Indian J Physiol Pharmacol 1998; 42 (2) : 172–188

REVIEW ARTICLE

AVERAGE EVOKED POTENTIALS – CLINICAL APPLICATIONS OF SHORT LATENCY RESPONSES

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(Received on July 3, 1997)

Abstract : Many clinical neurophysiology laboratories have added average evoked potential studies to their routine procedures as evoked potential recording methods are non invasive, highly objective and informative. Indeed, short latency brainstem auditory evoked potentials as well as short and intermediate latency cortical evoked potentials, lately have proved to be valuable clinical tools for objectively testing afferent functions in patients with neurological and sensory disorders. The averaged evoked potential responses (EPR) have been widely used in clinical practice to record the changes in the electrical potentials that occur within the central nervous system (CNS) of the patient in response to an external stimulus. Two types of evoked potentials are usually recorded. 1– Stimulus related, short latency evoked potentials, which represent an obligate neuronal response to a given stimulus and both the amplitudes and latencies of these depend on the physical characteristics of the eliciting stimulus. In this category brainstem auditory evoked potentials (BAEPs), visual evoked potentials (VEPs) and somatosensory evoked potentials (SEPs), have normal values for latencies, amplitudes of waves and characteristic wave form. Any abnormality of these reflects excitation, conduction block in the specific pathways in the CNS. Certain abnormalities in EPR reflect subclinical involvement of CNS even before the disease clinically manifests. Abnormality in BAEPs can in addition, depict the exact site of lesion in the brainstem auditory pathways. Same is true for SEPs where abnormalities in far-field or near-field components, reflect lesions at the plexus, spinal cord, brainstem or thalamo-cortical regions respectively. 2- The event related potentials (ERPs) can be recorded in response to an external stimulus to which person is attentive or an event requiring cognition, discrimination, or reaction to the target stimulus. P300 is one such ERP, helpful in distinguishing between disorders such as dementia and depression. This first review gives a bird's eyeview of the essentials, methods, interpretation and clinical applications of stimulus evoked short latency (brainstem auditory, visual and somatosensory) responses in human beings.

Key words : evoked potentials, auditory brainstem evoked potentials, visual evoked potentials, somatosensory evoked potentials, peak latency, interpeak latency, short latency

INTRODUCTION

It is well known that the sensory modalities are laid out in an orderly fashion throughout the brain right up to the level of the cerebral cortex. In the somatosensory system, for example, peripheral stimulation evokes electrical activity at the cortex that has topographical features – the familiar sensory homunculus. The possible clinical value of recording such evoked electrical activity from the brain to investigate sensory and neurological deficits is obvious and has long been recognised. On the other hand, the routine recording of evoked brain electrical activity by noninvasive procedures using scalp electrodes has only recently been realized, although the basic methods for doing so have long been available. For instance, EEG or spontaneous electrical activity of the brain is readily picked up and recorded from electrodes placed on the patient's scalp. Because the activity produced at the cortex by sensory stimulation is also electrical, it is reasonable to expect that this activity could be recorded by means of scalp electrodes as well. But while this is true in theory, serious problems are encountered in practice. When picked up by scalp electrodes, evoked electrical activity appears against a background of spontaneous electrical activity. In other words, what is seen in reality is a mixture of evoked and spontaneous electrical activity. More often than not, the spontaneous activity is of much greater amplitude than the evoked activity.

In technical language, the evoked activity is the "signal" we desire to record and the background activity is "noise". As we just noted, the signal is normally of much lower amplitude than the "noise" so that the proportion of signal in relation to noise – the signal-to-noise ratio-is low. A low signal–to noise ratio means that although a signal is present, it may go undetected because it is hidden or masked by the noise. To detect an evoked potential it is essential to increase the signal-to-noise ratio and one can do this either by increasing amplitude of the signal, decreasing amplitude of the noise, or both. Because amplitude of signal is governed by the intensity of stimulation, it is easy to see that the chief way of increasing signal-to-noise ratio is by reducing the amount of noise. One obvious way of doing this is to have the patient keep the eyes open. Under such conditions the alpha rhythm, which for purposes of evoked electrical activity is "noise" will be reduced in amplitude. In the awake, alert individual, this leaves a background consisting mostly of low amplitude activity in the alpha and beta frequency band. However, as cortical evoked potentials are commonly less than a few microvolts in amplitude, they still may be hidden in the remaining noise of the background activity. Hence the evoked potential signals which are about 1/100 the amplitude of ongoing spontaneous EEG activity must be extracted, by various means like superimposition, signal averaging, coherent averaging which are readily available in most of the modern sophisticated computers and averagers (Evoked potential Recorders). It is not possible to give details of all these methods, the interested reader can consult many books written on the subject from time to time. However, the presence of artifacts whether they are instrumental, environmental or physiological, can result in formidable problems which are obviated

by the use of various filters, artifact rejection devices, proper selection of stimulus parameters, patient's co–operation for proper relaxation and of course proper grounding of the equipment in the laboratory. A good clinical evoked potential laboratory must look after these technical procedural details for proper recording of evoked responses.

