Voluntary Alteration of Pattern Visual Evoked Responses

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Abstract: Pattern and flash visual evoked responses (VERs) were recorded from a large group of ophthalmologically normal subjects during two conditions: in one they were instructed to attend to the stimulus and in the other they were instructed to ignore the stimulus but maintain their gaze on the stimulus. Pattern VERs were recorded from 42 subjects. Fixation was constantly monitored during both attend and ignore conditions and no changes of fixation were noted at any time. The amplitude of the major positive wave of the pattern VERs produced by both 50- and 25-min checks was reduced significantly during the ignore condition. The implicit time of this positive wave did not differ significantly during the two conditions. The pattern VERs of eight subjects were extinguished and the VERs of another three subjects were unrecognizable during the ignore condition. Flash VERs produced by 10 flashes per second were recorded from 38 of the 42 subjects. There were no significant differences between the amplitudes recorded during the attend and ignore conditions. [Key words: conscious alteration, flash visual evoked response, malingering, pattern visual evoked response.] Ophthalmology 92:1356-1363, 1985

Visual evoked responses (VERs) produced by checkerboard reversal and flash stimuli often are used to detect evidence of an organic lesion in the visual pathways. Numerous studies have established the abnormal VER as a dependable indicator of multiple sclerosis, optic neuritis, and macular degeneration. The VER is also used to evaluate amblyopia, to assess visual function in neonates and young children, and to identify patients whose visual loss may be functional rather than organic. It is commonly assumed that a normal VER indicates intact visual pathways and that a diminished or absent VER indicates defective visual pathways. Results from several previous small series have suggested that this assumption is not true. In those studies, normal subjects could consciously alter their VERs, mimicking a significant visual or neurologic lesion. Our study was designed to assess the ability of subjects with normal visual acuity to alter their VERs to a variety of stimuli. The reproducibility of the VER to the same stimulus at different times during the test also was assessed. Our results demonstrate that some normal subjects can voluntarily diminish and even extinguish the VER produced by pattern stimulation.

MATERIALS AND METHODS

Forty-two subjects (14 men and 28 women) ranging in age from 23 to 60 years were tested. A complete ophthalmologic examination was performed on all prospective participants. Subjects in this series had normal color vision, pupillary responses, gross visual fields, slit-lamp exam, and normal fundus examinations conducted through dilated pupils. Thirty-eight subjects were corrected to 20/20. Four were correctable to at least 20/25 in the left eye (the eye used in all studies).

The VERs were recorded and stored using the UTAS-E1000 LKC system. Pattern stimuli were black and white checkerboards reversing two times per second. These patterns were generated on a video monitor driven by a Matrox pattern generator. The checkerboard pattern field subtended 8.6 by 10.6 degrees visual angle at one meter.
from the screen where the subjects were seated. Two check sizes, 50 and 25 min arc, were used. Contrast was 98% and space-averaged screen luminance was 10.9 ftL. Both contrast and mean luminance were measured with a Pritchard 1980A spot photometer. Each trial lasted 50 seconds (100 checkerboard reversals). The flash stimuli (Grass PS22) were presented in ganzfeld. Flash luminance was 1 ftL sec. The flash rate was 10 per second. The experimental area was kept quiet and the room lights were extinguished during testing.

Visual evoked responses were recorded with gold cup surface electrodes placed on mildly abraded scalp cleaned with alcohol. Conductive paste was used to establish good electrical contact and the electrodes were taped in place. Impedance between all electrodes was less than 5 kilohms before and after the testing procedure. The three active electrodes were placed 5 cm above the occipital electrode. One electrode was placed on the midline (M) and two were placed 5 cm to the left (L) and right (R) of the midline. The reference electrode was placed on the midline at one-third the measured distance from nasion to inion for pattern stimuli and on the midline of the chin for flash stimulus trials. An electrode placed behind the left ear was connected to ground. Signals were amplified, digitized (12 bit A to D), averaged, and recorded on diskette using the LKC system. The amplifier gain was 20,000 with a pass band of 0.3 to 100 Hz (3dB points), with an impedance of 5 megohms to ground for each input. Potentials larger than 100 µV occurring during any sweep caused it to be rejected, thus excluding large muscle and movement artifacts.

