PATTERN-SHIFT VISUAL EVOKED POTENTIALS. A LECTURE FOR THE WHO-NYI TRAINEES

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ABSTRACT

In this article, concerning the technical, scientific, and clinical aspects of Pattern-Shift Visual Evoked Potentials, the available data have been reviewed.

Keywords: Pattern-Shift Visual Evoked Potentials.

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ÖZET

Bu yazıda Pattern-Shift Visual Evoked potansiyeller hakkında bilinen teknik bilimsel ve klinik veriler gözden geçirildi.

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GENERAL DESCRIPTION of EPS

There are specific EEF responses to certain types of sensory stimulation. These responses, however, are generally hidden in background EEG activity in the conventional EEG recording. In evoked potential testing (EP), a stimulus from one sensory modality is presented to the subject repeatedly, and the EEG responses are recorded under standardized conditions. The brain electrical activity on EEG that follows each repeated stimulus is then averaged. It is therefore possible to average out most of the brain electrical activity thought not be directly related to the evoking stimulus; hence, the non-stimulus related background EEG is largely removed. What remains is a stimulus-related characteristic waveform, the evoked potential.

They consist of a sequence of deflections, or waves, each characterized by;

(1) positive or negative electric polarity,

(2) number of the wave in a sequence,

(3) Latency from the onset of the stimulus or from a precding peak,

(4) amplitude with respect to the baseline or to the preceding or subsequent peak of opposite polarity,

(5) waveshape, and

(6) distribution.

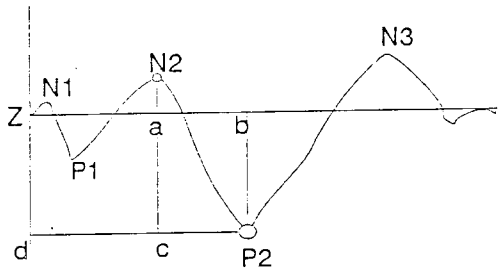

Figure 1. A schematic evoked potential output
1. b to P2 is the amplitude of the P2 wave
2. N2 to c is the peak to peak amplitude og the P2 wave
3. d to P2 is the latency of the P2
4. c to P2 (or a to b) is the peak to peak latency of the P2 wave

STIMULUS

The preferred stimulus for clinical invetigation of the visual pathways is a shift (reversal) of a checkerboard pattern (usually black and white) In the EP nomenclatur, it is called prolonged stimulus (Fig 2).

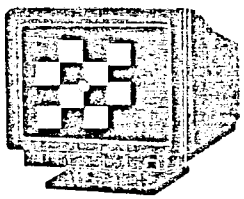

Figure 2. VEP Stimulator (Checkerboard)

(*) Psikiyatri Uzmanı, İ.Ü. Cerrahpaşa Tıp Fak. Psikiyatri ABD.

The squares simply reverse without change in total light output (luminance) from the screen. Initial clinical applications of VEPs employed a stroboscopic flash stimulus, but the utility of the flash evoked VEP is severely limited by the great varibility of responses among normal individuals and its relative insensitivity to clinical lesions. Occasionally, flash VEPs may provide limited information about the integrity of visual pathways twhen the preferred pattern-reversal stimulus cannot be used, as in infants or other patients unable to cooperate for more sensitive testing methods. A few investigator use the sinusoidal stimulators. This appears to enhance test sensitivity by permitting selective stimulation of retinal elements responsive to specific spatial frequencies, and of cortical elements sensitive to both spatial frequency and orientation (1).

Stimulus parameters:

1- Visual angle: This is a function of the distance from the subject's eye to the pattern an width of the pattern (or check). It may be calculated as follows:

1. Divide the width (height) of the pattern (or check) by 2.0

2. Divide that answer by the eye-pattern distance (measured in same units as width).

3. Take this number as a tangent value, and find the angle corresponding this value which can be found on a calculator or in a table.

4. Multiply this angle by 2.0. (Fig 3).

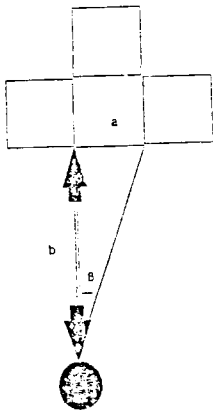

Figure 3. Calculation of the angle

The overall pattern jidth should be grater than 8 degree if only full field stimulation will be used or greater than 20 degree if partial field stimulation will be used. since the screen is usually placed at least 70 cm from the eye, the minimum dimensions of the entire pattern would be 10cm and 24 cm respectively. The individual check size most commonly used is about 35' (minutes) (7 mm at 70 cm), although checks as small as 15' (3 mm) are used. The smaller checks may have greater sensitivity in revealing abnormalities; however responses obtained with smaller checks are more likely to be affected by visual acuity and luminance changes which may lead adelay in latency.

2- Luminance (brightness): it must be very carefully controlled because small changes in luminance produce significant latency shifts in PSVEP. TV-type devices need to have the variable brightness control removed o otherwise locked. At present it is not important to be able to quantify screen luminance. However, it is recommended that a high quality, photographic light meter may be used to record the secreen luminance. The needle position on the light meter is all that needs to be follojed. In another word, it does not need to be translated into a standatd measure of brightness.)

PRETEST INSTRUCTIONS

1. The patient should bring eyegalsses used for reading

2. Hai should be washed.

3. A patient should not be sent for testing who has had mydriatic (pupilldilator) medication within 12 hours of testing, even if meiotic (pupilloconstrictor) were subsequently used. The increased pupillary diameter increases retinal illumination and has been reported to decrease P100 latency.