General principles of interpretation

The useful clinical information in an average evoked potential resides in the latencies and amplitudes of certain waves or components that are typically present in the waveform. Therefore, the first step in interpretation entails the identification of the various components of which the average evoked potential for a particular sensory modality is formed. This may be relatively easy to do in the case of a waveform that is readily replicable and has all of the usual waves present at the expected latencies. But if one or more of the usual components appear to be absent, or if the latency of one or more of the waves is prolonged, the interpreter may be faced with a dilemma. Delayed or absent waves are suggestive of pathology, but they may equally well be due to the presence of artifacts that obfuscate the waveform. Hence each neurophysiology laboratory at first instance, must obtain normative data of absolute peak and interpeak latencies of each wave of evoked responses. In certain cases amplitude also becomes an important entity. By and large, it has been agreed that any deviation of absolute or interpeak latency beyond 99% tolerance limit (Mean+3 SD) forms the basic criteria of abnormality. There are certain other minor criteria applicable to the specific evoked responses which will be dealt with subsequently under those responses.

Once the various components of a waveform have been identified the person interpreting the data is ready for the next step. This involves comparison of the relevant parameters of the patient's recorded waveforms with a set of norms. Normative data for average evoked potentials for the different sensory modalities have been published by a number of laboratories. These data continue to be updated, and so it is essential for the person interpreting average evoked potentials to keep abreast of the latest work in the area. As it is important to be familiar with the published norms, it is likewise important for each laboratory to have its own normative data as well.

In the following three major sections, the specific aspects of technique and interpretation relevant to Brainstem auditory evoked potentials (BAEPs), Visual Evoked potentials (VEPs), and Somatosensory evoked potentials (SEPs) are being discussed.

Brainstem auditory evoked potentials

Any adequate and specific stimulus given to the sensory organ, evokes action potentials in the sensory pathways which could be recorded by placement of suitable electrodes at different sites of these afferents. If one could record directly from several different levels of the subcortical auditory pathways of the humans, one would see, in the first 10 msec of the application of acoustic stimulus, a series of

short latency potentials corresponding to sequential activation of peripheral, pontomedullary, pontine and midbrain portions of the pathway. When these acoustic nerve and brainstem potentials are volume-conducted to surface recording electrodes at the vertex and ear lobe, they form a composite series of vertex positive and negative waves known as brainstem auditory evoked potentials. As peak to peak amplitude of these BAEPs recorded from the scalp are, at most, only 1/100 the emplitude of the ongoing spontaneous EEG activity and therefore must be extracted from this and other noise by the use of computer–averaging techniques. The normal BAEP recording consists of I-V vertex positive (ear-lobe negative) waves. Wave I is believed to reflect activity in the auditory nerve; Waves II and III, activity in the cochlear and superior olivary nuclei of the pons; and waves IV and V, activity in the lateral lemniscus and the inferior colliculi of the midbrain. Thus I to III interpeak latency (IPL) reflects conduction between auditory nerve and the pons; III to V interpeak latency reflects conduction between pontine and midbrain components of the brainstem auditory pathways. Thus interpeak latency I-V indirectly reflects neuronal conduction from acoustic nerve-pontomedullary, pontine – midbrain auditory pathways (1, 2). Proper use of this important test in clinical neurology requires a full appreciation of the technical, physiologic, otologic and pharmacological factors that may alter BAEPs in the absence of neurological disease (3). In order to obtain normative data of BAEPs, it is obligatory for each lab to spell out and properly control various non pathologic factors listed above.

Methodology

1) Stimulus parameters: Routinely click intensity of 60-70 dB above the patients hearing threshold, as determined at the time of testing for each ear is used as sound stimulus. Most of broadband clicks are used with audio frequency ranges from 100 Hz to 8 KHz so that entire cochlea is stimulated. These clicks are generated by passing 0.1 msec square pulses through shielded headphones (many headphones are fabricated for this purpose like Telephonics TDH–39, Telex 1470, Nihon Kohden DR–5138–6 Elega DR–531). The headphone output could be controlled through inbuilt computer in the stimulatory component of MEB 5200 Neuropack II Evoked Potential Recorder. The Polarity, intensity duration and frequency of click stimuli could also be changed by connecting the headphones with the output of MEB 4200 Stimulator (Nihon Kohden Japan).

