Principles and Practice of Clinical Electrophysiology of Vision

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A Year Book Medical Publishers imprint of Mosby-Year Book, Inc.

Mosby-Year Book, Inc.
11830 Westline Industrial Drive
St. Louis, MO 63146

1 2 3 4 5 6 7 8 9 0 CL CL MV 95 94 93 92 91

Library of Congress Cataloging-in-Publication Data
Principles and practice of visual electrophysiology / [edited by]
John R. Heckenlively, Geoffrey B. Arden.
p. cm.
Includes bibliographical references.
Includes index.
ISBN 0-8151-4290-0
1. Electroretinography. 2. Electrooculography. 3. Visual evoked response. I. Heckenlively, John R. II. Arden, Geoffrey B. (Geoffrey Bernard)
[DNLM: 1. Electrooculography. 2. Electrophysiology. 3. Electroretinography. 4. Evoked Potentials, Visual. 5. Vision Disorders—physiopathology. WW 270 P957]
RE79.E4P75 1991 91-13378
617.7 1547—dc20 CIP
DNLM/DLC
for Library of Congress

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Technical Issues in Visual Evoked Cortical Potential Recording

G. F. A. Harding

STIMULUS CONDITIONS

Certain principles of stimulation are essential for the identification of disorders involving the visual pathway and the cortex. For the identification of prechiasmal disorders it is essential that monocular stimulation to each eye always be performed, whatever stimulus is used. When monocular stimulation is combined with multichannel recording from both cerebral hemispheres, it assists in the location of prechiasmal and postchiasmal lesions as well as those lesions that involve the chiasm. Some forms of stimulation may need to be more specific and localized, although these techniques are usually only utilized with pattern stimulation. There are grave technical difficulties in providing local flash stimulation to particular areas of the retina.

Flash stimulation is normally performed by using a xenon gas discharge tube that is mounted in either a parabolic reflector or alternatively in a Ganzfeld stimulator. The luminance of such a stimulator is, of course, markedly suprathreshold and produces between 50 and 500 nit/sec. If the flash tube is mounted within a bowl for Ganzfeld stimulation, the patient usually places his head on a chin rest in the bowl, but with the usual parabolic reflector, the flash stimulator is held in front of the eye to be stimulated. With either technique the entoptic stray light generated in the eye helps produce an even distribution of the light falling on the retina. One complication that sometimes occurs with Ganzfeld stimulation is that the absence of any other visual stimulus in between the flashes of light may produce alpha rhythm in the electroencephalogram (EEG), with the visual evoked potential (VEP) being confounded by these rhythmic waves. Although the intensity of the flash stimulus can affect both latency and amplitude of the major P_2 component of the VEP, these variations are usually only found around the absolute threshold. It has been found that a 6-log-unit attenuation is necessary before any increase in latency of the flash VEP is observed.[38, 39] Although as the intensity is increased from threshold there is an initial shortening in latency, any further increase in the intensity does not produce a further reduction in latency since the stimulus has become markedly suprathreshold. It is therefore hardly surprising that pupil size has no significant effect on either the latency or amplitude of the flash evoked response.[29, 38]

With pattern stimulation there are a number of advantages. There is no overall change in luminance, and factors such as contour and contrast, level of luminance, and color can all be independently controlled.[33] All of these factors affect the latency of the VEP obtained. The pattern stimulation is usually provided in the form of a pattern of checks or bars that either reverse or appear and disappear into a gray background. For some studies the bars have no sharp edges but consist of gratings that al-

low independent studies of contrast without the interference of the effect of contour. The size of the pattern stimulus target and its position in the patient's field of vision affect both the amplitude and the lateralization of the VEP. The size of the stimulus field does affect the overall amplitude of the VEP,[32] but it has also been demonstrated that half-field stimulation using pattern reversal may produce the major positive component of the VEP on the surface of the scalp either ipsilateral or contralateral to the field stimulated, depending on the size of the half-field stimulation.[24] If large fields in excess of 0 to 10 degrees radius are used, the response that is elicited is undoubtedly ipsilateral.[3, 24, 27, 37] If small macular fields are used (0 to 2.5 degrees radius), the response is elicited cross-lateral to the field stimulated[24] (Fig 55–1, Plate 6).

