The visually evoked subcortical potential: is it related to the electroretinogram?

M. P. Rubinstein and G. F. A. Harding

The visually evoked subcortical potential (VESP) of mean latencies P21-N28-P36 has previously been recorded at an electrode site around the mastoid process. An initial topographical study of the potential indicated that it was independent of the electroretinogram (ERG), and monocular stimulation showed bilateral reduction, which suggests that the VESP is of postchiasmal origin. A more detailed topographical study of the scalp and facial distribution of the ERG and its oscillatory potentials has been carried out, with simultaneous recording of the VESP. Two monocular fields of ERG activity have been demonstrated, each having a wide area of distribution and interacting medially. Remnants of the ERG b-wave have been detected at many electrode sites, but they were of different amplitude and morphology from the VESP. Results are also presented from two atypical control subjects and two patients, providing further evidence of the separate genesis of the ERG and VESP.

Key words: electroretinogram, gold-foil electrode, noncorneal, oscillatory, topography, visual evoked subcortical potential

The existence of short-latency components of the visual evoked potential (VEP) has been known for many years,1-3 but detailed investigation of these components has remained unattractive due partly to their extreme variability and partly to their low amplitude as compared to the more consistent middle-latitude components, especially the major positive component (P100 or P2), which is more routinely considered in clinical electrodiagnosis. More recently, several reports have been presented suggesting the electroretinogram (ERG),4 the visual evoked cortical potential,5 the lateral geniculate body or geniculocalcarine tract,6 and the optic nerve7 as origins for these components.

In a previous communication,8 a human visually evoked subcortical potential (VESP) was described, having a triphasic configuration of mean peak latencies: P21.3 msec, N28.1 msec, and P35.9 msec. Topographically, this potential was found to be of maximum amplitude at or around the mastoid process and to be functionally independent of the ERG or optic nerve activity, therefore appearing to be of postchiasmal origin.

During evaluation of reference sites, an ERG-type signal was detected at certain scalp and facial sites distant from the cornea. In order to confirm independence of the VESP and ERG, a topographical study of the ERG has been carried out with simultaneous recording of the VESP. In addition, results are presented from two atypical control subjects and two patients.

Materials and method

For the topographical study, observations were made on 12 normal volunteer subjects (six male and six female) ages between 20 and 28 years (mean 23). All had visual acuities of 6/6 or better.
and had full visual fields. Electrodes were placed according to the International 10/20 system in a modified form, the standard sites used being FPz, Fz, Fp1, F8, F4, and T4. Additional electrodes were placed at N2, F12, T8 (10% lower than FPz, F8, and T4, respectively) and at M2 and F16 (20% lower than FP2 and F8, respectively). One electrode was placed in the center of the right lower lid as close as possible to the lid margin, at LL (Fig. 1).

The VESP was monitored with our standard electrodes sited at TVA and T3^ (midway between T4 and T6, and T3 and T5, respectively) and referred to the vertex, Cz.

A gold-foil electrode (GFE) was used to record a baseline ERG. During preliminary evaluation of this electrode, comparison was made on several subjects between the GFE and a standard Henkes contact lens electrode. High correlation of both a- and b-wave amplitude and latency was found, and the GFE was chosen for use in this study because it proved easily manageable and well tolerated by all subjects. In order to ensure an accurate topographical assessment, common reference recordings were made with the vertex (Cz), the contralateral occiput (Oi), and the anterior neck as comparator reference sites.

Standard silver/silver chloride EEG electrodes were affixed with collodion to the scalp and with adhesive discs to the face, and the resistance was maintained below 5 kOhms. The subjects were seated in a dimly lit room, and flash stimulation was delivered by a Grass PS22 Photostimulator from a distance of 25 cm. Direct viewing of the Photostimulator was maintained during all the recordings. The stimuli were presented binocularly and then monocularly to each eye. The unstimulated eye was carefully occluded.

Five hundred stimuli at high-intensity (3939 nits) at a rate of 6/sec were used, and a PDP8E computer averaged the response from each of eight EEG channels recorded on an Elema Svonander machine. The analysis time was 100 msec, and the bandpass of the equipment was from 66 to 700 Hz.