In laboratory, corrected visual acuity should be tested such as by fingers.

The technician should extract pertinent clinical information from the medical record and/or history of patient. The results of neuroophthalmological examinations including visual-field testing, are of perticular importance in considerations of clinical correlations. Patients with field defects are tested with laterally placed as well as midline electrodes if the midline responses are abnormal, because field defects are alter the potential-field distribution of the P100 waveform shifting the amplitude maximum away from the midline. Thus it is important to know of the field defect before performing the test if lateral electrodes are not used routinely.

RUNNING THE TEST

With the preliminaries accomplished, the subject is seated in front of the checkerbord at an eye-screen distance of 70 to 100 cm. At this distance it is more difficult to voluntarily defocus the pattern. The eyes are always tested one at a time (monocularly) and the opposite eye is covered with an eye patch.

The subject is instructed to stare at a dote in the center of the pattern being displayed. This dot may be colored or it may be a small light. Although precise fixation on this point is not important and minor wanderings of gaze do not singificantly affect P100 latency or amplitude, it is important that the subject maintain gaze fixation near the center of the screen. If this is not done, P100 amplitude will be diminished. If automatic artifact rejection is not available, the raw EEG signal must be monitored on an oscilloscope and averaign halted manually when excessive artifact is present, for example, during coughing, swallowing,

and moving. The PSVEP equipment is set up so that the subject can be seated at 1 m. Provision must also be made so that the technician can check to see whether or not the subjet is watching the screen. This can be accomplished by having the equipment aranged so that the technician, stationed at tha averager, is at an oblique angle in front of the subject.

AMPLIFIER CONTROL

PSVEPs are best recorded by using an amplification of 20.000 to 100.000. The filters are 1-3 Hz low cutoff (high pass) and 100 to 300 Hz high ctuoff (low pass). These values play a role on the results particularly on the latency.

AVERAGER

The electrical responses of the brain, brain stem, or spinal cord to a single stimulus, when recorded at the surface of the body, are small and obscured by EEG, EKG, muscle activity, and other biological and extraneous electric activity so that individual responses can not be clearly distinguished and seem to fluctuate in repeated recordings. Averagin serves to extract th responses, time-locked to the stimulus and considered signal in this context, from potential changes unrelated to the stimulus and here summarily considered noise. Averaging is done bya presenting sensory stimuli repeatedly, collecting and adding each response to the preceding ones, and dividing sum by the number of responses. This procedure enhances the signal by reducing the noise toward zero. Averaging is carried out by a digital computer that (1) records electric activity during the selected time period, (2) converts the continous voltage change of the recording (anolog recording) during that period intoa sequence of numbers (digital recording), (3) adds the number representing recordings after succesive stimuli to each other and scales them to the average (Fig. 4).

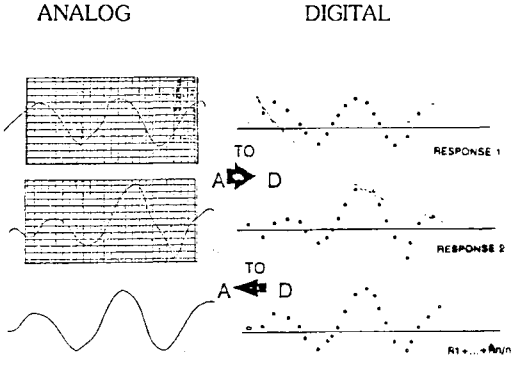

Figure 4. Averaging of EPs.

NUMBER OF RESPONSES TO BE AVERAGED (NOISE REDUCTION)

In practice, the number of responses collected should be large enough that succsively averaged EPs do not differ from each other. Each EP should be recorded at least twice, and the tracings should be superimposed to ascertain that they resemble each other closely enough in latency, amplitude and shape. If two succesive EPs do not replicat within these limits, more avarges must be obtained until it is clearly established. The aveager is set for a total sweep duration of 300 to 500 msec. Shorter durations spread out the P100 and make abnormal responses that may already have a long duration even more difgicult to recognize. Each channel should be composed of at least 256 points,sampled with a maximum intersample interval (dwel time) of 2 msec. The automatic sweep repatition control should be set to 100. It will be necessary sometimes to continue to 200 or 500 sweep repetitions if teh patient is noisy or the responses are nuclear for other reasons (abronmally low amplitude). Also, it is mandatory to repeat the trial and superimpose it on the previous trial to test waveform consistency. It may be necessary to repeat the test two or four times to arrive at a good measure of response variability.

In theory, for instance, a cortical response which has an amplitude of 10 microvolt and is embedded in EEG activity of 20 microvolt, has a signal-to-noise ratio 1:2. Averaging only four responses improves this ratio by a factor of 2. This illustrates the importance of using good recording methods to minimize artifacts and of using filters to exclude those portions of the frequency spectrum that do not contain signal components; both these measures reduce tha noise component, let the computer begin to work at a more favorable signal-to-noise ratio, and thereby effectively reduce the number of responses required for the definition of an EP. Of great practical importance arge gross deviations from random noise such as those cased by intermittent large transients, for instance artifacs or K complexes of the sleep EEG. If such a transient enters the average, it is not reduced by thef actor predicted for noise reduction because it does not represent randomly distirbuted noise.

CHANNES TO RECORD

Because of the normal anatomical variations of the occupital cortex around the calcarine fissure, maximum amplitude of P100 does not have an exact predictable location in the midline.Therefore it is better to use FZ, CZ, PZ, and Oz electrodes when recording the PSVEP. Reference sites used are earlobel or forehead. Both are active but to a degree that does not interfere singificantly with the posterior midline recordings.