The size of the individual elements or checks or bars of the stimulus can affect amplitude and latency. It can be demonstrated that optimum tuning of VEP amplitude and latency can be obtained for particular sizes of checks in particular targets and that this approximates the cortical representation of visual space.[11] The size of the check does not affect lateralization of the half-field response in half-field stimulation.[24] The overall luminance of pattern elements also affects both latency and amplitude. Latency increases and amplitude decreases as the stimulus intensity is lowered.[19, 22] If the contrast between the pattern elements is reduced, amplitude is also clearly reduced.[34]

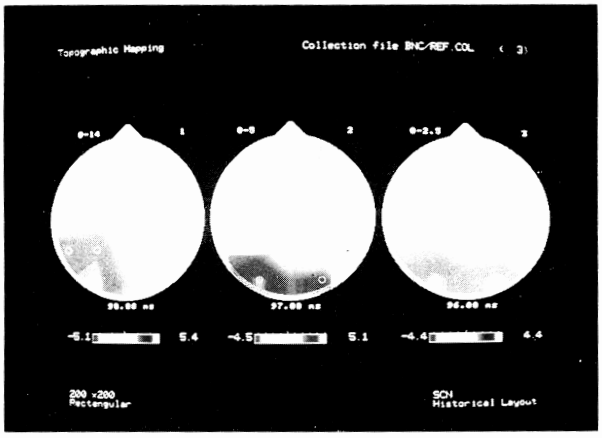

FIG 55–1.
Topographical distribution of the P_{100} component of the VEP in response to left half-field stimulation with differing check sizes with a 0- to 14-degree-radius checkerboard consisting of elements subtending 56 minutes of visual angle. It can be seen that the response is ipsilateral to the half-field stimulated as indicated as a marked positive component around 90 ms that is maximal over the left occiput (*white* and *red*). As the field size is reduced to a 0- to 5-degree radius, the response, although remaining ipsilateral to the field stimulated, becomes more bilateral. With a 0- to 2.5-degree-radius field the response becomes cross-lateral and is seen as a higher-amplitude response over the right occiput; this is indicated in *white* on the brain map. **(See also Color Plate 6.)**

Since in clinical investigations all these factors are considered to be intervening variables that interfere with the clinical robustness of the test, fairly standardized conditions have been developed. Large target fields (around 15 degrees radius) are usually used with relatively large checks approximating 1 degree. The stimulus is usually bright (around 100 cd/m^2) with a high contrast of approximately 75%. Many of the pattern stimulators used are of an optical type in which a slide is projected via a rotatable mirror onto a translucent screen so as to allow simple mirror movement to produce reversal of the elements of the stimulus.[15] Obviously the time of mirror movement may affect the latency of the response.[22] Similar optical techniques such as diffusing shutters can cause the pattern to appear and disappear with no change in luminance. The other pattern stimulation technique often used consists of either a domestic TV monitor or, alternatively, a special-purpose oscilloscope usually operating at high frequency.[1] These stimulators are far more flexible and allow a variety of patterns to be made to reverse or appear and disappear but unfortunately have the disadvantage that one complete cycle of the frame frequency is required to complete the entire pattern. If fixation wanders over the screen, then variability in the latency of the VEP occurs.[4] The specialized oscilloscopes operating at higher frequency reduce the error from this particular factor.

