management of similar studies in patients with retinal degenerations. Preliminary data have revealed that a rhythm in the ERG can be detected in a family with dominantly inherited retinitis pigmentosa after 3 days of entrainment.11

Key words: rod, electroretinogram, circadian, diurnal rhythm, disc shedding, entrainment, retinitis pigmentosa

From the Berman–Gund Laboratory for the Study of Retinal Degenerations, Harvard Medical School, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts. *Present address: Retina Foundation of the Southwest, 8220 Walnut Hill Lane, Suite 012, Dallas, Texas 75231, and Department of Ophthalmology, Southwestern Medical School, Dallas, Texas 75235. Supported in part by National Eye Institute Project Grant EY00169 and in part by the National Retinitis Pigmentosa Foundation, Baltimore, Maryland. Reprint requests: Michael A. Sandberg, PhD, Berman–Gund Laboratory, Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, MA 02114.

References

Rod and Cone ERGs and Their Oscillatory Potentials

P. Ewen King-Smith,* David H. Loffing,‡ and Ronald Jones*

Normal human ERGs were recorded from a dark-adapted subject using white and colored test flashes. Oscillatory potentials (OPs) were studied after high-pass digital filtering. When blue and red responses were compared at equivalent photopic intensities, OPs were visible at much lower intensities for the blue flashes. As the intensity was reduced from maximum, the first (negative) wave for red flashes maintained a latency of 20–25 msec before being lost in noise, whereas the first wave for blue flashes increased its latency progressively from 25 to 60 msec. These differences between photopically matched red and blue responses are interpreted to be due to rod-generated responses. When blue, orange, and white responses were compared at equivalent scotopic intensities, the latency of the largest negative wave was found to be similar for all three colors. The authors interpret this wave to be the beginning of the rod-generated OPs, so that the preceding waves (particularly evident for orange flashes) are cone-generated OPs, and they propose that the existence of separate rod and cone OPs should be borne in mind when investigating clinical changes in OPs. Invest Ophthalmol Vis Sci 27:270–273, 1986

The oscillatory potentials (OPs) of the human electroretinogram (ERG) are high frequency wavelets which occur during the rising phase of the b-wave.1–3

Considerable clinical interest in OPs has been generated by the demonstration that they may be selectively reduced in diseases of the inner retina.2,3 Despite this interest, there is still much uncertainty about the physiological origins of the OPs. For example, there is considerable disagreement about whether they are derived only from cones, or whether rod responses can also generate OPs.1 We believe that the results reported here unequivocally demonstrate that both rods and cones contribute to the OPs.

Materials and Methods. Potentials were recorded using a gold foil electrode4 (EL50, SC Electronics) and amplified by a Data Inc. 2124 amplifier (Fort Collins, CO) with low and high frequency cuts at 0.2 and 500 Hz. This amplified signal was sampled at 1-msec intervals and averaged by a North Star Horizon computer (San Leandro, CA). Oversize responses due to blinks or eye movements were rejected. Averages of 50 to 200 responses (to 1 flash per sec) were stored on magnetic disk and were later digitally high-pass filtered to emphasize the OPs by convolving the average with a weighting function w(t) consisting of a delta function minus a gaussian function defined by
\[ w(0) = 1 - k \]
\[ w(t) = -k \cdot \exp(-t^2/2s^2), \quad \text{for} \quad t = 0, \]

where \( t \) is time in msec, \( s \) is the standard deviation of the gaussian distribution which was 3.2 msec (equivalent to a cut-off frequency of 50 Hz), and \( k \) was adjusted so that the time integral (sum) of \( w(t) \) was zero.