2) Stimulus polarity: Two types of clicks may be produced, one that moves the ear–phone diaphragm away from the eardrum (rarefaction click), and one that moves it in the opposite direction (condensation or compression click). One may use rarefaction clicks, condensation clicks, or clicks with alternating polarity for the test. Since the response characteristics can vary, depending on click polarity, the type of stimulus used should be specified in the worksheet.

3) Stimulus rate: Many of the waveforms are reduced in amplitude at high rates of simulation. The preferred stimulus rate for BAEP is 10/s. Most machines on the market are capable of rates ranging from 1 to 70/s.

4) Stimulus intensity : There are many ways of defining the stimulus intensity. Most laboratories use two scales: hearing level (HL) and sensation level (SL). To establish the HL value, a number of normal persons are tested to determine the hearing threshold, or the lowest click intensity that can be heard, and the mean value is determined. This is taken as zero dbHL, and may vary from 5 to 30 dB, depending on the characteristics of the stimulator, earphone and laboratory environment. If we assume zero dbHL to be 20 dB, then a 60–dB click has an actual intensity of 60 minus 20, or 40 dBHL, which is 40 dB above hearing level. Alternatively, the patient's own hearing threshold may be taken as the zero measure. If the hearing threshold is 30dB and 60–dB click is used, then the actual intensity is 60 minus 30, or 30 dBSL, which is 30 dB above sensation level. The click intensity used should be recorded in dBHL or dBSL.

During monaural testing, it is important to mask the contralateral ear to avoid recording a crossover response from inadvertent stimulation of the contralateral ear via bone conduction of the stimulus. This is particularly important when a high-intensity click is used on the side with poor hearing, and the contralateral ear happens to be normal. Usually, white noise at 30 dB below the intensity of the stimulating click is used as the masking stimulus.

BAEP Recording Techniques

The volume conducted evoked responses are picked up from the scalp by using Ag/Agcl disc or ball type of electrodes placed as per 10–20 International system of placement. The evoked bipolar activity (mixed with EEG) recorded from CZ – A1 or CZ – A2 to acoustic stimulation is filtered (–6dB points 100 Hz and 3 KHz) and amplified (5×10^5) with inbuilt amplifiers or the type Gran P511J amplifiers and the activity time–locked to the stimulus is sampled at .25 to 100 KHz over the first 10–24 msec after the stimulus. This can be done by using Gran Model 10 or Nicolet CA–1000 signal averagers or the inbuilt averagers and address. Peak latencies are measured to the nearest 10 to 40 msec and peak to peak amplitudes to the nearest 10 nV by using digital cursors. At least two separate trials/averages of 2000–4000 (usually 2048) responses are recorded and superimposed per ear. The contralateral ear is masked with white noise of variable intensity (depending on audiogram) at least 40 dBHL. These four trials (both ear) are put into four quadrants of the computer memory. The number of responses to be averaged in each trial depends upon the degree of intertrial variability in IPLs. Each IPL i.e. I–III, III–V, I–V should not vary by more than 80 usec between trials, at the protocol for routine clinical use usually gives highly reprodcible waves of BAEPs. The basic protocol could be changed if need be by resetting of the programme of the computer.

Preparation of the patient

The patient should be put at ease and well informed about the testing procedure. He should be made to lie down, relaxed on a couch in sound proof and air conditioned examination room. With patient's relaxation, muscle artifacts would be minimal. Thoroughly, clean the electrode recording

sites on the scalp with cleansing material (skin pure or alcohol). Apply electrolyte paste (Elefix) on the recording surface of the disc electrodes. Position them and fix them with sticking tape. Connect these electrodes to Impedance meter and monitor the skin to electrode transition impedance, which should always be kept below 5 Kohms.

Examination procedures

After the electrodes have been connected, the patient prepared and the equipment switched on, it is important to confirm that the patient is fully relaxed. This can be done by checking the monitor display. Incoming signals when patient is supposed to be relaxed, should not exceed 50–60% of the display dimensions. If the incoming signals exceed this limit, it indicates that muscle potentials are also being added. In such cases, the whole procedure of preparation of patient and examination is redone.

Normal BAEPs

There are usually seven positive waves within 10 msec of application of stimulus. Of these first five constitutes the classical BAEPs. The typical recording of BAEPs from normal subject consists of a sharp peaked wave I which comes back to baseline, followed by an ascending big wave having four distinct peaks i.e. II, III, IV and V on its rising limb, then its descending limb falls below the base–line as far as wave I. This is followed by small VI and comparatively large VII wave. Of these first five originate from brainstem auditory pathways. These waves have definite peak and interpeak latencies. The normal values of peak latencies and IPLs have been reported by various clinical neurophysiology labs in different age group of subjects (4–8). Normative data of BAEPs from our lab is also comparable with Western reports (8–10) indicating that once standard techniques of BAEP recording are used, the inter-lab variation in normative data are minimal. The normative values of BAEPs obtained in our lab are given in Table I and II. The upper limit of interpeak latency values i.e. mean + 3SD as given by various authors (7) are, at a click rate of 10/sec, I – III, 2.6 ms, III – V, 2.4 ms; and I-V, 4.7ms for a group aged 15 to 50 yrs. these values are similar to ours (8–10). It should be obvious that identification of the various waveforms is crucial for proper interpretation of the BAEP. Absolute latency values are of less significance than interpeak latencies. This is because changes in wave I latency that

TABLE I : Showing the values of absolute peak latencies and amplitude of brainstem auditory evoked potentials in normal subjects.

