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Visual evoked potentials standard (2004)*

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Introduction

This document presents the current (2004) standard for the visual evoked potential (VEP). The VEP is an evoked electrophysiological potential that can be extracted, using signal averaging, from the electroencephalographic activity recorded at the scalp. The VEP can provide important diagnostic information regarding the functional integrity of the visual system.

The current standard presents basic responses elicited by three commonly used stimulus conditions using a single, midline recording channel with an occipital, active electrode. Because chiasmal and retrochiasmal diseases may be missed using a single channel, three channels using the midline and two lateral active electrodes are suggested when one goes beyond the standard and tests patients for chiasmal and retrochiasmal dysfunction.

Pattern reversal is the preferred technique for most clinical purposes. The results of pattern reversal stimuli are less variable in waveform and timing than the results elicited by other stimuli. The pattern onset/offset technique can be useful in the detection of malingering and in patients with nystagmus, and the flash VEP is particularly useful when optical factors or poor cooperation make the use of pattern stimulation inappropriate. The intent of this standard is that *at least one* of these techniques should be included in *every* clinical VEP recording session so that all laboratories will have a common core of information that can be shared or compared.

Having stated this goal, we also recognize that VEPs may be elicited by other stimuli, including moving, colored, spatially localized, or rapidly changing stimuli. These stimuli may be used to stimulate neural subsystems or to assist in localizing visual field defects. VEPs may be recorded using a full montage of electrodes covering all head regions to enable source localization. In addition to the commonly used technique of signal averaging, a variety of procedures including kernel analysis and Fourier analysis may be used to extract the VEP from background EEG activity. Some of these specialized VEPs, not covered by the standard, are listed in Table 1. Equipment manufacturers are encouraged to produce equipment that can perform as many of these specialized tests as possible. We particularly encourage the ability to record a minimum of five channels.

It is clear that this standard does not incorporate the full range of possibilities of VEP recording. However, in adopting the current standard for VEPs, the society, following a principle established in earlier standards [1–5], has selected a subset of stimulus and recording conditions which provide core clinical information and which can be performed by most of the world's clinical laboratories.

By limiting the standard conditions, the intention is that the standard method and responses will be incorporated *universally* into VEP protocols *along with* more specialized techniques (Table 1) that a laboratory may chose to use. The standard does not require that all stimuli should be used for every investigation on every patient. In most circumstances a single stimulus type will be appropriate. However, it is not the purpose of the standards to impede research progress, which might demonstrate that other tests are

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Table 1. Some specialized types of VEP not covered by the ISCEV standard

• Steady state VEP
• Sweep VEP
• Motion VEP
• Chromatic (Color) VEP
• Binocular (dichoptic) VEP
• Stereo-elicited VEP
• Multi-channel VEP
• Hemi-field VEP
• Multifocal VEP
• Multi-frequency VEP
• LED Goggle VEP

of equal or greater usefulness. This standard will be reviewed periodically and revised as needed.

The organization of this report is as follows:

Basic Technology

1. Stimulus parameters
   - A. Pattern stimulus
     - i. Pattern reversal stimulus
     - ii. Pattern onset/offset stimulus
   - B. Flash stimulus
2. Electrodes
   - A. Electrode Placement
3. Recording parameters
   - A. Amplification and averaging systems
   - B. Analysis time

Clinical Protocol

1. Preparation of the patient
2. Description of the three standard transient responses
   - A. Pattern reversal VEP
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   - C. Flash VEP
3. Pediatric VEP recording
4. Multi-channel recording for assessment of the central visual pathways
5. VEP measurement and reporting
   - A. Normal values
   - B. VEP reporting
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Basic technology

Stimulus parameters

There are two major classes of VEP stimulation, luminance and pattern. Luminance stimulation is usually delivered as a uniform flash of light and pattern stimulation may be either presented in a reversal or onset-offset fashion. The reader may refer to the ISCEV Calibration Guidelines [4] for further information regarding the measurement and definition of stimulus parameters.

Standard stimulus and recording conditions are described below and are summarized in Table 2.

