Principles and Practice of Clinical Electrophysiology of Vision

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18

Origin of Visual Evoked Cortical Potentials Components

G. F. A. Harding

FLASH VISUAL EVOKED RESPONSE

Waveform

The visual evoked response (VER) to flash stimulation consists of a series of components beginning with a negative around 30 ms and with succeeding waves consisting of a positivity around 55 ms, a negativity around 75 ms, a large major positivity at around 110 ms, a negative at 140 ms, a positive at 175 ms, and a negative around 220 ms (Fig 18–1).

Although there have been many descriptions of the evoked potentials with differing forms of nomenclature, the one that will be adhered to in this chapter is that of Harding.[41] Under this system the positivity or negativity is initialled followed by a sequential subscript. The use of this technique helps to differentiate between, for instance, the P2 component of flash and the P100 component of pattern reversal. Other commonly used systems are indicated in Figure 4–1. The early components of the evoked potential such as P^0N1 and P1 tend to be more variable and certainly appear to be susceptible to recording parameters, including the placement of electrodes and the stimulation conditions as well as subjective factors such as age. Early attempts to characterize the morphology of the flash VEP began with Ciganek,[16] who used a bipolar midline occipital parietal derivation to identify a series of waves that he labelled I, II, III, IV, V, VI, and VII, with average latencies of approximately 40, 55, 75, 95, 116, 135, and 195 ms, respectively. The first three waves he referred to as the primary response and suggested that they represented the response specific to area 17 of the visual cortex. The secondary response, waves IV to VII, was thought to be related to a more nonspecific diffusely organized system. Although waves V to VII do fit this categorization, later work suggested that wave IV was part of the primary response. Vaughan et al.[83] obtained similar early components to those of Ciganek, although with slightly different latency. Rietveld et al.[71] suggested that the discrepancies between various results, including those of Cobb and Dawson,[17] who identified a positive component around 22 ms, a negative at 45 ms, a positive at 60 ms, and a negative at 95 ms, were explicable in terms of variations in recording montage and stimulus and analysis parameters. Although matters have improved since these early days, similar problems of component analysis still exist.[34] Kooi and Bagchi[50] identified wave III of the Ciganek notation (N2 component) as being the most consistent and having a latency of between 80 and 126 ms. The test-retest reliability during the same session varied between 0.87 and 0.97 and was only slightly lower (0.88) over longer periods of time.

Gastaut and Regis[31] described a similar VEP to that of Ciganek,[16] who found that the most consistent component was a positive deflection occurring between 100 and 150 ms. Over the years it is this component that has been identified with most consistency in the results of many workers. Rietveld et al.[71] suggested that the major positive component (P2) and the preceding N2 component were related to the functioning of the central region of the fovea, the major positive component still being present when small targets that only covered the fovea were

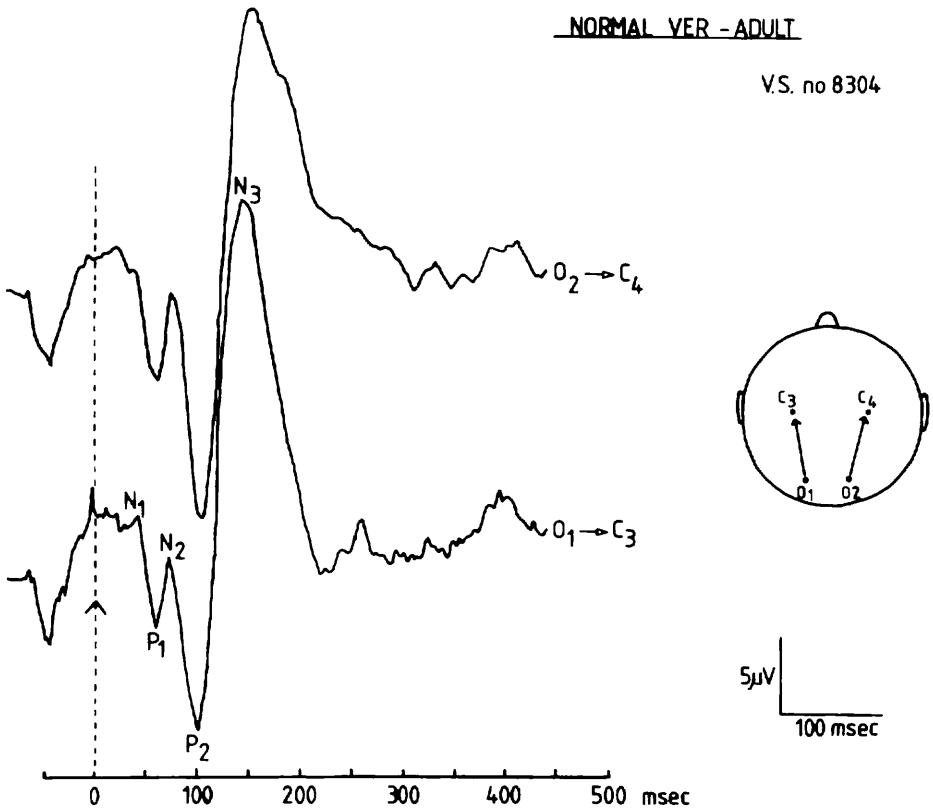

FIG 18–1.
Visual evoked potential (VEP) obtained from a normal adult. Negative in the illustration is indicated *upward* and positive *downward*. The nomenclature used for each component of the flash VEP is shown in this illustration. For comparison with earlier forms of nomenclature reference should be made to Figure 4–1. The most consistent component of the VEP is the P2 component seen just after 100 ms.

