Principles and Practice of Clinical Electrophysiology of Vision

Editors

JOHN R. HECKENLIVELY, M.D.
Professor of Ophthalmology
Jules Stein Eye Institute
Los Angeles, California

GEOFFREY B. ARDEN, M.D., PH.D.
Professor of Ophthalmology and
Neurophysiology
Institute of Ophthalmology
Moorfields Eye Hospital
London, England

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University of Oregon Health Science Center
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Adaptation Effects on the Electroretinogram

Peter Gouras
Cynthia Mackay

Studying visual adaptation of the human retina by using the electroretinogram (ERG) provides insights into the function of the photoreceptors and probably the retinal pigment epithelium, both likely candidates for containing the genetic defect in a large variety of different hereditary retinal degenerations. Visual adaptation depends on a number of different processes working together. They can be broadly grouped into those involving the transduction machinery of the photoreceptor and those involving regeneration of the photopigment. The former has been called the "neural" and the latter the "photochemical" components of adaptation.[7, 8]

GROWTH OF THE CONE ELECTRORETINOGRAM DURING LIGHT ADAPTATION

The cone ERG increases gradually in amplitude during light adaptation an average of 75% over a period of 20 minutes. This increase is initially fast and later slower so that after 20 minutes little further change is apparent. This increase involves both the a- and b-wave components of the ERG, and both waves follow a similar time course. This involvement of the a-wave strongly suggests that the photoreceptors are responsible for the effect. The action spectrum for the effects of light adaptation on the ERG parallels the cone action spectrum. The phenomenon is greatest at suprathreshold levels of stimulation and fails to occur at threshold levels, which suggests a significant change in the relationship between light absorbed and response produced during the course of light adaptation, i.e., the input/output function. An increase in the intensity of the adapting light shortens the time course of the ERG, measured as b-wave implicit time, but this occurs almost immediately, and the implicit time then remains constant during the subsequent slow increase in response amplitude. The stronger the adapting light, the smaller the overall ERG amplitude, but the percent growth during light adaptation appears to be the same. This slow increase in amplitude is thought to reflect the redepolarization of the cones after their initial hyperpolarization to the adapting field. It does not resemble light rise of the electro-oculogram.[9]

This is a somewhat surprising effect because psychophysical studies of sensitivity changes during light adaptation indicate that there may be a slight decrease or no change in sensitivity over comparable time periods and certainly no progressive increase in responsiveness.[2, 3] However, all these measurements were taken at threshold, and the ERG changes are also nonexistent at threshold but become quite large at suprathreshold levels. Granit and Therman[10] in 1935 indicated that the ERG response to flicker increased during the course of light adaptation. Previous workers have made observations that are in agreement with our observations (see Chapter 45). Burian[6] appears to have been the first to have noticed this effect in the single-flash ERG. Armington and Biersdorf[2] examined it quantitatively. They found a relatively small effect that involved only the b-wave and not the a-wave, but they only used a 22 degree field and did not separate cone from rod responses. The introduction of the Ganzfeld test and adapting fields greatly facilitates isolation of the cone ERG and dramatically exposes the large magnitude of this effect. Hood[11] reexamined this flicker effect in the frog retina and concluded that it involved cone adaptation and the a- as well as the b-wave, both of which conclusions are in complete agreement with our own results on the low-frequency, i.e., nonflickering, cone ERG. Recently Miyake et al.[12] have used this growth in the cone flicker ERG with light adaptation clinically and discovered an exaggerated growth of this response in an incomplete form of hereditary stationary nyctalopia.

This area of research is important in several respects. First it provides a means of minimizing variability between measurements of the cone ERG obtained by different laboratories or even within the same laboratory. Understanding this nonstationary nature of the light-adapted cone ERG enables one to take measures to control it. Second, the response itself provides a new insight into the physiology of cone adaptation and into certain forms of retinal degenerations.

EFFECT OF BACKGROUND ILLUMINATION ON THE CONE ELECTRORETINOGRAM

Increasing the level of background illumination decreases the amplitude and the implicit time (b-wave) of the cone ERG. There is a monotonic relationship between the strength of the adapting field and the percent reduction of the ERG and the decrease in implicit time (Figs 50–1 and 50–2). We have examined these changes in normal subjects and in subjects with various forms of retinal degeneration by using near-threshold cone stimuli to elicit the ERG, thus eliminating the growth that occurs with light adaptation (just discussed). Table 50–1 shows our current results.