Age group	*Peak latencies (mses)*					*Amplitude (μv)*		
	I	*II*	*III*	*IV*	*V*	*V*	*I*	*Ratio V/I*
Children	1.65 ± 0.25	2.69 ± 0.29	3.78 ± 0.29	4.83±0.37	5.60 ± 0.37	0.27 ± 0.13	0.20 ± 0.15	1.35
Adults								
a) Male	1.59 ± 0.17	2.68 ± 0.22	3.74 ± 0.21	4.91 ± 0.24	5.62 ± 0.26	0.26 ± 0.12	0.16 ± 0.09	1.62
b) Female	1.61 ± 0.20	2.64 ± 0.20	3.62 ± 0.26	4.80 ± 0.27	5.44 ± 0.29	0.36 ± 0.14	0.19 ± 0.13	1.89

TABLE II : Showing the mean values of various interpeak latencies along with 99% Tolerance limit of BAEPs (in msec) in normal subjects.

Age group	*No. of subjects*	I–III		III–V		I–V	
		Mean	*99%TL*	*Mean*	*99%TL*	*Mean*	*99%TL*
Children	74	2.11	2.5	1.84	2.38	4.01	4.67
Adults							
a) Male	148	2.13	2.58	1.86	2.30	4.03	4.48
b) Female	116	2.05	2.44	1.80	2.26	3.89	4.42

occur from cochlear or other ear disorders can prolong the latencies of the subsequent waves. Without identification of wave I, the interpretation becomes less specific, Sometimes wave I may be obscured by the stimulus artifact or by cochlear microphonics; in such cases, use of alternating clicks may be quite helpful. With alternating clicks, the cochlear potential reverses in polarity and cancels out during averaging so that wave I is easier to detect.

Abnormal BAEP

The most important criterion for BAEP abnormality which is routinely used is the prolongation of IPLs beyond 99% tolerance limit (Mean + 3SD). This is most acceptable as there is low inter individual variability of these IPLs. Abnormal IPL prolongation usually reflects a pathological disturbance of central auditory conduction. The morphology of BAEP is highly variable and not readily quantified, and therefore has little application in defining abnormality (7). However, we have shown that besides abnormality of the IPLs there could be abnormality of wave form in terms of absence of some waves in severely malnourished infants (11). Therefore the BAEP should be considered abnormal and suggestive of retrocochlear dysfunction when there is (1) abnormally prolonged IPL (beyond 99% TL) (2) complete loss of all waveforms (in absence of severe middle ear or cochlear disease) (3) absence of waveforms following waves I or III (4) abnormal inter ear difference in the I to V IPL. A low V/I amplitude is also considered to be abnormal.

Normal variations in BAEPs

The non pathological factors affecting IPLs of BAEPs must be emphasised and properly controlled in any clinical study involving evoked potentials. These factors are (1) physiological (2) due to variation in physical characteristics of the sound click stimulus (3) recording montages and (4) pharmacological.

Physiological factors:

These include age, sex, body temperature, pregnancy. Below the age of about 2 yrs, IPL are prolonged relative to adult values and vary inversely with age (12–13). Advancing age beyond 50 yrs prolongs the I–III IPLS (14). Females usually have significantly shorter IPLs as compared to males. This could be due to genetic anatomical, endocrinal factors (3). Pregnancy also affects the BAEPs (15–16)

causing variation within 2 SD of the normal. Hypothermia prolongs the IPLs of human BAEPs (17).

The physical characteristics of click stimulus i.e. its phase, intensity and rate influence BAEPs. Rarefaction clicks usually produce lesser absolute latencies and better resolution of BAEPs as compared to condensation clicks (3). The common practice in many electrodiagnostic labs including ours also, is to alternate the polarity of stimuli to minimise electrical and stimulus artifacts. The stimulus intensity does change absolute peak latency of wave I but IPLs are relatively independent of click intensity. Increasing rate of stimulus, increases the post stimulus latencies of all BAEP components as well as IPLs (3, 5). However, increase in rate of frequency from 10/sec to 30/sec does not have much effect on IPLs (7). As all these physical characteristics of sound click stimulus have profound influence on BAEP, each laboratory should have normal age, sex, stimulus specific data for their normal subjects.