used, although many of the earlier components disappeared,[68] and this suggests that their absence may be clinically significant. For this reason Jonkman[49] considered that the P2 component was better regarded as part of the primary response than the secondary response. It is certainly true that the major positive P2 component appears to be the most consistent response obtained by most authors, even though they use different stimulation and recording techniques.[24, 41, 74, 86]

The binocular response as a whole is said to be of higher amplitude as well as having shorter latency than the monocular responses.[8] If recordings are made over each cerebral hemisphere in normal control subjects, the responses are similar, although in normal subjects hemispheric amplitude asymmetries of 50% and asynchronies of 6 ms can be observed.[45, 51, 66, 82, 83] However, such asymmetries or asynchronies are stable in any individual and any asymmetries are greater for the earlier components.[45] Dustman et al.[25] showed that the response was of greater amplitude over the right hemisphere in females than in males, and similar differences between the sexes were reported by Buchsbaum et al.[11]

Scalp Localization

Early attempts to identify the scalp localization of components of the flash VEP really began in early studies in 1969. By using a bipolar chain of electrodes over the temporal lobes and the visual cortex Harding et al.[43] identified asymmetries in various components of the evoked potential in patients with hemianopias. Although early components were still seen over both visual hemispheres, the major positive P2 component was absent over the hemisphere contralateral to the missing half-field of vision. In the same year Lehmann et al.[56] investigated a patient with a split chiasm and bitemporal hemianopia. Using electrodes 5 cm lateral to the inion and 10 and 3 cm anterior, they showed a major positive P2 com-

ponent at around 140 ms that was only present at the ipsilateral occipital electrode when referred to the ipsilateral parietal electrode, that is, ipsilateral to the eye stimulated; this component represented the contralateral, i.e., nasal, field.

Bourne et al.[9] studied the topography of the flash VEP recorded from 17 electrodes concentrated over the occipital region. In one of the early attempts at brain mapping they showed how the potential spread over the occipital area. They found that the early part of the response, before 120 ms, appeared to have a source anterior to the occipital region, whereas the later components around 190 to 310 ms had a source at the occipital area. In the same year Nakamura and Biersdorf[65] investigated the topography of components before 100 ms in the flash VEP. They attempted to perform half-field stimulation by using red light with the subject sitting in a brightly illuminated hemisphere in which half the hemisphere could be occluded to provide the half-field stimulation. They found that the early P1 component around 60 ms was recorded maximally over the central parietal electrode and, on half-field stimulation, was located contralateral to the field stimulated. The later P2 component did not, however, show this lateralization and was located much nearer the midline, thus suggesting that the tangential dipoles for this component were located in the primary visual cortex.

Allison et al.[2] identified 22 components of the flash VER and suggested that the very early components consisting of a negative at 20 ms, a positive at 50 ms, and a positive at 65 ms were likely to be related to the electroretinogram (ERG). They did, however, clearly locate occipital potentials consisting of a positive at 40 ms, a negative at 70 ms, a positive at 80 ms, and a positive at 95 ms. No attempts were made at half-field stimulation. In a further study of the flash VEP with lesions in varying parts of postchiasmal pathways, Feinsod et al.[28] concluded that if the optic radiation was involved there was a delay in the early components. If the striate cortex was involved, both early and late components were absent. If, however, the involvement was suprastriate, there was only a selective loss of late components over the affected hemisphere. Corletto et al.[19] recorded the VEP from the scalp and visual cortex before and after surgical removal of the occipital pole in a patient with epilepsy. Prior to surgery the scalp components consisted of a positive around 28 ms, a negative at 40 ms, and several later components of alternating polarity. Similar findings were obtained when one electrode was placed approximately over Brodmann's area 17. Following surgical removal of the occipital pole, the VEP showed preservation of the initial positive component around 28 ms and the negative component at 40 ms. The later components were, however, significantly different and showed either an absence or gross delay. In a later study Lines et al.[60] demonstrated that when flash stimulation was confined to one visual half-field the P2 component was of earlier latency over the contralateral hemisphere. They suggested that the ipsilateral VEP might arise as a result of interhemispheric transmission to the temporal visual areas. Similar suggestions had been made by Kooi et al.[52] Although it is difficult to be sure that stray light into the other visual field is not producing a response, in a later paper[73] they demonstrated that the latency delays were unaffected by the distance of the stimulus from the fovea in each hemifield and that this therefore made contamination by stray light unlikely.

Spekreijse et al.[77] also studied the flash VEP on the basis of temporal stimulus frequency. They suggested that the primary response (around 30 ms) was thought to be generated in the striate area, as was the response to high-frequency flicker. With stimulation in each visual octant they could produce reversal of the polarity of the signal that would be consistent with the cruciform striate cortex within the calcarine fissure. More recent work by Maier et al.[61] has confirmed this suggestion. The secondary response (100 to 120 ms) showed maximal signal amplitude in the occipital area and was thought to originate in areas 18 and 19. These findings would of course be consistent with the areas of increased regional blood flow in both the mesial occipital lobe (area 17) and areas 18 and 19 reported by Celesia et al.[15] The late response (120 to 200 ms) was found to be widespread and not specific to visual cortex areas.

