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Light adaptation and the luminance-response function of the cone electroretinogram

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Abstract. Cone electroretinograms are typically isolated by presenting stimulus flashes against rod-desensitizing adapting fields. To investigate the manner in which adapting-field luminance affects cone electroretinogram response properties, we measured cone electroretinogram luminance-response functions of two normal subjects, with stimuli presented against adapting fields that ranged in luminance from −1.2 to 2.1 log cd/m^2. A flicker rate of 31.1 Hz was used to isolate cone electroretinograms under all adaptation conditions. A hyperbolic equation of the form $(R/R_{max}) = L^n/(L^n + K^n)$ was fitted to each luminance-response function by a least-squares criterion. As adapting field luminance increased, the best-fit values of the variables K and n increased, which is in general agreement with results of electrophysiologic studies of light adaptation in retinal neurons. However, R_{max} values also increased with adapting field luminance. The change in all three of these variables with adapting field luminance must be considered in the interpretation of cone electroretinogram luminance-response functions from patients with retinal disorders.

Introduction

The relationship between flash luminance and the amplitude of the electroretinogram (ERG) of the human rod system has been described by a hyperbolic equation of the following form

$$R/R_{max} = L^n/(L^n + K^n) .$$

In this equation, R represents the response to a flash of luminance L, R_{max} represents the response maximum, K represents the luminance required to generate a response one-half the amplitude of R_{max}, and n is a dimensionless slope variable. This analysis has been used to make inferences about the pathophysiologic mechanisms underlying retinal diseases [1–3]. For example, a selective decrease in R_{max} has been interpreted as indicating a decrease in the total number of generators contributing to the rod ERG

[1, 2], although it has been suggested that other mechanisms may contribute slightly to reductions in R_{max} [3].

The luminance-response function of the cone ERG can also be described by the above equation [4–6]. However, whereas rod ERGs are usually obtained under dark-adapted conditions, cone-mediated responses are typically isolated by presenting flash stimuli against a rod-desensitizing adapting field. Since patients with retinal disorders may have an altered response to the adapting field as well as to the flash stimuli, it is important to determine how changes in adapting-field luminance may influence the cone ERG luminance-response function. In the present study, we examined this question by recording cone ERG response functions under steady-state conditions of light adaptation spanning a 3.3-log unit range.

Subjects and methods

ERG records were obtained from two subjects, aged 44 years (subject 1) and 45 years (subject 2). Each subject had best-corrected Snellen visual acuity of 20/20 or better and had normal results of ophthalmic examination. Subject 1 had a mild deuteranomaly, whereas subject 2 had normal color vision.

ERGs were acquired by means of a Burian-Allen contact lens electrode referenced to a forehead electrode; the left earlobe was grounded. Recordings were obtained with a Nicolet Compact Four signal averaging system (amplifier frequency bandpass of 1–1000 Hz), stored on floppy diskettes and measured off-line.

White (xenon) strobe flashes were presented in a commercial ganzfeld (Nicolet) against an achromatic (tungsten) adapting field. To ensure that cone-mediated responses were isolated under all conditions of light adaptation, stimuli were presented as 31.1-Hz flicker trains. Stimulus luminance was controlled with Wratten No. 96 neutral-density filters and internal strobe settings. Adapting-field luminance was controlled with banks of incandescent bulbs. The photopic luminances of the flicker stimuli and adapting fields were calibrated with an EG&G Model 550 photometer equipped with a luminance probe and a flash integrator.

The pupil of the test eye was dilated with 1% tropicamide and 2.5% phenylephrine hydrochloride drops. The eye was then dark adapted for at least 40 minutes. Drops of 0.5% proparacaine hydrochloride anesthetized the cornea, and the contact lens was inserted under dim long-wavelength illumination. A steady adapting field was then presented at one of six luminances (-1.2, -0.6, 0.1, 0.7, 1.3 and 2.1 log cd/m^2), each used in a separate session. The subject was adapted to the field for 30 minutes, a period sufficient to achieve a stable level of response [7]. At the end of the light-adaptation period, a luminance-response function was obtained, with

the use of eight stimulus luminances ranging from −1.0 to 0.8 log cd s/m^2 (integrated luminances of individual flashes presented in isolation). Each flicker train was presented for approximately 1.3 s, with a 1-minute interval between stimulus presentations. No responses were recorded during the initial 0.5 s of stimulus presentation; then five 160-ms epochs were averaged.

