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Basic requirements for visual evoked potentials

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Visual evoked potentials (VEPs) are frequently used to assess the anterior and posterior visual pathways. In particular, the use of VEPs have been increasing in various fields such as evaluation of the optic nerves in patients with multiple sclerosis. The performance of VEP test can be affected by various factors such as stimulus type and subject condition, and its interpretation is also difficult. However, there have been no guidelines for performing and interpreting VEPs in Korea. Therefore, we aimed to provide comprehensive information regarding basic requirement and interpretation for VEPs.

Key words: Visual evoked potential; Optic nerve; Visual pathway

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INTRODUCTION

A visual evoked potential (VEP) measures an electrophysiological response of the visual pathway to a patterned or unpatterned visual stimulus. It is a reliable, sensitive, and non-invasive technique that can measure impairment of visual pathways.[1-4] While stimulation with a relatively low frequency (up to 4/s) generates transient VEPs, stimulation with a high frequency (over 10/s) generates responses corresponding to relatively simple waves in accordance to the stimulation. These are called steady-state VEPs.[5] Responses induced by a patterned stimulus are called patterned VEPs (PVEPs), while those induced by an unpatterned stimulus are called flash VEPs (FVEPs).[1-4] In this overview we describe comprehensive information regarding basic requirement and interpretation for VEPs.

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STANDARDS REGARDING VISUAL EVOKED POTENTIAL

Choice of stimulus

Patterned visual stimuli produce smaller inter- or intra-individual variability in comparison to unpatterned visual stimuli. The sensitivity and accuracy of PVEP testing is much higher than that of FVEP testing in detecting a visual pathway abnormality.[2,4] The most widely used patterned stimulus is checkerboard shape because of its relative simplicity and high reliability. To test a specific region in the visual pathway, check size, field size, and field location can be selected for testing with a patterned stimulus. In such testing, the stimulus should be determined according to the patient's clinical status, and it is advisable to use more than one stimulus. A nonpatterned stimulus is typically used in patients who cannot not focus on a stimulus or maintain attention.[2,4]

Subject conditions

It is very important to fixate on and maintain attention to the stimulus during PVEP testing.[2,4] During testing, the patient should precisely fixate on the stimulus. Eye position should be monitored during the test. In addition, visual acuity should be measured in all patients, and low vision should be adequately corrected with glasses or other means before testing. Fixation on a near stimulus can easily tire the patient, and to avoid patient fatigue, the stimulus should be presented at least 70 cm away from the patient. Patient arousal and focus are the most important factors of VEP testing, and an effort should be made so the patient is aroused and maintains focus. Changes in such factors during testing can affect the comparison of the measurements between left and right eyes and also the measurements with the second stimulus in the same eye, as well. If the patient cannot fixate on the stimulus and attend to the task, testing should be delayed because latency, amplitude, and waveform may be affected. Patients who feign illness can show abnormal responses if they intentionally do not fixate on the stimuli or maintain attention. Variations in pupil size also can affect test results. Very small pupils or severely asymmetrical pupils may show abnormal latency or amplitude, or asymmetrical findings, when co-occurring with cataract or lens opacity. Thus, pupil dilation medications are not generally used. If clinical decision-making could be influenced by pupil size, it should be mentioned in the test report. Because light adaptation in the retina is important in FVEP testing, stimuli should be presented in sufficiently bright light when FVEP testing is performed.

PERFORMANCE OF PATTERN REVERSAL VISUAL EVOKED POTENTIALS

Waveform generation and identification

The VEP usually is a triphasic potential with a major positive peak flanked by smaller negative peaks. Through phase reversal, waveforms with a positive peak and a latency of approximately 100 ms can be observed in the temporal and midoccipital areas.[2-4,6] Response components refer to the regions where polarity and peak latency are clearly observed. Negative and positive polarities are indicated as N and P, respectively, and peak latency is expressed in terms of msec post stimulation. Peak N75, P100, and N145 are recorded in the occiput, and N100 in the midfrontal area. Responses subsequently occurring after N145 are diverse and not used in the standard interpretation of test results.