The visual stimulator was a 50-cm ganzfeld illuminated by a Grass PS22 Photostimulator (Quincy, MA). Color was controlled by Grass colored filters (Model 5CF) and intensity was controlled by the photostimulator 'Flash Intensity' control and by Wratten neutral filters. Photopic intensities of white flashes and scotopic intensities of white and colored flashes were calibrated using a Pritchard 1980 Photometer; (Burbank, CA) care was taken to use relatively low photoc currents so that the brief (10-μsec) flashes did not overload the photometer. Relative intensity calibrations were confirmed using a United Detector Technology PIN 3DP silicon photocell (Culver City, CA) (and Schott KG3 heat filter) connected to a Keithley 610C Electrometer (Cleveland, OH) used as a coulombmeter. We estimated photopic intensity for blue and red flashes by matching the amplitudes of their 30-Hz flicker ERG to a corresponding response to white flicker; we used this technique (rather than using the Pritchard 'photopic' measurements for red and blue flashes) because the ERG is a response from the whole retina, whereas Pritchard photopic measurements reflect macular function (with corresponding absorption by the macular pigment). The ganzfeld could also be illuminated by a steady background field which was calibrated by the Pritchard photometer. For measurements in dark-adapted conditions, we waited until the amplitude of consecutive averages taken at 5-min intervals agreed to within 5%, and the ambient luminance of the ganzfeld was kept to a low level (about \( 2 \times 10^{-6} \) scotopic cd/m\(^2\)).

Results reported here are for the left eye of a 44 yr, normal white male (the first author) with his pupil dilated with 2 drops of 0.5% tropicamide. The major findings were confirmed in 2 other normal subjects.

**Results and Discussion.** Figure 1 shows dark-adapted responses to blue and red flashes and to red flashes on a blue background of 7 scotopic cd/m\(^2\); this background was chosen to eliminate most of the rod component of the ERG without having much effect on the cone response. The starting height of each trace indicates the photopic intensity of the test flash in log units. OPs are seen on the rising edge of the b-wave for all three conditions. The major finding is that these OPs can be seen for such low photopic intensities of blue flash that there is no significant response from the corresponding red flash. If OPs were derived only from cones, one would expect to see equal amplitude of oscillations from photopically matched blue and red flashes.

Figure 2 shows the results of Figure 1 replotted after high-pass digital filtering (see Methods). OPs are evident for much lower intensities of blue flash than for photopically matched red flashes. For red test flashes, the first OP maintains a latency of 20–25 msec and soon disappears into noise as intensity is reduced. For blue test flashes, the first OP remains visible over a much larger range of intensities.
Fig. 3. Unfiltered ERG responses for blue (left column, dominant wavelength 475 nm), orange (center, dominant wavelength 587 nm), and white (right) flashes in the dark adapted eye. The starting height of each response gives the corresponding value of log intensity in scotopic cd sec/m².

A wider range of intensities, and its latency gradually increases from about 25 msec at high intensities up to over 60 msec before it disappears into noise. The most reasonable explanation of the great difference between photopically matched blue and red responses is that the OPs generated by low-intensity blue flashes are derived from rod responses. (An alternative explanation in terms of responses from blue-sensitive cones would seem improbable in view of the relatively small contribution of these cones to the ERG and also because the corresponding unfiltered responses of Figure 1 have the characteristic wave form associated with rod responses.)

Figure 3 shows unfiltered responses to blue, orange, and white flashes, which in this case have been plotted according to their scotopic intensities. There is good agreement between corresponding responses at low intensities, confirming that these low level responses are derived from rods. At higher intensities, there are differences in the early part of the responses for the different colors that must be due to cone responses.

Corresponding high-pass filtered responses are shown in Figure 4. Because the height of any trace corresponds to its scotopic intensity, any wave which is generated by the rods should appear at corresponding latencies in all three columns. The largest negative wave in each trace does indeed occur with similar latencies in all three columns. This has been emphasized by marking with a dot the latency and corresponding scotopic intensity of the largest negative wave. For blue flashes (left column) these dots have been connected by lines, and these lines have been reproduced in the center and right columns. A striking agreement can be seen between the general trend of the dots and lines in both center and right columns; a slight discrepancy between dots and lines in the center column may indicate a small interaction between rod and cone ERGs.