The development of techniques of the topographical representation of brain activity began with the efforts of Walter and Shipton[84] to develop a topographic representation by using an array of cathode ray oscilloscopes. Unfortunately, although the array was visually meaningful at a moment in time, there was no way of representing the development of different potentials other than filming the array of oscilloscopes. In 1965 Remond[70] developed a technique that he entitled the chronotopogram. His technique allowed a spatial demonstration along a single meridan of the development of a potential over time. The y-ordinate therefore represented the scalp location along the single meridian, and the

x-axis represented time. In 1978 Ragot and Remond[69] developed a more elaborate method for plotting the potential gradients of evoked potentials from 48 electrode points. The most widely acceptable system, however, is that devised by Duffy et al.[23] in which recordings from 24 scalp electrodes allow the averaged evoked potential to be displayed, with each sample in time representing about 4 ms and presented on the monitor as a continuously developing display or alternatively as an instantaneous sample at any of the points (Fig 18–2; also see Plate 2). The system developed by Duffy has received wide acceptance and is now the standard system for multichannel recording and display. Other systems such as that of Buchsbaum et al.[12] utilized a gray scale from 16 electrode sites rather than the more acceptable color scaling used by Duffy.

By using these techniques Duffy[22] found that flash stimulation activates the cortex more widely than pattern reversal stimulation does. Similar findings have been reported by other authors.[44]

A recent study has been carried out in our laboratory of the topographical distribution of the P1 component and P2 component of the VEP.[47] In our study three different age groups (young, middle, and old) were investigated using 20-channel brain mapping. To make sure that the maps were unaffected by the reference site a noncephalic reference was used for this study. It was apparent from this study that although the P2 component can be recorded throughout life the incidence of the P1 component increases as the age of the subject increases. In addition, although age results in an increase in the latency of the P2 component, no such finding is apparent for the P1 component. The distribution of the two components is also different on the scalp. The occipital P1 component was also recordable over the parietal region, whereas the P2 component was confined to the occiputs (see Fig 18–2; also see Plate 2). Such findings do not fit well with the expected distribution proposed by Spekreijse et al.[77] It should also be noted that in our study the results that were obtained by using a balanced noncephalic reference were also compared with those obtained by using a midfrontal (FZ) reference. In Figure 18–2 (see also Plate 2) it is apparent from the traces that the P1 and P2 components of the flash VEP frequently coexist with a frontal negative potential. In examining the results of the different age groups it became apparent that although the negative potential was always associated with the P2 component, in the case of the P1 component the negative and positive potentials behaved independently. The frontal negative component, that is, N75, was seen in the middle age group before the development of the P1 component.

Many authors have of course reported the enhancement of the P1 component seen in older age[24, 38, 39, 44, 86]; it is therefore probable that the negative and positive components are the results of independent generators. On the basis of these results it is difficult to refute the suggestion of Spekreijse et al.[77] that the P1 component is generated in area 17 and the P2 component in areas 18 and 19. Mitzdorf and Singer[64] demonstrated using current

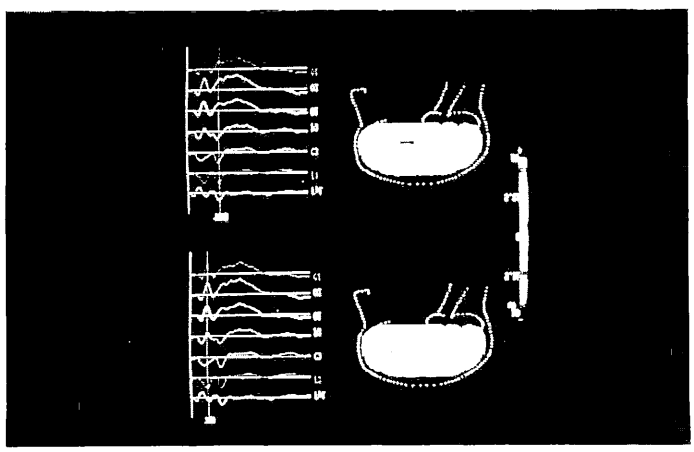

FIG 18–2.
Distribution of both the P1 and P2 components of the flash VEP. The P1 component seen in the *upper* block of traces and the upper anteroposterior brain map spreads more anteriorly than does the P2 component seen in the *lower* traces and lower brain map. It should be noted that the positivity of the P1 and P2 components (as indicated in the scale in the *right*) are accompanied by frontal negative potentials occurring at the same time. These recordings were made by using a balanced noncephalic reference. **(See also Color Plate 2.)**

source density techniques that the early components were the results of monosynaptic activity, probably in area 17, whereas later potentials were mediated by polysynaptic activity, probably from area 18. Kraut et al.[53] confirmed these findings by finding a large source in area 17 between 60 and 110 ms after the onset of flash stimulation and suggested that this response resulted from stimulation of the parvocellular cells of the lateral geniculate body. These findings would therefore suggest that the P2 component is a result of polysynaptic activity and may well be coming from area 18. Ducati et al.,[21] using intracerebral recordings in humans, showed that the generator of the P1 component was more superficial in the cortex than was the generator of the P2 component. This could of course explain the wider scalp topography of the P1 component. However, it should be realized that all these components are only a scalp representation and do not have a one-to-one relationship with activity recorded in underlying structures.