Methods for full-field stimulation

Full-field PVEP testing is a sensitive test to detect a lesion in the visual pathway anterior to the optic chiasm. Most of the P100 responses occur in the optic nerves in the area corresponding to 8–10 degrees of arc from the center of the visual field. A lesion in which central vision is maintained even though half- or partial-field is impaired does not greatly affect the latency and amplitude of P100 responses. Changes in response topography in the presence of a partial lesion in a prechiasmatic, retrochiasmatic, or chiasmatic area can best be assessed with the use of partial-visual field testing.

Stimulus

Full-field stimulation is performed monocularly. The eye of the subject is stimulated using a high-contrast (>50%), black-and-white checkerboard stimulus with a ratio less than 4/s. The subject should not be closer than 70 cm from the stimulus screen. A fixation point should be positioned in the center of the stimulus screen. Stimulus size and field size should be adequately chosen to best assess the clinical problem.[2-4,6,7] A small stimulus (12–16″) and a small field

(2–4°) selectively stimulates central vision, and the responses are particularly sensitive if the eyes are defocused or vision is low. A large stimulus (40–50") and a large stimulus field (16–32°) stimulate peripheral vision better and the responses are little affected even if the eyes are defocused or vision is low. First starting with a mid-sized stimulus (24–32") is an option and additionally, it is advisable to use more than one stimulus and more than one stimulus field.

Recording Methods

Filter setting

In the bandwidth of 1-100 Hz (-3 dB), the filter roll-off slope should not exceed 12 dB/octave for low frequencies and 24 dB/octave for high frequencies.[2,4]

Analysis time

For analysis time, 250 ms is adequate.[4] If response components are severely prolonged, a long analysis time of approximately 500 ms or a slow stimulus under 2/s is necessary.

Number of trials

Response outcomes should be obtained with at least two iterations. The average number of stimulations should be sufficiently high to confirm the reproducibility of main response components in each trial. In general, the measurement error of replicated responses should be within a difference of 2.5 msec for P100 latency, and within a difference of 15% for the interpeak amplitude of N75-P100 or P100-N145. Such values are usually achieved with 100–200 replications. To reproduce a low-amplitude response requires over 400 replications.

Electrode placement

A standard disk electrode is adequate for recording. In general, notations for the placements following the Queen Square System (labeling the electrodes in the occipital region as left occipital [LO], midline occipital [MO], and right occipital [RO]) and the International 10-20 system (labels like O1, O2, and O2) are used. Extratemporal leads are placed farther away from the midline in the Queen Square System than in the International 10-20 system. The Queen Square System is useful in recording the scalp distribution of PVEP in response to partial-field stimulation in adults or in response to total-field stimulation in subjects with a partial visual pathway lesion. In the international 10-20 system, the Fz lead is placed on average 11 cm above the nasion, and in the Queen Square System, the midline frontal (MF) lead is placed on average 12 cm above the nasion. In the Queen Square System, electrodes are placed and labeled in the following manner[2,4]:

1) MO: In the midline occipital area. Along the midline, 5 cm above the inion
2) LO and RO: In the lateral occipital area. 5 cm to the left or the right from the MO
3) MF: In the midline frontal area. Along the midline, 12 cm above the nasion
4) A1/A2: Left or right from the ear or mastoid
5) Ground: The vertex of the head

Recording montages

Recording should be made at least in 4 channels. In general, the following montage and derivatives are recommended[2,4]:

1) Channel 1: Left occipital to midline frontal = LO–MF
2) Channel 2: Midline occipital to midline frontal = MO–MF
3) Channel 3: Right occipital to midline frontal = RO–MF
4) Channel 4: Midline frontal to ear/mastoid = MF–A1 (A2)

Interpretation of the full-field visual evoked potential

Abnormality is manifest in terms of altered latency, amplitude, distribution, or waveform. Prolonged P100 latency is the most reliable index of a clinically significant abnormality, and is least influenced by technical factors or patient cooperation.[2-4,6,7] Amplitude and topography measurements are closely associated with each other, and may show a clinically significant abnormality. However, they are easily influenced by technical factors as well as patient cooperation, fixation, and arousal. Waveform abnormality is difficult to quantify, because it is generally subjective in nature. Thus, controversy may exist regarding misinterpretation or clinical relevance. Usually, normative VEP data are not interchangeable across laboratories, but can be interchanged between laboratories if identical instruments are used, and all stimulus recording parameters are also identical. To do so, light and dark parameters of the stimulus should be accurately calibrated (using a photometer) as well as other stimulus and recording parameters and they must be set identically in both laboratories.