Pattern stimulus

The recommended patterned stimulus is a black and white checkerboard. The stimulus should be defined by the visual angle subtended by the side of a single check. Visual angle is measured in degrees and minutes of arc subtended at the eye. All checks should be square and there should be an equal number of light and dark checks. Measurement of the physical check size in inches or millimeters should never be used to describe them.

Pattern stimulus luminance should be measured in candelas per meter squared ($cd \cdot m^{-2}$). The luminance of the white areas should be at least $80\,cd \cdot m^{-2}$. The mean luminance should be uniform between the center and the periphery of the field. We recognize that some optical and electronic systems do not provide truly uniform fields and may vary by up to 30%. We encourage those following the standards to use systems that come as close to uniform as possible. The surround of the stimulus should be homogenously lit, with an average luminance equal to or below the average stimulus luminance. Practically, this can be achieved by subdued room lighting with no bright sources visible to the subject.

The Michelson contrast ($\{[L_{max} - L_{min}]/[L_{max} + L_{min}]\} \times 100$) should be at least 75%, where L = luminance, max = maximum and min = minimum. The stimulus field size should be expressed in degrees of visual angle, with an indication of field shape, i.e., rectangular field a deg × b deg or a circular field of c deg diameter or radius. The location of the fixation point should also be defined in relation to this field; i.e., in the center or d deg to the left or right of the center. The fixation point should be positioned

Table 2A. ISCEV standard for VEP assessment: standard stimuli

	Field size (deg)	Stimulus type	Stimulation	Pattern element size	Luminance ($cd \cdot m^{-2}$)			Contrast (%)	Presentation rate
				Checks (min)	Background	Bright element	Mean		
Pattern Stimulation – Pre-chiasmal	>15	Pattern reversal or onset/offset	Monocular	60, 15	Equal to mean for onset/offset	>80	>40	>75%	<1–3 reversals or ⩽2 onsets per second
Flash Stimulation – Pre-chiasmal	>20	ISCEV standard luminance flash	Monocular	–	15–30	–	–	–	<1.5 flashes per second

Table 2B. ISCEV standard for VEP assessment: standard recording

	Electrode montage (International 10/20 channel system)		Filters (−3 dB)		
	Active	Common reference	Low freq.	High freq.	Sweeps averaged
Pattern Stimulation – Pre-chiasmal	Oz	Fz	<1	>100	⩾64
Flash stimulation – Pre-chiasmal	Oz	Fz	<1	>100	⩾64

at the corner of 4 checks when located at the center of the field.

Pattern reversal stimulus

The pattern reversal stimulus consists of black and white checks that change phase (i.e., black to white and white to black) abruptly and repeatedly at a specified number of reversals per second. There must be no overall change in the luminance of the screen. This requires equal numbers of light and dark elements in the display. Background luminance of screen and room should approximate the mean for onset/offset of each check. The stimulus should be defined in terms of the visual angle of each check, the reversal frequency, the number of reversals, the mean luminance the pattern contrast and the field size. For standard responses, at least two pattern element sizes should be used: 1 deg and 15 min per side checks. The visual field diameter should exceed 15 deg in its narrowest dimension. Reversal rates between 1 and 3 reversals per second (i.e., 0.5–1.5 Hz) should be used to elicit the standard pattern reversal response. The lower portion of this range is preferred. Stimulus rate should be reported in reversals per second to avoid the potential confusion related to the number of cycles (Hz) of a reversal stimulus being half of the number of reversals per second.

Pattern onset /offset stimulus

For pattern onset/offset a pattern is abruptly exchanged with a diffuse background. The pattern stimulus should be defined in terms of the visual angle of each check. At least two pattern element sizes should be used: checks of 1 deg and 15 min per side. The visual field stimulated should exceed 15 deg. The mean luminance of the diffuse blank screen and the patterned stimuli *must* be the same so there is no change of luminance during the transition from pattern to diffuse blank screen. This may be difficult to achieve. Background luminance should have this same value. We recommend a standard of 100 to 200 ms pattern presentations separated by 400 ms of diffuse background. The duration of pattern presentations and diffuse background in ms should always be indicated. The data acquisition system should be set to trigger at the appearance of the stimulus.