Results

Control ERG signals recorded with the GFE referred to the vertex revealed a mean
Table I. Mean amplitude and latency measurements of ERG-type waveforms

<table>
<thead>
<tr>
<th>Electrode site</th>
<th>a-Wave</th>
<th>b-Wave</th>
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<tbody>
<tr>
<td></td>
<td>Latency (msec)</td>
<td>Amplitude (μV)</td>
</tr>
<tr>
<td>Cornea</td>
<td>14 ± 1.16</td>
<td>15.40 ± 4.71</td>
</tr>
<tr>
<td>LL</td>
<td>18.83 ± 1.46</td>
<td>4.13 ± 3.20</td>
</tr>
<tr>
<td>N1</td>
<td>12.75 ± 2.38</td>
<td>1.75 ± 0.55</td>
</tr>
<tr>
<td>Fp2</td>
<td>12.75 ± 4.41</td>
<td>1.11 ± 0.63</td>
</tr>
<tr>
<td>FPz</td>
<td>11.5 ± 5.37</td>
<td>1.12 ± 0.71</td>
</tr>
<tr>
<td>F12</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>M1</td>
<td>14.5 ± 1.25</td>
<td>0.36 ± 0.44</td>
</tr>
<tr>
<td>F2</td>
<td>12.1 ± 2.4</td>
<td>0.05 ± 0.19</td>
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<tr>
<td>F4</td>
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<td>F6</td>
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<td>F8</td>
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*Latency of components remains remarkably constant, but amplitude diminishes acutely at noncorneal sites in proportion to the cornea-electrode distance. a-wave remnants are abolished at electrodes relatively close to the cornea, but a vestigial, low amplitude b-wave remnant is present at most electrode sites.

— = no measurable response.

a-wave latency of 14.82 msec (±1.16) and mean amplitude of 15.40 μV (±4.71), and a mean b-wave latency of 37.36 msec (±1.85) and mean amplitude of 57.58 μV (±16.67). Two oscillatory potentials (OPs) were seen on the b-wave of the ERG in most subjects with mean latencies of 17.22 msec (±1.09) and 25.22 msec (±1.48).

The use of either an anterior neck or a contralateral occipital reference site produced negligible effect on amplitude or latency of the ERG; indeed, the anterior neck site produced increased myogenic artifact in the response, which made the identification of OPs more difficult.

Amplitude and latency measurements of the waveforms derived from the various electrode sites were made manually, and the mean values of the amplitude of any detectable ERG-type signal were expressed as a percentage of the corneal ERG amplitude (Table I).

The amplitude of the ERG response from skin electrodes was found to diminish acutely as distance from the eye increased an artifact became accentuated, but latencies, however, remained almost identical to those from the GFE. The amplitude of the response from the lower lid was found to be the highest of the noncorneal sites; amplitude of the a-wave was 26.8% and that of the b-wave was 31.16% of the control ERG signal.

Fig. 2 illustrates the scalp and facial distribution of ERG-type signals in five subjects with various amplitudes of corneal ERG. As distance between the cornea and the recording electrode increased, the a-wave was abolished earlier than the b-wave, as would be expected from their relative amplitudes. A remnant of the b-wave was, however, detectable in most subjects at almost all electrode sites, although it often appeared as an extremely low amplitude deflection difficult to discern from myogenic artifact except by the superimposition of consecutive tracings. Similarly, the amplitude of the OPs reduced rapidly as the distance from the cornea increased.

Myogenic and lid-blink artifact varied between subjects and in some cases confounded the ERG signal at skin electrodes relatively close to the cornea. The extent of the field of activity produced was directly proportional to the amplitude of the corneal ERG (Fig. 2), with Subject 5 demonstrating a wider distribution of ERG-type signals than Subject 2.

On binocular stimulation, the responses at sites N2 and FPw were found to be twice that produced on monocular stimulation of either eye, and the response at Fp1 was around
Fig. 2. Scalp and facial distribution of ERG-type signals in five subjects. Note that the corneal signal is recorded with a GFE at half the gain of all other channels. All electrodes are referred to the vertex, and recordings are made in accordance with electroencephalogram convention, positive at grid 1 downward. All subjects show similar distributions of signals, the extent of the field being in direct proportion to the amplitude of the corneal signal. At temporal sites T4 and T8, a very low amplitude b-wave remnant is seen in some cases.

one-and one-half times the monocular response from the right eye, indicating interaction of the two monocular ERG fields. The response at LL was not enhanced on binocular stimulation and neither was that at any other electrode site.