RELATION TO ACUITY

There is no simple relationship between the flash VEP and visual acuity. Many authors have shown that the flash VEP is relatively insensitive to refractive errors and that blurring by as much as 5 D will cause no significant change in the latency of the VEP.[44] However, some authors have shown that the amplitude of the flash VEP does bear some crude relationship to visual acuity, although only in indicating lesions at the neuroretinal level. Copenhaver and Perry[18] compared normal controls with patients with refractive errors, patients with opacities of the media, and patients with neural lesions. In patients with neuronal retinal lesions there was no doubt that the amplitude of the flash VEP was significantly smaller and that this relationship was more marked than for the group with refractive errors or opacities of the media. These techniques have been used by Thompson and Harding[79] to predict the outcome of surgery in patients with dense unilateral cataracts. Patients who showed an amplitude reduction of 33% or a delay in latency of 12 ms invariably had a poor outcome to surgery, that is, their vision was 6/24 or worse postoperatively. The presence or absence of the lens had no effect on the VEP, which suggests that these techniques were appropriate for measuring retinal or neural lesions and were unaffected by the blurring of the image by the opacity of the medium.

There is little doubt that the VEP to flash stimulation reflects the integrity of the central retina. Patients with macular degeneration frequently show a reduction in amplitude of the P2 component of the flash evoked potentials.[40] On the other hand, patients with retinitis pigmentosa very frequently have well-preserved VEPs reflecting this varying of macular function. As has been stated earlier, the majority of the P2 component to the flash VEP is probably generated from the central 5 degrees of vision reflecting the cortical representation of visual space.[20]

PATTERN REVERSAL

Waveforms

The VEP elicited by a pattern-reversing checkerboard occupying a radius of say 0 to 15 degrees is of fairly simple morphology. It consists of a negative wave around 75 ms, a positive high-amplitude component around 100 ms, and a negative of around 145 ms (Fig 18–3). The positive component is by far the most consistent and usually of highest amplitude and shows remarkably little variation in latency between or within individuals. The variation in amplitude is similar between flash and pattern reversal. When using a midfrontal reference the response is of maximal amplitude at the midoccipital electrode and spreads laterally but to a less marked extent than does the flash response. The relative rapid fall-off in amplitude of the response at lateral occipital electrodes around positions O3 and O4 on the International 10/20 System[48] is probably artifactual and due to cancellation of components on either side of the head due to both half fields having been stimulated.[7]

Distribution of the VEP across the scalp in relation to the part of the visual field that is being stimulated by pattern reversal has been studied by Halliday's group, who used large 50-minute checks. In studying right and left half-field stimulation it became apparent that the N75-P100-N145 complex described as maximal at the midline becomes markedly asymmetrical when only half the visual field is stimulated. Under these conditions and when using large targets, usually around 15-degrees radius, there is no doubt that the response is recorded at the midline, and ipsilateral to the half-fields stimulated.[3] This response also showed a more lateral spread than under full-field stimulation and was still clearly present at the lateral occipital electrodes. On the contralateral side of the head the response was smaller and of opposite polarity, consisting of a positive at 75, a negative at 105, and a later positive at 135 ms. This component had an entirely different distribution