Norms may differ according to age and sex.

Delayed P100 peak latency

Delayed P100 peak latency suggests a visual pathway abnormality if disease in the eye or the retina is excluded by an appropriate test. When these factors are excluded, a monocular latency abnormality is indicative of a unilateral optic nerve disorder. In addition, abnormally prolonged P100 interocular latency difference is indicative of an abnormality in the eye with prolonged latency.[2,4] A bilaterally prolonged latency indicates a disorder in the bilateral visual pathway, but whether the disorder is limited to the prechiasmatic or retrochiasmatic area cannot be determined just by examining the amplitude and the topographical pattern in further detail. In most laboratories, an abnormality is determined if P100 latency or interocular latency difference exceeds 2.5 or 3 standard deviations away from the mean of the age-matched normal control group.

Reduced amplitude of the P100

The amplitude in the midoccipital area can be reduced because of patient factors, impaired fixation, defocusing, tears, inattention, or sleepiness. If these factors are excluded, monocular abnormality suggests a unilateral disorder in the prechiasmatic area.[2,4,8,9] A binocular abnormality is indicative of a bilateral disorder, but it cannot be accurately localized whether the disorder is present in the prechiasmatic area without a detailed examination of responses to partial-field stimulation or topographical characteristics.

If low P100 amplitude is recorded without asymmetry between left- and right-sided responses, its clinical significance is unclear. The presence of an abnormality may be confirmed by performing an additional test with half-field or partial-field stimulation.

Double-peaked or "W"-shaped P100 waveform

A double-peaked or "W"-shaped P100 waveform may difficult to interpret. To analyze such responses, it is inappropriate to try to determine which is the true P100 peak. Rather, the response's clinical significance should be determined by adding half- or partial-field stimulation or stimuli of a different size. It is possible that neither waveform is P100, as in central scotoma. In that case, the first, the second, or both waveforms could be P100. Double-peaked P100 waveform may be present in the presence of various disorders in the partial visual pathway.

Half-field visual evoked potential

Half-field PVEP testing is more useful than full-field testing in detecting a lesion in the chiasmatic or retrochiasmatic area. The test often clarifies an ambiguous finding of full-field testing. Half-field testing requires a higher level of patient cooperation and is also technically more demanding.

Recording methods

The recording procedure is generally the same as with full-field testing. At least 4 channels should be recorded.[4]

Regarding the left half-field stimulation,

1) Channel 1: From left occipital to midfrontal = LO–MF
2) Channel 2: From midoccipital to midfrontal = MO–MF
3) Channel 3: From right occipital to midfrontal = RO–MF
4) Channel 4: From right posterior temporal to midfrontal = right posterior temporal (RT)–MF

Regarding the right half-field stimulation,

1) Channel 1: From left posterior temporal to midfrontal = left posterior temporal (LT)–MF
2) Channel 2: From left occipital to midfrontal = LO–MF
3) Channel 3: From midoccipital to midfrontal = MO–MF
4) Channel 4: From right occipital to midfrontal = RO–MF

Interpretation

To accurately interpret the results of half-field PVEP testing, first, it is important to determine whether P100 is abnormal and prolonged. Half-field responses have lower amplitude and larger variability than full-field responses. Other than those, the criteria for clinically significant abnormal findings are identical to the criteria and cautions for full-field VEP.

Because various testing procedures can be used to obtain half-field responses, it is possible to misinterpret the results based on small variability. Accordingly, the following stepwise approach is necessary for proper interpretation. The first step is to use $p < 0.01$ as the criterion to be more conservative in determining abnormality. Clinical significance is more likely to be high, because the score is more strongly deviated from the central value. The second step is to observe internally consistent abnormality in one or more measurements. For example, it will be necessary to deter-

mine clinical significance if prolonged latency in response to half-field stimulation exceeds the symmetry criterion for stimulation in the other half-field. Technical difficulty in testing influences amplitude measurements rather than latency measurements. Accordingly, more conservative criteria are needed in determining abnormalities in amplitude than in latency.