Although the sample is still small, it seems that all retinitis pigmentosa (RP) patients, including Usher's syndrome and Leber's amaurosis, are less affected by the adapting field than are normals. This is true for the reduction both in b-wave amplitude and in b-wave implicit time. The most striking finding is that patients with Leber's amaurosis have implicit times that are unaffected by our brightest adapting lights. This is most remarkable considering that their ERG amplitudes at high levels of background illumination are similar to many of the other RP patients. Our tentative interpretation of this is that they have a relatively large number of functioning cones but these cones have virtually no photopigment. This is what one might expect to find under such circumstances: normal implicit times in the dark but prolonged ones in the light because the adapting light is being absorbed ineffectively and therefore these cones remain relatively dark-adapted. The implicit times of test flashes on a zero background are larger in other forms of RP than in normal individuals. This implies that other differences occur in these conditions. We have also found that older normal subjects' ERGs are less changed by adapting lights than are those of younger ones. This occurs for both

TABLE 50–1.

Results of Background Illumination on Normal Subjects and Those With Various Forms of Retinal Degeneration

				Log Photopic Trolands					
		Dark		1.7		2.8		4.1	
Subjects	No.*	%B	ms	%B	ms	%B	ms	%B	ms
Normals <40 years	11	98	34	87	32	51	28	13	23
Normals >40 years	9	97	37	90	35	54	29	15	24
RP simplex	7	97	43	85	39	76	38	37	33
RP dominant	5	97	48	93	46	70	41	27	35
Cone/rod	2	93	41	97	40	82	38	19	31
Leber's amaurosis	3	92	35	95	35	91	35	73	35
Usher's syndrome	1	87	37	74	43	100	35	74	27

*No. = number of subjects; %B = percent maximum b-wave amplitude; ms = implicit time; RP = retinitis pigmentosa.

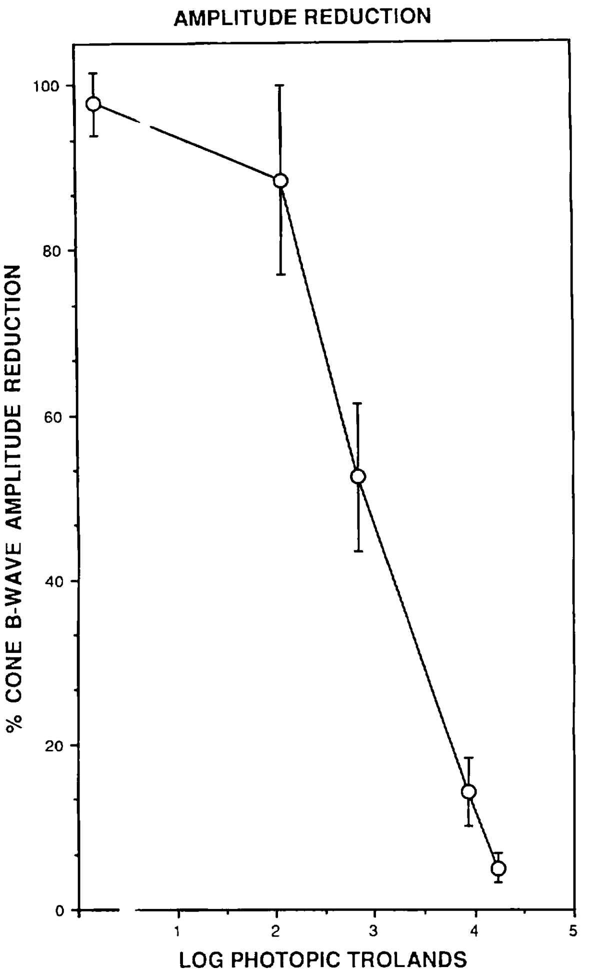

FIG 50–1.