A suggested six-channel montage for recording PSCAPs produced by full-field or partial-field stimulation is:

Channel 1: Fz to reference.

Channel 2: Cz to reference.

Channel 3: Pz to reference.

Channel 4: Oz to reference.

Channel 5: L5 to reference.

Channel 6: R5 to reference.

L5 and R5 refer to electrode locations 5 cm up from the inion and 5 cm lateral to mitline on the left and irfght, repectively. this mantage provides some information about the horizontal distribution Of P100, thus eliminating the need to repeat the test as is required when midline montages show abnormal responses.

PRECHIASMAL, CHIASMAL, RETROCHIASMAL STRATEGIES

Different combinations of monocular and half-field stimulation and of recording from midline and lateral occipital electrodes are used to detect lesions in the three major portions of the visual pathway, namely (1) the prechiasmal part, consisting of retina and optic nerve (2) the optic chiasm, (3) the retrochiasmal portion, consisting of optic tract, lateral geniculate body, optic radiation, and visual cortex.

1. Prechiasmal Staregy: Monocular full field stimulation and midline recording needs to be used.

2. Chiasmal Staregy: Monocular half-field stimulation and bilateral occipital recording is needed.

3. Retrochiasmal startegy: Monocular half-field stimulation and bilateral occipital recording is needed.

Choice of strategies: Clinically most useful is the prechiasmatic strategly. If this strategy shows an abrormal VEP pattern, particularly bilateral monocular abnormality,it requires further investigations with half-field studies.

TROUBLESHOOTHING

If no responses are obtained, consideration should be first given to the following principles;

1. Biological errors: If some waveforms are clearly seen but others are poorly seen or absent, this is likely due to a biological error (lesion in the patient, conduction defect).

2. Technical Error: If no waves at all are seen after trial repetition, especially, if no stimulus artifact is present, it is most likely due to a technical error. In this case, the problem may be related to the stimulus, amplifier, or averager.

Stimulus:

1. If the patient can see the stimulus?

2. Is the stimulator power ON?

3. Are the stimulator parameters set properly (freqency, duration, intensity, repeat mode)?

4. Is there a brak in the wires going to the stimulating electtrodes (this is a common problem)?

5. Is the synchronization pulse gettin to the averager? (trigger)

Amplifier:

1. Are the patient electurodes plugged into the electrode interface panel (headbox)?

2. Is the headbox connected to the amplifiers?

3. Are the channel derivations selected properly?

4. Are the amplifiers ON? (not set to stand by or cal)

5. Are the gain and filter controls set poperly?

6. Does it have a 60 HZ (in Europe 50 HZ) artifact?

If there is question, you may want to look at a known calibration signal.

Averager:

1. Is the averager synchorized properly with the stimulus or is it being controlled by another stimulator or free-running?

2. Was the memory erased before you began the trial?

If the answer still has not been discovered, then you must avarage a calibariton signal to test the entire system.

If the amplitude is low, there may be a problem with fixation or watching the pattern. If there are no recognizable waveforms, the patient's visual acuity may be too poor to distinguish the checks. The visual angle subtended by the checks must be increased (by making the checks larger of moving the patient closer to the pattern).

READING THE RESULTS, NORMATIVE DATA, AND VARIATIONS

The latency of an EP compenent is generally measured from the onset of the stimulus to the point of makximum waveform amplitude (either positive or negative). Interpeak latencies are by measuring the time differential betweenpeaks on the same EP. Waveshape variability is a measure of how much the waveform of the EP changes for the same subject without changes in the stimulus or recording conditions.

The latency and amplitude values are compared to the laboratory's normative data and a conclusion reached regarding whether the responses are normal or abnormal. Finally, the clinical significance of the findings should be interpreted, whenever possible, in light of other relevant clinical data.

In case of PSVEP recording from the region of OZ and the inion, three peaks can usually be identified in normal subjects (Fig. 5).

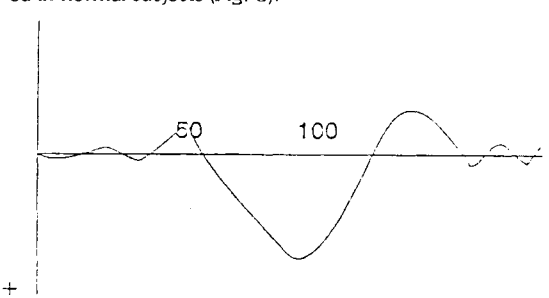

Figure 5. Normal PSEVP.

The peak polarities are negative, positive, and negative, respectively, and mean peak latencies are 70, 100, and 135 msec. The first negative wave may be difficult to indentify in some normal subjects and many patients, and the second negative peak is too inconsistent in latency and amplitude to be of clinical utility. Only the first, large, positive peak, labelad P100 or P2, is seen in all normal subjects and has a variability small enough to make it reliable in clinical situations.

For full-field stimulation, P100 measurements taken from midline recording derivations are:

1. Absolute latency

P100: 89.5-117 (Suggested by some laboratories. Each lab. has to calibrate its own normative data.)

2. Interocular absolute latency difference

P100: 0-6 msec.

3. Amplitude

P100: 3-21 microvolt.

4. Interocular amplitude difference ratio

P100: < 2.5

5. Duration (No generally accepted normative value is available Bach lab. has develop its own value.)

In case of bifid, or W-shaped P100, location of the latency can be determined by extrapolating from the side limbs.

SMOOTHING

High frequency noise components are often superimposed on EPs and can be reduced by smoothing, a fairly simple digital filtering method. Smoothing operation must be used with caution. Even though it does not distort the phase relationship between EP peaks, it may change the EP shape by reducing the amplitude of short waves more than that of long ones.

