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RELATION OF THE *e*-WAVE TO GANGLION CELL ACTIVITY AND ROD RESPONSES IN THE FROG

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Abstract—The *e*-wave of the electroretinogram was recorded intraretinally from dark-adapted frog eyecups. *e*-Wave latency was roughly proportional to log stimulus intensity, varying from 2 to 65 sec. The delayed response of ganglion cell units (types 3 and 4) began simultaneously with the *e*-wave. The *e*-wave response had similar latencies as the onset of the decay phase of the saturated rod response (determined by recording the mass receptor response and by monitoring *b*-wave threshold). These results suggest that the *e*-wave and the delayed ganglion cell response represent closely-linked retinal phenomena which are initiated by rod response decay.

INTRODUCTION

The *e*-wave is a slow retinal voltage response of 5–15 sec duration and approximately 300 μV amplitude. The response differs from all other components of the electroretinogram (ERG) in that it has extremely long latencies to its onset, as great as 20 sec or more. The response has been described by Crescitelli and Sickel who have recorded *e*-waves across the isolated, perfused retina of the frog (Sickel and Crescitelli, 1967; Crescitelli and Sickel, 1968) and from the tadpole eyeball (Crescitelli, 1970).

A second retinal delayed response can be recorded from retinal ganglion cells, a delayed cell activation evoked by short light flashes. This "delayed ganglion cell response" has been described by Pickering and Varjú (1967, 1969; Pickering, 1968) in the intact eye of the frog. It has also been recorded in the frog by Chung, Raymond and Lettvin (1970), Chino and Sturr (1975a) and Lurie (1976), and in the mudpuppy by Karwoski and Burkhardt (1976).

The *e*-wave and the delayed ganglion cell response share several properties. The latencies to the onsets of both responses are roughly proportional to the log of stimulus intensity. Latencies of from 2 sec to greater than 20 sec have been observed in both cases. In addition, both responses are found only in the dark adapted eye.

Crescitelli and Sickel (1968) and Pickering and Varjú (1969), noting the similarities between the two responses, have suggested that they might be related. An earlier investigation by Sickel and Crescitelli (1967) showed a correlation between times of occurrence of the two responses. However, a firm demonstration linking the two responses has been needed.

The striking feature of both responses is their long delays. Several investigators have proposed hypotheses to account for these delays (Varjú and Pickering, 1969; Chino and Sturr, 1975b; Lurie, 1976). In the simplest notion, Sickel (1972a,b) has suggested that the delay to onset of the *e*-wave is determined by the time to recovery of the rod receptor response. Intracellular studies of the scotopic retina have shown that brief light flashes can evoke prolonged rod responses lasting tens of seconds (Toyoda, Anno and Tomita, 1970; Lipton, Ostroy and Dowling, 1977). The onset of the decay phase of such rod responses could occasion the *e*-wave and the delayed ganglion cell response. But no comparison of the latencies of rod response decay and the *e*-wave has been made to test this "receptor" hypothesis.

The temporal relation of the *e*-wave to the delayed ganglion cell response and the prolonged rod response has been studied by us. The *e*-wave and ganglion cell activity were recorded simultaneously in the dark-adapted retina under a wide range of stimulus intensities. The time course of the rod response was monitored and compared to *e*-wave latencies. The results show that the *e*-wave and the delayed ganglion cell response occur at the same time as the onset of decay of the rod response.

METHODS

Eyecup preparations of the northern leopard frog, *Rana pipiens*, were used in this study. The eyes were removed from pithed frogs previously dark-adapted for at least 4 hr and were then transected under dim red illumination using a sharp razor blade. The vitreous humor was soaked up from the eyecup with absorbent tissue, leaving a thin layer over the retinal surface. The eyecup was placed on a piece of Ringer's-soaked gauze, put in a Plexiglas moist chamber and cooled to 15°C. The chamber was ventilated by a steady flow of humidified 95% O_2 and 5% CO_2.

Except when otherwise noted, light stimuli consisted of 100 msec flashes of diffuse white light presented in the dark. The light from a quartz–iodine fiber-optic illuminator (Model 11–80, American Optical Corp., operated at lowest intensity) was gated by an electromagnetic shutter (Model 23X, Vincent Associates) and attenuated by two back-to-back logarithmic circular neutral-density wedges (having a total range of over 8 decades). Light from the attenuator was led through a fiber-optics bundle into a light-tight box containing the preparation. The end of the fiber bundle was placed above the eyecup and illuminated the entire retina.

