, 8 or 8.75 Hz. All temporal frequencies were presented in the above order for each run. There were four test sessions, separated by several days, for each subject. Each test session lasted approximately 1 1/2 hours.

Experiment III:

The fourth subject was tested once, using the same procedure as in Experiment II.

ANALYSIS:

A measure of the apparent latency of the response can be derived from the phase measurements in the following way. Assume that there are three stimulus conditions, each a single temporal sinusoid at frequencies of 2.5, 5 and 10 Hz. A pure delay between stimulus and response, 100 msec. for example, will cause a particular phase lag at each frequency that increases linearly with frequency of stimulation (figure 3). Thus, if the stimulus frequency is doubled the phase lag of the response will be doubled. It is then possible to plot phase lag as a function of stimulus frequency and use this plot to calculate apparent latency. If the delay is constant, and the phase lag changes are due only to the delay, then this plot will be a straight line, the slope of which will give a measure of the apparent delay in the system. A steeper line, giving a larger slope, would indicate a greater delay (figure 4). However, frequency independent

Figure 3

Hypothetical sinusoidal responses to stimuli at frequencies of 2.5, 5 and 10 Hz are plotted. The solid line indicates the phase lag resulting from a 100 msec delay. In this example, a 100 msec delay causes a 90 degree phase lag for the 2.5 Hz response, a 180 degree phase lag for the 5 Hz response and a 360 degree phase lag for the 10 Hz response. The dashed line indicates the phase lag resulting from a 50 msec delay which causes a 45 degree phase lag for the 2.5 Hz response, a 90 degree phase lag for the 5 Hz response and a 180 degree phase lag for the 10 Hz response.

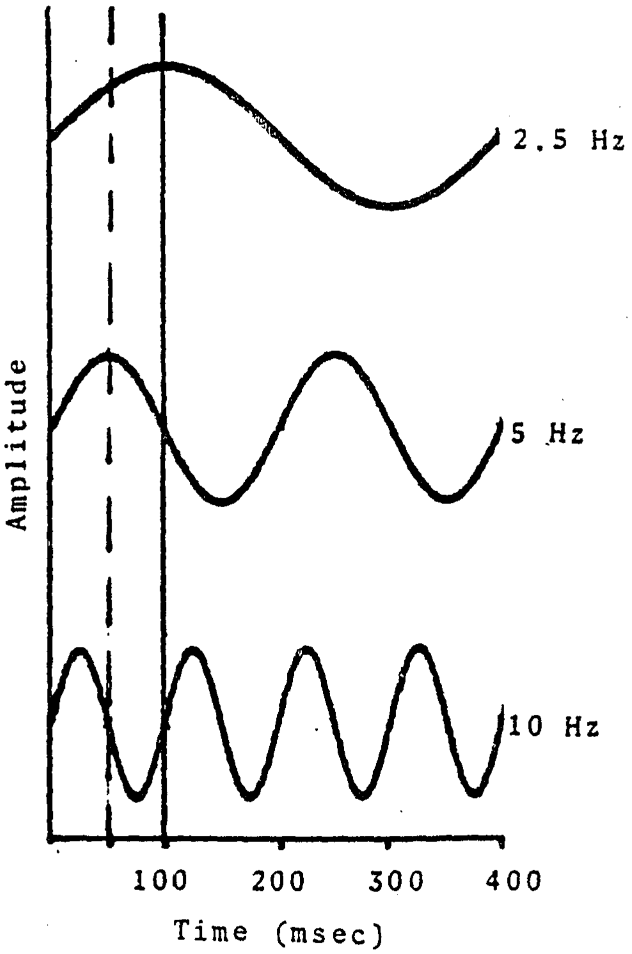


Figure 3

Figure 4

Phase lag as a function of frequency is plotted from the data in figure 2. The solid line is the function as a result of the 100 msec delay and the dashed line of the 50 msec delay.

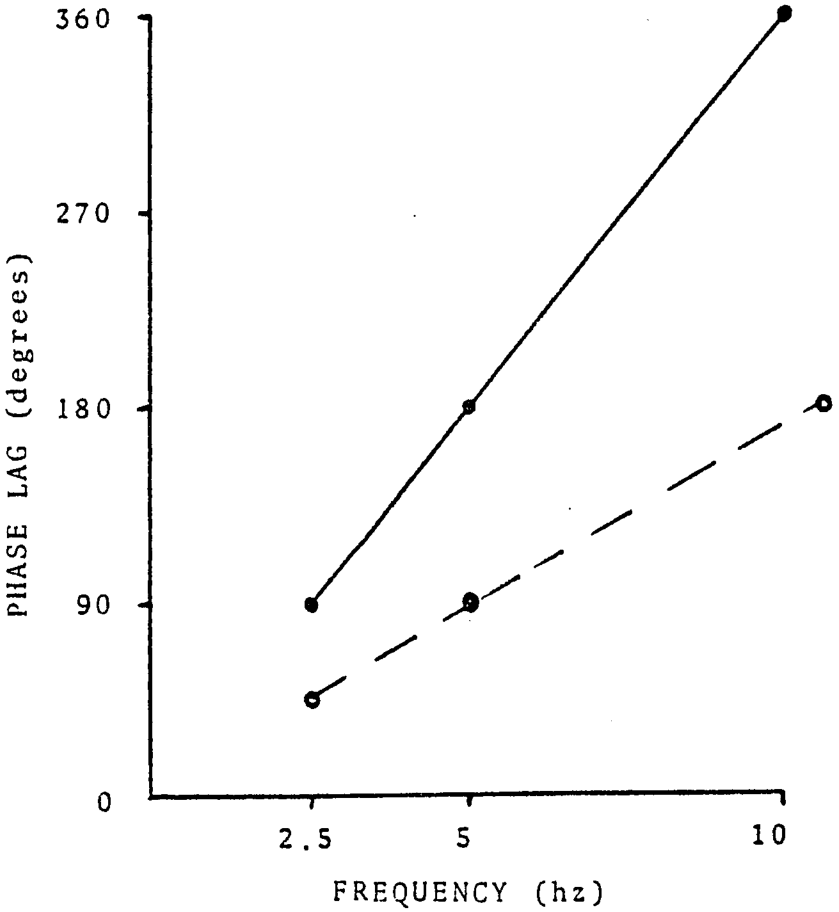


Figure 4

Figure 5

Representative phase lag as a function of frequency plotted from the data obtained from Fourier analysis measurements yield curve a) and the dashed curves. In order to have an indication of possible frequency independent phase shifts, curve a) must be shifted by 360 degrees yielding curve b). The data plotted is subject B's response as recorded from the bipolar placement over the right hemisphere as a result of direct stimulation of the right hemisphere through the left eye.

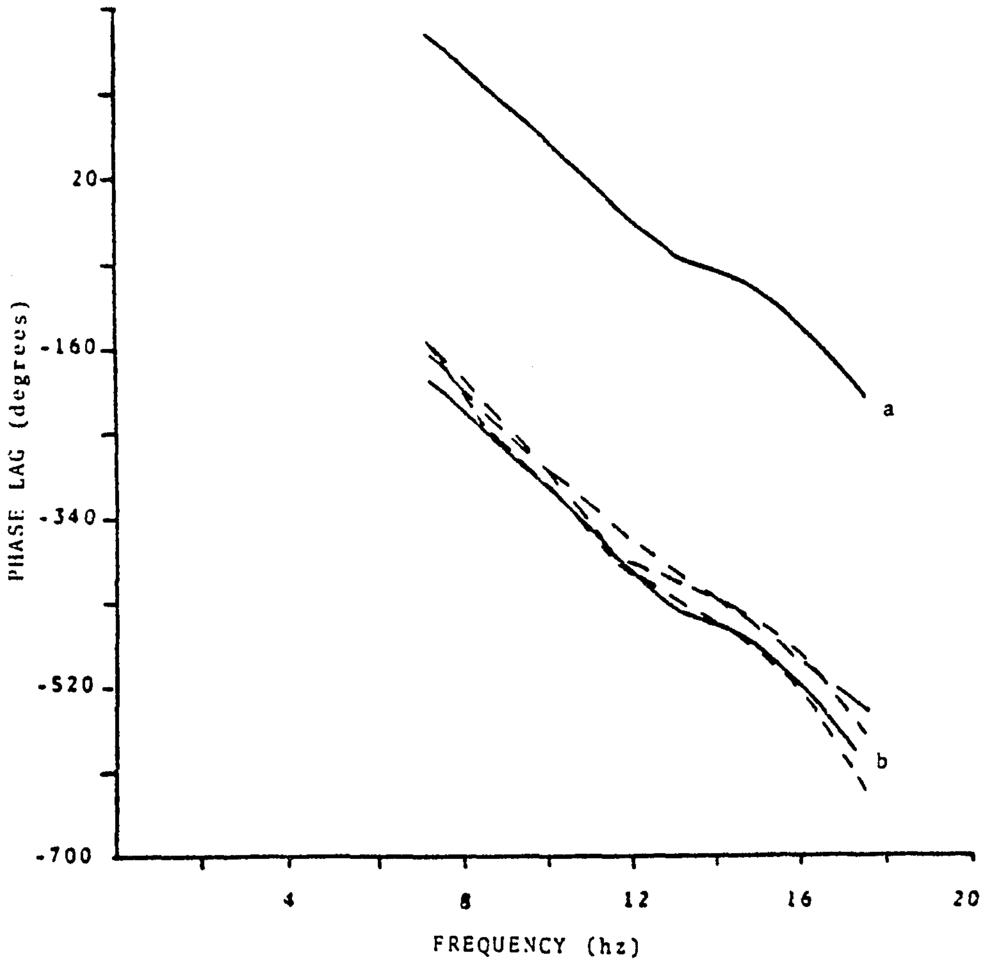

20
-160
-340
-520
-700
PHASE LAG (degrees)
4
8
12
16
20
FREQUENCY (hz)
a
b

Figure 5

phase shifts are possible, in which the entire functions are shifted (figure 5). Since the absolute zero point of the phase is uncertain, the slope of the phase-by-frequency function and not the absolute phase lag is related to the delay. Therefore, such measures are still reliable but should be interpreted as measures of "apparent latency" and should be used as relative rather than absolute measures (Regan, 1982).