CURSOS

A cursor is a marker represented by an increased brightness of one dot in the line of dots forming a digital display or by a vertical line above or below that display. The cursor can be placed on any point of the digital display. The cursor can be placed on any point of the digital display. The numerical values of the amplitude and latency of the point indicated by the cursor are shown on the oscilloscope screen.

Most averagers provide a selection of one or more cursor. If one cursor is selected for a measurement, the readout indicates amplitude and latennсy of the selected point with reference to the first point of the display. If two cursors are selected, the readout indicates the difference in amplitude and time between the two points marked by the cursors.

NONPATHOLOGICAL FACTORS AFFECTING RESULTS

Technical Factors:

1. Luminance: It has marked effect on latency. Latency increases as luminance decreased.

2. Contrast: (Luminance difference between light and dark checks) Reductions in the contrast caused increased latency and decreased amplitude.

3. Stimulus field size: Dimunition in field size results in a decline in P100 amplitude but little change in latency .

4. Check Szie: Smaller checks produce larger amplitude P100s unless they are not smaller than the visual acuity for the eye. Another important point is that, as check size is increased above 2 degree the contribution of luminance overcome the pattern reversal effect, and this results in excessive variability of P100 latency and shape. Because of this, the clinical use of checks of 2 degree or greater is contrindicated.

5. Reversal Frequency: If you increase tha stimulus rate (frequency of pattern reversal) from 1 to 4, the P100 latency is increased about 5 msec. At faster rates, the waveform becomes less distinct.

6. Monocular versus binocular stimulation: VEPs to stimulation of either eyes normlly very similar to each other. The VEP to stimulation of both eyes may have slightly larger amplitude but normally has tha same latency. In patient with an abrormal VEP to stimulation of one eye, the EP to binocular stimulation is usually normal.

7. VEPs to full-field stimulation: normal monocular full-field pattern VEPs have a maximum at the midline of the hedadand are usually fairly symmetrical on the two sides.

8. VEPs to half-field stimulation: stimulatin of each half-field produces occipital VEPs that have maximum amplitude, and peaks similar to those of the full-field VEP, at the midline and ipsilateral to the stimulated half-field, opposite the stimulated hemisphere.

Subject/Patient Factors:

1. Age: After the fifth decade there is an increase of latency, 2 to 5 msec per decade. The latency reach the adult values in 5 or 6 years. But adults. Durng the adult life, it remains quite stable.

For the normal preterm infants below 32 weeks, VEP consists of a broad negative deflection only. At 32 to 35 weeks postmenstrual age a small positive deflection appears before the negativity which increases in amplitude with the age. Maturation of the VEP with development of the positive wave in a normal infant is shown on the left side of the (fig. 6)

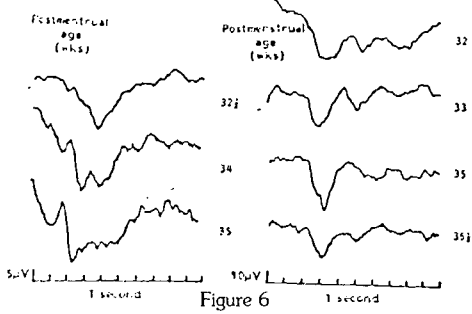

Figure 6

abnormal maturation withdelayed appearence of the positive wave in an infant with a Grade III periventricular hemorrhage is shown on the right side. A correlation is found between the presence or absence of an acuity and the presence or absence of a positivity in the VEP. This assessment of visual function in newborn infants provides information on the integrity of the visual pathway, and has been claimed to be a reliable predictor of a later intellectual performance(2).

2. Reproducibility and reliability: The latency of P100 is reasonably stable and not affected by the level of attention or concentration. While the waveshape and amplide is vulnerable to the changes and may show variability within case himself and interindividually.

3. Body Temperature: It does not affect the result.

4. Gender: Females have been found to have slightly shorter P100 latencies and greater amplitudes than males.

5. Eye Dominance: P100 amplitudes are higher in the dominant eye thanthe other one.

6. Drugs: There have been few reports of the effects of common therapeutic medications on PSVEPs. It is found that lithium had no effect on latencies, although amplitude changes were seen.

7. Hyperventilation: Small decrease in P100 latency is reported in subjects jith hyperventiltion.

8. Background Activity: VEPs vary with amplitude (3) and phase (4) of alpha rhytm.

9. Heart rate and blood pressure: These are not important except in very small EPs.

10. Time beween averages: EPs recorded from the same subject in different sessions vary more than EPs recorded durging the same session.

11. Difference between laboratories:EPs recorded from the subjects in different laboratories vary more than EPs recorded from the same subject at different times in the same laboratory (5).

ANATOMIC AND PHYSIOLOGIC BASIS OF PSVEP

Because of the lens properties of the eye, the right half of the visual field is projected onto the left half of the retina and vice versa. The retinal areas then map into the lateral geniculate bodies in the thalamus and from there to the occipital cortex.

%80 of response arise from the fovea-central 8 degree. However, the peripheral 8 to 32 degree still produce a signicant contribution to the P100 amplitude. Similarly, patients with progressive constriction of their cvisual fields because of retinitis pigmentosa may have a P100 of low central areas are larger than the peripheral areas.

The major effect of the pattern-shift stimulator is located on the fovea. Fovea is thinned-out rod-free portion of the retina where the cones are densely packed and ae few cells and no blood vesels overlying the receptors. The fovea is highly developed in humans. It is the point where visual acuity is greatest. When attention is attracted to or fixed on an object, the eyes are normally moved so that light rays coming from the object fall on the fovea.