Finally, mention should be made of the rate at which stimulation takes place. Obviously, this can have a marked effect on the morphology of the VEP. In general, there has recently been a growing dominance of the use of transient evoked potentials in clinical practice. For these techniques stimuli are usually produced at a rate of between one and two per second, thus allowing each evoked potential to develop before the following stimulus occurs. It has been clearly shown that at rates above three stimuli per second the VEP is markedly affected and begins to take on the appearance of a sinusoidal response.[26] Some groups have utilized this technique to produce what is known as the steady-state evoked potential and, in order to deal with the difficulties of measuring latency, have developed a variety of waveform analysis techniques. So far they have not demonstrated clear clinical advantages over the transient evoked potential with its simple measurement of la-

tency and amplitude and descriptions of morphology. However, they occasionally have special use as in the rapid assessment of visual acuity in children.

NORMATIVE STUDIES

For all diagnostic VEP investigations it is absolutely essential that the limits of normalcy for latency and amplitude be known for each age band and in addition that the normal range of interocular variation be known. Such parameters should be determined by each laboratory with its own stimulators and recording apparatus since technical factors can markedly affect latencies. In general, ten normal volunteers are usually sufficient for each of the decades of life to obtain statistically acceptable means and standard deviations. There is a good deal of discussion over the number of standard deviations that should be allowed for a normal limit, and this appears to vary between 2 and 3 SD, 2.5 SD being an acceptable compromise. Although 2 SD appears to carry an unacceptable risk of misdiagnosis (5%), it should be remembered that almost all clinical conditions cause an increase in the latency of the VEP and therefore the risk of misdiagnosis is, in fact, only 2.5%.

Studies of the flash VEP over the normal population have shown that the normal latency of the P_2 component (125 ms) shows an increase with age.[7, 13, 18, 23] Studies of amplitude variation show that high values often seen in childhood slowly decrease and stabilize.[23] It should be noted, however, that in the 60- to 70-year-old age group there is a clear increase in the P_1 component (70 ms) in comparison to the amplitude of the P_2 component.[7, 12, 17, 23, 40] The latency changes of the P_2 component that are marked over the age span cannot be explained in terms of optical factors such as the reduction in pupil size with age. This factor can only account for a 3- to 4-ms increase in the latency of both flash and pattern-reversal VEPs, whereas the latency increase that is seen with flash stimulation is much larger.[25]

The VEP to pattern reversal shows a slight increase in the latency of the P_{100} component of around 5 to 10 ms over the life span, depending on the size of the pattern elements. Large elements around 1 degree show little change, and the greatest change is seen with small checks.[2, 8, 21, 31, 35, 40] The change that can be seen can be clearly attributed to the decrease in pupil size with age. Amplitude tends to be higher in the under-25-year-old age group and to show little significant change during the rest of the age span.[8, 21, 30] Pattern–onset-offset stimulation is less often used in clinical studies, and few normative studies have been performed. Most of these studies have shown greater variability over the life span of the C_1, C_2, and C_3 components, particularly in the young age group.[14, 40]

We have carried out a study to determine the normative data for flash, pattern-reversal, and pattern–onset-offset stimulation in the same subjects in each decade of life from 10 to 70 years of age.[25] The results are shown in Table 55–1. It can be seen that the flash P_2 latency significantly increases with age and shows a mean latency increase of 20 ms over the age span and that this must represent neural aging. At the same time the increase in the latency of the pattern-reversal P100 response is only 3 ms. Greater changes were seen in the C_2 component of the pattern onset-offset, but it should be noted that the C_2 component could not be reliably identified in the young age group.

TABLE 55–1.