Each cumulative average of 25 responses was displayed on a monitor for viewing during testing. For each trial, 100 responses were averaged and the average response was printed out for permanent record on a printer-plotter. Amplitudes and implicit times were automatically calculated. Implicit time is the time in milliseconds between the onset of the stimulus (flash or checkerboard reversal) and the peak of the positive wave which occurs at around 100 msec. Amplitude is the voltage in µV between the previously defined positive peak and the trough of the preceding negative wave (Fig 1).

The right eye of each subject was patched so that light stimulated only the left eye. When necessary, subjects wore trial frame lenses to correct the visual acuity to at least 20/25 in the left eye. Six pattern trials were presented to each subject in a dim, quiet room. During each trial, one examiner sat beside the stimulus screen to observe the subject carefully. Fifty-min checks were used in the first two trials. In the first trial (attend condition), the subject was asked to keep the left eye open and fixated on the center of the video screen, actively concentrating on its image. In the second trial (ignore condition), the subject was instructed to attempt to ignore the checkerboard reversal stimulus. Although the subject was allowed to use whatever means he chose, he was required to keep his left eye open and his gaze fixed on the center of the screen. Any deviation from this gaze, prolonged closing of the eye, or ocular convergence requiring the subject to turn his head even slightly to maintain fixation in the center of the video screen was detected easily by the observer, who then stopped the recording. Twenty-five-min arc checks were used in the third and fourth trials with attend and ignore conditions, respectively. The fifth trial consisted of a repeat of the 50-min arc check stimulus identical to the stimulus in the first trial to test for fatigue and order effects on the VER produced while attending. The sixth trial provided an estimate of averaged amplifier and physiological noise by recording with the screen completely covered. Between trials the subject was told to look away from the screen or close his eyes to avoid adaptation to the static check pattern that remained on the screen.

Of the 42 subjects who participated in the pattern VER study, 38 participated in the VER study. On completion of the pattern VERs, each of the 38 subjects was then positioned at the ganzfeld. The right eye remained occluded. The ganzfeld apparatus prevented direct observation of the left eye during recording of flash VERs. In the first of three flash stimulus trials, the subject was told to keep his left eye open while concentrating on a stimulus of ten flashes per second. During the second trial, the subject was instructed to keep his eye open but to attempt to avoid perception of the ten flashes per second stimulus. Finally, a noise trial with the light occluded but flashing at a rate of ten per second was performed.

RESULTS

Means and standard deviations of the amplitudes and implicit times produced by the 50-min checks during the test and retest conditions are seen in Table 1. The results of the t-test (paired data) comparing data recorded during the two conditions are also seen in Table 1. There were no significant differences between the amplitudes of these VERs. The implicit time of the positive peak near 100 msec recorded from electrode M was significantly prolonged during the retest condition relative to the implicit
Table 1. Amplitudes and Implicit Times of Visual Evoked Responses Recorded During Test and Retest Attend Conditions (50 min arc checks)

<table>
<thead>
<tr>
<th>Electrode</th>
<th>Amplitude (μV)</th>
<th>Implicit Time (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Middle</td>
<td>Left</td>
</tr>
<tr>
<td>Test</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.89 ± 4.32</td>
<td>8.17 ± 3.79</td>
</tr>
<tr>
<td>Retest</td>
<td>10.45 ± 4.29</td>
<td>7.82 ± 3.25</td>
</tr>
<tr>
<td>t values*</td>
<td>1.38</td>
<td>1.29</td>
</tr>
<tr>
<td>N</td>
<td>41</td>
<td>41</td>
</tr>
</tbody>
</table>

* t values ≥ ±2.7 were significant at α = 0.01 for N = 41. †significant α = 0.01.

Time recorded during the test condition. Neither the mean implicit time nor the implicit times of the VERs of individual subjects exceeded a value 2½ standard deviations greater than the mean established during the test condition.