Light intensities used in this study are given with reference to that intensity which produced a threshold response

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in the completely dark-adapted eye. This threshold stimulus, a 100 msec flash at log $I = 0$ produced a 10 μV ERG response in the most sensitive preparations. Increasingly positive log I values indicate brighter stimulus intensities. Flashes of 500 nm light, produced by a narrow-band interference filter, were used in *b*-wave threshold experiments. The intensities of these stimuli were adjusted to equal scotopic luminance for the exposed retina of the frog.

The neutral density attenuator was calibrated using a PIN photodiode (PIN-3DP, United Detector Technology). The quantal content of the threshold stimulus was determined with the photodiode by the method of Green, Dowling, Siegel and Ripps (1975). A 100 msec, log $I = 0$ white stimulus was found to contain the scotopic equivalent of 7.8×10^{-4} photons/μm^2 of 500 nm light.

Both ERG and intraretinal voltages were recorded with Ringer's-filled Ag/AgCl micropipettes. Microelectrode tips were broken to a 5 μm tip diameter for intraretinal electrodes and 30–40 μm for vitreal and scleral electrodes. Low drift Ag/AgCl wires were prepared by slow plating for 8 hr (Newman, 1977).

Retinal slow potentials were amplified with two differential electrometers (Model AK-47, Metametrics). Signals were recorded d.c. with a high frequency cut-off determined by one stage of RC filtering ($\tau = 25$ msec). Recordings were made on a linear pen recorder (Mark 260, Gould Inc.) and photographed for reproduction from a CRT screen (Model 565 oscilloscope, Tektronix).

Ganglion cell activity was recorded with metal-filled micropipettes (Dowben and Rose, 1953; Gesteland, Howland, Lettvin and Pitts, 1959) whose tips were flashed with gold and then plated with platinum black. Single-unit activity was recorded from the cell bodies of ganglion cells. This activity was easily distinguished from the activity of fibers of passage, for it consisted of spikes of longer duration (Karwoski and Burkhardt, 1976) at a deeper location within the retina and with a receptive field location which was coincident with the position of the recording electrode. Signals were a.c. coupled to a third amplifier and filtered with a bandpass filter centered on 1 kHz.

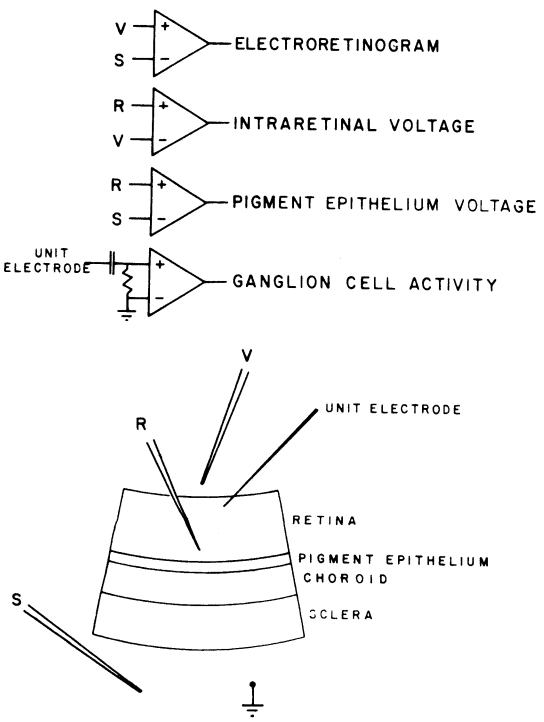

Fig. 1. Schematic diagram of recording arrangement. See text for details.

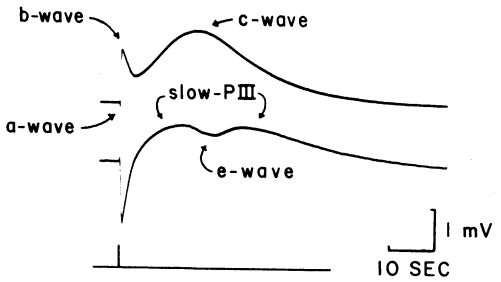

Fig. 2. The ERG (top trace) and intraretinal voltage (middle trace) evoked by a stimulus flash (indicated in the bottom trace). Log $I = 5.7$. Upward deflections represent positive voltages in this and all other figures.

Normal Ringer's solution, modified from Oakley and Green (1976), contained 112 mM NaCl, 2.4 mM KCl, 4.0 mM $NaHCO_3$, 1.0 mM $MgCl_2$ and 0.9 mM $CaCl_2$. An aspartate Ringer's was prepared by replacing the NaCl of the normal Ringer's solution with 112 mM aspartic acid. The aspartate Ringer's was titrated to pH 7.0 with NaOH.