Flash stimulus

The flash VEP should be elicited by a flash that subtends a visual field of at least 20 deg. The

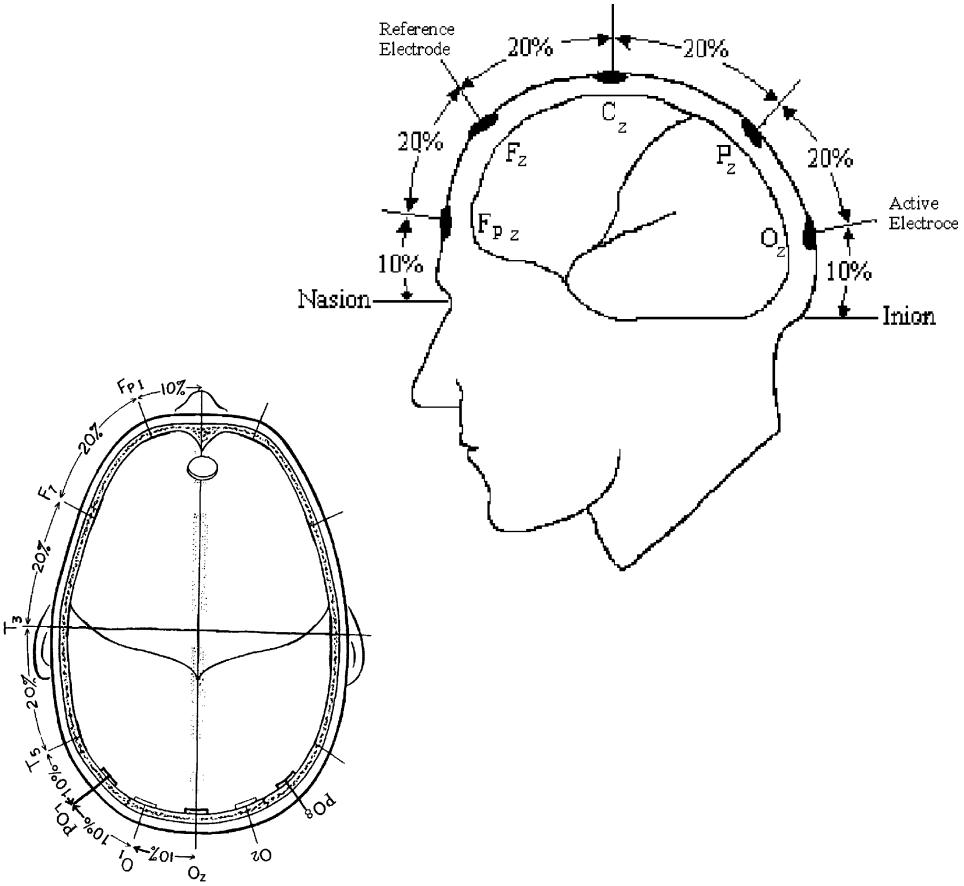

Figure 1. Electrode Locations. 1A. Location of Active and Reference Electrodes for Standard Responses. The active electrode is located along the midline at Oz. The reference electrode is located at location Fz. The subscript z indicates a midline position. 1B. The locations of the lateral active electrodes, O_1, O_2, PO_7, and PO_8 are indicated along with the midline active electrode location, O_Z.

stimulus should be presented in a dimly illuminated room. The strength (time integrated luminance) of the flash stimulus should be measured in photopic candelas seconds per meter squared ($cd{\cdot}s{\cdot}m^{-2}$). The background on which the flash is presented should be measured in candelas per meter squared ($cd{\cdot}m^{-2}$). The flash should have a stimulus strength of 1.5–3 $cd{\cdot}s{\cdot}m^{-2}$ with a background of 15–30 $cd{\cdot}m^{-2}$ as described in the ERG standards for the standard flash [2] and should be presented less than 1.5 times per second (<1.5 Hz).

Electrodes

Standard silver-silver chloride or gold disc surface electrodes are recommended for recording VEPs. The electrodes should be fixed to the scalp and maintained using procedures recommended by the manufacturer. The electrode impedances should be below 5 kΩ and equal to reduce electrical interference.