Filter settings

The ideal band pass for clinical purposes is 100 to 3000 Hz. This will not allow EMG, EEG artifacts and improve BAEP resolution.

Recording montages

Relative amplitude of BAEPs are highly dependent on ear reference site. Clearer and larger wave I of BAEPs is obtained if periaural sites are used as reference. It is customary to use electrode hook up as follows : Active (+) : CZ, Reference (–) : Ear lobe ground (E) : Forehead. Transition impedance: < 5 Kohms

Pharmacological factors

Interpeak latencies of BAEPs are relatively resistant to pharmacological insults including nonspecific CNS depressants. The anaesthetic agents like isoflurane which causes absence of spontaneous EEG, still show normal IPLs. Drugs affecting specific neurotransmitters involved in the generation and modulation of BAEP (e. g. Serotonin, Ach–muscarinic receptors) alter relative amplitudes and IPLs of BAEPs (18). Recently in our laboratory, it has been shown that premedicant Diazepam prolongs the peak and IPLs particularly I–III in the elderly patients undergoing elective eye surgery (19). Acute ethanol intoxication has been reported to prolong IPLs (20).

Clinical applications of BAEPs

The neurological applications in which BAEPs have proved most useful include (i) assessment of auditory function including evaluation of auditory pathways in children (ii) diagnosis of demyelinating diseases like multiple sclerosis (iii) the early detection and localisation of posterior fossa tumours in the brain (iv) intraoperative monitoring of the patient to assess hearing sensibility and (v) the evaluation of the cause and reversibility of coma. We have employed this method to assess the course of meningitis, enteric fever and correlated the changes in IPLs to grade of malnutrition in infants and children (11). However, BAEP abnormalities are, not often specific for any type of brainstem abnormality and can occur with

various other neurological syndromes like hereditary sensorimotor neuropathy, sleep apnoea and cranial polyneuritis. As BAEPs are highly dependent upon a number of physiological and technical variables, it is therefore very important to control and minimise these before statistical criteria of abnormality can be meaningfully applied. Proper attention to technical details and patient characteristics greatly reduces normal BAEP variability. Each lab should, therefore, operationally define that irreducible BAEP variability for itself with the methods intended for use on patients (21).

Clinical correlation of abnormal BAEP

Eighth–nerve Tumour : The BAEP is a very sensitive indicator for tumours that arise from or compress the eighth nerve. In the case of an acoustic neurinoma, wave I may be absent on the side of the lesion or the I – III interpeak latency may be prolonged. The test has been found to be highly sensitive in this regard, with some studies suggesting 90% to 95% sensitively. With a large cerebellopontine angle tumour compressing the brainstem, the III – V interpeak latency may be prolonged, often on the contralateral side. In the case of intra–axial tumours, such as brainstem glioma, bilateral prolongation of III – V interpeak latency is the more common finding (21).

Demyelinating disease : In a patient with a single episode of neurological deficit such as optic neuropathy or diplopia, it is often difficult to make a diagnosis of multiple sclerosis. Although the magnetic resonance imaging (MRI) scan has become the most useful tool for diagnosing this condition, multiple pathway dysfunction is best documented by a battery of evoked–potential tests. In this context, the BAEP is a very useful technique, particularly to document subclinical lesions. A high incidence of abnormalities has been reported in definite cases of multiple sclerosis. The abnormalities may be in the form of prolonged interpeak latencies and absence or distortion of the waveforms. Recently reports from our lab have shown sub–clinical involvement of auditory pathways in the rubber factory workers (22) and the patients suffering from primary hypertension (23).

Coma : Since the BAEPs are not affected to any significant degree by metabolic derangements or by drugs, BAEP is a good test for detecting structural abnormalities of the brain stem in patients in coma. Thus, if a good wave I is present and all the subsequent waveforms are absent or disorganised, or the interpeak latencies are prolonged, one may conclude that there is some structural abnormality of the brain stem. Of course, if wave I is also absent, such a conclusion cannot be drawn because of the possibility that the clicks may not be stimulating the cochlea and triggering signals in the auditory nerve. Total absence of all waves subsequent to wave I in a patient with suspected brain death may be used as a confirmatory test for the lack of brain stem function. The BAEP also serves to distinguish between metabolic coma and coma resulting from structural lesions of the brain stem.

Apart from the above indications, the BAEP studies are very useful in assessing hearing in paediatric patients who cannot cooperate in standard audiometric testing.