The relationship between the percentage of cone ERG b-wave amplitude reduction and Ganzfeld fields of different photopic luminances. These results were obtained from 20 normal subjects except for the highest luminance, which represents only 3 subjects. The *vertical lines* are the standard deviations. The response is obtained with a red (Wratten 29) filter that produces an identifiable cone ERG at all background fields.

implicit time and amplitude reduction. Again the implicit times of older normals are longer than younger normals even in the dark. Again this implies that another factor than cone pigment density alone may be operating here to produce these changes, perhaps media transparency.

Using the Ganzfeld adapting field as the independent variable and leaving the deep red stimulus flash constant provide a new dimension to studying the electrophysiology of retinal disease: it can be examined independently of absolute ERG amplitude. The amplitude of the ERG to a first approximation reflects the number of functioning photoreceptors and diminishes with the progression of the disease. The change in amplitude and implicit time that is produced by light adaptation is presumably independent of the number of photoreceptors, depending on the ability of each photoreceptor itself to adapt. Therefore early and advanced forms of degeneration become more comparable. These changes reflect unique physiological aspects of the retina that can now be studied. It is very conceivable that the percent reduction in b-wave amplitude varies independently of the reduction in implicit time so that some degenerations may be distinguishable by comparing these two parameters. For example, the one case of Usher's syndrome we have now studied (Table 50–1) shows a very slight reduction in response amplitude that is comparable to subjects with Leber's amaurosis, but with Usher's syndrome the pa-

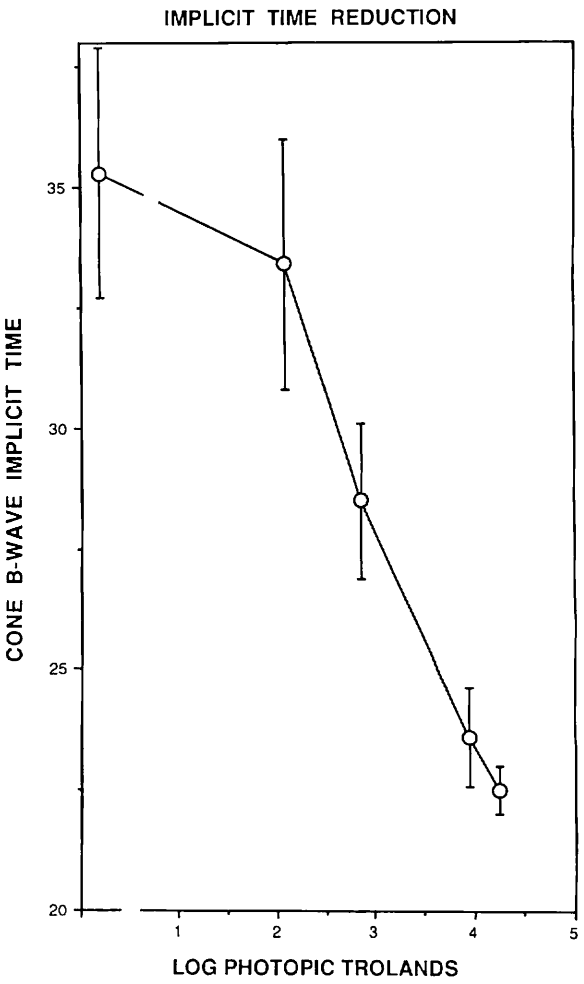

FIG 50–2.

The relationship between cone b-wave implicit time in milliseconds and Ganzfeld fields of different photopic luminances. Otherwise everything is the same as Figure 50–1.

tient has a significant reduction in his implicit time that none of the patient with Leber's amaurosis have. Larger sampling of these and other forms of RP may more clearly demonstrate whether this new method can distinguish different forms of RP by differences in the way the cone photoreceptor light-adapts.

DARK ADAPTATION OF THE CONE ELECTRORETINOGRAM

It is necessary to understand prior light adaptation before beginning to examine what would happen in the dark. For example, if RP cones are not absorbing as well as normal cones, then it would be misleading to measure dark adaptation following exposure to the same physical adapting light. Such a light might not adapt RP cones as much as normal cones, and their recovery might occur more rapidly than normal. Such a result has in fact been reported.[4] Other authors[1, 5] have reported that some RP patients adapt more slowly than normal. These observations were made on rod rather than cone adaptation, however, but the cones might also dark-adapt slowly.