Measures of apparent latency in milliseconds can be derived from the slope of the phase lag by frequency function using the formula:

$$\frac{\text{phase difference in degrees}}{\text{frequency interval in Hz}} \times \frac{1000}{360} \text{ msec}$$

(Duwaer and Spekreijse, 1978).

RESULTS AND DISCUSSION

EXPERIMENT I:

The first series of experiments was designed to determine those stimulus parameters and electrode placements which would evoke the largest amplitude and most consistent VERs. Thus, the amplitude and phase information derived from the Fourier analysis of the results would be as accurate as possible.

Amplitude and phase measurements for the second harmonic response were obtained from Fourier analysis of the VER. The responses to the unidimensional stimuli used (sinusoidally modulated gratings) were quite small in amplitude, so a sinusoidally modulated checkerboard pattern was tried. The checkerboard is a simple patterned stimulus having a lot of contour that is easily controlled in terms of check size, overall intensity and contrast between light and dark areas. VERs to the checkerboards were considerably larger than those to gratings when presented in the peripheral retina. Note that to a contrast reversing checkerboard there is no response at the fundamental frequency because those responses cancel out in the ER (Zemon and Ratliff, 1982). As shown in figure 6, the response to such a pattern is at twice the stimulus frequency and the largest measureable Fourier component is the second harmonic.

Steady-state VER amplitudes and phases were compared for several

Figure 6

The visually evoked response to a sinusoidally modulated contrast reversing checkerboard. At the top of the figure the checkerboard stimulus is shown in two phases; at the starting point (its peak) and shifted 180 degrees (where the originally white squares are now black and vice versa). As described in the text, the major portion of the VER to a checkerboard modulated in this fashion is at the second harmonic to the fundamental stimulus frequency, as shown at the bottom of the figure.

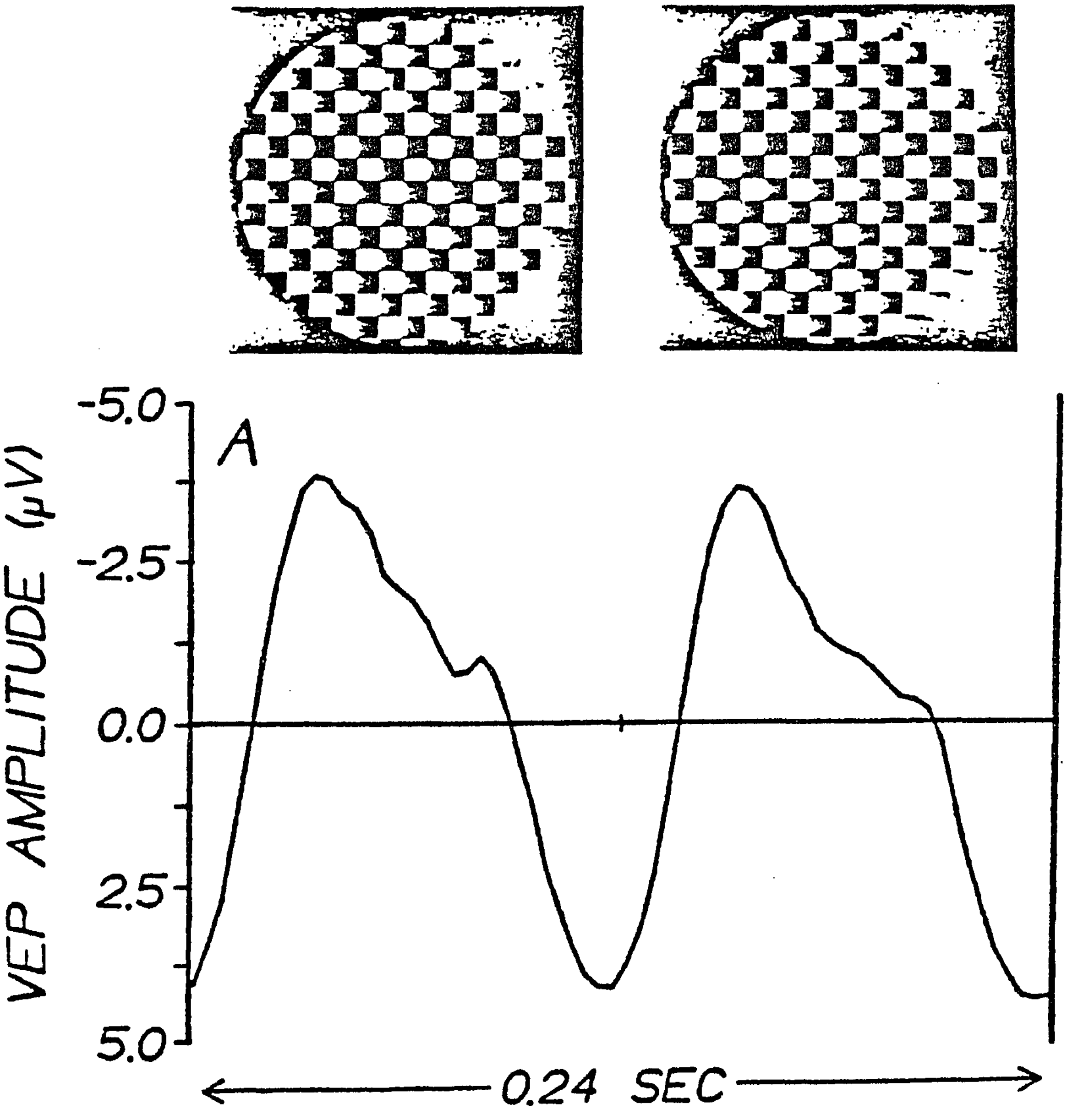


Figure 6

stimulus and recording conditions at a stimulus frequency of 6.27 Hz. A field size of 17.6 degrees of visual angle made up of checks of 1.5 cycles per degree was found to evoke the largest amplitude response for all three subjects.

Each cortical hemisphere was to be stimulated separately by presenting stimuli monocularly to either a right or left hemiretina. In order to be sure that the central area of the fovea (having projections to both hemispheres) is avoided, it is necessary to present the boundary of the stimulus field slightly lateral to the point of central fixation. Even when a central fixation marker is replaced by eccentric targets, eye movements have been found to be less than 25 minutes of arc (Sansbury et al, 1973) so that a fixation point at least .5 degrees lateral to the stimulus boundary should assure that eye movements will not move the stimulus into the central foveal area.

The stimulus field size was increased from 8.8 degrees by a factor of four (to 17.6 degrees) and a factor of 16 (to 35.2 degrees) at all eccentricities tested (central fixation, .5, 1 and 5 degrees). If it is assumed that the amount of cortex involved is inversely proportional to the eccentricity of the stimulus (the cortical magnification factor), such an increase should yield VEP amplitudes as a result of peripheral stimulation that are at the very least comparable to those evoked by foveal stimulation. In fact, a two degree field has been shown to evoke comparable responses at central fixation and two degrees lateral to central fixation, and a sixteenfold increase in stimulus field size has been shown to yield comparable amplitudes as compared to foveal stimulation at an eccentricity of 8 degrees, (Tyler et al, 1980; Tyler and Apkarian, 1982). However, in this experiment, even when the stimulus field was made sixteen times larger than the field presented foveally, response amplitudes to stimuli presented at eccentricities of 1 degree and 5 degrees were severely attenuated. Taking the cortical magnification factor into account as well as testing at various spatial frequencies did not yield amplitudes of the magnitude predicted by the magnification factor.

Responses from a number of electrode placements were studied. Unipolar VER recordings taken from a lateral array with electrodes placed at O_z and at 3.5 cm intervals to its left and right and referenced to C_z yielded the largest amplitude signals generated by the stimulus parameters chosen. Amplitudes of bipolar recordings of VERs from sites between O_z and the placement 3.5 cm immediately to its left and right were not as reliable. However, since phase data is not totaly dependent upon absolute amplitudes, the bipolar placements were chosen to be used as an additional comparative measure in experiment II.