Visual evoked potential (VEP)

Unlike the BAEPs, the generators for VEP waves, volume-conducted to the scalp are not definitely known. Areas in the brain suggested to be involved in the electrogenesis of VEP are area 17 of the striate cortex and associate visual cortical areas (24–25). The potentials may also be influenced by limbic and frontal cortex (26). There are reports that VEP persists even in cortical blindness (27). The normal VEP, thus, only reflects the functional integrity of the visual pathways from retina to occipital striate area. However, abnormalities in the initial NPN components of VEP do reflect lesion in optic nerve or pathways. Thus VEP is an important diagnostic tool in the investigation of adult and paediatric ophthalmic and neurological disorders.

Methodology

Like BAEP recording, patient is prepared in a dark sound proof, air conditioned room. Scalp areas for recording like 01, 02, FPZ, A1, A2 are prepared and electrodes mounted. Usual recording montages taken are active electrode (–): Occipital 01 or 02, Reference (+): A1 or A2 Ground (E) : FPZ. Response to visual stimulus (flash, transient pattern reversal or steady state pattern) are amplified, averaged into a computer and displayed on the CRT screen or on paper using X–Y plotter. At least two trials, each of 256 responses are recorded to ensure replicability of the findings. The patient is seated in front of a TV monitor (producing pattern of different sizes) at a distance of 1 metre. With one eye closed, he fixates his other eye in the centre of TV screen. The pattern alternates of a fixed rate and VEP responses picked up. Thus VEP is primarily a reflection of activity originating in the central 3° to 6° of the visual field (mainly cone activity). However, if large pattern (check size greater than 30 minute of arc) are used as the stimulus signals outside the central 3° but not beyond 10° of visual field can be recorded (26).

Stimuli used to record VEP

Two general types of visual stimuli are most often used: (i). Unpatterned flashing lights from photostimulator (ii) patterned stimuli (checker board). The pattern stimuli can be presented in three ways. The first, a flashing patterned stimulus is produced by placing a photostimulator behind a large photographic transparency of black and white checks. As luminance changes can not be controlled it is offset or pattern reversed. In the former, pattern is immediately replaced by an unpatterned diffuse field of same size with same average luminance as previously seen in patterned stimulus. The diffuse field remains on for an equal amount of time (i.e. 500 msec) and the pattern then reappears. In the pattern reversal situation, checks are visible at all times. To maintain constant luminance one half of the checks increase in luminance while the other half decrease. This can be done by electronic checker generator which is inherent in the Evoked Potential Recorder. The black and white squares are made to reverse without there being any change in the luminance, or total light output of the screen. A number of stimulus parameters are known to influence the VEP. These include the rates of pattern reversal,the size of the checks, and the luminance. There are also patient–

related factors that affect the degree of retinal stimulation, namely, visual acuity, visual fixation, and pupillary size.

A pattern–reversal rate of 1 to 2/s has been found to be optimal for recording the visual evoked potential, which is used most often in routine clinical practice. A steady–state evoked potential is recorded when the stimulus rate exceeds 10 per second. Although the VEP can be obtained with even slower rates of stimulation, there are disadvantages. With a slower rate, the test becomes more time consuming and there is a greater chance that the patient may not fixate on the screen. If the stimulus rate is too fast, the response to one stimulus may contaminate the response to the subsequent stimulus.

The visual angle, or the angle that the individual checks subtend at the retina, has a significant effect on the latency of the response and, hence, needs to be standardized. It depends upon the height or width of the checks, as well as the distance between screen and eye. The formula used for the calculation is: Visual angle = 57.3 (W/D), where W is the width of one check and D is the distance berween eye and screen, both in centimeters,

The brightness setting of the monitor should be kept constant to maintain the same mean luminance of the checkerboard pattern. Similarly, ambient luminance of the room needs to be kept at a constant level. Consistency of these settings is essential for obtaining consistent data. The luminance can be measured using a spot photometer.

The patient is asked to fixate on a dot placed in the center of the TV monitor screen. The purpose of the fixation point is to ensure that the macular and perimacular areas of the retina are stimulated. The visual-evoked potential becomes smaller in amplitude whenever good visual fixation is not achieved.

The size of the pupil determines the amount of light that enters the eye and, hence, can affect the VEP. The patient should not have mydriatics or cycloplegics for at least 12 hours prior to the test. Visual acuity can also influence the latency and amplitude of VEP. The patient should wear corrective glasses, if any, during the test. If there is a marked deficiency in visual acuity, the checks should be made larger so that the patient can see them clearly. The technician should assess the patient's visual acuity, using a Snellen chart-and pupillary size and enter these data in the worksheet before commencing the test.

Transient VEPs have the advantage of component analysis. The initial positive wave (referred) to as P1 or P100 occurs between 95 to 110 msec after pattern reversal is clinically measured. When steady state VEPs are recorded (checkerboard alternation rate 6–8/sec), specific component analysis is no longer possible, amplitude and phase are then measured (29).