PERFORMANCE OF FLASH VISUAL EVOKED POTENTIALS

The FVEP test is not as sensitive as the PVEP test for visual pathway abnormalities. In general, its clinical use is limited, but it may be performed in the following cases: 1) Subjects who cannot see patterned stimuli due to visual impairment or a disorder in their lens, and 2) subjects who are too young or too uncooperative and cannot fixate on a patterned stimulus (PVEP testing can be used in infants or toddlers, but it takes a long time).[4]

Test results show peak positive responses reproducible with flash stimulation, if there is no movement induced by the stimulus, artifactual wave of muscular origin, or auditory response occurring in response to a sound accompanying the stimulus. They are labeled as I, II, III, IV, V, and VI in sequence. Any of the peaks can be replaced with a faster peak. The latency of individual peaks shows considerable inter-individual variability, and also differ according to arousal level. Such characteristics often make it difficult to compare particular response components across subjects.

Methods for stimulation and recording

Stimulator

Unpatterned visual stimuli consist of a brief flash of light of an indistinguishable pattern and shape. Stimuli are presented by a photostimulator lamp, which is an light emitting diode (LED) or a Ganzfeld stimulator. A photostimulator lamp is the most readily available means to present stimuli, and generates brief flashes of light from a Xenon light discharge tube like the one used in a stroboscope. The LED screen can be shown at the same distance, or a pair of LED goggles can be placed directly over the eyes. Goggles are useful because they have a wide stimulation field to minimize the effect of changes in gaze orientation. A disadvantage of using goggles is that the eyes cannot be observed, but stimulation takes place even when the eyes are closed. Stimuli can be quantified or calibrated through the Ganzfeld stimulator. This consists of a ball shape reflected and diffused through an opening on the wall of a hemi-sphere. A brief and bright flash is delivered to the subject's full visual field in a specific illuminance and waveform against limited background illumination. This can generate precisely calibrated stimulations, but the test requires a high level of cooperation from the subject.

Stimulus rate

Stimuli are presented approximately at 1/s. The rate should be lower in young infants.

Stimulus intensity

It is not practical to measure the intensity of a photostimulator lamp. The best way is to make a note of the stimulus type and the intensity setting and constantly maintain them. Main decisions regarding intensity depend on the distance between the subject and lamp. The lamp is positioned in front of the subject at a distance of 30–45 cm, and stimuli are presented with the subject gazing at the lamp with the eyes open. Background light should be adequate for observing the subject's eyes without causing glare or discomfort. The LED stimulator can be measured by a photographic light meter.

Recording montage

A simple screening test to determine the absence or presence of a response may be performed with a single channel attached in the midoccipital area. However, if a response is absent, multiple channel recordings should be performed for quite a long time. Here, a simple recording montage with four channels is as follows[2,4]:

1) Channel 1: From the left occipital area to the reference lead: LO–reference
2) Channel 2: From the midoccipital area to the reference lead: MO–reference
3) Channel 3: From the right occipital area to the reference lead: RO–reference
4) Channel 4: From the vertex of the head to the reference lead: vertex of the head (V)–reference

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A lead connecting unilateral or bilateral ears/mastoids can serve as a reference.

Interpretation of the flash visual evoked potential

Reproducible peaks, different from irregular variability in the baseline, should be identified, and peak latency and peak-to-peak amplitude should be measured. The amplitude ratios of responses in the left and right sides should be computed.

Because of considerable variability of FVEPs across individuals, abnormality is certain only when identifiable responses are absent. Low amplitude and long latency due to marked asymmetries of amplitude and latency are indicative of a unilateral abnormality in the eye.[2,4,10] The absence of FVEP in the occipital area means that no stimulation has reached the occipital cortex. The values of latency and amplitude should be referenced against the norms collected by the laboratory in aroused normal subjects of a similar age. Particularly, vague waveforms and changes in latency or interocular symmetry should be interpreted with caution.

Normal FVEP means that some visual stimulation has reached the occipital cortex. However, it does not tell whether the visual stimulation took place in the macula or in the peripheral retina. In infants and subjects with communication difficulties, the presence of normal FVEP does not imply conscious visual perception

CONCLUSIONS

VEP is a useful test that is widely used to evaluate anterior and posterior visual pathways. It is most important to choose the appropriate methods of VEP test and to interpret the results according to the patient's characteristics and condition. In this regard, we hope that this paper will help physicians learn and understand the proper testing and interpretation of VEP.

Conflicts of Interest

We have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest. The authors report no disclosures.

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