Once the best stimulus location, spatial frequency and recording parameters were determined, amplitudes and phases were compared for stimuli modulated over a wide range of temporal frequencies. In order to derive apparent delay measures from phase data, it is necessary to measure responses at more than one rate of stimulus presentation. As described earlier, if the delay of transmission of information is constant, and the phase lag changes are due only to the delay, then the plot of phase lag as a function of stimulus frequency will be linear and the response of the system can be modeled in terms of a pure delay due to neural transmission time. This model assumes negligible phase shifts introduced by volume conduction of the responses to the surface of the head. The volume conduction model accounts for current flow over a spherical shape with areas of different impedences. However, since the brain is not truly spherical, and there are areas of irregularity consisting of concavities, convexities, different densities and open areas in the skull, the applicability of this model is not always certain (Vaughan, 1974). This is even more tenuous in the present study since the probable sources of the VERs as a result of stimulation of the peripheral retina are located within the fissures of the brain.

If there is any additional processing occuring the phase lag by frequency function may not be linear. In light of the above, in order to obtain a better indication of the characteristics of transmission, it was deemed necessary to test a wide range of frequencies at close intervals so that any deviations from linearity could be detected.

It was determined that a maximum of eight temporal frequencies could be tested during one session without making the duration of the session too long. Frequencies at 1.5 Hz intervals ranging from 3.5 to 14 Hz were tested. VER amplitudes were consistent and the phase lag by frequency functions were linear and consistent between 3.5 and 8 Hz. For frequencies above 8 Hz, however, amplitudes were quite low and the phase by frequency function deteriorated in a non-regular manner. Since the data in this range were shown to be unreliable, and the frequency range between 3.5 and 8.75 Hz was large enough to yield good measures of apparent latency, the 8 temporal frequencies chosen to be used in Experiment II were 3.5, 4.25, 5, 5.75, 6.5, 7.25 and 8.75 Hz.

EXPERIMENT II:

Again, amplitude and phase measurements for the second harmonic response were obtained from Fourier analysis of the VER for each of the stimulus frequencies. Amplitude and phase measurements for each stimulus frequency for each condition were averaged for the four sessions for each of the three subjects. All of the frequency labels on the following plots derived from the data refer to response frequency, and are double the stimulus frequency since, as mentioned above, the largest measurable Fourier components of the VER to a contrast reversing checkerboard pattern is at twice the stimulus frequency.

As illustrated in figure 7, the averaged amplitude curves are good indicators of the shape of the individual amplitude curves. To

Figure 7

Representative amplitude by frequency and phase lag by frequency functions.

Amplitudes and phase lags for each of the four sessions (-----) were averaged to yield one function per condition (——). The top panel shows amplitude plotted as a function of frequency, and the bottom panel shows phase lag as a function of frequency.

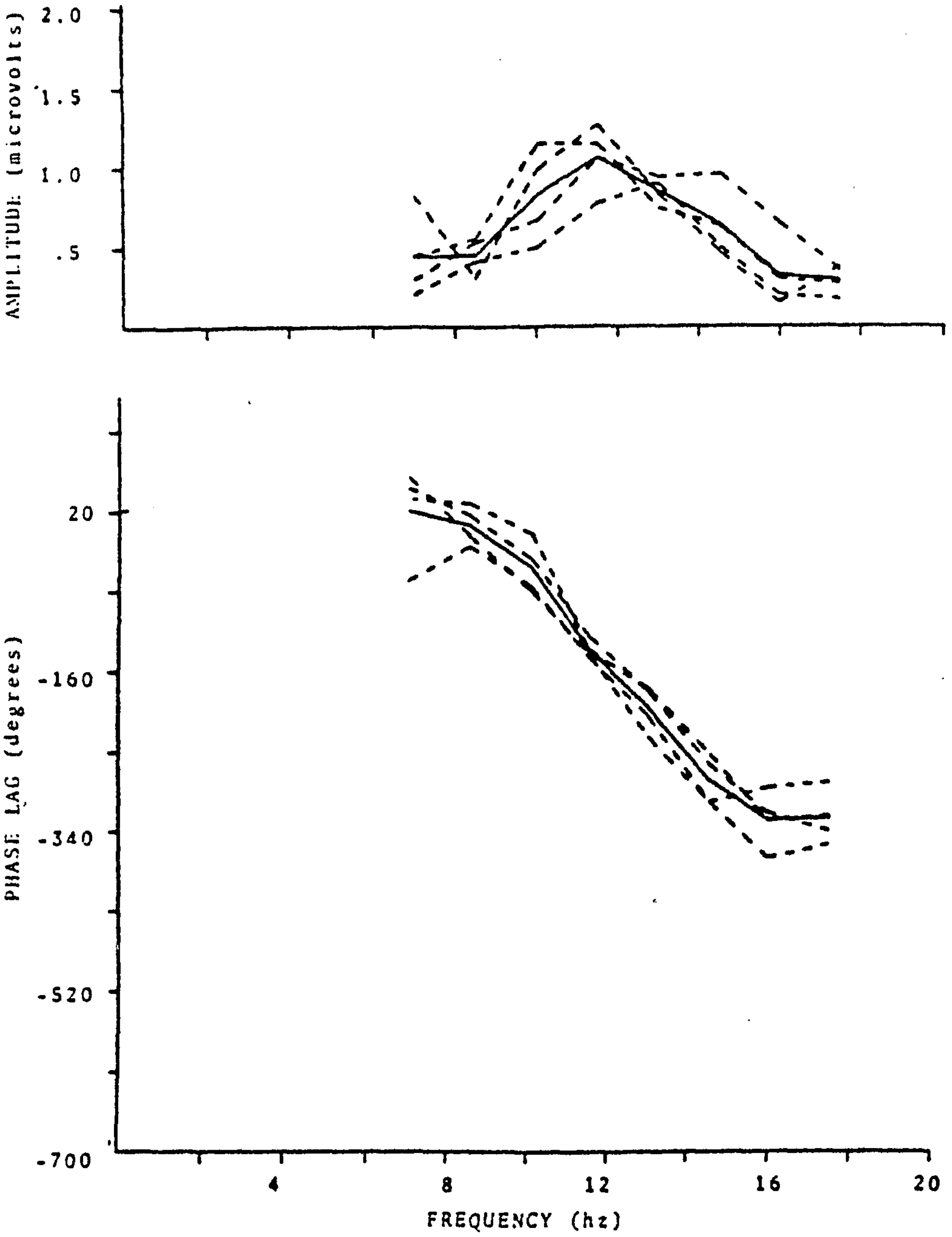

AMPLITUDE (microvolts)
2.0
1.5
1.0
.5
PHASE LAG (degrees)
20
-160
-340
-520
-700
4
8
12
16
20
FREQUENCY (hz)

Figure 7

simplify comparisons between recording sites, the VER recordings will be referred to as follows: Unipolar recordings from placements 7 cm lateral to O_z and referenced to C_z are the outer pair, records from placements 3.5 cm lateral to O_z and referenced to C_z are the inner pair, and records from O_z and referenced to C_z is midline. Records from placement 3.5 cm lateral to O_z and referenced to O_z are referred to as the bipolar pair.

Amplitude Data:

Steady-state VER amplitudes for the paradigm used in this study are generally quite low. However, one of the advantages of the Fourier analysis of steady state ERs is the accuracy with which it can detect and differentiate low signals from noise (Regan, 1982).

Several interesting patterns of responding became evident when the averaged amplitude by frequency functions were plotted. Most of these patterns were consistent within each subject's data, but not necessarily between subjects, so comparisons are made individually for each subject.

A. Peak amplitude as a function of stimulus location

Stimuli were presented directly to the left or right hemisphere through the left or right eye. Bipolar recordings from all three subjects showed the largest amplitude peaks from electrode placements over the directly stimulated hemisphere (figure 8).

Subject N showed the largest peak amplitudes from recordings over the directly stimulated hemisphere for all electrode pairs for all conditions.

Subject B showed the largest peak amplitudes when records were taken from over the left hemisphere for the outer pairs and at midline no matter which hemisphere was directly stimulated. Recordings from the inner pairs also showed this relationship, but not to the same extent.

Subject H showed the largest peak amplitudes from recordings over the hemisphere that was not directly stimulated when the left hemisphere was directly stimulated for both outer and inner pairs. When the right hemisphere was directly stimulated the largest peak amplitudes were recorded from midline.

B. Peak amplitude as a function of recording site

For subject B, VEPs from all unipolar sites and the bipolar site located over the right hemisphere showed the largest amplitude peaks when that hemisphere was directly stimulated. Stimulation via the contralateral eye evoked slightly higher amplitudes than stimulation via the ipsilateral eye. The opposite relationship was seen from recordings from the bipolar site over the right hemisphere.

Figure 8

VER amplitudes as a function of frequency recorded from the bipolar pair of electrodes. Recordings were taken from over the directly stimulated hemisphere (———) and from over the non-directly stimulated hemisphere (-----) for all three subjects as identified by the initial in the upper right corner of each plot.
Conditions were as follows:
Subject N - direct stimulation of the right hemisphere through the left eye
Subject B - direct stimulation of the right hemisphere through the right eye
Subject H - direct stimulation of the left hemisphere through the left eye
Note that in this figure and the following data figures all functions plotted are the averaged response from the four sessions as described in figure 7.