The brain areas activated by visual stimuli have been investigated in monkeys by means of radioactive 2-deoxyglucose. Activation occurs not only in the occipital lobe but also in parts of the inferior temporal cortex, and portions of the frontal cortex. The subcortical structures activated colliculus, pulvinar, caudate nucleus, putamen, claustrum, amygdala.

What is cone: They have a high threshold, but have a greater acity. It is the system responsible for vision in bright light (photopic vision) and for color vision.

What is rod: It is another receptor of the vision located in the retina except fovea centarils. They are extremely sensitive to light and are the receptors for night vision (scotopic vision). The scotopic visual apparatus is capapble of resolving the details and bonudaries of obwects or determining their color.

PHYSILOGICAL BASIS OF PSVEPs

The electrical events that occur in the cortex after stimulation of a sense organ can be monitored with an exploring electrode connected to another electrode at an indifferent point some distance away. A characteristic response is seen in animals under barbituralte anesthesia. If the exploring electrode is over the primary receiving area for the particular sense, surface-positive wave appears with a latency of 5-12 msec. This is followed by a small negative wave and then by a larger, more prolonged positive defletction with a latency of 20-80 msec (6). This sequence of potential changes is illustrated in (Fig 7).

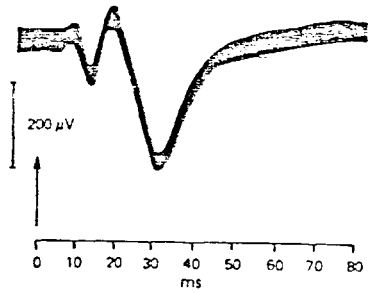

Figure 7

The first positive-negative wave sequence is the primary evoked potential; the second is the diffuse secondary response.

Primary Evoked Potential.

The primary evoked potential is highly specific in tits location and can be observed only where the pathways from a particular sonse organ end. Indeed, it is so discrete that it has been used to map the spe-

cific cortical sensory areas. An electrode on the pial surface of the cortex samples activity to a depth of only 0,3 - 0,6 mm. The primary response is negative rather than positive when it is recorded with a microelectrode inserted in layers 2-6 of the unedrlying cortex, and the negative wave within the cortex is followed by a positive wave. This indicates depolarization on the denrtires and somas of the ccells in the cortex, followed by hyperpolarization. The positive-negative wave sequence recorded from the surface of the cortex occurs because the superficial cortical layers are positive relative to the initial negativity, then negative relative to tho deep hyperpolarization. In unanesthesized animals, the primary evoked potential is largely obscured by the spontaneous activity of the brain, but in can be demonstrated with special techniques. It is somewhat more diffuse in unanesthesized animals but still well localized compared with the diffuse secondary response.

Diffuse Secondary Response.

The surface-positive secondary response is sometimes followed by a negative wave or series of waves. Unlike the primary response,tha secondary response is not highlt localized. It appears at the same time over most of the cortex and in many onther parts of the brain. The uniform latency in different parts of the cortex and the fact that it is not affected by a circular cut through the cortical gray matter that isolates an area from all lateral connections indicate that the secondary response can not be due to lateral spread of the primary evoked response. It, teherefore, must be due to activity ascending from below the cortex. The pathway involved is the nonspeicif thalamic projection system from the midline and related thalamic nuclei.

The features of an EP only very grossly suggested its origin. In general, peaks of relatively high amplitude and restricted distribution on the scalp are likely to be generated in the cortex under one of the recording electrodes, especially if the latency is long enough to be accounted for by conduction through the afferebt pathway. Peaks of low amplicude and by conduction through the afferebt pathway. Peaks of low amplicude and by conduction through the afferebt pathway. Peaks of low amplicude and wide distribution are more likely to be generated in subcortical structures, especially if they have short latency.

The location of EP generators may be studied by delineating the distributinion of the peaks in simulatneous recordings from many scalp electrode positions. In a common method of analysis, the magnitude of an EP deflection at a certain latency is plotted for each recording point on a head diagram; points of equal potential are connected to give a map of concentric isopotential lines which outline the maximum of the scalp potential and its gradient Fram the map of the elecktric field on the surface one may infere the location of a central generator in the depth, often illustrated as a center of opposing charges, or dipole.

Although the location of the dipole may suggeste the approximate location of the anatomical structures generating the electric field of the EP peak, the definite identification of these structures as genarators requires further validation by clinical correlations or direct recordings with depth electrodes. So far, the generators of most EP peaks have been determined only approximately. There is much debate about the brain stem generators of each of the peaks of the short-latency AEP; it seems that a precise correlation between each peak and one structure cannot be made because more than one structure may contribute to the production of one peak, and each generator may contribute to more than one peak. Discussions of the generators of the scalp SEP have not yet answered the question of which peak indicates arrival of the afferent volley at the cortical level. Although the generator of the major peak of the VEP must be visual cortex, it is not known to what extent the primary visual cortex on the mesial surface and the secondary visual cortex on the lateral surface contribute to the VEP.

The general principles of the production of EPs by elements of the nervous system have been the subject of many experimental studies that suggest some general conclusions of practical importance. Two types of nerve cell activity seem to contribute, in different proportions, to (1) cortical EPs, (2) subcortical EPs, and (3) EPs recorded from sensory nerves.

1. Cortical EPs are due largely to the spatial and temporal summation of excitatory and inhibitory postsynaptic potentials generated at the membrane of nerve cell bodies and dendrites in response to the input produced by the stimulus. The resulting potential differences generate pcurrents which penetrate to the cortical surface and scalp and produce intervening structures.