RESULTS

The e-wave and ganglion cell activity

A schematic diagram of the recording arrangement used in this study is shown in Fig. 1. The electroretinogram (ERG) was recorded between vitreal (V) and scleral (S) electrodes. The *e*-wave was monitored by recording the intraretinal voltage between an intraretinal electrode (R) and the vitreal electrode. *c*-Wave latencies were monitored between intraretinal and scleral electrodes, and ganglion cell activity was recorded with a microelectrode in the ganglion cell layer of the retina. Intraretinal and ganglion cell electrodes were placed within 0.5 mm of each other on the retinal surface.

The eyecup was kept as completely dark-adapted as possible throughout the experiment in order to standardize response latencies. The preparation was dark-adapted for 1½–2 hr following the initial dissection, conducted under dim red illumination, until maximum retinal sensitivity was achieved. The eye was permitted to dark-adapt following each stimulus flash. A 7 min recovery time was used for bright stimuli (log $I = 7.7$).

Typical voltage responses evoked by a light flash in a dark-adapted eyecup are shown in Fig. 2. The *a*-, *b*- and *c*-waves of the ERG are seen in the upper trace of this record. The intraretinal voltage is shown in the lower trace. A slow positive potential, having roughly the same time course as the ERG *c*-wave, follows the intraretinal equivalents of the *a*- and *b*-waves (Brown and Wiesel, 1961). This is the slow PIII response (Faber's terminology, 1969). Superimposed on the slow PIII potential is a negative dip or notch—the *e*-wave. The *e*-waves shown in this and the following figures were recorded with the intraretinal electrode tip in the distal retina, although large *e*-waves can be recorded almost anywhere within the retina (Newman, 1977).

e-Waves evoked by a series of increasing intensity stimuli are shown in the intraretinal (middle) traces

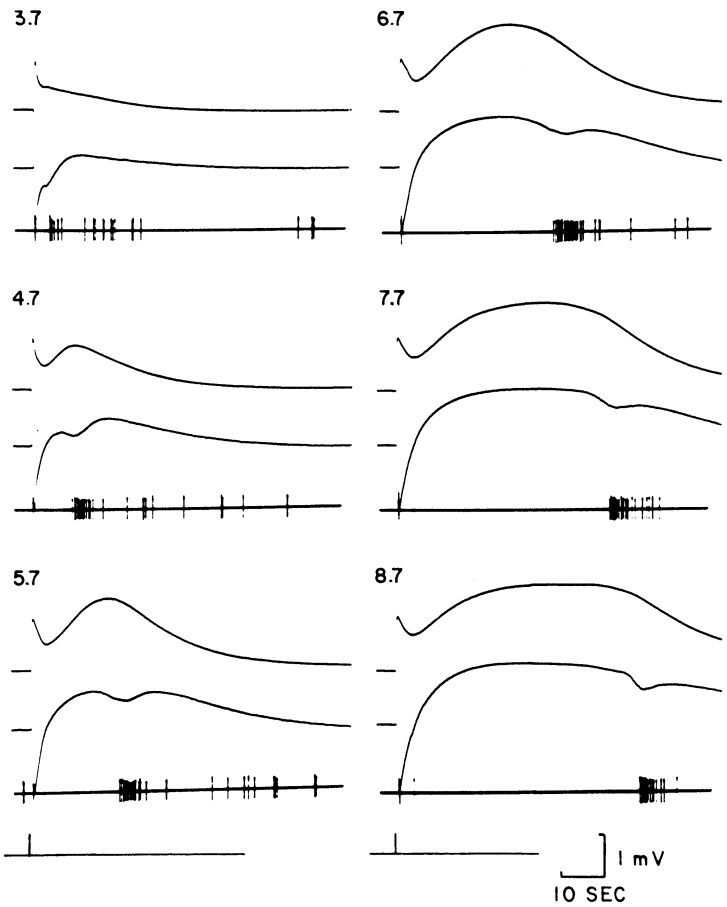

Fig. 3. The ERG (top traces), intraretinal voltage (middle traces) and ganglion cell activity (bottom traces; a type 3 unit) recorded at six flash intensities. Numbers indicate log stimulus intensity. The vertical scale refers to the top two traces only.

of Fig. 3. At dim intensities (log $I = 3.7$) a flash produces a small *e*-wave which appears on the trailing phase of the intraretinal *b*-wave. Brighter flashes elicit *e*-waves with progressively longer latencies to their onset. The *e*-wave response does not appear in the ERG, the upper trace of each record.

The shape of the *e*-wave varied somewhat in different preparations. *e*-Waves sometimes had much sharper turn-ons and shorter total durations than those shown in Fig. 3. In other experiments, *e*-waves had smooth transitions and small amplitudes and were barely visible. The waveforms sometimes changed during the course of a single experiment, suggesting that their shapes are partly determined by the state of the preparation.