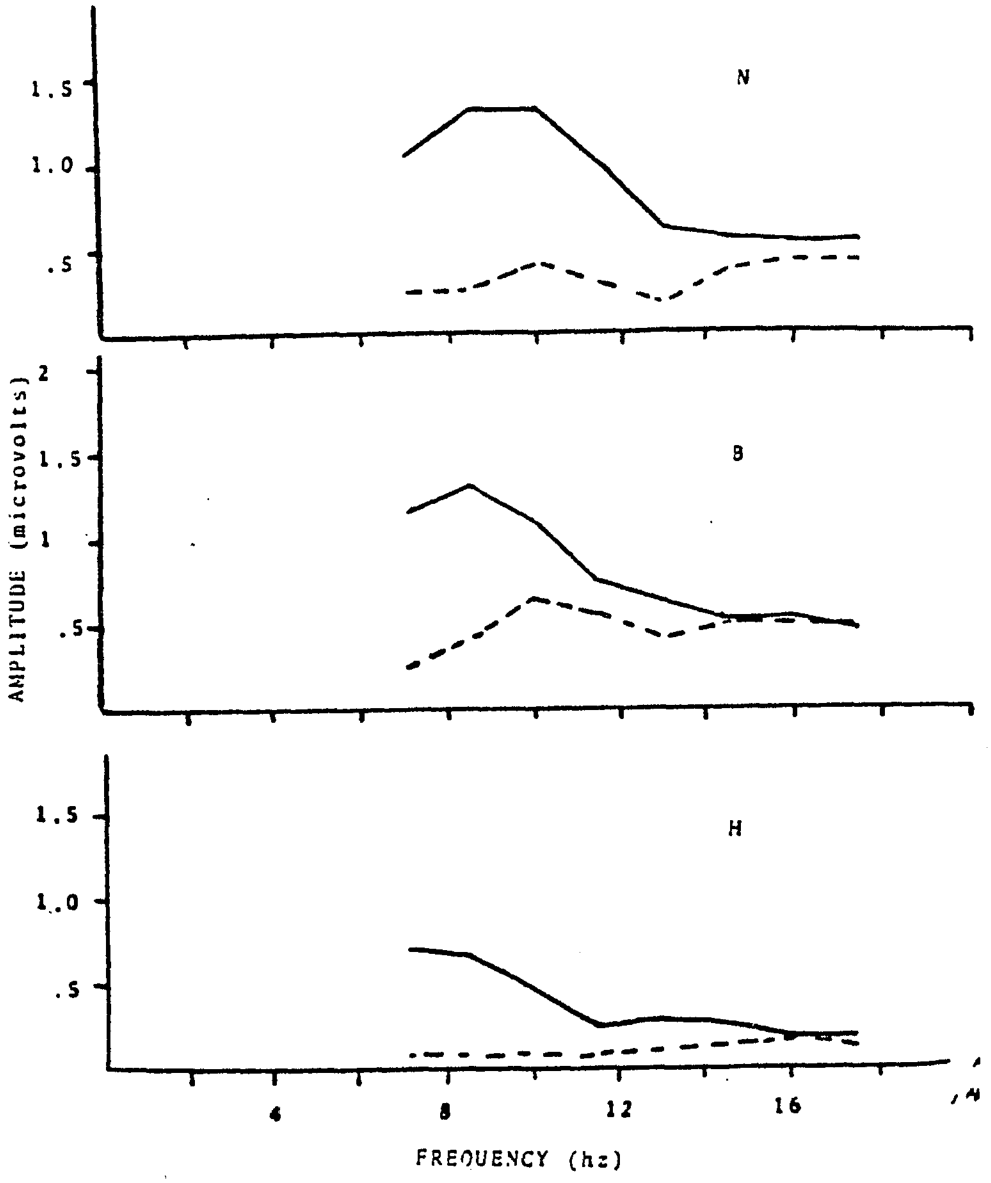

N
1.5
1.0
.5
B
AMPLITUDE (microvolts)
2
1.5
1
.5
H
1.5
1.0
.5
4
8
12
16
FREQUENCY (hz)

Figure 8

VEPs from placements over the directly stimulated hemisphere (whether it was the left or right hemisphere) for all electrode placements showed the largest peak amplitudes for subject N. The midline response showed the largest amplitude when the left hemisphere was stimulated via the ipsilateral eye followed closely by the right hemisphere stimulated via the ipsilateral eye.

H's bipolar recordings from over the directly stimulated hemisphere (left or right) showed the largest amplitude peaks. For the outer pairs amplitudes were largest from placements over the non-directly stimulated hemisphere. The inner pair placement over the left hemisphere showed largest amplitude responding as a result of stimulation via the ipsilateral eye to either hemisphere. The inner placement over the right hemisphere showed largest amplitude responding as a result of indirect stimulation.

C. Amplitude as a function of frequency

In general, VEP amplitudes vary as a function of frequency (Regan, 1968). By plotting amplitude as a function of frequency a subject's "temporal tuning" can be determined. Amplitude by frequency functions for the three subjects in this experiment showed very consistent patterns, not necessarily resembling classical temporal tuning functions.

H's data is closest to what a temporal tuning curve of a simple band pass filter might look like. For all conditions stimulation at the lower frequencies evoked the largest amplitude response (figure 9). There is some decrease in amplitude at the lowest frequency and at higher frequencies the amplitudes declined substantially.

B's data showed the largest amplitude VERs as a result of stimulation at the higher frequencies when recording from the directly stimulated hemisphere, and as a result of stimulation at the lower frequencies when recording from the non directly stimulated hemisphere. This relationship was evident for all conditions as illustrated in figure 10 with just a few exceptions.

N's amplitude by frequency functions were U or inverted U shaped as seen in figure 11. When recording from the directly stimulated hemisphere peak amplitudes were a result of stimulation at about 14-15 Hz and 8-9 Hz with a dip in the middle frequency range. The function was inverted in recordings from the nondirectly stimulated hemisphere, with the largest amplitude responding in the mid-frequency range, at about 12 Hz.

In all three subjects recordings from the unipolar midline placement were closest to unipolar recordings from the non directly stimulated hemisphere with respect to absolute amplitudes and the shape of the amplitude by frequency function as can be seen in figures 9, 10 and 11.

Figure 9

Amplitude by frequency function for Subject H. The right hemisphere was directly stimulated through the left eye. Unipolar recordings from the inner pair of electrodes were taken from over the directly stimulated hemisphere (——) and the non-directly stimulated hemisphere (-----). Unipolar recordings were also taken from the midline placement (.....).

Figure 10

Amplitude by frequency function for Subject B. The left hemisphere was directly stimulated through the right eye. Unipolar recordings from the inner pair of electrodes were taken from over the directly stimulated hemisphere (——) and the non-directly stimulated hemisphere (-----). Unipolar recordings were also taken from the midline placement (.....).

Figure 11

Amplitude by frequency function for Subject N. The right hemisphere was directly stimulated through the left eye. Unipolar recordings from the inner pair of electrodes were taken from over the directly stimulated hemisphere (——) and the non-directly stimulated hemisphere (-----). Unipolar recordings were also taken from the midline placement (.....).