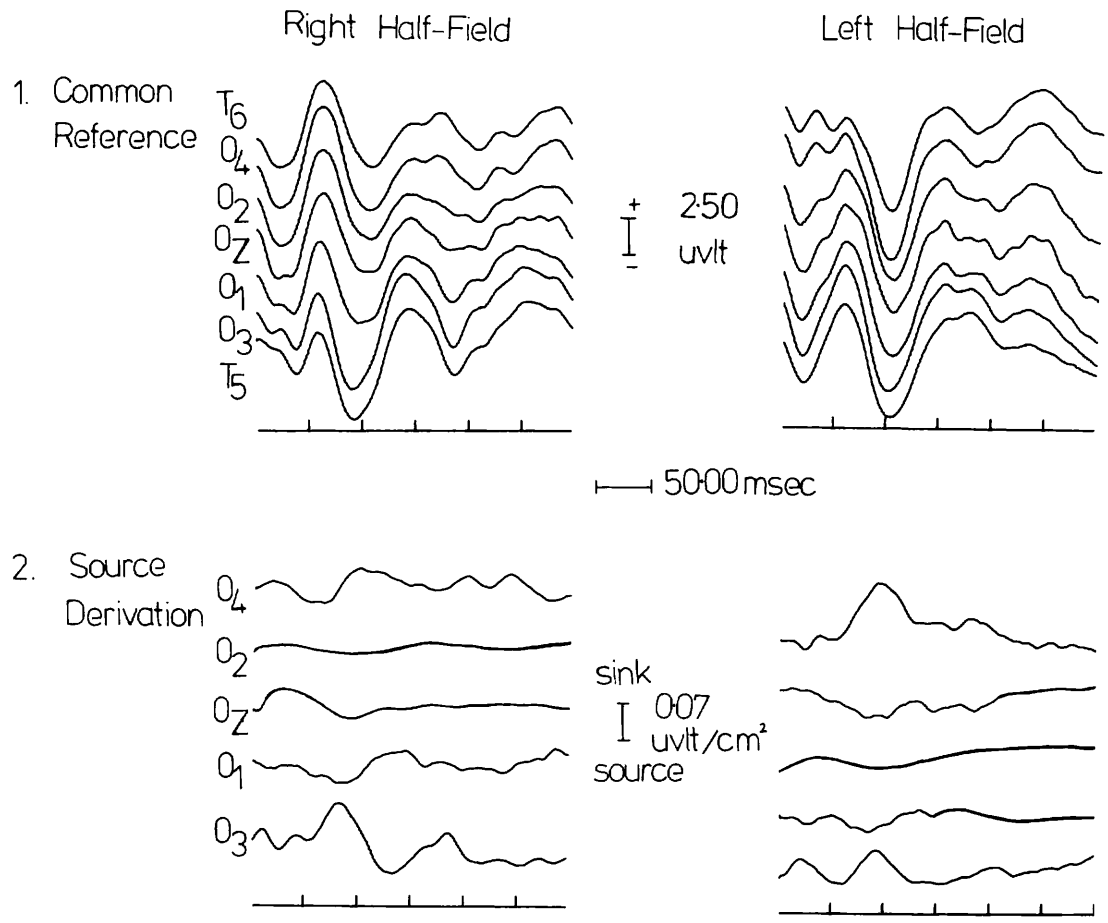

FIG 18–3.
VEP and source derivations of right and left half-field stimulation. The derivations are those of the 10:20 system and indicated on the *left* of the figure. All derivations are referenced to a midfrontal electrode, and it can be seen that the derivations used represent a chain of electrodes around the rear of the head. These responses were recorded by using a 14-degree-radius checkerboard stimulation. These responses represent the group average of ten subjects. It can be seen that on half-field stimulation it is extremely difficult to deduce the lateralization of the evoked potential. The response is often of higher amplitude on the lateral occipital electrode ipsilateral to the half-field stimulated (right half-field, O4; left half-field, O3). However, source derivation makes the results remarkably clear, as seen in the *lower* traces. It can be seen that the midoccipital derivation consistently shows the source whichever half-field is stimulated. Sources are indicated downward, and the major positive component (P100) occurs just before 100 ms. When the right half-field is stimulated, however, the sink (indicated upward on the trace) can be seen to occur contralateral to the field stimulated at O3. When the left half-field is stimulated, however, the larger sink clearly occurs at O4.

from the P100 component, being clearly maximal at the most lateral occipital position and being of low amplitude around the midline.[6] Blumhardt and Halliday[7] demonstrated that the full-field response is in actual fact an algebraic summation of the responses to each half-field. The P100 complex is of highest amplitude at the midoccipital point simply because the contralateral negativity is of lowest amplitude at the midoccipital point, whichever half-field is stimulated. Thus, when both half-fields are being stimulated (as in full-field stimulation) the positivity is clearly maximal at the occiput since it is not cancelled by the contralateral negativities, whereas at the most lateral occipital electrode the falloff of the P100 response is most marked because it is there that the two contralateral negative components are at their maxima.

These authors point out, however, that although the scalp distribution appears to suggest two independent sources of signals there is clear evidence that all the components of the half-field pattern reversal response, including both the ipsilateral P100

and the contralateral negative complex, can be obtained when the preserved half-field is stimulated in a patient who has had one cerebral hemisphere removed. Barrett et al.[3] suggested that although the major positivity is obviously generated by the visual cortex contralateral to the field stimulated, the major positivity appears at the midline and ipsilateral electrodes because their orientation, in relation to a midfrontal reference, positions them maximally for a radial source. The electrodes on the correct side of the head see the source as tangential and therefore do not receive a clear signal. Obviously, with large fields of stimulation the response is represented for a great distance down the calcarine fissure. If the size of the visual field stimulated is reduced below 8 degrees, then the response would be represented in the striate cortex posterior to the calcarine fissure.[75] Barrett et al.[3] showed that reducing the size of the stimulated half-field down to 0- to 4-degrees radius had little effect on the distribution of the response; a 0- to 2-degree-radius stimulus, however, resulted in less clear lateralization and on some occasions a contralateral maximum. Harding et al.[42] showed that when the size of visual half-field stimulated was reduced to 0 to 2.5 degrees, the response clearly became cross-lateral in normal subjects. This change in lateralization with decreased field size has been demonstrated by other authors.[10, 62] Although Harding et al.[42] showed that reducing the check size had no effect on the lateralization of the half-field response, Brecely and Cunningham[10] showed that a reduction in the check size increased the contralateral spread of the major positive component. Obviously this would be predicted since a foveal response should be maximal at the occipital pole and therefore the electrodes on the same side of the head and close to the midline would be expected to pick up the response most clearly.