2. Subcortical EPs are probably a mixture of two components: Postsynaptic potentials generated in groups of neuronsof subcortical relay nuclei, and action potentials of the connecting axonal tracts. The first component, consisting of stationary generators of electric fields, is probably responsible for those sabcortical potentials tht can be recorded with consisting of propagated waves of depolarization, may explain some subcortical EPs that appear with delays of up to a few milliseconds at different recording sites.

3. EPs recorded from sonsory nerves are due to a wave of depolarization propagated synchoronously along the membrane of the nerve fibers. When passing under a satationary recording electrode on the skin, tha wave produces mawor surface-negative deflection taht may be precedend and followed by minor positive deflections due to the approaching and disappearing wave. The compound action potential may include later deflections generated by fiber groups of lower conduction velocity, but these deflections are of low amlitude due to the greater temporal dispersion of slowly conducted impulses.

For all three kinds of EPs, the shape, size, and timing of an EP recorded from the scalp or skin dpend on many factors, including the duration of the potential change, the size and spatial orientation of the generator to the recording electrodes, the distances between generator and electrodes and between the

electrodes themselves, and the electric conductivity of the intervening structures. In general, it seems that long-lasting potential changes generated by stationary sources in large structures with uniform geometrical orientation have a better chance of being recorded than brief potentials generated by traveling waves in small structures with disparate geometrical orientation. In both cases, the chances for a potential to be recorded decrease as the distence between the sorce and the recording electrodes increases, but even relatively long distances can be overcome with far-field recording methods.

TYPES OF EPs ACCORDING TO THE PHYSIOLOGICAL BASIS

1. Cortical EPs: Cortical EPs generated by primary sensory and hihger cortical areas. They have latencies of over 10-20 msec and amplitudes of up to 10 microvolt or more. Cortical EPs generally are derived with elecryodes placed near the primary receiving areas in the occipital and parietal areas respectively. Cortical AEPs are recorded with elecrodes not directly overlying the auditory cortex. In all three modalities, cortical EP peaks may be preceded by peaks generated by subcortical structures. The usual clinical VEP test records only cortical EPs.

2. Subcortical EPs: Subcortical EPs are generated by the chains of neurons in a sensory pathway to the cortical receiving area. These EPs have latencies of less than 10-20 msec. Because the brain stem and cord are relatively far away from recoding electrodes on the head and neck, potentials generated in the auditory and somatosensory afferent pathways are much atenuated by the intervening tissues, have amplitudes of usually less than 1 microvolt at surface recoding electrodes, an must be recorded with far field methods.

What is far field, and near field methods?

1. Near field recordings: Near field recordings are used to record cortical EPs. One electrode is placed close to the area under study, and the other electrode is placed over an electrically more quite area severalcentimeters away. A recording between these electrodes yields responses of 1-10 microvolt and requires collection of only about 100 responses for a clear definition of the cortical EP. Repetition rates of 1-2/sec are usually used for transient cortical EPs because these EPs have relatively long latencies and durations and may interact with each other at higher rates.

2. Far-field recordings: Far-field recording methods are used mainly for recording of patentials produced in the brain stem and spinal cord, namely, far away from surface electrodes. The electric field generated deep in the brain has a wide distribution at the surface so that the exact location of recording electrodes is not critical, although they must be fairly far apart to pick up the small voltage differcences on the surface. The amplitude of the potentials is much attenuated at the surface and usually measures less than 1 microvolt, requiring averages of 1000 or more responses for a clearly defined EP. Because subcortical EPs have short latency and duration and are fairly resistant to fast repetition, stimulus rates of 5-10/sec or more may be used. Far-field recordings may contain peaks generated by structures seperated by relatively long distance: AEP ecordings between electrodes on vertex and ear can show peaks that are generated by the acoustic nerve and its relays in the brain stem. SEPs recorded between an electrode on the scalp and another electrode on the shoulder or knee may reflect subcortical EPs from the entire afferent pathway.

3. Mixed far-field and near-field recordings: Recordings of AEPs and SEPs between a scalp electrode ner the cortical sensory area and a distant electrode may show small ealy peaks which represent far-field recordings from distant, subcortical structures and precede the larger cortical potentials generated near the scalp electrode.

CLINICAL USE of EPS:

In case of PSVEP, it is used mainly to test conduction in the visual system. It is so sensitive that it can detect lesions not discovered by clinical or other laboratory techniques. Furthermore, EPs often help to localize lesions in certain segments of a central sensory pathway. EPs therefore hove become valuable diagnostic tools in clinical neurology. They are especially helpful in the diagnosis of muhtiple scleroisis where the demonstration in clinically silent defects my prove the presence of multiple lesions. EPs may e usefl in the diagnosis of other structural lesions, some degenrative diseases, and even a few metabolic encephalophathies. EPs are also abnormal in many other disorders such as dementia, schizophrenia etc. In cases of diffuse disorders, EPs may be used to show involvemet of a particular sensory pathway. Tablo 1(7).