Means and standard deviations of amplitudes and implicit times of the VERs produced by pattern stimulation (50- and 25-min checks) during attend and ignore conditions are seen in Table 2. The results of t-tests, comparing data recorded during the ignore and attend conditions, also are seen in this table. The data of 11 subjects were excluded from the t-tests of the pattern VER data either because the responses were extinguished (Fig 2; eight subjects) or because they were not interpretable (Fig 2). Except for the VERs recorded from electrode R and produced by 50-min checks, the amplitudes of the VERs produced by both check sizes were reduced significantly during the ignore condition compared to those recorded during the attend condition. Except for the VER produced by 50-min checks and recorded from electrode M, there were no significant differences between the implicit times of the VERs recorded during the ignore and attend conditions.

Because the implicit time of the VER produced by 50-min checks and recorded from electrode M was significantly prolonged during the retest attend condition compared to that during the test attend condition, t-tests were done to compare the responses produced by the 50-min checks during the retest condition and those produced by the 50-min checks during the ignore condition. These tests showed no significant difference between the implicit times produced during the ignore and retest conditions; however, the amplitudes produced by 50-min checks and recorded from electrodes M, R, and L were reduced significantly during the ignore condition compared to those produced during the retest condition. Thus, the change in amplitude, but not implicit time, produced by ignoring the pattern stimuli was robust enough to be seen when compared to either the test or retest data.

For the VERs produced by the 50-min checks, 57% of all the amplitudes were decreased by greater than 25% during the ignore condition when data from the three electrodes were combined. For those 31 subjects with interpretable responses, neither the amplitudes nor the implicit times of the VERs from any individual exceeded 2.5 standard deviations from the mean response produced during the attend condition. For the VERs produced by the 25-min checks, 62% of all the amplitudes were decreased by greater than 25% during the ignore condition. For the 31 subjects with interpretable responses, no VER

Table 2. Amplitudes and Implicit Times of Visual Evoked Responses Recorded During Attend and Ignore Conditions

<table>
<thead>
<tr>
<th>Electrode</th>
<th>Amplitude (μV)</th>
<th>Implicit Time (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Middle</td>
<td>Left</td>
</tr>
<tr>
<td>50 min arc checks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attend</td>
<td>10.86 ± 4.26</td>
<td>8.53 ± 3.75</td>
</tr>
<tr>
<td>Ignore</td>
<td>7.82 ± 4.25</td>
<td>6.48 ± 3.66</td>
</tr>
<tr>
<td>t values*</td>
<td>5.96†</td>
<td>4.67†</td>
</tr>
<tr>
<td>N</td>
<td>31</td>
<td>31</td>
</tr>
</tbody>
</table>

| 25 min arc checks |        |      |       |        |      |       |
| Attend    | 10.44 ± 3.74 | 8.40 ± 2.78 | 9.34 ± 5.90 | 103.10 ± 5.9 | 103.72 ± 6.23 | 103.62 ± 7.54 |
| Ignore    | 7.48 ± 4.06 | 6.54 ± 3.75 | 6.51 ± 2.9 | 106.52 ± 10.25 | 107.03 ± 10.13 | 106.58 ± 11.31 |
| t values* | 5.21† | 3.24† | 4.76† | -2.13 | -1.98 | -1.92 |
| N         | 31 | 29 | 26 | 31 | 29 | 26 |

* t values ≥ ±2.75 were significant at α = 0.01 for N = 29, 30, or 31. †significant α = 0.01.
amplitudes exceeded 2.5 standard deviations from the mean response during the attend condition for electrodes M and L. The amplitudes of the VERs of two subjects exceeded 2.5 standard deviations from this mean for electrode R.

Means and standard deviations of the amplitudes of the VERs produced by the 10 per second flash are seen in Table 3, along with the results of the t-tests comparing the data from the attend and ignore conditions. No significant effects in amplitude data were found from any electrode. When data from all electrodes were combined, only 7% of the amplitudes were decreased by 25% or more during the ignore condition. No flash VERs were extinguished during the ignore condition. Many flash VERs were larger during the ignore condition than during the attend condition (Fig 3).