The results of simultaneous recording of corneal ERG and VESPs in the same five subjects are shown in Fig. 3. Subjects 1, 2, 3, and 5 demonstrate well-formed bilateral VESP components, all with clear triphasic configurations. The latencies of the VESPs recorded in Subjects 1, 2, and 3 were clearly unrelated to those of the ERG, but in Subject 5 there was a closer relationship between the peak of the ERG b-wave and the final, positive peak of the VESP. The results from Subject 4 are atypical. This is a subject from whom no VESP had ever been recorded despite repeated attempts on a number of occasions over a period of 14 months and the use of variations in electrode montage and stimulus parameters. A normal corneal ERG, however, was recorded in this subject, as was a visual evoked cortical potential (VECP) to both flash and pattern-reversal stimulation. No neurological or oph-
Later components were seen at certain electrode sites consisting, in 10 subjects, of a positive peak around 45 to 55 msec latency. In three subjects, a negative peak of latency around 60 to 70 msec was also seen. The origin of these components was determined by comparison of responses between the three reference sites. The positive component around 45 to 55 msec was present on recordings from electrodes F12, T4, and T8, and M2 when Cz was a reference (Fig. 2) but was absent when an anterior neck reference was used, although ERG topography remained the same. The use of O1 as reference revealed similar responses to those obtained with the vertex site. This would suggest that the component may be surface-negative around Cz and therefore probably of cortical origin, possibly spreading from the occiput. In accordance with electroencephalogram convention, when the electrode connected to grid 1 (in this case the “active” electrode) becomes electronegative in relation to the electrode connected to grid 2 (in this case the “reference” electrode Cz), there will be a downwards deflection of the recording pen. Thus, if Cz becomes relatively electronegative compared with the active electrode, a similar deflection will occur. Indeed, this component may well constitute the N1 component of the VECP, since trials in our laboratory with flash stimulation showed that the N1 component had a mean latency of 56.1 msec (±6.8).

The second atypical control subject was a 20-year-old male who revealed markedly asymmetric ERG responses; the amplitude of that from the right eye was almost half that thalmological abnormality could be detected.
Fig. 4. Recordings in a normal control subject showed ERG signals recorded from electrode sites FP_1 and FP_2 to be consistently asymmetrical, response from the right eye being almost half the amplitude of that from the left eye. However, simultaneously recorded VESPs recorded at electrodes T3/2 and T4/2 were of almost identical amplitudes. The early components of the occipital response (recorded at electrodes O1 and O2) were also symmetrical.

Two patients with distinct and discrete pathological conditions have also been examined. Patient 1 was a 39-year-old male who during a fall had sustained a fracture of the left zygoma and orbit, with an associated left optic nerve injury. Vision in the left eye was reduced to zero light perception, and the optic disc was pale and atrophic. Electrophysiological assessment (Fig. 5) revealed normal photopic ERGs from both eyes. Stimulation of the affected eye failed to elicit any consistent VESPs, and VECPs were also absent even from the left eye although the latencies were approximately the same (Fig. 4). The VESPs were, however, found to be of approximately equal amplitude and of similar latency, as were the initial VECP components detected with occipital electrodes. This was a consistent, repeatable asymmetry, which was not found to be caused by the electrodes or recording technique. On examination, the subject had visual acuities of 6/5 in both eyes and full visual fields, and ophthalmoscopic examination was normal.
Fig. 5. Recordings from a 39-year-old male who had sustained a left optic nerve injury. Normal photopic ERGs were recorded from either eye, but stimulation of the affected eye failed to reveal any consistent VESP or VECP. Recordings of VESP and VECP from the unaffected eye were normal.
when high-intensity flash stimulation was used. These responses were of normal latency and amplitude from the unaffected eye, and despite the VECPs being of higher amplitude over the left occiput, there was no significant asymmetry in the monitoring EEG.

Patient 2 was a 22-year-old male who had suffered a penetrating wound with a metallic intraocular foreign body in the left eye. Subsequent to its removal, the retina detached, involving the macular area and reducing the vision to accurate projection of light. Electrophysiological assessment (Fig. 6) revealed abolition of the ERG of the affected eye. VESPs were present bilaterally at normal latency and were of normal amplitude for monocular stimulation, and a VECP could be consistently recorded bilaterally with flash stimulation, although no response could be elicited with pattern-reversal stimulation of any check size. The VECPs from the affected eye were slightly delayed compared with those from the unaffected eye, although the VESPs were of compatible latency and amplitude.