Electrode placement

The scalp electrodes should be placed relative to bony landmarks, in proportion to the size of the head, according to the International 10/20 system [6] (see Figure 1a). The anterior/posterior midline measurements are based on the distance between the nasion and the inion over the vertex. The active electrode is placed on the scalp over the visual cortex at Oz with the reference electrode at Fz. Commonly used ground electrode positions include the forehead, vertex (Cz), mastoid, earlobe (A1 or A2) or linked earlobes.

Recording parameters

The details of equipment calibration are given in the ISCEV Calibration Guidelines [5] and should be adhered to. The Guidelines include details on the measurement of electrode impedance as well as amplifier filtering and gain.

Amplification and averaging systems

Analogue high pass and low pass filters [−3 dB points] should be set at 1 Hz or less (corresponding to a time constant 0.16 s or more) and at 100 Hz or more, respectively. Analogue filter roll-off slopes should not exceed 12 dB per octave for low frequencies and 24 dB per octave for the high frequencies. While other filter settings may be required in particular circumstances, it must be realized that all analogue filters produce an apparent change in the timing or peak latency of the components of the VEP particularly if low pass filters below 100 Hz are used. The use of notch or comb line frequency filters is not recommended.

Amplification of the input signal by 20,000–50,000 times is usually appropriate for recording the VEP. The input impedance of the pre-amplifiers must be at least 100 MΩ and the common mode rejection ratio should ideally be in excess of 120 dB. The amplifiers must be electrically isolated from the patient and international standards for safety of biological recording systems in humans should be used (IEC-601-1 type BF specification). The analogue signal should be digitized at a minimum sample rate of 500 samples per second per channel with a minimum resolution of 12 bits. Automatic artifact rejection based on signal amplitude should be used to exclude signals exceeding ± 50–100 μV in amplitude. The amplifiers must return to baseline rapidly following artifactual signals.

The number of sweeps per average depends upon the signal to noise ratio between the VEP and the background noise. In most clinical settings, the minimum number of sweeps per average should be 64. At least two averages should be performed to verify the reproducibility of the findings. In pediatric practice, particularly with infants, a smaller number of sweeps per average may sometimes produce a clearer response. The longer recording time required to increase sample size introduces the possibility of increased variability due to loss of attention and/or increased movement.

Analysis time

The analysis time (sweep duration) for all transient flash and pattern reversal VEPs should be at least 250 ms. If one analyzes both the pattern onset and offset responses elicited by onset-offset stimuli, the analysis time (sweep duration) must be extended to at least 500 ms.

Clinical protocol

Preparation of the patient

Pattern stimuli for VEPs should be presented when the pupils of the eyes are unaltered by mydriatic or miotic drugs. Pupils need not be dilated for the flash VEP.

Extreme pupil sizes and any anisocoria should be noted. For pattern stimulation, the visual acuity of the patient should be recorded and the patient should be optimally refracted for the viewing distance of the screen. Monocular stimulation should be performed. This may not be practical in infants or some other special populations, when binocular stimulation may be used to assess whether any afferent signals are reaching primary visual cortex. When a flash stimulus is used with monocular stimulation, care should be taken to ensure that no light enters the unstimulated eye. Usually this requires a light-tight opaque patch to be placed over the unstimulated eye. Care must be taken to have the patient in a comfortable, well supported position to minimize muscle and other artifacts.

The pattern onset/offset response shows a greater intersubject variability than the pattern reversal VEP but shows less sensitivity to confounding factors such as poor fixation or eye movements. It is difficult to deliberately defocus a transient pattern onset/offset stimulus. Therefore, it is an effective stimulus for detection or confirmation of malingering or evaluation of patients with nystagmus.

Description of the three standard transient responses

The waveform of the VEP depends upon the temporal frequency of the stimulus. At rapid rates of stimulation, the waveform becomes approximately sinusoidal and is termed steady-state. At low temporal frequencies, the waveform consists of a number of

discrete deflections and is termed a transient VEP. Only transient VEPs form a part of this standard.