CLINICAL UTILITY OF EVOKED POTENTIAL STUDIES İN PSYCHIATRY

As mentioned earlier (8), EP testing has some established indications in clinical neurology and neurosurgical practice, especially in the evaluation of demyelinating disorders, such as multiple sclerosis (Fig 8),

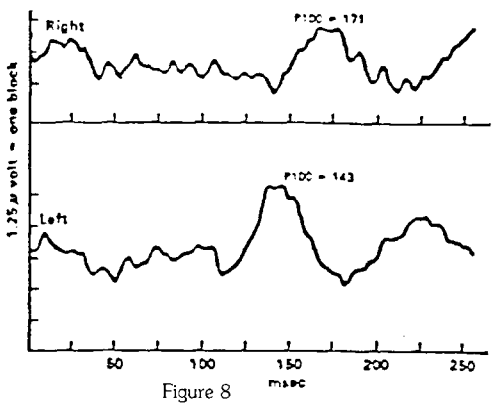

Figure 8

and the intraoperative evaluation of nerve integrity during certain neurosurgical procedures. There is,

however, no consensus as to the current clinical utility of EP testing in the evaluaion of idiopathic psychiatric disorder. EP studies are unique's among electrophysiological and brain-imaging methodologiesin the EP technique's ability to detect the cerebral processing of stimuli and information that takes place within miliseconds of the occurence of the stimulus. Some cognitive processes of special interest to psychiatrists and neuroscientists occur on this chronological order of magnitude. Abnormalities of early, middle, and late EP components have been reported in psychiatric disorders, but non seem diagnostically definitive or of clear clinical usefulness as of this date. However, this is an area of active investigation. It is hoped that the value of EP testing to psychiatrists will be enhanced with additional careful clinical studies and by the application of advences in the computer analysis of EP data (e.g. computerized topoghraphic EP mapping).

COMPUTERIZED TOPOGRAPHIC MAPPING OF ELECTROPHYSIOLOGICAL DATA

Indeed, topographic techniques to display EEG or EP data have been under development for more than three decades. The technique by which this process is applied to both EEG and EP data has been called computerized Generation of Topographic Maps:

Evoked potentials for the entire cortical surface can also be topographically visualized using computerized electrophysiological mapping systems. Generally, the EPs are averaged over epochs (time intervals) measured in milliseconds (e.g. 4 msec), and the EP data can be viewed for each epoch. As with the mapping of EEG data, the EPs are displayed within outlines of the head with different colors or gry tones corresponding to different EP voltage ranges (Fig. 9).

Both positive and negative voltages can usually be visualized on the same map by assigning different color ranges to positive and negative (e.g. blue-purple as negative, orange-red as positive). Topographic maps may be used to represent statistical relations between individuals and groups or between two populations of subwect (e.g. patients with schizophrenia as compared with control subjects). In this case a z-transform or a t-transform is used to highlight regional differences between an individual and a group or between two groups. This technique has been called-significance probability mapping or T-Statistic maps and represants a form of exploratory daha analysis that does not address the overall significance of group differences. This issue may be investigated using multivariate discriminant analysis based on the electrophysiological measures delineted by these topographic approaches.

APPLICATION OF COMPUTERIZED TOPOGRAPHIC MAPPING TO PSYCIATRY

Some advantages of computerized topographic mapping systems over other types of brain imaging research techniques (SPECT, or PET) include:

1. The absence of ratiation exposure,

2. Greater chronologic rsolution for the computerized electrophysiological mapping systems (specifically computerized EP mapping), which is of the order of milliseconds versus minutes with other brain-imaging techniques (e.g. PET),

3. The generally lower cost of computerized EEG as compared with other brain imaging procedures.

As in conventional EEG and EP testing, computerized testing procedures require vigilance for possible artifactual contamination of the data.