Discussion

It is clear that the ERG signal produced under the same conditions used to elicit the VESP is distributed over a wide field around the orbit, and this is in agreement with the results of other authors. The measureable extent of the field of activity of the ERG is dependent partly on the amplitude of the corneal signal and partly on the degree of myogenic artifact present. The fields from either eye clearly overlap medially but are separated by the nasal insulator. Because the interaction of the fields does not extend to the lower lid site, the recording of monocular responses without occlusion of the opposite eye is possible and may be of value in the clinical situation.

At the more posterior sites used in this study, i.e., T4 and T8, any measureable remnant of the ERG b-wave takes the form of a small monophasic deflection, generally much less than 1 \( \mu \)Volt in amplitude, dependent on corneal ERG amplitude. The VESP, however, assumes a triphasic P-N-P configuration, and its peak-to-peak amplitudes are of the order of 1.5 \( \mu \)V and 2.5 \( \mu \)V, respectively.

The subject (Fig. 2, No. 4) from whom VESP signals could not be recorded is unusual and is one of three out of 60 seen in our laboratory, all neurologically normal. The ERG from the cornea is of equally high amplitude when compared with that of other subjects, and scalp and facial distribution of the ERG-type response is also being similar to that of other subjects.

The existence of amplitude asymmetries of ERG and VEP is well known, but the coexistence of an almost 50% asymmetry in ERG with symmetrical VESP and VECP must indicate independence of the respective evoked potentials.

The results obtained from Patient 1 demonstrate that because of unilateral optic nerve trauma despite the survival of an ERG of normal amplitude and latency from the affected eye, the VESP and VECP are absent. Patient 2 shows that extinction of the ERG in one eye due to retinal detachment can coexist with bilateral survival of both VESP and VECP from the same eye.

Cobb and Morton noted an early component of the occipital response to high-intensity flashes and excluded direct spread of the retinal potential over the scalp but did not discount spread across the base of the brain. Cobb and Dawson used a bipolar recording technique and reported early components of the occipital response beginning 20 to 25 msec after stimulation. On comparison with a simultaneously recorded ERG, they suggested that these components were unrelated to current spread from the ERG, although the location of the signal in their illustration appears more anterior than the occiput.

Monnier observed that a negative wave resembling the ERG c-wave could be recorded from the nonilluminated eye in response to light stimulation of the contralateral eye, and the activity of the efferent centrifugal pathway of the optic nerve was regarded as its origin. Horsten et al. showed in cats and in one patient that when one eye was enucleated
Fig. 6. Recordings from a 22-year-old male with retinal detachment of the left eye after a penetrating injury. The ERG from the affected eye was totally extinguished; VESP and VECP (to flash stimulation) were present bilaterally although no VECP could be elicited from the affected eye with pattern-reversal stimulation. Recordings of ERG, VESP, and VECP from the unaffected eye were normal.
and replaced with a saline-soaked gauze pad, an inverted complete ERG signal could be recorded from the socket if the intact eye was very strongly illuminated. These findings were also reported in cats after transection of the optic nerve or coagulation of the chiasma, and it was concluded that this transmission of signals did not take place via the nervous pathway but rather by direct electrical spread via the surrounding tissues. Similar results were reported in cats by Yonemura et al.17 Honda7 described the recording of high-frequency wavelets in the region of the lateral canthus while the eye was rotated nasally and postulated that their origin was probably the optic nerve. Siegfreid18 reported similar findings of possible optic nerve potentials around the temple and discounted passive conduction of the ERG at this site.

The distinct difference in morphology between the VESP and the ERG b-wave remnant recordable at the temporal sites described and the relative disparity in amplitudes strongly suggest that the VESP is not attributable to a volume-conducted ERG response.

In conclusion, on the basis of the evidence of the present topographical study, the co-existence of intact ERG and extinct VESP and vice versa in pathological states, the results presented of atypical control subjects, and the effect of monocular vs. binocular stimulation on the VESP,8 we suggest that the VESP and ERG are distinct and unrelated electrophysiological phenomena.

We are most grateful to Mrs. Margaret Geddes and Mrs. Ann Davies for secretarial assistance and to Mr. Neville Drasdo for continued advice and encouragement. We also acknowledge the cooperation of the Consultants at the Birmingham and Midland Eye Hospital in allowing us to study their patients.

REFERENCES