Blumhardt et al.[6] showed that occlusion of the central part of a 0- to 16-degree-radius half-field markedly attenuated the ipsilateral P100 component while at the same time enhanced the contralateral negative component. In addition, a clear progression could be demonstrated in which for a 0- to 2.5-degree-radius occlusion the P100 component was markedly attenuated whereas the contralateral negativity was enhanced. Similar findings applied to a 5-degree occlusion, and a negative component only began to decrease in size when the central area of occlusion reached 0 to 10 degrees. Conversely, restriction of the outer field markedly attenuated the contralateral negativity so that by the time the target had been restricted to a 0- to 5-degree radius the contralateral negativity was entirely absent. On the basis of these findings Blumhardt et al.[6] considered that the P100 component was largely associated with stimulation of the central 0 to 8 degrees of the visual field, thus explaining its maxima at the midline occipital electrode. The contralateral positive-negative-positive (PNP) component would be diminished by such stimulation. However, Beauchamp et al.[4] and Wildberger et al.[85] had suggested that transcallosal transmission could explain the ipsilateral response.

However, the studies of Blumhardt and Halliday[7] on patients with hemispherectomies clearly demonstrated that although the response was ipsilateral to the field stimulated the response did originate in the contralateral cortex. Lehmann et al.[55] studied right and left half-field stimulation and used dipole modeling to locate the position of the VEP generators. They found that with large targets the dipole was clearly situated in the contralateral hemisphere, with the positive end pointing toward the electrodes on the ipsilateral scalp. However, for the small targets the dipole had a less ipsilateral orientation, that is, the positive end of the dipole moved toward the midline. They were also able to demonstrate contralateral negativity, and with intercerebral recordings in patients for large half-field stimulation, they found a clear ipsilateral positivity and contralateral negativity that they suggested arose from a midline surface positive generator with ipsilateral orientation. They felt that the estimated position and orientation would be compatible with an origin in the extrastriate visual cortex.

Flanagan and Harding[30] investigated the distribution of the pattern reversal response to large fields (0- to 14-degree radius) by using source derivation. Using a similar check size to Halliday and his coworkers (56 minutes), they showed that whichever half-field was stimulated the source was maximal at the midline occipital electrode but that a sink was always contralateral to the half-field stimulated (Fig 18–3). Edwards and Drasdo[26] showed that when using a central target of 4 degrees and making use of a brain-mapping system with the entire 20-electrode configuration constricted to the posterior portion of the head, there is clear evidence that on full-field stimulation the P100 component was maximal at the midline with relatively little lateral spread and that it appeared contralaterally over each occiput on half-field stimulation.

Similar studies have been carried out of the changes that result from the stimulation of upper and lower half-fields. In an early study Halliday and Michael[37] stimulated octants of the central 8 degrees of the visual field. The P100 component underwent an inversion in polarity from positive for lower half-

field stimulation to negative for upper half-field stimulation. With both upper and lower half-field stimulation the maximal signal occurred between 5 and 7.5 cm above the inion. They felt that since this polarity reversal occurred the results were not consistent with a P100 origin in the calcarine cortex. This they deduced because if the signal did originate in that area more prominent responses and greater polarity inversion would be seen for horizontal octants (right and left field) since these are represented inside the sulcus and are inverted with respect to each other in terms of the upper and lower field. For the vertical octants, represented as they are on medial cortical surface upper and lower field, neurons lie parallel, and therefore less clear polarity reversal would be expected. They therefore suggested that there is probably an extrastriate origin for the P100 component, with the generators for the lower half-field response on the upper surface of the occipital lobe, whereas the upper field generators would be on the undersurface. However, if this was true, one would expect that the upper-field response would be of lower amplitude, which was not what was found. In a later study[63] they discovered that the reference points that they used (linked ears) were in fact active and that the midfrontal electrode was a far less active reference point. By using this new reference point they found that lower-field targets elicit a positivity that is above the inion whereas the upper field targets produce a positivity below the inion with a negative potential more anterior. These findings were later confirmed by Halliday et al.,[35] who used a more extensive electrode array. Blumhardt and Halliday[7] showed that the stimulation of upper-field quadrants enhances the contralateral N105 component whereas lower-quadrant stimulation produces a greater spread of the P100 component across the midline. Confusingly, enhancement of the contralateral complex with upper-field stimulation can result in blurring of the midline P100 signal and cause an apparent increase in latency. These findings again, they suggest, would be consistent with the P100 signal arising from lower-field projections on the upper surface of the occipital lobe. An enhanced contralateral N105 component when the upper field was stimulated would be consistent with extension of the upper-field projection area onto the undersurface of the occipital lobe. Under these circumstances, of course, a dipole that has an outward positivity would be facing toward the electrodes when the lower half-field is stimulated and would be facing away from the electrodes when the upper half-field is stimulated. The electrodes would then see the negative end of the dipole. Lehmann et al.,[57] using a 0- to 16-degree-radius target and 50-minute checks, compared the distribution of responses to upper and lower half-field stimulation. They confirmed that stimulation of the lower half-field produces a P100 component that can be found around 103 ms. By careful mapping they showed that the most prominent component of the upper half-field response was in actual fact a positivity that was maximal at the inion and had a latency of 146 ms. Although upper-field stimulation also revealed a negativity around 103 ms, this was of much lower amplitude. They suggested that the P103 response on lower-field stimulation and the P146 response on upper-field stimulation were related and that the results demonstrated a delay in latency with the upper half-field stimulation and not polarity inversion since the maps of the two components at their times of peak amplitude were much the same. They suggested that the latency difference might be related to various anatomical features and pointed out that receptor density and therefore visual acuity were higher in the upper hemiretina than in the lower hemiretina and that this might reflect the greater importance in humans of the lower half-field of vision. Later studies by Lehmann and Skrandies[58, 59] have confirmed these results, as have the studies of Flanagan and Harding (Fig 18–4).[30]