Greatly enlarged *e*-waves were sometimes recorded from unhealthy preparations (as judged by the ERG). Figure 4 shows one such example where the *b*- and *c*-waves of the ERG (top traces) were smaller than normal. Abnormally large *e*-waves with superimposed oscillations of approximately 1 Hz were recorded intraretinally (lower traces). Under these conditions a component of the *e*-wave is seen in the ERG records.

The activity of a type 3 ganglion cell (changing contrast detector or ON–OFF unit; Maturana, Lettvin, McCulloch and Pitts, 1960), is shown in the lower traces of Fig. 3. Responses consist of an initial brief burst of spikes coincident with the *b*-wave and a prolonged period of delayed activity which follows a silent period. As demonstrated by these records, the delayed ganglion cell response begins at nearly the same time as the *e*-wave.

The latencies of the two delayed responses are graphed as a function of log intensity in Fig. 5, which represents data from a preparation having a sharply defined *e*-wave. The latency relations of the delayed ganglion cell response and the *e*-wave (onset) are almost identical over a wide range of stimulus intensities. Latency vs log I relations are roughly linear for both over a range of 3 decades in stimulus intensity. The latency of the peak of the *c*-wave is also plotted as a function of log I in Fig. 5. Although *c*-wave (peak) latencies of greater than 30 sec are attained, the *c*-wave peak latency relation differs significantly from those of the two delayed responses.

In general, ganglion cell activity of type 3 and type 4 (dimming detector) units began simultaneously with the *e*-wave response or within seconds of its onset (during the initial negative phase of the response). (Diffuse light flashes do not elicit responses in type 1 and 2 units—Maturana *et al.*, 1960.) All spontaneous ganglion cell activity was blocked during the

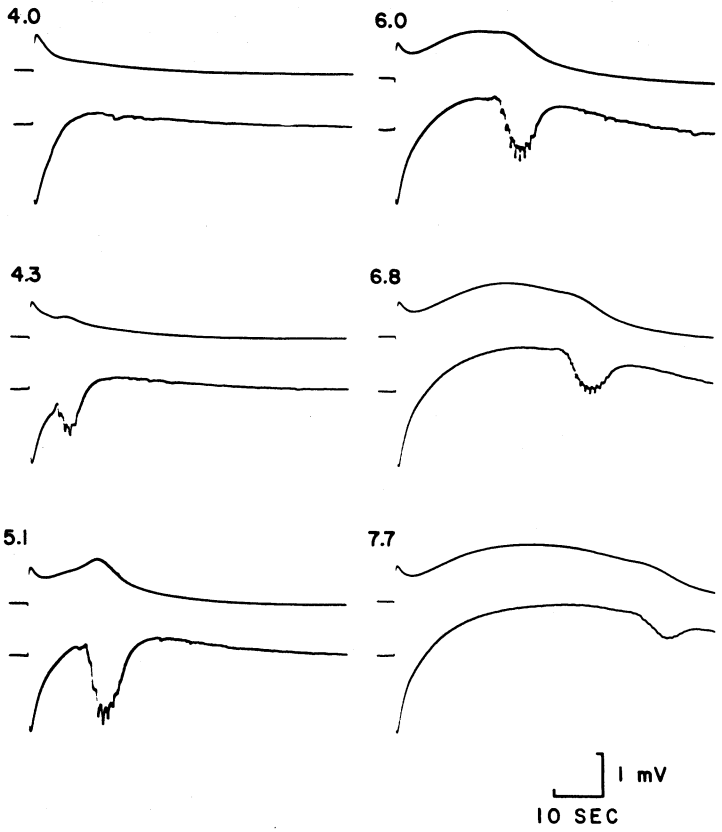

Fig. 4. Large *e*-waves recorded from an abnormal eyecup preparation. Top trace: ERG; bottom trace: intraretinal voltage. An *e*-wave was not elicited by the dimmest stimulus flash (4.0).