Results

Figure 1 presents two representative sets of flicker ERG waveforms obtained from subject 2. Responses on the left were obtained with a luminance series presented against an adapting field of 0.1 log cd/m^2; responses on the right were obtained with the same series presented against an adapting field of 1.3 log cd/m^2. For both adapting-field luminances, flicker ERG amplitude increased systematically with stimulus luminance. For stimuli of low luminance, increasing the adapting-field luminance reduced the response amplitude, as expected. In contrast, when stimuli of high luminance were used, increasing the adapting-field luminance increased the response amplitude.

Figure 2 illustrates the luminance-response functions derived from the waveforms of Fig. 1. Each data point represents the average of the peak-to-trough amplitudes of the individual responses composing each of the waveforms. The solid lines in Fig. 2 represent the least-squares fit solutions to the equation given in the Introduction for these two data sets. The values of R_{max}, log K and n were each increased at the higher adapting-field luminance.

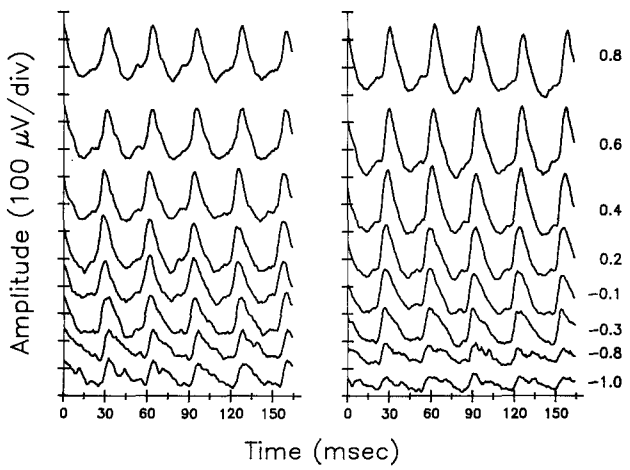

Fig. 1. Cone flicker ERGs obtained from subject 2 to stimuli presented against an adapting field of 0.1 (left) or 1.3 (right) log cd/m^2. The luminance (log cd s/m^2) of the stimulus used for a particular waveform is indicated at right.

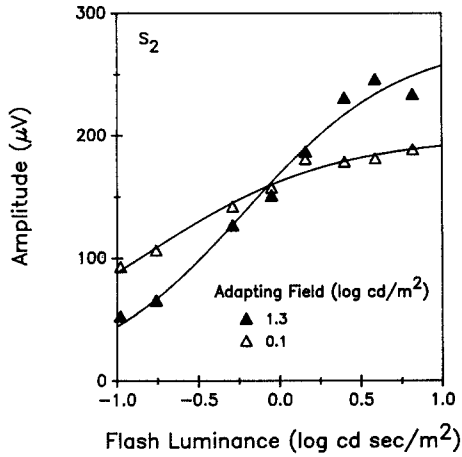

Fig. 2. Cone flicker ERG luminance-response functions derived from the waveforms shown in Fig. 1. Solid lines represent the least-squares fits of the equation to the data; rms errors were 5.5 and 12.2 for adapting fields of 0.1 and 1.3 log cd/m^2, respectively.

The luminance-response functions obtained at each of the six adapting conditions were analyzed in a similar manner. Figure 3 plots the values of the least-squares fit variables of the equation as a function of adapting-field luminance. In general, values of log K (Fig. 3A) and n (Fig. 3B) increased with increasing adapting-field luminance. In addition, values of R_{max} became larger with increasing adapting-field luminance (Fig. 3C). In fact, R_{max} values obtained for the highest-luminance adapting fields were more than 100 μV above those obtained for the lowest-luminance fields.