VEP peak latency, amplitude, and waveform are age-dependent. The description of standard responses below reflects the typical response of an adult aged 18–60 years of age. VEP peak latency refers to the time from stimulus onset to the maximum positive or negative deflection or excursion; thus, the term VEP peak latency corresponds to the term implicit time used to describe the time from the stimulus to the maximum deflection of electroretinograms. VEP peak latency may also be referred to as 'time to peak' or peak time.

Pattern reversal VEP

The pattern reversal VEP has relatively low variability of waveform and peak latency both within a subject and over the normal population. Therefore, it is the preferred procedure in most circumstances. For pattern reversal, the VEP consists of N75, P100 and N135 peaks. The nomenclature consists of designating peaks as negative and positive followed by the typical mean peak latency (see Figure 2). It is recommended to measure the amplitude of P100 from the preceding N75 peak. The peak latency of P100 shows relatively little variation between subjects, minimal within-subject interocular difference, and minimal variation with repeated measurements over time. P100 peak latency is affected by non-pathophysiologic parameters such as pattern size, pattern contrast, pattern mean luminance, refractive error, poor fixation and miosis.

Pattern onset/offset VEP

The onset/offset VEP is more variable in appearance than the pattern reversal VEP. The response to pattern onset/offset stimulation typically consists of three main peaks in adults; C1 (positive approximately 75 ms), C2 (negative approximately 125 ms) and C3 (positive, approximately 150 ms) (see Figure 3). Amplitudes are measured from the preceding negative peak.

Flash VEP

Flash VEPs are much more variable across subjects than pattern responses but show little interocular asymmetry. They may be useful in patients who are unable or unwilling to cooperate for pattern VEPs, and when optical factors such as media opacities prevent the valid use of pattern stimuli.

The visual evoked potential to flash stimulation consists of a series of negative and positive waves. The earliest detectable response has a peak latency of approximately 30 ms post-stimulus and components are recordable with peak latencies of up to 300 ms. Peaks are designated as negative and positive in a numerical sequence (see Figure 4). This nomenclature is recommended to automatically differentiate the flash VEP from the pattern reversal VEP. For the flash VEP, the most robust components are the N2 and P2 peaks. Measurements of P2 amplitude should be made from the positive P2 peak at around 120 ms to the preceding N2 negative peak at around 90 ms.

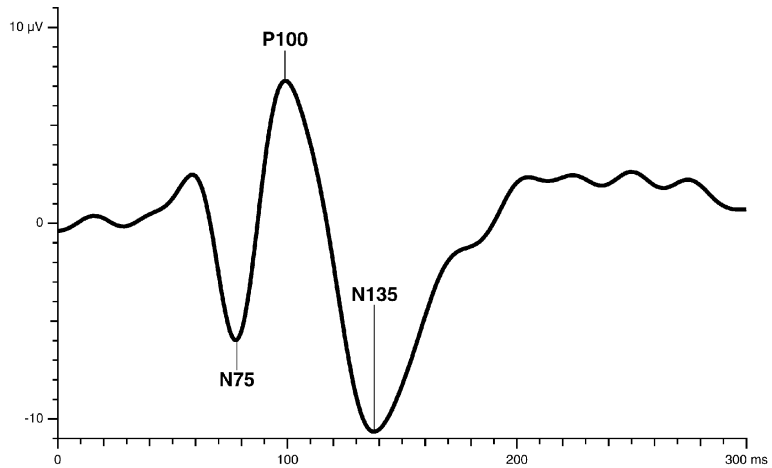

Figure 2. A normal pattern reversal VEP.

Pediatric VEP recording

Modifications to VEP recording methods and testing strategies may be required to optimize results in infants, young children or people with disabilities. In principle, the stimulation and recording methods recommended in the ISCEV standard can be applied to all populations. However, in these special populations modifications to VEP recording methods and testing strategies may be required to optimize the quality and pertinence of the result to diagnosis and visual assessment to the clinical question.

All VEPs in children should be compared with appropriate age related normal values. When recording the VEP in infants the sweep duration should be increased due to the increased peak latency in this population. By six months of age the peak latency of the main positive peak of the pattern reversal VEP for larger checks (>30') is usually within 10% of adult values.