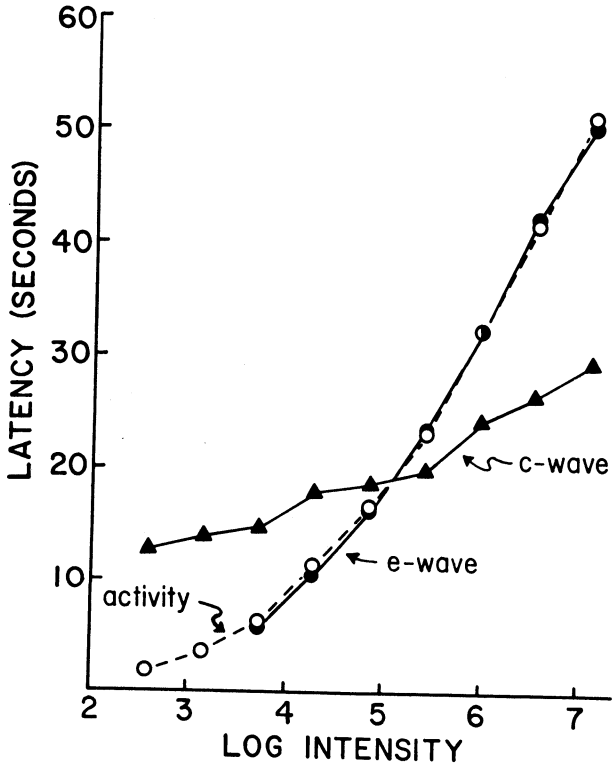

Fig. 5. A comparison of the latencies of the *e*-wave (●), the delayed ganglion cell response (○) and the *c*-wave peak (▲) graphed as a function of log intensity. The ganglion cell plot represents the activity of a type 3 unit.

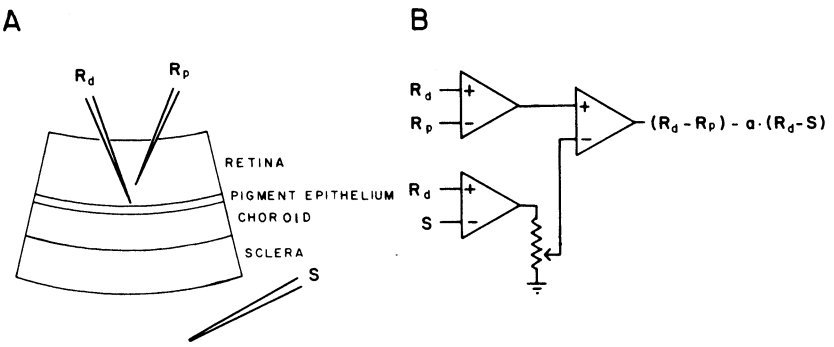

Fig. 6. Arrangement used in recording the mass receptor response. (A) Distal (R_d) and proximal (R_p) intraretinal electrodes were placed on opposite sides of the receptor layer in the retina. (B) The corrected receptor response was obtained by subtracting a fraction (a) of the *c*-wave response ($R_d - S$) from the receptor response ($R_d - R_p$).

silent period preceding the delayed response. This inhibitory period was particularly marked in type 4 units, which normally have high activity rates in the dark.

The durations as well as the latencies of the two delayed responses showed close correlations in many preparations. As illustrated in Fig. 3, the *e*-wave and the initial high frequency portion of the delayed ganglion cell response had similar durations. Preparations having short, sharply defined *e*-waves had short delayed ganglion responses with sharply defined turn-ons and turn-offs. Other preparations, having prolonged *e*-waves with smooth transitions, had longer delayed ganglion cell responses with gradually increasing and gradually declining periods of spike activity.

The rod response

The relation between the *e*-wave and rod activity was investigated by recording the mass receptor response in aspartate-treated eyecups (Sillman, Ito and Tomita, 1969). The receptor response was recorded between two intraretinal electrodes placed across the receptor layer in the distal retina (Fig. 6A). This differential recording method minimized the contribution of the *c*-wave and the slow PIII responses to the recorded receptor potential. Any residual slow response component was reduced by subtracting a fraction of the *c*-wave potential ($R_d - S$) from the receptor response ($R_d - R_p$) (Fig. 6B). This fraction, *a*, was adjusted so that saturated receptor responses with flat plateaus were obtained. In most cases, *a* did not exceed 1/20.

The *e*-wave latency was initially determined as a function of log *I* in normal, untreated eyecups. 5 µl of aspartate Ringer's solution (resulting in a final vitreous concentration of ~11 mM aspartate) were then added to the preparation under dim red illumination. The mass receptor response was then recorded over a range of stimulus intensities. The retina was thoroughly dark-adapted before recording *e*-wave and receptor potentials so that the latencies of the two responses could be compared properly.

Figure 7 shows a series of receptor responses recorded from an aspartate-treated preparation. As intensity is increased, the response amplitude saturates, and duration of the total response increases. At high intensities, the response is composed of an initial transient cone contribution followed by a prolonged, saturated rod response (Brown, Watanabe and Murakami, 1965). The latency to the onset of the decay of the rod response increases with stimulus intensity. The onset of the *e*-wave response, recorded in the same preparation before aspartate treatment, is indicated by the arrow heads in Fig. 7. The *e*-wave and the decay phase of the rod response begin almost simultaneously at all stimulus intensities.