Our own attempts to examine cone ERG dark adaptation were influenced by reports[13] that there was a slow rod influence that increased the amplitude of the dark-adapting cone ERG, a sort of rod/cone inhibition that was turning off. We now have repeatedly studied the dark-adapting cone ERG by using a deep red flash, and we do not find any slow increase in amplitude that follows the time course of rhodopsin regeneration. If, however, we use a stimulus that also affects the rods, we do see a gradual increase in amplitude that parallels the slower adaptation of the rods. We have concluded that dark adaptation of the cone ERG does not result in a change in amplitude after the first few minutes when using 10^4 photopic trolands of prior Ganzfeld light adaptation. The major change in the cone ERG occurs within the first 2 minutes of dark adaptation. Following our strongest Ganzfeld light-adapting field (17,000 photopic trolands), the cone b-wave of both a normal and an RP simplex subject increases rapidly during the first 100 seconds in the dark, with a slight suggestion of an "overshoot." The same relative amplitude intensity relationship and time course holds for both, although the RP response is only 1/10 of the normal amplitude. With this adapting light (11,000 photopic trolands) we are mainly studying neural rather than photochemical adaptation.

DARK ADAPTATION OF THE ROD ELECTRORETINOGRAM

Dark adaptation of the rod ERG is a slow process, and because of this, rod adaptation has seldom been examined clinically by means of the ERG.

Figure 50–3 shows the time course of adaptation of the rod ERG in a rhesus macaque following a 5-minute exposure to 7,000 photopic trolands. Results are shown for two different test lights, both blue, but one is 1/10 the strength of the other. The greatest changes occur within the first 10 to 15 minutes, especially with the brighter light. The time course at which the dark-adapted response is approached seems similar for both tests light, which

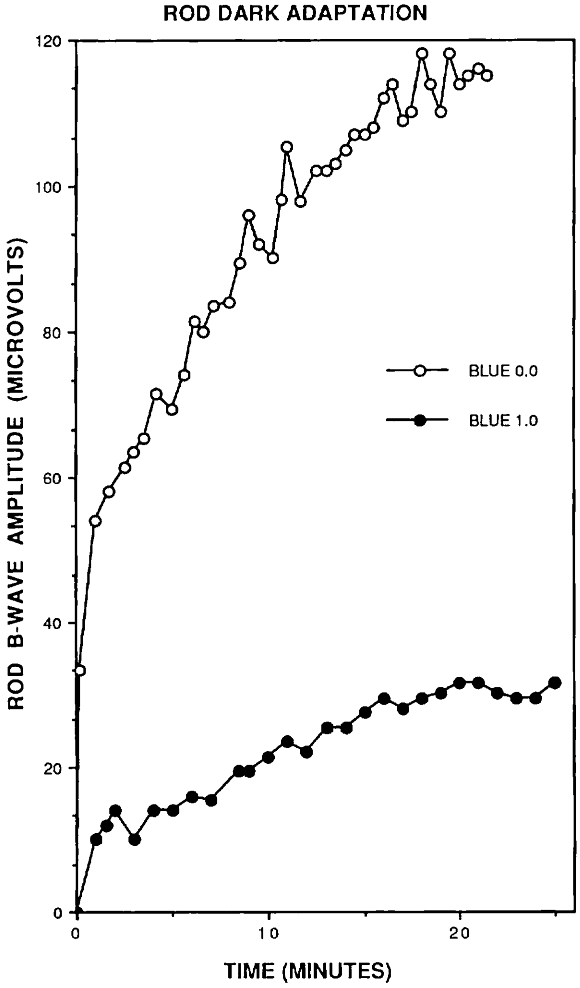

FIG 50–3.
The change in rod b-wave amplitude in the dark after exposure to a Ganzfeld field of 500 photopic trolands. The test light is blue (Wratten 98), of two different intensities (maximum and 1/10 of this), 10 μs in duration, and presented every second.

implies that the brighter light is not itself producing any significant degree of light adaptation.

We have been determining the time that it takes for the response obtained at 1 minute to double in amplitude. This doubling time is about 10 minutes in normal subjects. This strategy has the advantage of limiting the study of rod dark adaptation to a more reasonable amount of time, and it leads to a number that reflects the kinetics of rod dark adaptation.

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