Factors affecting pattern VEPs

Besides luminance and alternation rate, there are a number of factors like size of pupil, state of refraction, field of vision, check size which affect pattern VEP (30). Therefore, caution must be exercised in comparing peak latencies of patients who have miotic or dilated pupils with a normal control group. Like BAEPs, VEPs are also

affected by age and sex. Peak latency of P1 shortens rapidly during the first year of life and levels off at approximately 6–7 years of age, latency remains stable until 60 years of age and then increases (31–32).

Normal VEP and criteria of abnormality

The typical normal pattern VEP in an adult individual consists of three negative and three positive waves within span of 350 msec after application of stimulus. Of these first three waves i.e. N1,P1 & N2 (NPN) complex and particularly P1 latency and amplitude is clinically important. In order to obtain normative data, each lab should determine its own values after carefully controlling all factors influencing pattern VEP. Many laboratories have reported normative data of transient pattern reversal VEP (33–34). Our data in children and adults (Table III) is comparable with the ones reported by other workers (35, 36). The used criterion of abnormal VEP is taken as prolonged latency of P1 or P100 beyond 99% tolerance limit. More than 50% reduction in the amplitude of P1 is also taken as abnormal. Also an interocular difference in P1 latency of more than 10 ms is often considered abnormal. These abnormalities of VEP reflect decrease in conduction processes in visual pathways.

Abnormal VEP

The abnormalities include absence of a VEP, prolonged P_{100} latency, and an excessive interocular difference in P_{100} latency.

When the technician discovers that the VEP is absent, a number of steps have to be taken to ensure that a technical problem is not to blame. These include : (i) making sure that the TV monitor is connected to the evoked-potential machine and that the two are synchronized so that a pattern shift occurs each time the averager is triggered; (ii) ensuring that the patient is focusing on the checks; and (iii) making sure that the electrodes are properly applied, that their impedances are less than 3k ohms, and that the electrode box is connected to the machine. Once these conditions are satisfied, the test should be run again using a 500–ms sweep so that a possible delayed response is not missed. If the VEP is still absent, the finding is definitely abnormal. If monocular full-field stimulation results in an absent response on one side and a

TABLE III : Absolute peak values of VEP (msec) and amplitude of P_1 (μv) in normal subjects. (Data are mean±SD)

Age group	*Age (yrs)*	N_1	P_1 (P_{100})	N_2	P_2	*Amp.* P_1
Children (n=84)	9.9 ± 2.61	68.9 ± 5.9	101.63 ± 9.7	141.4 ± 29.6	180.30 ± 29.7	6.6 ± 3.4
Adults Male (n=20)	23.72 ± 8.5	75.72 ± 7.86	95.37 ± 6.85	129.75 ± 10.50	150.30 ± 12.64	6.40 ± 2.38
Female (n=7)	25.71 ± 7.7	71.35 ± 6.3	91.07 ± 7.4	117.07 ± 10.04	149.28 ± 17.53	6.88 ± 2.79

normal response on the other, a lesion of the ipsilateral optic nerve is most likely, provided ocular pathology, including retinal lesions, is excluded. Absence of the VEP on monocular stimulation of right and left eyes suggests either bilateral optic nerve or chiasmal lesions, or less commonly, bilateral retrochiasmal lesions.

Clinical applications

VEP has clinical application in neurooptthalmology and neurology. Abnormal VEP has been reported in disorders of optic nerve and anterior visual pathways like optic neuritis, ischaemic optic neuropathy, toxic amblyopia, optic atrophy, optic nerve hypoplasia, glaucoma, papilloedema, tumours and various neurologic or metabolic disorders as multiple sclerosis, B12 deficiency, Parkinsons' disease, ataxias Phenylketonuria (37).

Therefore, the latency of the pattern VEP (particularly P1) provides a sensitive means of detecting subclinical lesions of the optic nerve and enables the clinician to make a diagnosis of demyelinating diseases earlier than otherwise. We have also reported changes in VEP in children suffering from different grades of xerophthalmia due to vitamin A deficiency and their reversal on therapy (38). Subclinical involvement of optic nerve in ocular leprosy patient, for the first time, has also been reported by us using VEP (39). Work place environment of the rubber factory also subclinically involves the optic pathways (40). Like BAEPs, it should be kept in mind that latency abnormalities are not specific to any one disorder and are certainly not pathognomic of any particular disorder as abnormalities from retina to cortex can produce abnormal peak latencies of VEP.