A comparison of the duration to decay of the receptor response and the latency of the *e*-wave in a second preparation is plotted as a function of log intensity and shown in Fig. 8. As demonstrated in Fig. 7, the

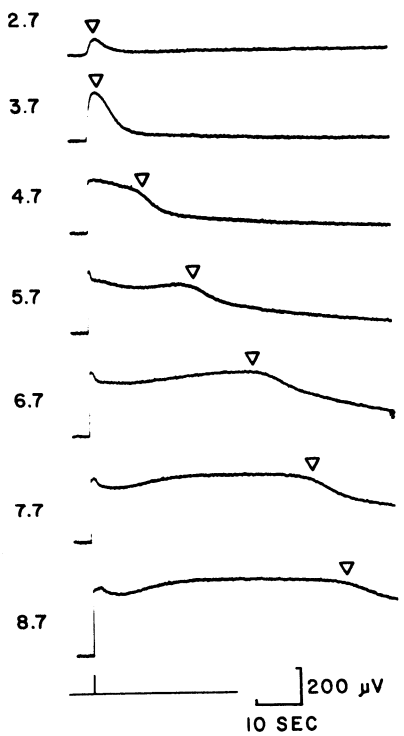

Fig. 7. The corrected receptor response, $(R_d - R_p) - a(R_d - S)$, recorded at different flash intensities. Correction factor, $a = 0.04$. The onset of the *e*-wave, recorded before aspartate treatment, is indicated above each trace (▽).

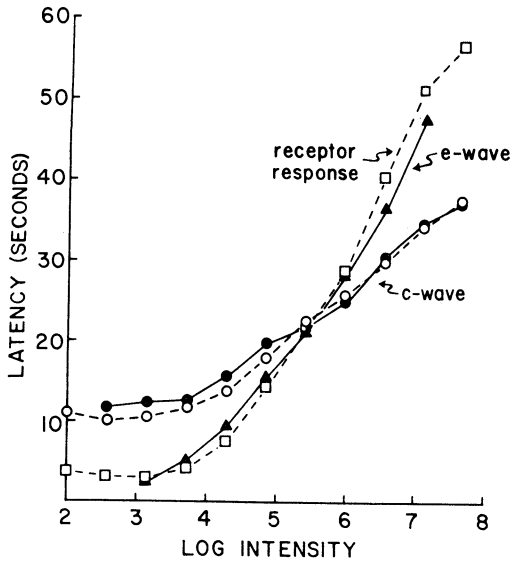

Fig. 8. A comparison of the latencies of receptor response decay (□), the *e*-wave (▲) and the *c*-wave peak plotted as a function of log intensity. *c*-Wave latency relations were determined both before (●) and after (○) aspartate treatment.

two latency relations are nearly identical. The *c*-wave response, which is believed to reflect rod activity (Oakley and Green, 1976) and is not substantially affected by aspartate treatment, was used as a control measure in this experiment. The latency vs log *I* relations of the *c*-wave peak, determined both before and after aspartate treatment, are plotted in Fig. 8. The two relations are nearly identical, indicating that receptor activity was not substantially altered by the aspartate treatment.

Retinal threshold

The onset of rod response decay was also determined by monitoring the threshold of the intraretinal *b*-wave. This method permitted the simultaneous determination of *e*-wave latency and rod response decay latency in a normal, untreated preparation. The threshold of the rod system drops rapidly from an immeasurably high value as the rod response decays from a saturated, plateau level (Lipton *et al.*, 1977).

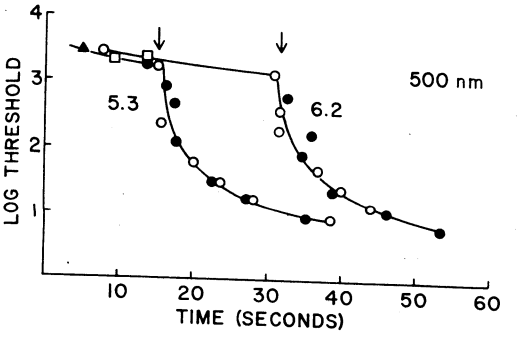

Fig. 9. Log threshold of the intraretinal *b*-wave response following adapting flashes of two intensities: Log $I = 5.3$ and 6.2. Vertical arrows indicate the onset of the *e*-wave. Criterion *b*-wave responses used in calculating threshold were: 37 μV (□), 50 μV (○), 75 μV (▲) and 100 μV (●).

Thus, the onset of rod response decay can be determined by monitoring the rod component of retinal threshold.

The threshold of the intraretinal *b*-wave was monitored by applying test flashes at 5 sec intervals following a bright adapting stimulus. The test flash intensities needed to produce criterion *b*-wave responses at times following the adapting flash were then determined. A 500 nm light was used for adapting and test stimuli in order to elevate the measured cone threshold with respect to the rod system.