Adachi-Usami and Lehmann[1] investigated the upper and lower half-field responses to both monocular and binocular stimulation. For lower half-field stimulation they found that the maximum on monocular stimulation was more posterior than on binocular stimulation, but when the upper half-field was stimulated, the maxima for binocular stimulation was more posterior than for the monocular stimulation. This finding they felt could be related to the expected proportions of monocular-driven cortical neurons, which are greater in striate areas, whereas binocular-driven cortical neurons would be greater in extrastriate visual areas. Since areas 18 and 19 are more anterior than area 17 above the calcarine fissure whereas below the fissure area 17 is more anterior and areas 18 and 19 more posterior, this would explain their results. However, although the position of maximum amplitude of the P100 response was confirmed in the study of Flanagan and Harding[30] they point out that source derivation shows no change in location. They did, however, find a delay in latency of 7.5 ms for the upper-field stimulus, thus supporting the earlier work of Lehmann et al.[37]

An entirely separate line of investigation has been taken by Haimovic and Pedley.[32] They predicted that the problems of locating the P100 and N100

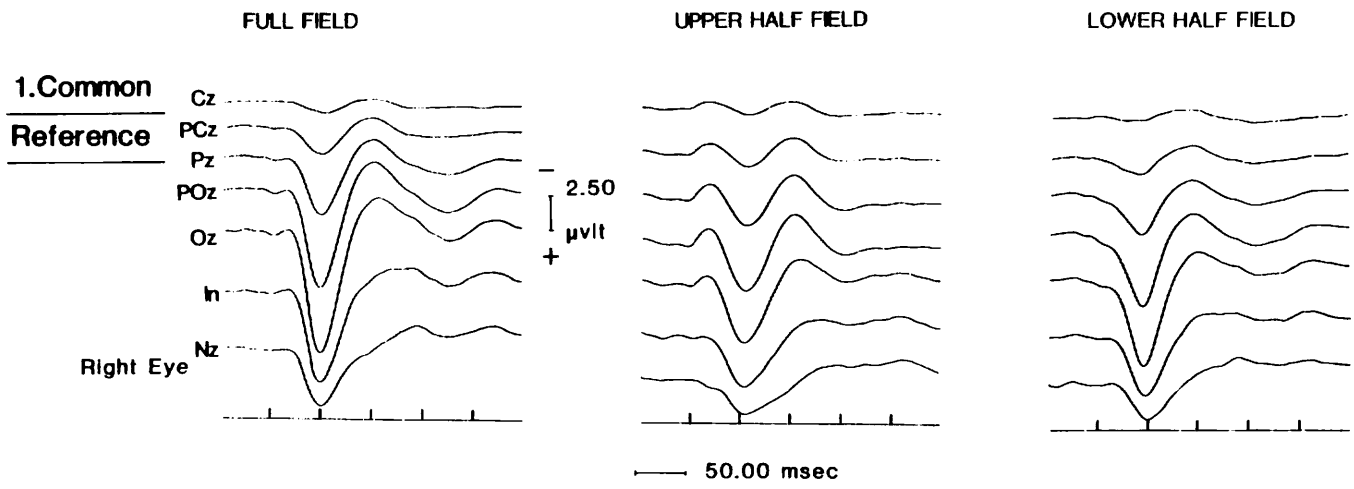

FIG 18–4.
Normal pattern reversal VEP elicited by full-field stimulation, upper half-field stimulation, and lower half-field stimulation. The derivations of the VEP are indicated on the *left* and refer from *top* to *bottom* to the vertex electrode *(Cz)*, the parietocentral electrode *(PCz)*, a parietal electrode *(Pz)*, a parieto-occipital electrode *(POz)*, an occipital electrode *(Oz)*, an inion electrode *(In)*, and a neck electrode *(Nz)*. It can be seen that on full-field stimulation the response is maximal at the occiput as it is on both upper and lower half-field stimulation. However, it should be noted that the response to upper half-field stimulation is slightly delayed as compared with that of lower half-field stimulation, a common finding in the literature. All derivations are referenced to a midfrontal electrode. (From Flanagan JG, Harding GFA: *Doc Ophthalmol* 1986; 62:97–105. Used by permission.)

components could be solved by investigating patients who had cortical lesions associated with similar homonymous hemianopic field losses but who had different lesions. If the geniculostriate pathway or area 17 were affected, they would predict that the entire VEP would be eliminated or attenuated. However, if the patient had lesions affecting only the parastriate areas, they predicted that the N100 response would disappear and that P100 would remain intact. When they investigated patients with these types of lesions, the results confirmed the suggestion that the P100 was generated in striate areas and the N100 in parastriate ones.