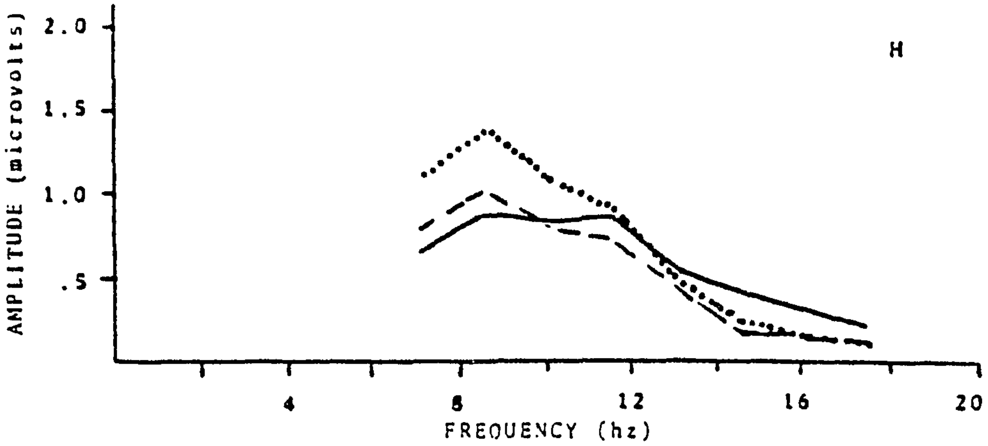


Figure 9

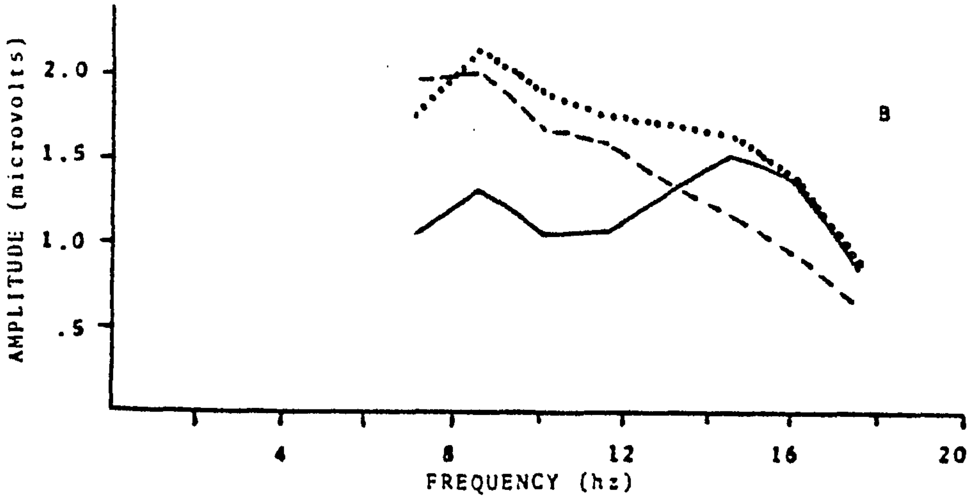


Figure 10

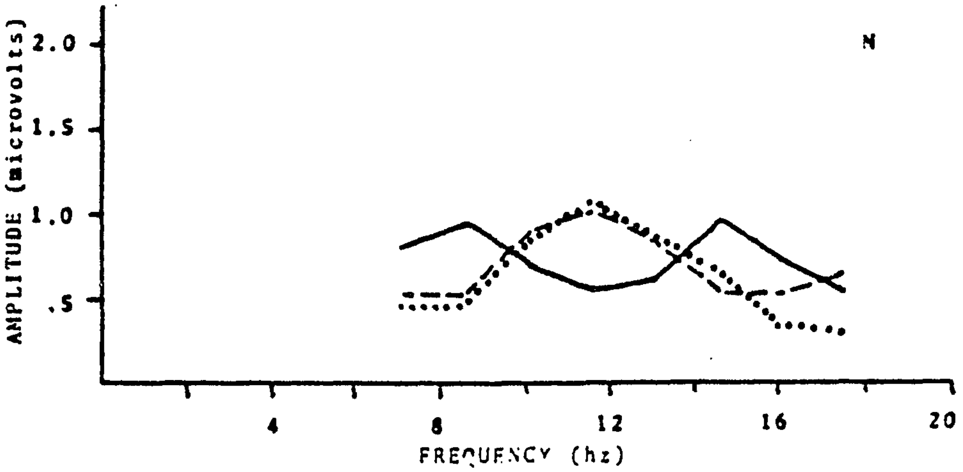


Figure 11

These data cannot be interpreted as simple volume conduction or simple neural transmission from one hemisphere to the other. The inverted nature of the frequency by amplitude function when recording from the directly and non directly stimulated hemisphere for two of the subjects and the differences in the amplitude curves for the third subject can be interpreted as an indication of some additional processing or filtering occurring during the interhemispheric transfer of information. The nature of this additional filtering is not clear, however, since while all subjects show differences the intersubject differences are not consistent.

Van Essen et al (1982) have found a high degree of individual variability in the complexity and structure of the callosal projections. They have suggested several, not necessarily independent, possibilities as to the functional significance of the callosal fibers. First, as an indication of the extent to which receptive fields extend to the ipsilateral hemifield. Second, as a possible modulator for nonvisual processes such as eye movements or attention. And finally, as having a role in the nonvisual processes of pattern discrimination such as memory or strategies. Any of these possibilities, as well as the fact that only the extrastriatal cortical areas have callosal origins and terminations (Van Essen et al, 1982), may indeed be influencing the specific individual interhemispheric differences seen in the VER amplitude data as well as the interhemispheric differences in the phase data described below.

Phase Data:

As described earlier, if there is a constant delay in the transmission of the neural response to the cortex then the phase lag will increase linearly with increasing frequency of stimulation (see figures 3 and 4).

As increasingly higher stimulus frequencies are used, or if the delay is long, the system may not show a response to the stimulus until after the first or even second stimulus cycle. When that happens the phase measurement obtained from Fourier analysis is the phase of the point on that particular stimulus cycle where responding begins. Therefore, a phase measurement of 90° on the second cycle would in fact be a phase lag of 450° -- 360 of the entire first cycle plus 90° of the second cycle (figure 12a). If a phase lag by frequency function were to be plotted for responses over a large frequency range directly from the Fourier analysis measurements it would look like figure 12b. Since the phase measurements at the higher frequencies give no indication of the cycle on which they lie, the measurements must be "rolled over" by adding or subtracting a multiple of 360° to those assumed to be on cycles after the first. Rolling over and plotting the phase measurements from figures 12 a and b would yield the functions shown in figures 12 c and d. Measurement of the degree of linearity of the function is dependent on appropriately rolling over the phase measurements. Since the absolute zero point is not known (that is, on which cycle the response

Figure 12

a) Hypothetical sinusoidal responses to stimuli at frequencies of 1, 2, 4 and 8 Hz. The dashed line indicates the phase lag resulting from a 625 msec delay at each of the frequencies (as in figure 2).

b) Phase lag as a function of frequency plotted directly from the data in a) (as in figure 3).

c) Phase lag as a function of frequency plotted from "rolled over" data from a).

d) Phase lag as a function of frequency plotted from "rolled over" data from a). This plot differs from plot c) in that the data was rolled over using the convention of phase lags being negative.

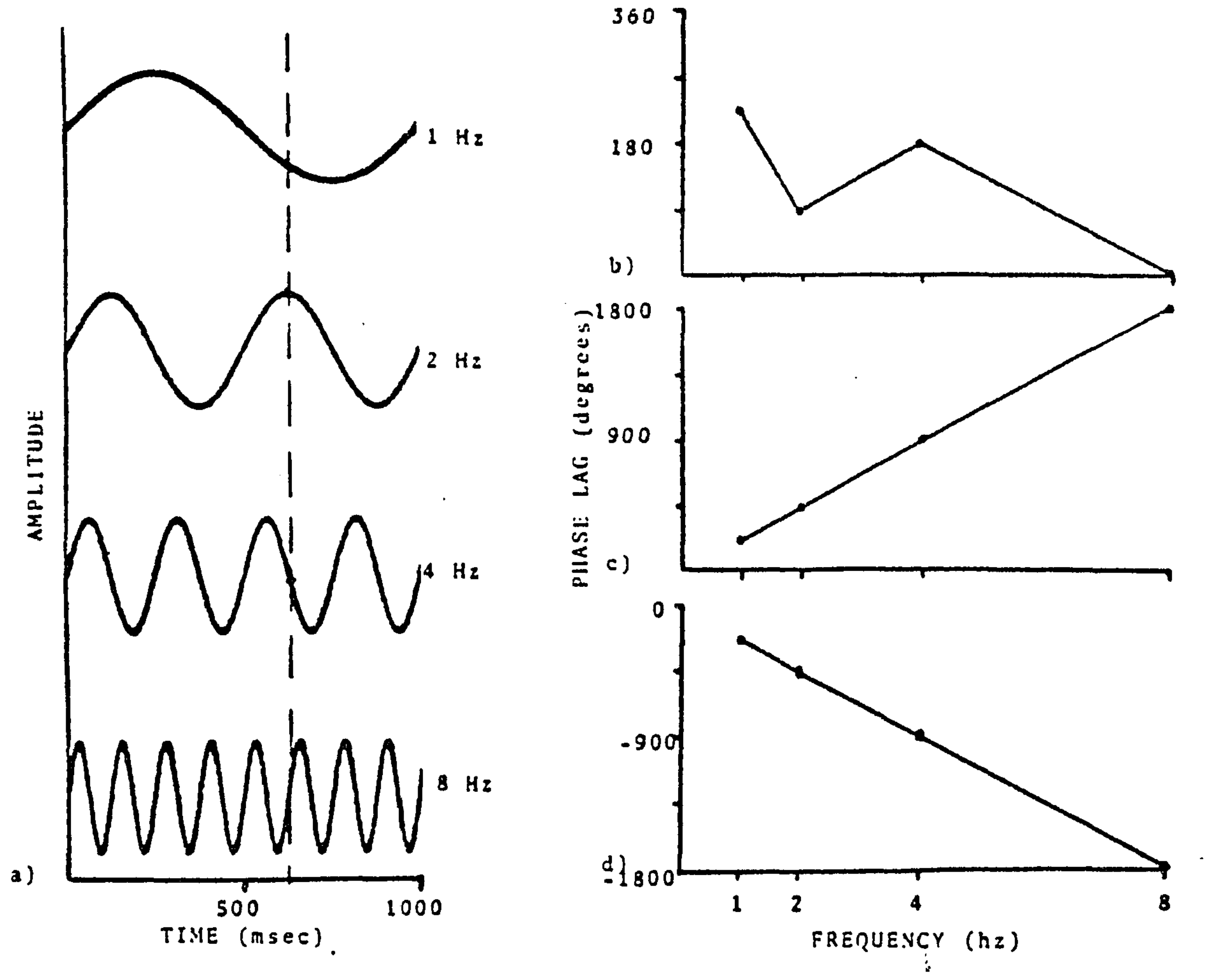

AMPLITUDE
1 Hz
2 Hz
4 Hz
8 Hz
a)
500
1000
TIME (msec)
PHASE LAG (degrees)
360
180
b)
1800
900
c)
0
-900
d)
-1800
1
2
4
8
FREQUENCY (hz)

Figure 12

to the lowest frequency begins) the delay in milliseconds derived from the slope of the phase by frequency function is therefore a relative measure of "apparent latency" (Regan, 1982).