Normal Values for VEP Latency Throughout the Adult Life Span*

Decades (yr)	Flash P_2 Component Latency (ms)	Pattern-Reversal P_{100} (56-Minute Check) Latency (ms)	Pattern-Onset C_{II} (56-Minute Check) Latency (ms)
10–19	114.5 ± 9.84†	108.56 ± 10.9	‡
20–29	120.75 ± 10.99	101.78 ± 7.64	98.0 ± 14.0
30–39	121.7 ± 7.8	106.78 ± 4.91	99.0 ± 4.6
40–49	126.8 ± 11.26	104.6 ± 5.15	102.9 ± 9.95
50–59	122.5 ± 15.45	102.89 ± 6.75	105.6 ± 13.1
60–69	127.28 ± 11.28	109.22 ± 10.45	110.5 ± 9.8
70–79	134.25 ± 12.72	111.00 ± 8.7	116.4 ± 9.2

*Normal values for VEP latency throughout the adult life span to flash stimulation, pattern-reversal stimulation, and pattern-onset stimulation. No data could be obtained in the younger age group for pattern-onset stimulation due to variability of the components. It should be noted that the smaller standard deviations seen for pattern-reversal stimulation are only apparent over a limited age group between 20 and 60 years of age.
†Values are means ± 1 SD.
‡Pattern-onset data not available due to ambiguity of the waveform.

TABLE 55–2.
Normal Values for Mean Monocular Latency Variation*

Decades (yr)	Flash P_2 (ms)	Pattern-Reversal P_{100} (ms)	Pattern-Onset C_{II} (ms)
10–19	3.5 ± 1.87†	6.3 ± 4.81	—
20–29	5.4 ± 3.55	6.7 ± 6.49	6.5 ± 3.87
30–39	5.5 ± 5.42	2.45 ± 1.62	4.25 ± 3.39
40–49	5.3 ± 4.04	3.55 ± 2.14	4.4 ± 2.51
50–59	4.65 ± 2.98	2.1 ± 1.58	3.85 ± 4.43
60–69	4.6 ± 4.55	5.4 ± 6.83	2.42 ± 1.36
70–79	5.0 ± 3.72	7.05 ± 5.98	4.20 ± 3.9

*Mean monocular latency variation for flash, pattern-reversal, and pattern–onset-offset principal components. No data are available for pattern onset in the 10 to 19 decade due to the variability of components. Again it is clearly apparent that the smaller standard deviations of the pattern-reversal P100 component are only apparent between the ages of 30 and 59 years.
†Values are means ± 1 SD.

For the same subjects we obtained normative values for mean monocular variation in latency since in diagnostic studies it is essential to compare the affected eye with the fellow eye of the same patient. These data are shown in Table 55–2. It can be seen that the mean monocular variation is very similar for the three types of stimuli. The superiority of the pattern-reversal stimulus in producing a relatively narrow normal range of monocular variation[20] is actually only apparent for the age groups between 30 and 60 years.

A number of studies have demonstrated that small but significant differences exist in the mean latency of the checkerboard pattern-reversal evoked potential between the two sexes. Stockard et al.[35] compared the responses of 15 age-matched men and women and showed a mean latency of 98.8 (SD, 5.78) ms for women and 111.5 (SD, 6.2) ms for men. There was no sex difference in interocular latency variation. These findings have been confirmed by Halliday[20] in a study of 69 healthy women and 65 healthy men who were not age matched. The reason for these differences has not been established, although similar small sex differences in the flash response have also been reported.[5, 7]

DIURNAL PATTERNS

Circadian variations have been reported for the pattern-reversal VEP latencies and amplitudes. The longest latency is said to occur in the early morning between 2 and 5 A.M. when the amplitude is also the lowest. The shortest latency is around 5 P.M., the difference in latency being of the order of 6 ms.[36]

The effect on the flash VEP is not as clear, and it is suggested that the P_2 latency varied by less than ±5%, but there was a clear amplitude difference of around ±15%.[28] They also suggest, however, that this variation may be partly due to alterations in the level of attention.