**DISCUSSION**

The use of VERs to assess dysfunction in visual pathways is based on the assumption that normal subjects will reproducibly demonstrate an electrical response to a visual stimulus. A few investigators have questioned this assumption and suggested that normal subjects can suppress their VERs with no apparent change in their concentration or cooperation. Bumgartner and Epstein observed that one-third of their 15 subjects could produce abnormal VERs by means not apparent to the observer. These studies, however, have not been widely acknowledged because they involved few subjects and because data confirming the normal neurologic and ophthalmologic status of the subjects was not clearly presented. Our study was designed to test this basic hypothesis on which the interpretation of the VER is based, with a larger group of clearly normal subjects. Our results confirm the observations of Bumgartner and Epstein that many normal subjects can consciously suppress and even extinguish their VERs.

Since normal variations of VER parameters may be
affected by age, sex, and different test days,\textsuperscript{21,–27} we compared attend vs. ignore responses during a single test session for each subject. This study was designed to determine if it was possible by conscious maneuvers to produce significantly different pattern and flash VERs with differences that would be considered clinically abnormal. The pattern VERs of eight subjects were extinguished and three were not interpretable with certainty. Eleven extinguished or uninterpretable responses are many more than could be expected from chance based on data from the attend condition. The VERs of the 11 subjects were significantly different during the ignore condition. We also determined that the amplitudes of the VERs of the other 31 subjects were significantly reduced during the ignore condition compared to the amplitudes produced during either the test or retest attend condition.

The results of the implicit time analysis were clear for the 25-min check data. No significant differences were found between the implicit times of the responses recorded during the attend and ignore conditions. However, for the 50-min check data, the implicit time of the VER recorded from the electrode most commonly used in clinical testing (M) was significantly prolonged during the ignore condition relative to that produced during the test attend condition. However, no significant differences were found between the implicit times recorded during the retest attend condition and the ignore condition. Since for this electrode there was also a significant prolongation of the VER recorded during the retest attend condition relative to that recorded during the test attend condition, the significant prolongation in implicit time for electrode M produced during the ignore condition relative to that during the test attend condition may reflect fatigue. The difference between the test-attend implicit time and the ignore implicit time was small. A t value of 3.23 is necessary to account for 25\% of the variance with this sample size. The difference in implicit time for these two conditions may have been a chance occurrence. Differences of this magnitude will be incorrectly classified as significant 1\% of the time. The difference between the retest-attend and the ignore implicit times was not significant. These results could be summarized most succinctly by saying that subjects can voluntarily extinguish their VERs or significantly decrease the amplitude of the response, but that they cannot alter significantly the implicit time of the VER if it is not extinguished or uninterpretable.

Over one-half of the amplitudes recorded during the ignore condition were decreased greater than 25\% compared to baseline attend VERs. Twenty percent of our subjects could extinguish responses in all electrodes for 25- or 50-min arc checks. An extinguished response is considered abnormal.\textsuperscript{4,15,20,21} Halliday\textsuperscript{28} states that a VER peak amplitude of less than 2.0 \( \mu \text{V} \) indicates an organically caused lesion in the visual pathway. The same author, as well as others,\textsuperscript{21,22,29} has noted that a better criterion for determining pattern VER amplitude abnormality is based on comparison of amplitudes produced by stimulation of the two eyes monocularly. These authors have maintained that, with monored fixation, an amplitude difference of greater than 6–7 \( \mu \text{V} \) should be considered abnormal. Although we tested only one eye in each individual, we assumed that a normal person able to decrease the amplitude of a response produced by stimulation of one eye could effect a significant difference in the amplitudes of the responses produced by stimulation of the two eyes monocularly. The normal subjects in our study who were able to mimic an abnormality by fulfilling the requirement of decreasing the amplitude in one eye by greater than 7 \( \mu \text{V} \) were, for the most part, those who could extinguish the responses from all electrodes for VERs produced by both check sizes. Therefore, by our criteria for normal, as well as by those reported by others, many subjects can alter the pattern VER amplitude to an extent that would be considered “abnormal.”