Frequency independent phase shifts are also possible (Regan, 1982). These phase shifts can be used as an indication of additional processing occuring. It is uncertain as to the cycle on which the response to the lowest frequency tested starts unless VERs to very low frequencies are recorded. Here again, since the absolute zero point of the phase by frequency function is unknown, in order to have an indication of frequency independent phase shifts between functions it may be necessary to shift entire curves by a multiple of 360^o (see figure 5). It was necessary to shift several entire functions in this study by 360^o so that they would be more coincidental with the other functions and any displacements of functions could be examined. Only <u>relative</u> comparisons of these phase shifts can be made.

Each subject's phase information for each condition for each session was rolled over as appropriate and a phase by frequency function was plotted. Note that the phase measurements on all of these functions are negative because I used the convention of phase lags being negative as illustrated in figure 12d. Slopes were calculated for each function and measures of apparent latency were derived from those slopes. Comparisons of apparent latencies will be considered below.

A. Linearity of the phase by frequency functions

Linear regression analysis yielded significant correlation coefficients for all of the phase by frequency functions at the .05 level or above.

Although there is a high degree of linearity, examination of N's and B's phase by frequency plots show evidence of "breaks" in approximately 1/3 to 1/2 of the functions. The breaks occur more frequently in VEPs recorded over the directly stimulated hemisphere and are at the same frequencies at which there is evidence of an amplitude change (figure 13). The fact that the phase plots are different in shape for the directly vs. the indirectly stimulated hemisphere can be interpreted as further evidence for rejecting a simple volume conduction or relay model of inter hemispheric transfer of information and is explored in more detail in Experiment III.

B. Measures of apparent latency

Measures of apparent latency derived from the phase and frequency functions indicate an apparent temporal delay in the transfer of information from the directly stimulated hemisphere to the non directly stimulated hemisphere for all subjects in nearly all conditions (figure 14). That is the apparent delay for the nondirectly stimulated hemisphere is greater than for the directly stimulated hemisphere.

Figure 13

An example of a "break" in a phase lag by frequency function occuring at the same frequency where there is evidence of amplitude changes. The data shown, as recorded from subject N when the left hemisphere was stimulated through the left eye, is representative of the breaks in the functions as described in the text. Unipolar recordings from the inner pair of electrodes were taken from over the directly stimulated hemisphere (———) and the non-directly stimulated hemisphere (-----). Unipolar recordings were also taken from the midline placement (.....).

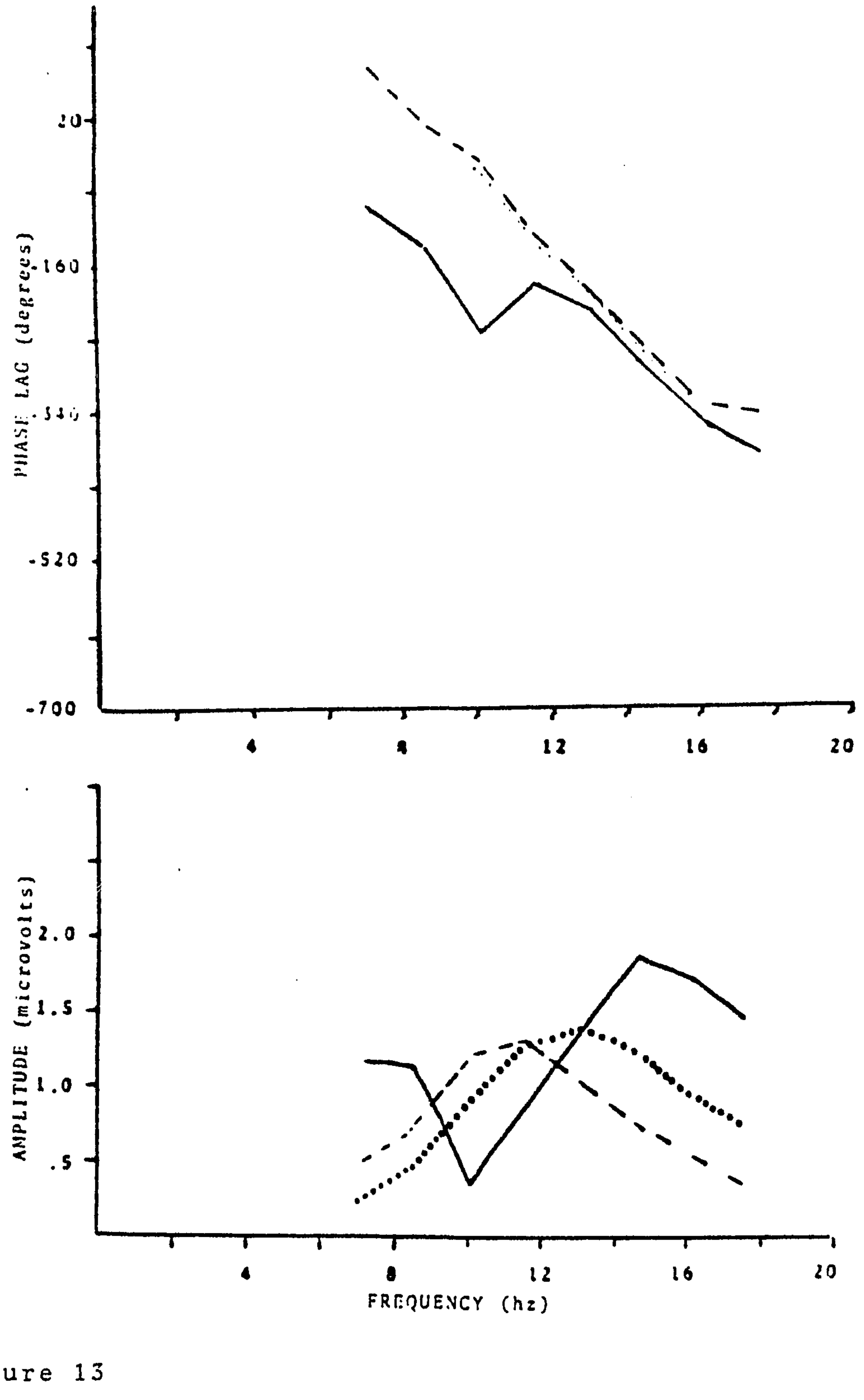

PHASE LAG (degrees)
20
-160
-340
-520
-700
4
8
12
16
20
AMPLITUDE (microvolts)
2.0
1.5
1.0
.5
4
8
12
16
20
FREQUENCY (hz)

Figure 13

Figure 14

Apparent delay measurements (in msec) for each subject for each condition.

Each subject's data is identified by the initial in the upper right corner of each plot.

Conditions are identified as follows:
RR - Right eye, Right visual field
Stimulation of the left hemisphere through the right eye.
RL - Right eye, Left visual field
Stimulation of the right hemisphere through the right eye.
LR - Left eye, Right visual field
Stimulation of the left hemisphere through the left eye.
LL - Left eye, Left visual field
Stimulation of the right hemisphere through the left eye.

Recording sites are as follows (see figure 4 for electrode configuration):
1 - Unipolar recording taken between Cz and the electrode 7 cm lateral and to the left of Oz.
2 - Unipolar recording taken between Cz and the electrode 3.5 cm lateral and to the left of Oz.
3 - Unipolar recording taken between Cz and Oz.
4 - Unipolar recording taken between Cz and the electrode 3.5 cm lateral and to the right of Oz.
5 - Unipolar recording taken between Cz and the electrode 7 cm lateral and to the right of Oz.
6 - Bipolar recording taken between Oz and the electrode 3.5 cm lateral and to the left of Oz.
7 - Bipolar recording taken between Oz and the electrode 3.5 cm lateral and to the right of Oz.

The solid lines indicate that recordings were taken from over the directly stimulated hemisphere, the dashed lines from over the nondirectly stimulated hemisphere and the dotted lines from over the midline placement.