Somatosensory Evoked Potentials (SEPs)

It is only within the last 10–15 years that the clinical uses and limitations of SEPs have come to be better appreciated. The peripheral stimulus routinely used to elicit SEP activates predominantly large diameter, fast conducting group Ia muscle and group II cutaneous afferents. Although this is usually accomplished by electrical stimulation, it can also be achieved by a variety of a mechanical stimuli (41). The ideal stimulus probably induces a mixed nerve action potentials greater than 50% of its maximum amplitude and clinically produces slight muscle twitch. A stimulus of 200–300 usec duration, 3Hz-15 Hz to the median or ulnar nerves at the writ, posterior tibial at the ankle and peroneal at the knee is commonly given to elicit SEPs from scalp.

Recording and filtering of SEPs

Recording montages can be either of the cephalic bipolar variety or referential montages with the referential electrode placed off the head. A cephalic bipolar montage is relatively noise free but for field potentials are not recordable. Therefore, a compromise is made where electrode hook up is as follows : Active electrode (–) : 2 cm to the rear of C3 or C4 (contralateral to stimulus) Reference (+) : Ear lobe ground (E) : Wrist, Stimulation : Median nerve. The preparation of the patient and examination procedures are similar to BAEPs and VEPs. Make sure that patient is fully relaxed. For general purposes, a relatively broad band

pass (10 to 2500 Hz) is most suitable for recording SEPs. Recommended filter settings are 5 to 30 Hz low and 2500 to 4000 Hz high frequency. For upper extremity studies a 50 ms and lower extremity studies 100 ms analysis time is sufficient. This should be increased if no cortical responses are observed so as not to miss a delayed, response. Usually number of response averaged vary from 500 to 2000.

Measures of SEPs

The latency, interpeak latencies and amplitude of various positive and negative waves should be carefully measured. Like BAEPs and VEPs there are also sex and age variation in peak latencies of SEPs (41). The classical SEP record shows for field components like P9, P11, N12, P13, P14 indicating generators in brachial, proximal, plexus, spinal cord entry, dorsal column volley, dorsal column nuclei and brainstem generator respectively from median nerve SEP. Whereas near field potentials like N17, N19 reflect thalamic and cortical generators respectively. It, therefore, appears that no less than six far field potentials and are recordable with median nerve stimulation. Similarly SEPs on posterior tibial stimulation can be recorded and like median nerve SEPs, they have far field components and near field components N35, N37. Their recognition can be enhanced by restricted analog or preferably, digital filtering.

It is to be stressed that small amplitude far-field potentials are not always recoverable, and may be absent in as many as 30 percent of normal subjects; their absence can not be regarded as indicating disease. However, it is important again to point that each laboratory should have its own normative data. Variation of more than 3 SDs from the mean of the normal is considered abnormal. The latencies of SEPs also show variations with normal physical parameters of the subjects like height, arm span length & muscle mass (42).

Abnormal SEPs

In case of median nerve the IPL between N9 and N13 as well as N13 and N20 should be considered. Abnormal IPL, N9 and N13 suggests slowing of conduction in the cervical nerve roots/cervical dorsal columns. A prolonged IPL N13 and N20 suggests delayed conduction in the pathway between medulla sensory cortex. Absence of cortical potential (N20) in presence of a normal N13 indicates lesion involving medial lemniscus/thalamocortical projections. Likewise corresponding IPLs become abnormal in lower limb nerves.

Clinical applications

The main clinical reasons to records SEPs is to identify and localise a lesion involving the somatosensory pathways. However, the presence of SEP abnormality does not indicate, the nature of the diseased process. SEPs have a definite role in the investigation of peripheral nervous system. Scalp recorded SEPs were found to be absent or delayed in patients with variety of polyneuropathies and motoneuropathies. Focal nerve lesions may be detected and evaluated with SEPs (43, 44). These potentials have also been used to evaluated lesions involving inaccessible segments of nerves and limb plexus and spinal roots. Finally SEPs may also be useful in patients with nerve conduction problems. Moreover,

SEPs have definite role to play in assessing plexus lesions, thoracic outlet syndrome, cervical and lmbosacral radiculopathies and of course multiple sclerosis (45, 46). Abnormality in SEPs in most of these patients consists of absence or delay of far-field components or their altered morphology. Near-field potentials may be useful in determining brainstem or hemispheric lesions and various other hereditary alaxias and juvenile diabetes indicating impairment in sensory motor conduction. Therefore, the major disorders for which SEPs are of value include multiple sclerosis, spinal cord lesions (traumatic, compressive and other etiology) and lesions of brachial and lumbosacral plexuses. These are also useful in head trauma and in determination of brain death. For further details regarding SEPs, one can read excellent chapter on SEPs by Eisen and Aminoff (47). Recently using median nerve somatosensory evoked potentials, reports from our lab have shown interaction of pain and somatosensory afferents in patients receiving electroacupuncture analgesia (48). Rubber factory workers also showed trend of increase in latency of various components of SEP's indicating that sojourn in rubber factor environment does affect sensory conduction (49).

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