The threshold of the intraretinal *b*-wave following adapting flashes of two intensities is shown in Fig. 9. The threshold plots are composed of an initial cone phase followed by a steeply declining rod phase. The beginning of the *e*-wave (vertical arrows), recorded concurrently with threshold measurements, occurs precisely at the onset of rod threshold decline. This correlation was seen following adapting flashes producing delays ranging from 15 to 50 sec.

DISCUSSION

The e-wave and ganglion cell activity

Similarities in the properties of the *e*-wave and the delayed ganglion cell response have prompted suggestions of a relation between the two responses (Crescitelli and Sickel, 1968; Pickering and Varjú, 1969). The experiments conducted in this work demonstrate that the two delayed responses are closely linked in time. The latency to the onset of the *e*-wave and the delayed ganglion cell response are nearly identical over at least a 5-decade range of stimulus intensity (Figs 3 and 5). The durations of the two delayed responses are also similar (Fig. 3; see also Newman, 1977).

The close temporal relation between the *e*-wave and the delayed ganglion cell response suggests that the two responses reflect closely linked retinal phenomena. This relation is consistent with the preliminary results of a source-density analysis of the *e*-wave (Newman, 1977), which indicate that the *e*-wave is primarily generated by a current source near the ganglion cell layer and a current sink near the border between the inner plexiform and inner nuclear layers. This source–sink distribution suggests that the *e*-wave is mainly generated by proximal elements in the retina.

Origin of delayed response delays

The most striking feature of the delayed ganglion cell response is its long latency. Several hypotheses have been offered accounting for these long delays. Varjú and Pickering (1969) and Pickering and Varjú (1971) have suggested that the latencies are generated by an interaction of inhibitory and excitatory responses within the retina. This theory invokes retinal processes which have not been demonstrated experimentally.

Chino and Sturr (1975b) have suggested that the cone system plays a key role in the generation of delayed response delays. However, the spectral sensitivity of both the *e*-wave (Crescitelli and Sickel, 1968)

and the delayed ganglion cell response (Chino and Sturr, 1975b) have been shown to resemble the absorption spectrum of the rod pigment rhodopsin. In addition, the light and dark adaptation properties of the delayed ganglion cell response (Pickering and Varjú, 1969) suggest a rod origin of the response. Thus, it is unlikely that the cone system contributes significantly to the delayed retinal responses.

Lurie (1976), in a study of the *c*-wave and type 4 ganglion cell activity, has suggested that currents generated by the pigment epithelium might modulate ganglion cell activity. As demonstrated in this work (Fig. 5), the *c*-wave latency vs log *I* relation differs significantly from the latency relations of the delayed retinal responses. It seems unlikely, therefore, that the pigment epithelium, which generates the *c*-wave (Noell, 1952; Schmidt and Steinberg, 1971), controls the onset of the delayed retinal responses.

Intracellular recordings have demonstrated that brief stimuli can evoke rod responses which remain at a saturated plateau level for tens of seconds before the onset of response decay (Toyoda *et al.*, 1970; Lipton *et al.*, 1977). Sickel (1972a,b), noting this property, suggested that the onset of rod response decay could initiate the *e*-wave response. This hypothesis, in contrast to the theories discussed above, is based solely on the delays inherent in the rod response itself.

The results presented in this work strongly support Sickel's "receptor response" hypothesis. As shown in Figs 7 and 8, the onset of the decay phase of the rod response corresponds closely to the onset of the *e*-wave recorded in the same preparation before aspartate treatment. The time course of the receptor response has also been determined by monitoring the threshold of the intraretinal *b*-wave. The nearly vertical beginning of the rod component of *b*-wave threshold marks the onset of the decay phase of the rod response from a saturated level. As illustrated in Fig. 9, the onset of the *e*-wave occurs at this same time.

These experiments demonstrate that the onset of the *e*-wave (and thus the delayed ganglion cell response as well) occurs as the plateau phase of the prolonged rod response begins to decay. Although this correspondence does not prove a causal relationship, it strongly implies that the latencies of the *e*-wave and the delayed ganglion cell response are determined by the rods. In these terms, the two delayed responses can be interpreted as "scotopic off effects" (using Sickel's terminology, 1972a) triggered by the declining phase of the prolonged rod response.

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REFERENCES

Brown K. T., Watanabe K. and Murakami M. (1965) The early and late receptor potentials of monkey cones and rods. *Cold Spring Harb. Symp. quant. Biol.* **30,** 457–482.

Brown K. T. and Wiesel T. N. (1961) Localization of origins of electroretinogram components by intraretinal recording in the intact cat eye. *J. Physiol., Lond.* **158,** 257–280.