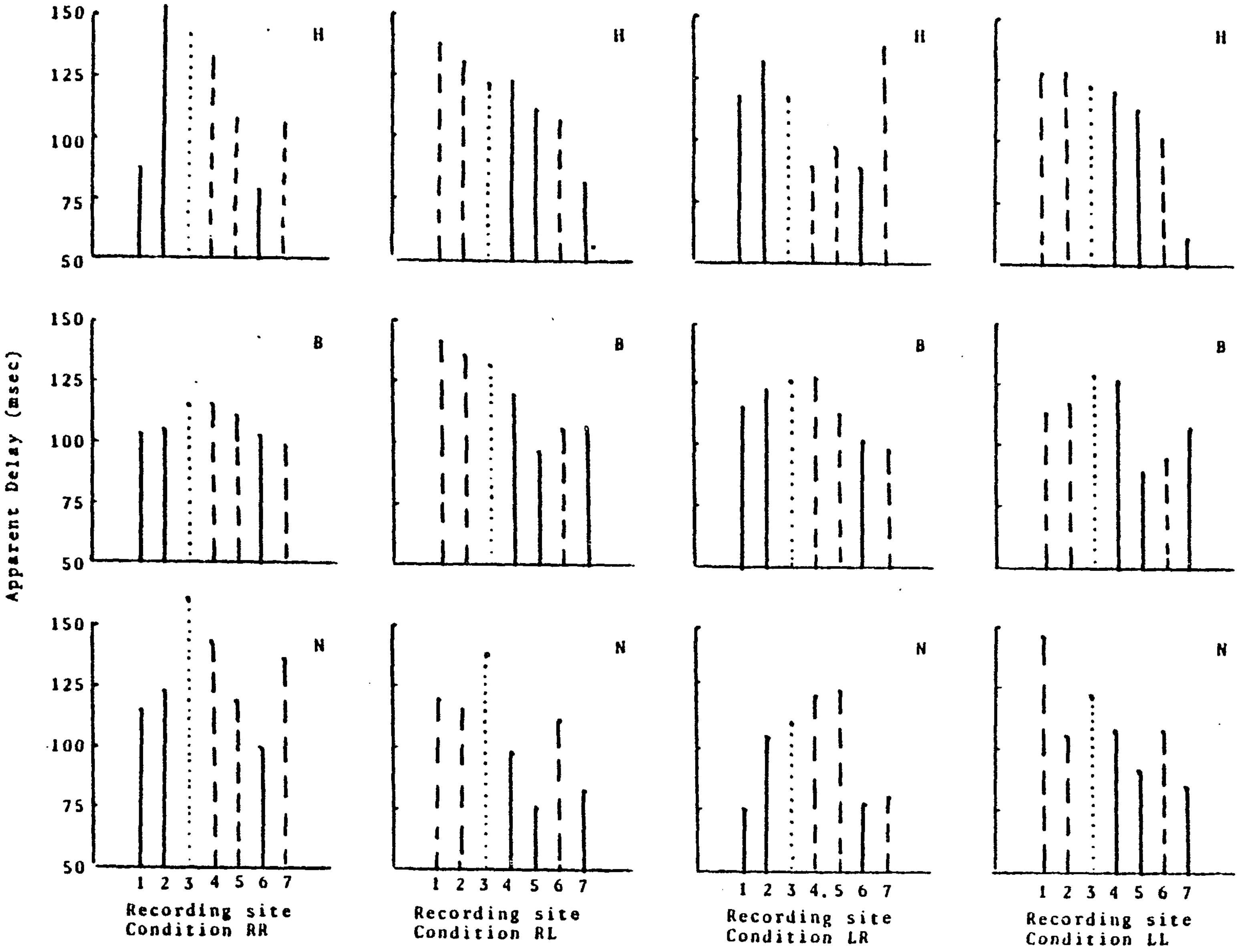

150
125
100
75
50
Apparent Delay (msec)
H
B
N
1 2 3 4 5 6 7
Recording site
Condition RR
1 2 3 4 5 6 7
Recording site
Condition RL
1 2 3 4.5 6 7
Recording site
Condition LR
1 2 3 4 5 6 7
Recording site
Condition LL

Figure 14

Of the 36 combination compared (inner pair, outer pair and bipolar pair for four conditions for three subjects) 28 showed this relationship. T tests performed on all combinations showed significance at the .05 level or above for 10 of the 28 comparisons showing a temporal delay in interhemispheric transmission to the indirectly stimulated hemisphere (table 1).

Fixation errors may have on occasion moved the stimulus to the central fovea. This would decrease the apparent delay by reducing the slope of the phase by frequency function for the indirectly stimulated hemisphere. Thus the difference in apparent delay between direct and indirect measurements are minimum estimates. Fixation errors could never increase the delay difference values. In addition, direct observation of subjects indicated no eye or head movements of sufficient magnitude to have moved the stimulus into the foveal area.

C. Frequency independent phase shifts

Further indication of additional inter hemispheric processing can be seen by comparing the starting points of the phase and frequency functions at each pair of electrode sites.

Evidence of frequency independent phase shifts were seen in more than 66% of the comparisons of inner pair, outer pair and bipolar phase by frequency functions for all subjects. Displacements ranged from 10 to 180 degrees with no particular interaction between degree

Table 1

Comparisons of mean apparent latencies for each subject for each condition.

Conditions are identified as follows:
- RR - Right eye, Right visual field
  Stimulation of the left hemisphere through the right eye.
- RL - Right eye, Left visual field
  Stimulation of the right hemisphere through the right eye.
- LR - Left eye, Right visual field
  Stimulation of the left hemisphere through the left eye.
- LL - Left eye, Left visual field
  Stimulation of the right hemisphere through the left eye.

Comparisons are as follows (see figure 14 for identification of recording sites):
- Outer pair - L = site 1; R = site 5
- Inner pair - L = site 2; R = site 4
- Bipolar pair - L = site 6; R = site 7

MEAN APPARENT LATENCIES (msec)

	Outer pair			Inner pair			Bipolar pair		
	L	R		L	R		L	R	
Subject B									
RR	101.32	110.42	t=-1.95	103.76	114.87	t=-2.37	101.75	99.36	t=.7
RL	140.3	95.17	t=5.84*	136.81	119.21	t=1.44	105.83	106.74	t=.08
LR	107.89	112.5	t=-1.18	111.96	117.3	t=-1.74	102.78	99.18	t=1.10
LL	100.07	89.34	t=.54	117.58	127.34	t=-.54	95.69	107.13	t=-1.2
Subject N									
RR	112.91	118.76	t=-.11	108.03	141.29	t=-.91	99.7	135.57	t=-.74
RL	119.46	76.3	t=10.71*	114.54	87.98	t=3.86*	110.75	83.97	t=2.41*
LR	72.51	122.46	t=-9.34*	104.94	120.8	t=-.53	77.31	79.92	t=-.51
LL	146.98	90.68	t=1.67	106.66	108.44	t=-.05	108.155	84.35	t=2.76*
Subject H									
RR	86.53	108.82	t=-.87	151.15	131.51	t=1.55	79.67	82.79	t=-.1
RL	138.52	111.78	t=2.39*	130.8	122.41	t=2.07	107.3	81.68	t=3.4*
LR	118.5	97.84	t=.84	131.59	89.5	t=1.87	89.09	139.13	t=-1.93
LL	128.12	113.19	t=.66	128.22	120.4	t=.77	101.58	60.52	t=5.07*

* indicates significance at the .05 level or above (3 df)

Table 1 Mean appparent latencies for electrode comparisons of displacement and stimulus condition. Here again, since the absolute zero point of the phase by frequency function is unknown, it is impossible to determine whether the function derived from the directly stimulated hemisphere actually lies above or below that of the indirectly stimulated hemisphere. In light of that, no speculations as to the specific nature of the additional processing obviously occuring during the interhemispheric transmission of visual information can be made.

EXPERIMENT III:

The breaks in linearity of the phase by frequency functions and their correspondence to amplitude changes as a function of frequency raised questions as to relationships between phase information and "temporal tuning" functions.

In order to examine these relationships, an additional subject (J) was chosen to be tested using the same procedure as in Experiment II. Temporal tuning functions had previously been obtained for J in this laboratory using the same equipment. Conte et al (1983) had modulated a grating pattern in an appearance-disappearance paradigm. The pattern was modulated about a particular contrast where instead of the pattern components reversing from dark to light as in Experiments I and II of this study, the pattern faded away and reappeared. Although the major portion of the response is seen at the fundamental frequency there is still a significant second harmonic response. As can be seen in figure 15, there is an amplitude peak evident at a stimulus frequency of about 5 Hz which corresponds to the second harmonic response frequency of 10 Hz. This peak shows the temporal frequency that will evoke the best response for this subject.

J's phase by frequency functions from Experiment III show a high degree of linearity as tested by linear regression analysis at the .05 level or above. As with N's and B's data in Experiment II, J's functions show similar breaks in linearity. The breaks in J's functions measured in Experiment III with contrast reversing checkerboards are at the same temporal frequency (about 10 hz) as the peak in the temporal frequency tuning function measured with appearing-disappearing gratings (figure 16).

Figure 15

Second harmonic response amplitude as a function of temporal frequency for Subject J (from Conte et al, 1983). VERs to appearing-disappearing gratings were recorded from midline placements.