In pattern VER testing, an abnormal implicit time is more reliable than an abnormal amplitude as an indicator of a true organic lesion in the visual pathway.\textsuperscript{22,26,28} As with amplitude measurements, differences in implicit times produced by stimulation of the two eyes monocularly are a more reliable indicator of a lesion when differences of 6–8 msec occur.\textsuperscript{3,5,21,30} Six subjects in our series could prolong the implicit time 8 msec in only one eye from the M electrode when presented the 50-min arc checks. Six is statistically far more than would be expected by chance alone. However, if an abnormal VER implicit time is defined as greater than 2.5 standard deviations above the mean implicit time for the attend pattern VER, only three subjects in this study fulfill that criterion from any lead and check size. For 11 subjects, implicit time could not be determined accurately during the ignore condition because of broad, equivocal peaks or extinguished responses.

Chiappa and Ropper\textsuperscript{22} have stated that the flash stimulus elicits a greater variation in the VER than does the checkerboard reversal stimulus, and that the sensitivity of the flash VER to conduction defects is lower. With this in mind, we also tested our normal subjects for their ability to alter VERs produced by flashes. No significant differences were noted when a given subject’s ignore flash VER amplitude was compared to the attend flash amplitude. No subject extinguished the response to the 10 Hz flash stimulus. These data suggest that this stimulus may be a more reliable parameter to assess visual conduction defects.

One obvious strategy for ignoring the stimulus would be to defocus consciously the image of the stimulus on the retina by fixating in front of or beyond the plane of the stimulus. To rule out the possibility of this strategy, cycloplegia could serve as a control. Cycloplegia was induced in one of the eight subjects who were able to extinguish VER during the ignore condition. The subject was still able to extinguish the responses produced by 50- and 25-min checks during cycloplegia. In a previous study by Regan and Richards,\textsuperscript{31} 10 diopters of defocus had no significant effect on the amplitudes of the VERs produced by 50-min checks. Three to four diopters of defocus caused a significant increase of amplitude. It has long been known that defocus has less effect on pattern responses produced
by larger checks (40 min or greater). Amplitudes of VERs to large checks can be decreased by defocus but only with displays subtending significantly larger angles (eg. 32°) than those used in this experiment. If defocus were the strategy employed by the subjects significantly altering their VERs during the ignore condition, one might expect a larger number of subjects to be able to alter the amplitude of the VER produced by 25-min checks than by 50-min checks. However, the same number of subjects were able to alter the VERs produced by both check sizes.

If a defocused retinal image were a significant factor, one might expect a significant difference in implicit time during ignore and attend conditions because defocus of even small checkerboard displays of large checks has been shown to cause a prolongation of the implicit time of the VER. However, for the 31 subjects with interpretable responses during both conditions, no significant prolongation of the implicit time of the VER was recorded during the ignore condition.

We do not believe that defocus was a significant variable in producing the effects on the VER demonstrated in this study. Even if it were, the conclusion would be that cycloplegia with correction for the distance of the screen should be used to control for malingering with questionable VERs in a clinical setting. This precaution should be taken in all clinical laboratories, but it may not always be used.

Our data indicate that a significant number of normals can, by conscious maneuvers, produce extinguished or unrecognizable pattern VERs although they were observed to have their gaze directed toward the stimulus. Thus, an extinguished or unrecognizable VER cannot be used with certainty to distinguish between organic and functional loss of vision. It is difficult to gauge the magnitude of this problem of clinical interpretation. Our data show that approximately 20% of our subjects were able to extinguish or alter their VERs when they were prompted to do so by the experimental conditions. Certainly during clinical testing the bias of instructions, atmosphere, and information is toward reducing the percentage of those patients able to alter the VER consciously, rather than increasing it as in this study. A recent report by Towle et al may provide a method helpful in determining whether individuals with extinguished or unrecognizable VERs have organic or functional loss of vision. In this study, infrequently presented patterns, with stripes narrower than the patients admitted seeing, produced a P300 in three of the three patients with functional loss of vision.