INTERTEST VARIABILITY

Within an individual there is really remarkably little variation in the VEP over months or even years. This is true for the flash VEP as well as for the pattern-reversal and pattern–onset-offset VEP.[20] Ciganek[9] found that most of the trial-to-trial variability of flash VEPs was due to contamination with the background activity of the EEG since there is some tendency toward phase locking of the background activity. Obviously, the averaging process does not entirely get rid of the background activity since the number of trials required to entirely remove this activity would be infinite. Ciganek pointed out that there was a marked reduction in the variance of the VEP that occurs about 80 ms after the flash and thus the N_2 and P_2 components are relatively little affected. Contamin and Cathala[11] found only a 15% variability in latency. In a similar manner, variability of the pattern-reversal VEP is small and shows remarkably little variation over 11 consecutive averages of 200 pattern reversals.[6] All evoked potentials show much more variation between individuals than they do within an individual, and in any single individual the latency factor shows less variability than does amplitude.

ARTIFACT RECOGNITION

Problems of artifacts have been dealt with in Chapter 49. It should be remembered when examining evoked potentials that in general any artifact is

unlikely to be time locked to the stimulus, with the exception of photomyoclonic responses and intention tremors or the electroretinogram. Obviously it is essential to repeat each averaged VEP under each stimulus condition so that any artifact that has occurred during one particular series of responses and contaminates that average is unlikely to be present on a second occasion.

PATIENT COMPLIANCE

In general, patient compliance is not a great difficulty, and many of the artifacts accidentally generated by patients have been dealt with in Chapter 49. One factor that has not been thoroughly dealt with, however, is the problem of optical blurring affecting the latency of the VEP. As might be expected, the VEP to pattern stimuli containing clear contours are markedly affected by any optical blur. A number of studies have been made of the effect of optical blurring on pattern VEPs.[10, 25, 35] Optical blurring clearly increases the latency of the pattern-reversal VEP, the effect being more pronounced the smaller the pattern elements. Often a 3-D blur increases the latency of the P100 component by around 4.5 ms in response to 56-minute checks and by *20.4 ms in* response to 14-minute checks. If pattern onset-offset is used, then it is found that the C_2 component (the one normally associated with contour) is the most sensitive, and massive shifts in latency can be seen at relatively low amounts of defocusing (Fig 55–2).