The good agreement between dots and lines demonstrates that the largest negative wave of each response is generated by a rod mechanism. For blue flashes, this largest wave is the first wave at all but the highest intensities, and this is consistent with the previous demonstration (Fig. 2) that most blue-flash OPs are rod-generated. For orange flashes, the largest negative wave is the second one at high intensities and the third at medium intensities; the preceding waves are presumably cone-generated. For white flashes, an early cone wave can be seen at high intensities.

In summary, we conclude that in a dark-adapted subject, there is a large rod contribution to the OPs. The rod-generated OPs are generally delayed relative to the cone-generated OPs and, with our technique of digital high-pass filtering, the beginning of the rod OPs corresponds to the largest negative wave. We believe that it is important to keep the subject well dark-adapted to demonstrate the rod OPs, and failure to achieve good dark adaptation may explain why rod OPs have not been more frequently demonstrated.

The clearest demonstration in the literature of separate rod and cone contributions to the OPs of the normal human ERG is probably that of Stodtmeister. He has shown that the action spectrum for generating
OPs in the dark-adapted eye is similar to the scotopic luminosity function. In addition, his results show some of the features of the present study—particularly the large variation in the latency of rod-generated responses as a function of flash intensity and some of the changes in waveform of responses to orange flashes as intensity is reduced. The spectral sensitivity measurements of Wachtmeister also support the proposal that there is a rod contribution. The clinical finding of greatly reduced OPs in some types of congenital stationary night blindness is also indicative of a rod contribution.

We believe that the evidence for rod-generated OPs is now unequivocal. This paper indicates how separate rod and cone contributions may be recorded and recognized. We propose that the existence of separate rod and cone OPs should be borne in mind when investigating clinical changes in OPs.

Key words: ERG, rod ERG, cone ERG, oscillatory potentials, digital filtering

Acknowledgments. We thank Drs. John Armington, Glenn A. Fry, and Peter Gouras for their advice.

From the College of Optometry and Biomedical Engineering Center, The Ohio State University, Columbus, Ohio. Supported by NIH grant EY-04948 and the Ohio Lion’s Eye Research Foundation.

Submitted for publication: April 23, 1985. Reprint requests: Dr. Ewen King-Smith, College of Optometry, 338 W. 10th Ave., Columbus, OH 43210.

References


Prognostic Value of Laser Interferometric Visual Acuity in Amblyopia Therapy

Arkady Selenev, Kenneth J. Cuffreda, Rochelle Mozlin, and David Rump

There has been no simple clinical test which accurately predicts post-therapy visual acuity in amblyopic eyes. Since grading test patterns generally yield optimal visual acuity in amblyopic eyes, the authors sought to determine if pre-therapy laser interferometric grating visual acuity would predict conventional post-therapy visual acuity in functional amblyopia. In 90% of the patients who completed therapy, the pre-therapy laser visual acuity was within two lines of the post-therapy Snellen visual acuity. Thus, pre-therapy laser visual acuity is a good prognostic indicator of conventional post-therapy visual acuity in amblyopic eyes. Invest Ophthalmol Vis Sci 27:273–277, 1986

Treatment for remediation of amblyopia involves several months of occlusion of the dominant eye, frequently in conjunction with specific visuo-motor training procedures, all of which are aimed at improving visual acuity as well as overall sensory-motor ability in the amblyopic eye. Unfortunately, there has not been any simple clinical test which predicts post-therapy visual acuity with a high degree of accuracy. Over a decade ago, it was reported that laser interferometrically determined assessments of visual acuity in amblyopic eyes resulted in gross overestimations when compared to standard Snellen measures (as well as high contrast, square-wave grating estimates of visual acuity) when targets were equated for luminance. However, if these laser-generated grating targets represented an optimal stimulus arrangement, then such measures may instead reflect visual acuity potential. In our experiment, we tested this hypothesis by comparing pre-therapy laser visual acuity to pre- and post-therapy clinical measures of visual acuity in a group of patients with functional amblyopia.

Materials and Methods. A commercially available, clinically based, low-energy, helium–neon laser interferometer (Rodenstock Retinometer) was used to produce high luminance (450 cd/m²) interference fringes. The target consisted of a circular (5.5°), high contrast (96%), sinusoidal grating that could be oriented at either