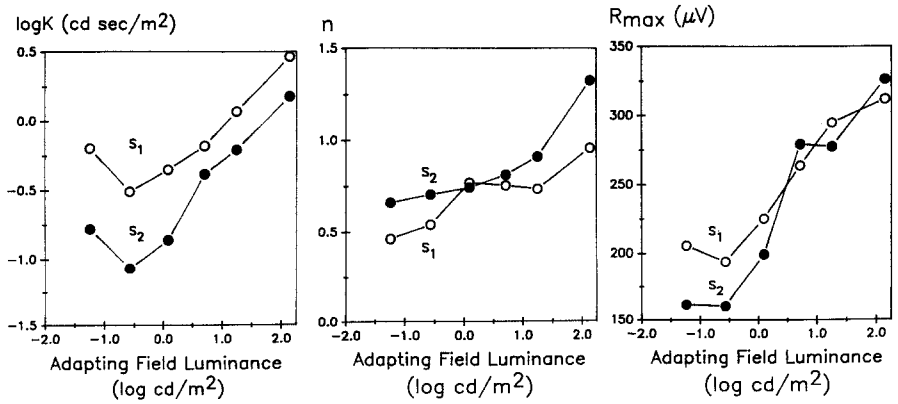

Fig. 3. Variables derived from least-squares fit of the equation to each luminance-response function, plotted as a function of adapting field luminance, for subjects 1 (open circles) and 2 (filled circles).

Discussion

There are several parallels between the present results and those obtained from electrophysiologic recordings in vertebrate retina. For example, as the level of light adaptation increases, stimulus-response functions of retinal neurons in the cone pathway are normally translated along the stimulus luminance axis such that a higher luminance is required to evoke a response of a criterion amplitude [8–12]. The increase in log K of the cone ERG with increasing adapting-field luminance (Fig. 3A) is likely to reflect this feature of light adaptation. The slope of the cone photoreceptor stimulus-response function changes little as the level of light adaptation increases [8, 9, 11], but response functions of second-order neurons become steeper [10, 12]. Therefore, the increase in n with increasing adapting-field luminance (Fig. 3B) is not unexpected, since the cone ERG is likely to include a substantial contribution from postreceptoral neurons [13].

In contrast to the increase in R_{max} observed in the present study (Fig. 3C), most single cell studies of the cone pathway have not reported an increase in response amplitude with increasing levels of light adaptation [11, 12]. However, an exception can be found in white perch cone horizontal cells, the responses of which are smallest under conditions of dark adaptation and are enhanced by light adaptation [14, 15]. The adaptation-induced enhancement of white perch horizontal cell responses appears to reflect a neuromodulatory influence involving dopamine [15]. However, the relationship between the response properties of these cells and of the human cone ERG remains to be determined.

Our results indicate that the interpretation of changes in the luminance-response function of the cone ERG that might occur in patients with retinal disorders may be more complex than for the rod ERG function. This is primarily because an adapting field is used to isolate the cone ERG, whereas the rod ERG is typically obtained under dark-adapted conditions. For example, if a disease acts to decrease the total number of retinal generators contributing to the ERG, but those that remain are normal, then the luminance-response function of the rod system will show a selective reduction in R_{max}, while the value of log K will be normal [1–3]. In comparison, if a disorder reduces the absorption of light by the photoreceptors, then the rod ERG luminance-response function will show an increase in log K, due to the decreased effectiveness of the test stimulus, but the value of R_{max} will be normal.

For the cone system, a decrease in the total number of ERG generators will produce changes in the luminance-response function that are comparable to those for the rod system. Specifically, there will be a selective decrease in the value of R_{max}. However, reduced light absorption by the photoreceptors will reduce the effectiveness of both the test stimulus and the adapting field used to isolate the cone system response. As a result, the cone

ERG luminance-response function will show an increase in the value of log K but will also have a decrease in R_{max}. This decrease in R_{max} occurs because the reduced absorption of light from the adapting field will in turn reduce the magnitude of the adaptation-induced increase in R_{max} (Fig. 3C). Therefore, both disease mechanisms will produce a reduction in R_{max} for the cone system.

In conclusion, an interpretation of abnormalities in the luminance-response function of the cone ERG is complicated by the presence of the adapting field used to isolate cone system responses. Recording cone ERGs in the absence of any adapting field (for example, by using flicker stimuli in the dark) will not yield a solution to this problem, since the cone ERG appears to be suppressed under dark-adapted conditions [7, 16, 17]. Further work will be necessary to determine whether other methods can be used to derive the cone ERG luminance-response function to make more accurate assessments of the pathophysiology underlying retinal disorders affecting the cone system.

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