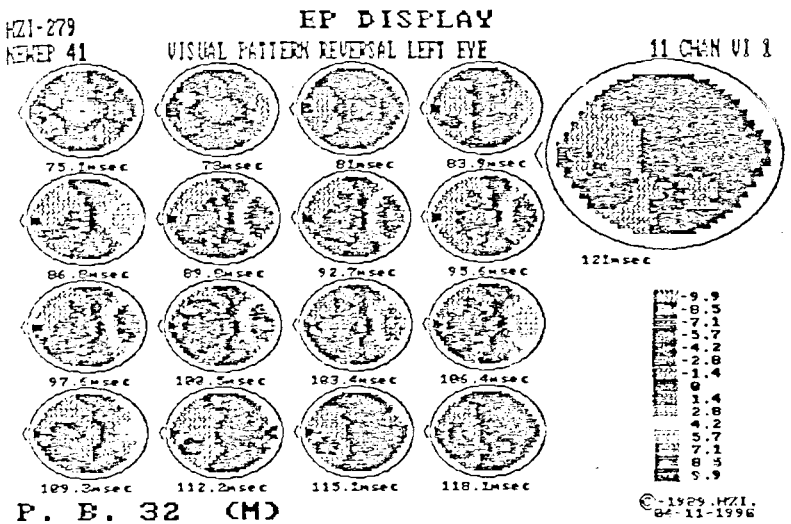

Figure 9

DIAGNOSIS	INCIDENCE ABNORMALITY	CHANGES	SOURCE
ALCOHOLISM (CHRONIC)	37%	INCREASED P100 LATENCY (IMPROVEMENT FOLLOWED A 6 MONTH PERIOD OF ABSTINENCE)	EDEMA OR DEMYELINATION IN CNS
ALZHEIMER'S DISEASE		INCREASED P100-P2 FLASH LAT.	UNKNOWN
AMBLYOPIA - TOXIC (QUININE, ETHAMBUTOL. ALCOHOL, TOBACCO) - LEBER'S OPTIC ATROHY		DECREASED AMPLITUDE DISTROTION IN WAVES INCREASED LATENCIES	OPTIC NEUROPATHY
COMPRESSION ON ANTERIOR VISUAL PATHWAYS		WAVEFORM ABNORMALITIES AND LOSS OF AMPLITUDES	CONDUCTION DEFECTS IN THE VISUAL PATHWAYS
CORTICAL BLIDNESS		ABSENT OR ABRONKAL LATENCIES	ANATAMOPATHOLOGICAL CHANGES IN OCCIPITAL AREAS OF 17, 18, 19.
DIABETES MELLITUS		INCREASED P100 LATENCY	DIABETIC NEUROPATHY IN VISUAL PATHWAYS
FRIEDRICH'S ATAXIA	66%	INCREASED P100 LATENCY	CONDUCTION DEFECTS IN THE VISUAL PATWAYS
GLAUCOMA		DECREASED AMPLITUDE	GLAUCOMATOSE LESIONS IN OPTIC NERVE
HYSTRIA (AND MALINGERING)		NO ABNORMALITIES	PSYCHOLOGICAL
INTRAOPERATIVE MONITORING		CHANGES IN EP COMPONENTS (AMPLITUDE, LATENCY, MORPHOLOGY)	POSSIBLE COMPRESSION OR DEMAGE IN OPTIC NERVE DURING SURGERY
ISCHEMIC OPTIC NEUROPATHY		DECREASED AMPLITUDE THEN INCREASED LATENCIES (AS ILNESS PROGRESSES)	ISCHEMIC CHANGES IN RETINA
MULTIPLE SCLEROSIS	90%	-INCREASED P100 ABSOLUTE LATENCY - INTEROCULAR LATENCY DIFFERENCES	CONDUCTION DEFT IN THE OPTIC NERVE. (EITHER DUE TO OPTIC NEURITIS OR INFLAMATION IN THE FURTHER ANATOMIC STRUCTURES)
PARKINSON'S DISEASE		-INCREASED P100 LATENCY - INTEROCULAR DIFFRENCES	INSUFFICIENCY OF THE DOPAMIMERGIC CELLS IN THE INTERPLEXIFORM LAYER IN THE RETINA
POLYNEUROPATHY (CHRONIIC, INFLAMATORY DEMYELINATING)	50%	-INCREASED P100 LATENCY -DECREASED P100 AMPLITUDE	CONDUCTION DEFECTS IN VISUAL PATHWAYS
POSTERIOR VISUAL PATHWAY DISEASES - ASSOCIATED WITH NEOPLASM - ASSOCIATED WITH VASCULAR DISORDERS - ASSOCIATED WITH INFLAMATORY DIS.		AMPLITUDE AND LATENCY ABNORMAL ITIES IN SEQUENTIAL PARTIAL FIELD STIMULATION	CONDUCTION DEFECTS DUE TO CHIASMATIC OR RETHORCHIASMATIC LESIONS
PROGRESSIVE MYELOPATHY (MAJOR INDICATION IS WHETHER MYLEOGRAM IS NECESSARY)	76%	INCREASED P100 LATENCY	CONDUCTION DEFECTS IN VISUAL TRACTS
TRANSIENT RETINAL ISHEMIA		DERCREASED AMPLITUDE (ONLY)	ISCHEMIA IN RETINA
VISUAL DEFECTS IN AT RISK IN FANTS (SCREENING)		IMPROVEMENT IN AMPLITUDE FROM 20/150 AT 2 MONTH OF AGE TO 20/20 BY 6 MONTH OF AGE	

PROBLEMS PERHAPS SPECIFIC TO COMPUTERIZED TOPOGRAPHIC SYSTEMS

1. Possible limitations or flows in the software design (e.g. possible built-in erroRneous assumptions, oversimplifications, compromises).

2. Possible mathematical or statistical inaccuracies.

3. Possible overinterpretation of the color maps beyond what can be justified by the available research data.

Rationals for Use of PSVEP in a Research Related to the Depression:

1. Just measuring the EPs, we may ignore both neurophysiological and psychological rationales in the hope that multivariate statistics will make sense of the results. This can benamed agnostic, ampirical appraoch. It can be used as a trait phenomenon or as a dignostic pattern

2. It is worthy to study the effect of antidepressants and anti-oxidants on VEP.

3. It may be hypothesized that the psychiatric disorders with the profile of alpha increase, like depression, may be monitored, even diagnosed with this test.

REFERENCES

1. Bodis-Wollner I, Ghilardi MF., Mylin LH The importance of stimulus selection in VEP practice; the clinical relevance of visual physiology. In: Cracco RQ, Bodis-Wollner I, eds. Evoked Potentials. New York: Alan R Liss; 1986: 354-65.
2. Placzek M., Mushin J., Dubowitz LMS, Maturation of the Visual Evoked Response and its Correlation with Visual Acuity in Preterm Infants, Dev. Med. Child Neurol, 1985, 27, 448-454.
3. Johns JK, The removal of alpha from the VECP by means of selective averaging, Vision Res. 1977, 17:949-50.
4. Trimble N., Ongoing Occipital Rhytms and the Ve. I. Stimulation at peaks of the alpha rhytm. Invest. Ophthalmol. Visual. Sci. 1975, 14: 537-546.
5. Aunon RT. VEP and AEP variability: Interlaboratory vs. intralaboratory and intersession vs intrasession variability. Electroencephalogr. Clin. neurophysiol. 1977, 42, 705-708.
6. Ganong WF., Review of Mdical Physiology, 1991, Appleton & Lange, pp. 179-180.
7. Itil TM., Eralp E., Lebars P., Mucci A., Saito A., Arikan MK. PSVEP in: Evoked Potential and Dynamic Brain mapping Professional Manual. HZI Foundation Publication (1991) pp. 33.
8. Rosse RB., Warden DL., Morihisa JM. Applied Electrophysiology. In: Comprehensive Textbook of Psychiatry/C Kaplan HI., Sadcok BJ (eds) Wilkams & Wilkins (USA) 1989, pp. 74-85.