Our data with 25- and 50-min check stimuli show that the implicit time of pattern VERs not extinguished or unrecognizable are not susceptible to alteration by conscious maneuvers. When patients have normal pattern VERs and claim vision inconsistent with the VER results, this is useful information. Therefore, extinguished or unrecognizable pattern VERs should be interpreted with caution, but the implicit times of even small VERs produced by 25- or 50-min checks provide information that can be interpreted without considering conscious maneuvers as a possible artifact.

REFERENCES

The authors have confirmed the results of other workers before them, demonstrating that normal volunteers subjected to pattern reversal visually evoked potential (VER) testing can willingly alter the recorded response, even if they appear to be looking at the target screen. The results of this study included the recording of a number of unreadable responses, a consistent decrease in amplitude of the P-100 wave in many patients, and a rare prolongation in the implicit time (stimulus to peak of P-100 wave). In contrast, Uren et al demonstrated that, by eccentrically fixing on the target monitor, consistent changes could be produced in the implicit time, including delays on the order of 20 msec in response to VER stimuli. Tan et al similarly found delays in the implicit time in 4 of 12 patients. Bumgartner and Epstein demonstrated that fully one-third of normal patients could spontaneously alter or obliterate the VEP to pattern shifts and that 70% of the remainder could alter the VEP response by convergence efforts. They postulated that the degradation of response could be produced by convergence maneuvers as well as by daydreaming and meditation.

The authors mentioned that one strategy for ignoring the stimulus is to consciously defocus the image. This possibility could be experimentally tested by cycloplegia and appropriate correction. For some reason, the authors chose to do this in only one patient with no noted change, confirming the work of Regan and Richards in 1973. On the other hand, Van Lith et al and Sokol and Moskowitz demonstrated that defocusing the image, especially to small checks, can produce changes in both the latency and amplitude of the VEP.

Unfortunately, the present study does not shed a great deal of light on the mechanisms underlying this important observation. Using a flash pattern stimulus, Ellenberger and Shuttleworth demonstrated an increase in the P-100 wave under binocular conditions. Using a pattern reversal stimulus, Lenerbrand demonstrated similar changes in response under binocular conditions. It would be interesting to test patients suspected of volitionally altering the VEP response under binocular conditions and to determine if the presence of an additive effect would be useful in making the diagnosis of conscious blurring. Tan et al demonstrated that two patients who altered the VEP by using convergence mechanisms could not alter the VER under binocular conditions without the observer becoming aware of the induced movement.

Since recorded responses can be volitionally altered, immature patients with normal potential can have abnormal VERs, and patients with severe central nervous system disease can have relatively normal VERs, can evoked potentials (in this case, visually-evoked potentials) have a role in the everyday care of your patients? At the present time, with the exception of the electroretinogram, the answer is an unequivocal "no." If a patient is symptomatic a complete neuro-ophthalmologic examination, establishing a diagnosis will not give a pathoanatomical diagnosis as well.

If the patient is visually asymptomatic and an abnormality is found during your examination, establishing a diagnosis will not be aided by doing a VER. By the very presence and degree of the abnormality found on examination, one can predict that the VER will or will not be altered. What if the patient has had signs and symptoms of neurologic disease elsewhere (eg, suggestive of demyelination)? The visual examination is normal. What will a VER tell you first that will help the patient, and second, that you will tell the patient? Let us assume there is a 10-msec delay in the VER in one eye. On the basis of an electrophysiologic test in an otherwise visually asymptomatic patient, are you going to make the diagnosis of disseminated disease? I think not and hope not.

I believe that the VEP is an interesting experimental, but not clinically useful, tool. Visual evoked response data, if obtained, should be done on a prospective basis, and there should...
be only a minimal charge for this examination. In a child with obviously poor vision, the one evoked potential that will be consistently helpful is an electroretinogram. It will tell you in no uncertain terms whether or not the outer layers of the retina are functioning.

References