VEPs should be recorded when the infant or child is in an attentive behavioral state. Direct interaction with the child can help maintain attention and fixation, and two testers are beneficial; one to work with the child and the other to control data acquisition. Data quality and reliability will be improved if a recording trial can be paused or interrupted when fixation wanders and then resumed as the child resumes adequate cooperation. To facilitate compliance, an infant may view the stimulus while lying across a lap, or held over the shoulder. The order of stimulus presentation also should be flexible and selected to ensure that responses most critical to the diagnostic question are obtained within an individual child's attention span. Binocular pattern stimulation, which facilitates attention and fixation, may be useful to evaluate overall visual function. Monocular testing to at least one stimulus is desirable to assess the function of each eye. It is particularly important to obtain replicate responses from children to assure that the response measured is a reliable signal and not an artifact. As for adults, additional channels of recording may be important for diagnosis of chiasmal and post-chiasmal dysfunction. When pattern VEPs cannot be reliably recorded, flash testing which is less dependent upon co-operation can usually be achieved. Pattern reversal VEPs recorded from patients with nystagmus or unstable fixation should be interpreted with caution. Pattern onset/offset stimuli can be helpful in gaining attention of children and are usually more robust in cases of nystagmus, but the waveform components change with age. Reports should note the degree of cooperation and arousal of the child.

Multi-channel recording for assessment of the central visual pathways

Multi-channel recording is not covered by the standard. However, intracranial visual pathway dysfunction may require multi-channel recording for accurate

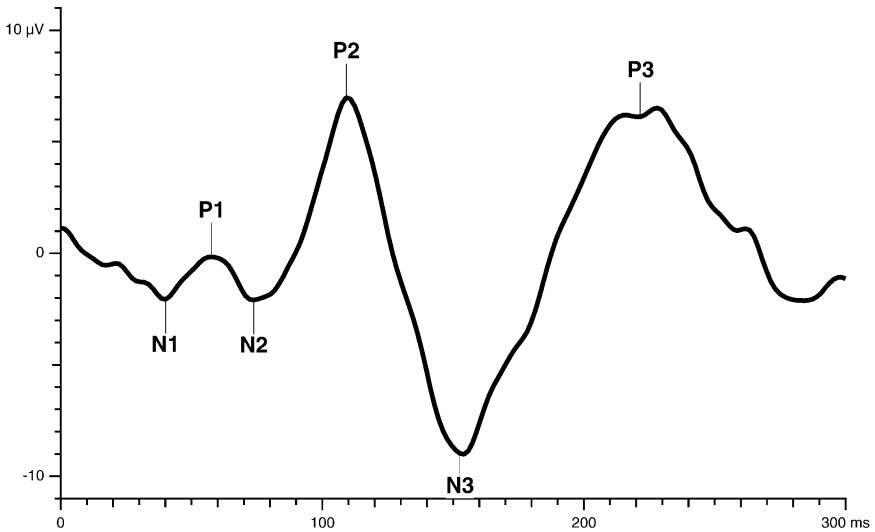

Figure 4. A normal flash VEP.

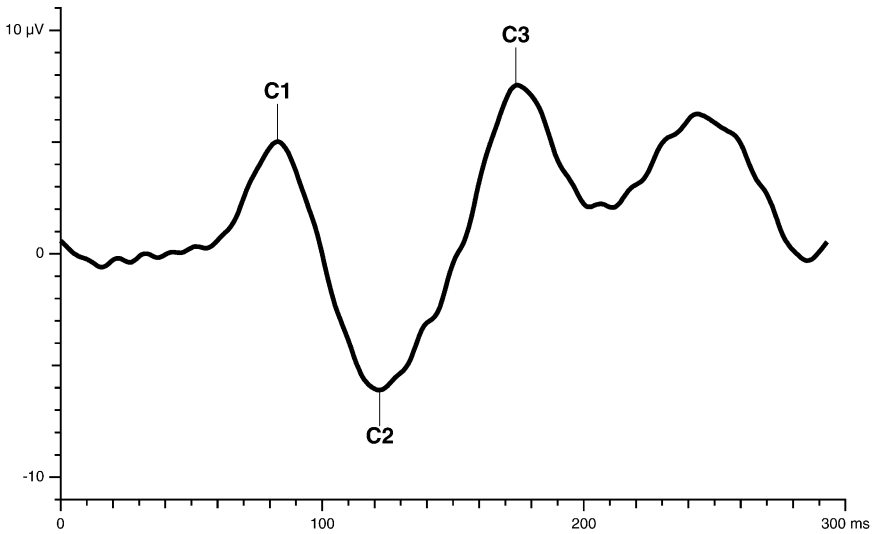

Figure 3. A normal pattern onset/offset VEP. Note that with a 300 ms sweep only the pattern onset response is recorded.