Chino Y. M. and Sturr J. F. (1975a) The time course of inhibition during the delayed response of the ON–OFF ganglion cell in the frog. *Vision Res.* **15,** 185–191.

Chino Y. M. and Sturr J. F. (1975b) Rod and cone contributions to the delayed response of the ON–OFF ganglion cell in the frog. *Vision Res.* **15,** 193–202.

Chung S. H., Raymond S. A. and Lettvin J. Y. (1970) Multiple meaning in single visual units. *Brain Behav. Evol.* **3,** 72–101.

Crescitelli F. (1970) The *e*-wave and inhibition in the developing retina of the frog. *Vision Res.* **10,** 1077–1091.

Crescitelli F. and Sickel E. (1968) Delayed OFF responses from the isolated frog retina. *Vision Res.* **8,** 801–816.

Dowben R. M. and Rose J. E. (1953) A metal-filled microelectrode. *Science* **118,** 22–24.

Faber D. S. (1969) Analyses of slow transretinal potentials in response to light. Ph.D. thesis, University of New York, Buffalo.

Gesteland R. C., Howland B., Lettvin J. Y. and Pitts W. H. (1959) Comments on microelectrodes. *Proc. Instn Radio Engrs* **47,** 1856–1862.

Green G., Dowling J., Siegel I. and Ripps H. (1975) Retinal mechanisms of visual adaptation in the skate. *J. gen. Physiol.* **65,** 483–502.

Karwoski C. J. and Burkhardt D. A. (1976) Ganglion cell responses of the mudpuppy retina to flashing and moving stimuli. *Vision Res.* **16,** 1483–1495.

Lipton S. A., Ostroy S. E. and Dowling J. E. (1977) Electrical and adaptive properties of rod photoreceptors in *Bufo marinus*. I. Effects of altered extracellular Ca^{2+} levels. *J. gen. Physiol.* **70,** 747–770.

Lurie M. (1976) Some observations on the *c*-wave of the electroretinogram in the intact frog eye. *Expl Eye Res.* **23,** 197–207.

Maturana H. R., Lettvin J. Y., McCulloch W. S. and Pitts W. H. (1960) Anatomy and physiology of vision in the frog (*Rana pipiens*). *J. gen. Physiol.* **43,** 129–175.

Newman E. A. (1977) The *e*-wave of the frog retina: its origin and relation to the delayed ganglion cell response and the prolonged rod response. Ph.D. thesis, Massachusetts Institute of Technology, Cambridge.

Noell W. (1952) Azide-sensitive potential across the eyebulb. *Am. J. Physiol.* **170,** 217–238.

Oakley B. II and Green D. G. (1976) Correlation of light-induced changes in retinal extracellular potassium concentration with the *c*-wave of the electroretinogram. *J. Neurophysiol.* **39,** 1117–1133.

Pickering S. G. (1968) The extremely long latency response from ON–OFF retinal ganglion cells: relationship to dark adaptation. *Vision Res.* **8,** 383–387.

Pickering S. G. and Varjú D. (1967) Ganglion cells in the frog retina: inhibitory receptive field and long latency response. *Nature, Lond.* **215,** 545–546.

Pickering S. G. and Varjú D. (1969) Delayed responses of ganglion cells in the frog retina: the influence of stimulus parameters upon the length of the delay time. *Vision Res.* **9,** 865–879.

Pickering S. G. and Varjú D. (1971) The retinal ON–OFF components giving rise to the delayed response. *Kybernetik* **8,** 145–150.

Schmidt R. and Steinberg R. H. (1971) Rod-dependent intracellular responses to light recorded from the pigment epithelium of the cat retina. *J. Physiol., Lond.* **217,** 71–91.

Sickel W. (1972a) Retinal metabolism in light and dark. *Handbook of sensory physiology*, Vol. VII/2, pp. 667–727 (edited by Fuortes M. G. F.). Springer–Verlag.

Sickel W. (1972b) Electrical and metabolic manifestations of receptor and higher order neuron activity in vertebrate retina. *Adv. Med. Biol.* **24,** 101–118.

Sickel W. and Crescitelli F. (1967) Delayed electrical responses from the isolated frog retina. *Pflügers Arch. ges Physiol.* **297,** 266–269.

Sillman A. J., Ito H. and Tomita T. (1969) Studies on the mass receptor potential of the isolated frog retina. I. General properties of the response. *Vision Res.* **9,** 1435–1442.

Toyoda H., Anno H. and Tomita T. (1970) The rod response in the frog as studied by intracellular recording. *Vision Res.* **10,** 1093–1100.

Varjú D. and Pickering S. G. (1969) Delayed responses of ganglion cells in the frog retina: the influence of stimulus parameters upon the discharge pattern. *Kybernetik* **6,** 112–119.