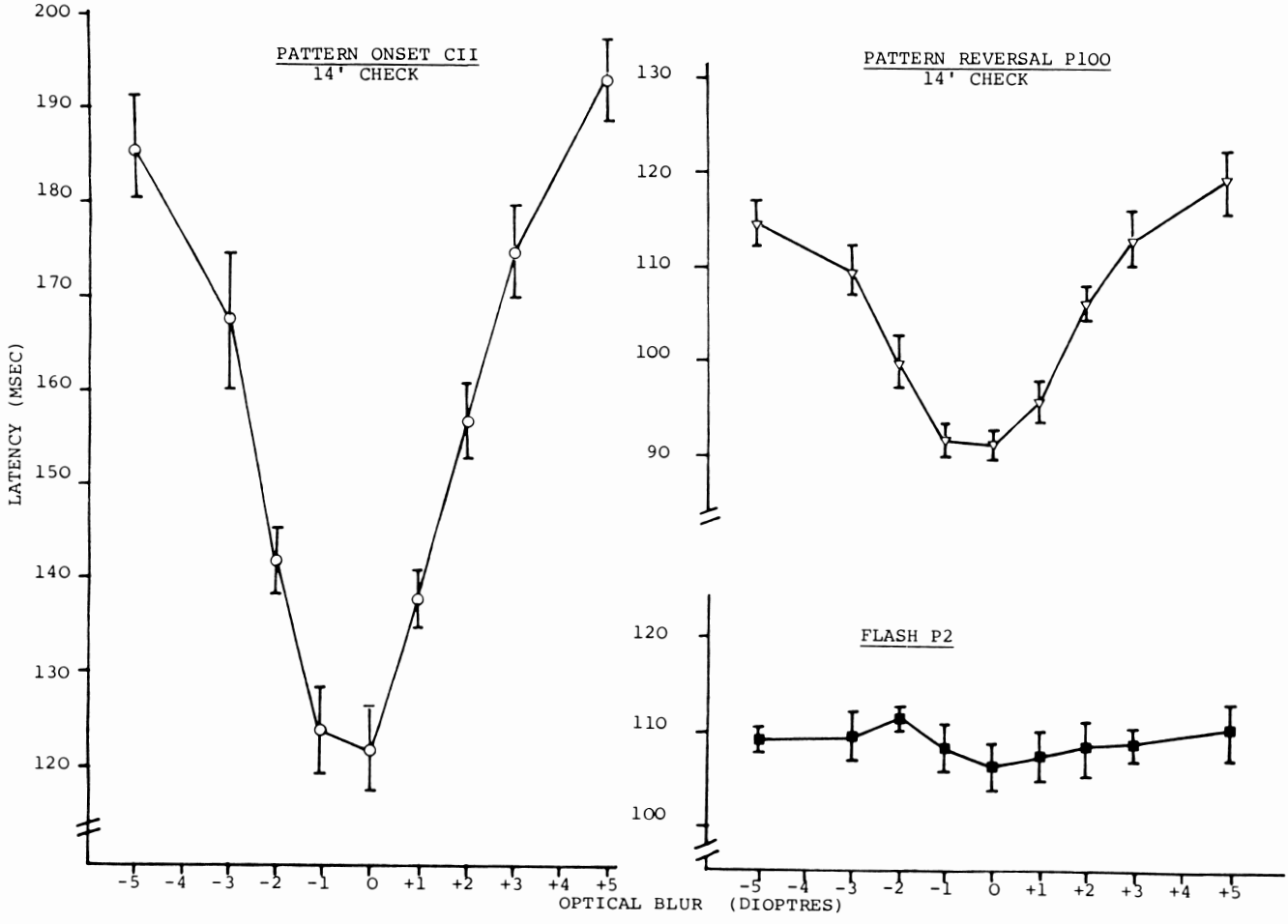

FIG 55–2.

Effect of defocusing on the latency of the C_2 component of pattern-onset stimulation, the P_{100} component to pattern reversal, and the P_2 component of flash stimulation. It can be seen that defocusing has the most marked effect on the C_2 component of pattern onset, even a shift of 1 D markedly affecting the latency of the component. Similar effects are seen in the pattern-reversal P100 component, although here shifts of more than 1 D are needed. Both components show a marked sensitivity to positive optical blurring, probably representing the eyes' differential ability to accommodate to positive and negative defocusing. It should be noted that the flash P_2 component is completely uneffected by any degree of defocusing, thus indicating that correct refraction is not required for flash stimulation since it is of course a diffuse stimulus.

As is to be expected, however, the P_2 component of the flash VEP is not altered by any amount of defocusing since it is, of course, a diffuse stimulus. This does, of course, provide the flash response with a degree of clinical robustness that often is useful in conditions where patients cannot or will not fixate on patterns or where refractive errors are unknown. It is therefore useful in conditions involving opacity of the media or in conditions where the patient is anesthetized. When pattern stimulation is used, the patient's visual acuity should be checked and correctly refracted for the viewing distance of the visual stimulator.

With regard to patient compliance, the method of obscuring the eye not under investigation is clearly important. Whereas this can be relatively easily achieved with pattern-reversal stimulation, successful occlusion is much more difficult with flash stimulation. Occlusion using an eye patch that is carefully taped around the edges of the orbit should be used for bright flash stimuli. A response can still be apparently obtained from a blind eye if there is light leakage past the occlusion into the fellow eye of the patient. In patients suspected of functional or hysterical blindness, care should be taken to make sure that they do not close their eyes when presented with either a flash or a patterned stimulus, and as far as possible they should be made to fixate on the center of the pattern stimulus. It is often found that in difficult patients the use of pattern–onset-offset stimuli is frequently advantageous in demonstrating the integrity of vision since this stimulus appears more difficult to actively defocus than the more common pattern-reversal stimulator.

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