Other authors have investigated the effect of different stimulus parameters on the pattern reversal VEP. The interest in spatial frequency and orientation that was generated by the studies of Campbell and his coworkers[5, 13, 14] developed the concept of two separate channels of information in the visual system. The sustained channel is thought to be sensitive to stationary patterns at high spatial frequencies, whereas transient channels are responsive to lower spatial frequencies or, alternatively, high repetition rates or moving stimuli. Obviously, this is of great interest to VEP studies, particularly in pattern reversal where quite commonly the apparent reversal is produced by movement. Obviously, the two-channel theory could indicate that gratings with lower spatial frequencies will be dealt with by the transient system, although of course, with checkerboard patterns, since there are edges to the checks, high frequencies are always present.[54] It is to be expected that as retinal eccentricity increases the size of the check that will elicit a maximum response must also increase. Meredith and Celesia,[62] using a pattern-reversing checkerboard, found that indeed the optimum spatial frequency decreases as targets become more peripheral. Their findings confirmed the results of Harter,[46] who showed that small checks around 7.5 to 30 minutes of visual angle elicited maximal responses within a 0- to 1.5-degree radius whereas large checks (30 to 60 minutes) produced the highest amplitude at around 4.5- to 7.5-degree eccentricity. His original results were obtained by using the patterned flash VEP. At greater eccentricities check size appears to have less influence on amplitude. In the 1982 study of Meredith and Celesia,[62] they also compared the timing of the waveforms and the effect of different stimulus target sizes with the appropriate size of checks as obtained from the first part of their study. A 2-degree stimulus elicited almost no response beyond the central 4 degrees of the visual field. To obtain comparable results to the effect of the 2-degree field within the fovea they found that field sizes of 16 or 30 degrees were required outside the 8- and 14-degree meridans of the visual field, respectively. These targets were designed using the M-scaling of

Rovamo and Virsu.[72] Flanagan and Harding[30] used the magnification equations of Drasdo[20] and used fields of 3-, 10-, and 30-degree diameter designed to stimulate cortical areas in the ratio of 1:3:6. The amplitude of the pattern reversal response obtained, however, did not correlate with the theoretical ratio being of the order of 1:1.5:2. It would therefore appear that a linear summation of the cortical responses is too simple a concept. We have already discussed the problems of the differing signal that may be elicited from different points in the visual field by the same stimulus, and this may be an explanation for these findings.

Pattern reversal transient responses to gratings are rarely studied, although in a careful study of the effect of spatial frequency and the P100 response Plant et al.[67] showed that with increasing spatial frequency above 2 cycles per degree there is an increase in latency of the early component. There have of course been many studies of steady-state potentials elicited by contrast gratings. By using these techniques Kulikowski[54] has shown that a stimulus of 6 cycles per degree alternating at 1.67 Hz elicits pattern reversal VEPs that are dominated by both pattern-related, that is, sustained, channels as well as transient channels. As the spatial frequencies are reduced, the pattern reversal VEP becomes dominated by transient mechanisms related to the movement of the pattern. When a high spatial frequency is introduced, the response becomes dominated by the sustained or pattern-related channels. Tyler and Apkarian[80] found that selected local regions in the visual field did not give one but rather two peaks in the spatial frequency tuning curves. They suggested that these different peaks might be related to the different population of cortical neurons that were being stimulated; this in turn suggested that the most likely areas were V1 and V2. In a later paper[81] they suggested that since the peaks changed with changed temporal frequency this may be related to resonance characteristics of the neural circuitry in the visual cortex.

The problem of reversal and motion was studied originally by Fenwick and Turner,[29] who demonstrated a linear relationship between the proportion of pattern movement (25%, 50%, or 100% of the check size) and the amplitude of the VEP. In a later study Spekreijse et al.[76] showed that the abrupt displacement of a stationary checkerboard up to one-check width produced a response that was essentially similar to the pattern reversal VEP. They demonstrated that both onset and offset of the movement elicited separate signals but that if the time interval between onset and offset was small, the response appeared to be very similar to the pattern reversal VEP. These findings of course support the work of Kulikowski.[54]

The contrast between the pattern elements has also been shown to have a clear effect on both amplitude and latency of the VEP. Campbell and Maffei[14] showed that the VEP amplitude produced by steady-state alternating patterns consisted of two linear functions, one elicited by high contrast and the other by low contrast. Spekreijse et al.[78] reported that under conditions of lower contrast the checkerboard response was low in amplitude and long in latency, and it has become general practice for most pattern reversal studies to use a high-contrast stimulus. Estévez and Spekreijse[27] demonstrated that the pattern reversal VEP contained a contribution from the pattern offset or contrast response, and other authors have confirmed the similarity between the pattern reversal response and the pattern offset response.

An alteration to the luminance level of the checkerboard stimulus has a clear effect on the P100 component of pattern reversal. A reduction of 3 log units in brightness decreases the amplitude of the evoked potential by almost 50% and, in addition, extends the latency of the P100 component by almost 50 ms.[36] Conversely, a reduction in the level of illuminance reaching the retina has been implicated in the change of P100 latency with old age.[86] Equally, the effect of blurring of the pattern edges has a marked effect on the VEP, particularly with small check sizes.[44] When using check sizes of around 14 minutes of visual angle it was found that just 2 D of blurring would produce changes in the latency of the pattern reversal P100 component of between 5 and 8 ms, whereas for larger check sizes of 50 minutes to 1 degree little change is found in the latency.[33] The sensitivity of P100 component to changes in focus have allowed its use in VEP refractometry, although the C2 component of the pattern-onset response is far more sensitive.[44]

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