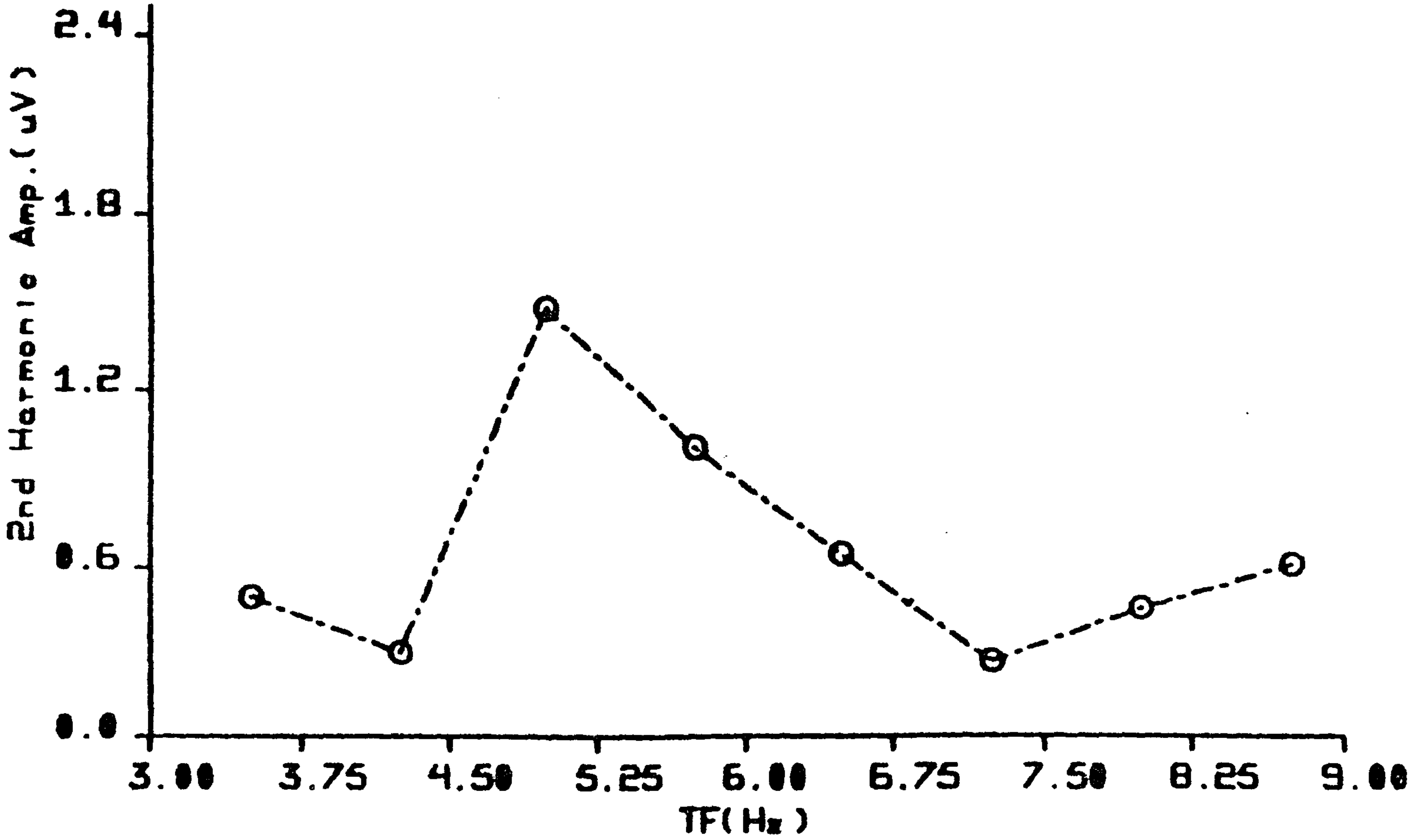

2nd Harmonic Amp.(uV)
2.4
1.8
1.2
0.6
0.0
3.00
3.75
4.50
5.25
6.00
6.75
7.50
8.25
9.00
TF(Hz)

Figure 15

Figure 16

Phase lag by frequency functions for Subject J. Unipolar recordings from the inner pair of electrodes were taken from over the directly stimulated hemisphere (———) and the non-directly stimulated hemisphere (-----). The data in the upper panel was recorded when the left hemisphere was stimulated through the left eye and the data in the lowere panel was recorded when the left hemisphere was stimulated through the right eye.

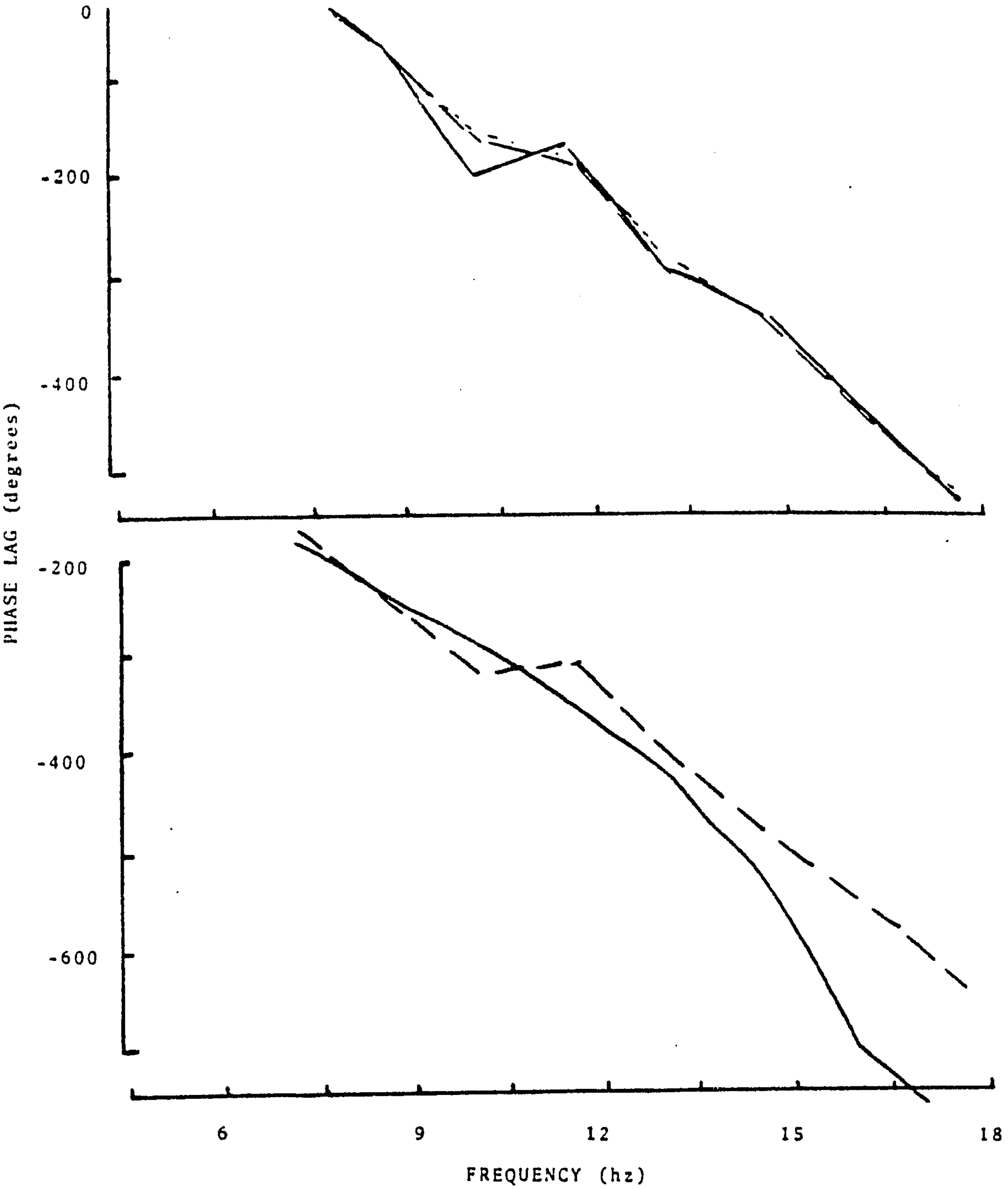

0
-200
-400
-200
-400
-600
PHASE LAG (degrees)
6
9
12
15
18
FREQUENCY (hz)

Figure 16

SUMMARY

Direct visual stimulation of one cerebral hemisphere resulted in reliable VERs from recording sites over both hemispheres. A temporal delay was found between the recordings from over the directly stimulated hemisphere and from those over the non-directly stimulated hemisphere as measured by apparent latencies. No consistent differences were found when apparent latencies were compared for direct stimulation of the left and right hemispheres or when stimuli were presented through the eye ipsilateral or contralateral to the directly stimulated hemisphere. However, a simple delay in interhemispheric transmission due to neural transmission time or volume conduction cannot account for the consistent patterns found in the amplitude and latency measurements for each of the three subjects. The individual differences found in these patterns may be due to individual differences in the convolutions of the cortex, the shape of the head or visual information processing. In spite of the individual differences seen, the data indicate evidence of additional processing or filtering occuring during the interhemispheric transfer of visual information.

There are several ways in which the underlying neural processes and specific filtering properties could be explored using direct visual stimulation of only one cerebral hemisphere. Modulation transfer functions and spatio-temporal mapping using wide ranges of spatial and temporal frequencies would yield information as to the specific areas in the spatial and temporal frequency spectra and their interactions affected during interhemispheric transmission.

Modulation of more complex stimulus patterns than those described above have been used to identify and localize lateral interactions in the visual system (Ratliff and Zemon, 1982). Underlying neural mechanisms in the interhemispheric visual pathways can be explored in a similar manner.

Split-brain patients have few if any direct interhemispheric pathways. Using the same experimental design as decribed in this paper, a study with split-brain patients could rule out any influence of volume conduction, since any responses found in the nondirectly stimulated hemisphere of such patients could be assumed to be due primarily to volume conduction.

One other interesting result was derived from these data. As described in Experiment I, several stimulus field sizes were tested at different eccentricities into the peripheral retina. The cortical magnification factor, as outlined above, does not account for the degree of the attenuation of the VER as recorded from both the directly and nondirectly stimulated hemispheres when stimuli were presented more than .5 degrees lateral to central fixation. The stimulus field size was increased so that VEP amplitudes should have been, at the very least, comparable to those evoked by centrally fixated stimuli (as in Tyler and Apkarian, 1982; Tyler et al, 1980).

An additional confounding factor might be the fact that cortical projections from the peripheral retina are buried deeper in the cortex and cortical fissures and are therefore less accessible to surface electrodes than are foveal projections. Cortical mapping studies such as those by Dobelle et al (1979) have been conducted with direct cortical stimulation and/or recording techniques. Steady state VERs may not be accurate enough to yield data that conforms to Dobelle et al's findings.

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