diagnosis. With dysfunction at or posterior to the optic chiasm, or in the presence of chiasmal misrouting (as seen in ocular albinism), there is an asymmetrical distribution of the VEP over the posterior scalp. Chiasmal dysfunction gives a 'crossed' asymmetry whereby the findings obtained on stimulation of one eye show an asymmetrical distribution that is reversed when the other eye is stimulated. Retrochiasmal dysfunction gives an 'uncrossed' asymmetry such that the findings obtained on stimulation of each eye show an asymmetrical distribution across the hemispheres that is similar when either eye is stimulated. We suggest that for pattern reversal stimulation the stimulus should consist of high contrast black and white checks of 60' in a field of 30 deg (full-field). A minimum of two channels is needed for detection of lateral asymmetries. We suggest the use of three active electrodes, two lateral electrodes placed at O_1 and O_2, and a third midline active electrode at Oz. All three active electrodes should be referenced to Fz. This three channel montage provides the preferred montage for simultaneous detection of prechiasmal and central pathway dysfunction. Additional electrodes placed at PO_7 and PO_8, also referred to Fz, may increase sensitivity to lateral asymmetries in some cases. The position of the lateral electrodes is illustrated in Figure 1B. For all stimulus conditions, normative data should include amplitude and peak latency comparisons between homologous left and right occipital channels. Particular caution is needed when interpreting the multichannel pattern reversal VEP due to the phenomenon of paradoxical lateralization. This phenomenon, in which the response recorded at a lateral head position is generated by activity in the contralateral hemisphere of the brain, occurs with a large field, large check reversal stimulus and common reference recording to Fz.

VEP measurement and reporting

Standardization of VEP measurement and reporting is critical to the goal of having comparable data worldwide.

Normal values

Even though standardization should ensure similar responses across laboratories, each laboratory must establish its own normative values using its own stimulus and recording parameters. The construction of a normal sample for laboratory norms should include the factors of age, gender, and interocular asymmetry. Adult normative data cannot be generalized to pediatric or elderly populations. Interocular amplitude and peak latency analysis increases the sensitivity of the VEP to monocular diseases. We recommend that laboratory norms make use of descriptive statistics that do not assume a normal distribution, but are based on the calculation of the median and percentiles from the observed sample distribution. We recommend the 95% reference

interval as the minimum limit of normal (i.e., the range from 2.5% to 97.5%).

VEP reporting

A minimum of two recordings of each VEP condition should be acquired, measured and displayed. Reports of the standardized conditions should specify the stimulus parameter; the field size of the stimulus, the strength (time integrated luminance) of the flash or mean luminance of the pattern, the pattern element size and contrast of pattern stimuli, the frequency of stimulation, the eye tested and the recording parameters; the filter settings and the locations of the positive (i.e., active) and negative (i.e., reference) and indifferent (i.e., ground) electrodes.

Traces should have a clear indication of polarity, time in milliseconds, and amplitude in microvolts. We recommend that VEP traces be presented as positive upwards. All VEP reports, even for non-standard responses (whether for local records or publications) should include normative values and the limits of normal.

The report should indicate whether the recordings meet this international standard. We recommend that the numerical measurements of obtained peak latency and amplitude be reported along with the normal values and the limits of normal.

VEP interpretation

VEP abnormalities are not specific and can occur in a wide variety of ophthalmological and neurological problems. The interpretation should include statements about the normality and abnormality of the result in relation to normative data as well as comparison between the eyes or with previous records. The type of abnormality in the response should be described and this should be related to the clinical picture and other visual electrodiagnostic results.

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