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Cone phototransduction and growth of the ERG *b*-wave during light adaptation

Kenneth R. Alexander [a,b,*], Aparna Raghuram [a], Aruna S. Rajagopalan [a]

[a] *Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, 1855 W. Taylor St., Chicago, IL 60612, USA*
[b] *Department of Psychology, University of Illinois at Chicago, 1007 W. Harrison St., Chicago, IL 60612, USA*

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Abstract

The purpose of this study was to determine whether cone redepolarization accounts for the amplitude increase of the *b*-wave of the human electroretinogram (ERG) during light adaptation. The time course of the *b*-wave amplitude increase was compared to the time course of the change in the activation phase of cone phototransduction, as derived from a delayed Gaussian model applied to the leading edge of the ERG *a*-wave. ERG recordings were obtained from five visually normal subjects, alternately in the presence of the adapting field (*adapt-on* condition) and 300 ms after its temporary extinction (*adapt-off* condition). The proportional increase in amplitude was less for R_{mp3} (maximum amplitude of P3, the massed cone photoreceptor response) than for the *b*-wave for both adaptation conditions, and the time course of the amplitude increase for R_{mp3} was faster than that for the *b*-wave in the *adapt-off* condition. The results demonstrate that time-dependent changes in the activation phase of cone phototransduction have only a minimal role in governing the increase in the amplitude of the human cone-derived ERG *b*-wave during light adaptation. In addition, the systematic increase in *b*-wave amplitude and the decrease in *b*-wave implicit time in the *adapt-off* condition indicates that the ERG response measured shortly after adapting field offset does not necessarily represent the waveform of the dark-adapted cone ERG.

Keywords: *a*-wave; *b*-wave; Adaptation; Cone; Electroretinogram (ERG)

1. Introduction

The amplitude of the full-field, light-adapted ERG response to a brief flash is a common clinical index of the functional integrity of the cone system. However, the amplitude of the ERG response is known to depend on the duration of light adaptation. If the eye is continually exposed to an adapting field following a period of dark adaptation, the ERG *b*-wave shows a systematic increase in amplitude with a time course of several minutes (e.g., Armington & Biersdorf, 1958; Burian, 1954; Gouras & MacKay, 1989; Peachey, Alexander, Fishman, & Derlacki, 1989). There can also be a systematic decrease in the implicit time or time-to-peak of the *b*-wave during light adaptation (Peachey et al., 1989), although this is not a universal finding (Gouras & MacKay, 1989). Other components of the brief-flash ERG response also increase in amplitude during light adaptation, including the *a*-wave (Gouras & MacKay, 1989), the *i*-wave (Peachey et al., 1989), and the oscillatory potentials (OPs; Benoit & Lachapelle, 1995). An amplitude increase occurs in response to a long-duration stimulus, affecting the *d*-wave as well as the *b*-wave, although the time course of the amplitude increase is not equivalent for these two ERG components in either human or monkey (Murayama & Sieving, 1992). There is an increase in ERG amplitude in response to full-field flicker (Peachey, Alexander, Derlacki, & Fishman, 1992a; Peachey, Arakawa, Alexander, & Marchese, 1992b) and in the focal ERG (Weiner & Sandberg, 1991). The relative amplitude increase is smaller in the fovea than in the retinal periphery, as determined from the multifocal ERG (mfERG; Kondo et al., 1999).

* Corresponding author. Fax: +1 312 996 7770.
E-mail address: kennalex@uic.edu (K.R. Alexander).

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The mechanism underlying the amplitude increase of the *b*-wave during the course of light adaptation is presently uncertain. Based on the observation that the ERG *a*-wave increased in amplitude during light adaptation with a time course and magnitude similar to that of the *b*-wave, it was proposed that cone redepolarization is the primary underlying mechanism (Gouras & MacKay, 1989). In support of this hypothesis, it was reported recently that changes in the cone photoresponse during light adaptation are sufficient to account for the increase in *b*-wave amplitude in the rat retina (Bui & Fortune, 2005). However, the increase in the amplitude of the isolated P3 of the carp retina during light adaptation is less than for the *b*-wave (Horiguchi, Takabayashi, & Miyake, 1986). Furthermore, in primate retina, the amplitude increase of the *a*-wave may not have the same time course as that of the *b*-wave (Murayama & Sieving, 1992), which has led to the proposal that two different sites of adaptation, one photoreceptoral and one postreceptoral, are involved. A further consideration is that the amplitude of the *a*-wave is typically measured from the prestimulus baseline to the *a*-wave trough, and this measure may include a contribution from postreceptoral neurons (Bush & Sieving, 1994; Friedburg, Allen, Mason, & Lamb, 2004; Ueno, Kondo, Niwa, Terasaki, & Miyake, 2004). Therefore, the exact relationship between changes in the cone photoreceptor response and the amplitude increase of the *b*-wave of the human ERG during light adaptation remains to be clarified.

To address this issue, the present study investigated the extent to which changes in the activation phase of cone phototransduction contribute to the growth of *b*-wave amplitude during light adaptation in human subjects. The activation phase of the massed photoreceptor response (P3) of the cone system was derived by fitting a delayed Gaussian model (Hood & Birch, 1995) to the leading edge of the *a*-wave obtained at successive time points during light adaptation. There are two parameters in this model: R_{mp3}, which refers to the maximum amplitude of the P3 response, and *S*, which represents the sensitivity of the activation phase of phototransduction. Either or both of these parameters could change during light adaptation. Therefore, the time course of the change in these parameters of cone phototransduction was compared to the growth of the ERG *a*- and *b*-waves during light adaptation in visually normal human subjects.

In addition to defining the adaptational properties of the light-adapted cone ERG, it is of interest to derive the waveform of the brief-flash ERG of the cone system under dark-adapted conditions (Verdon, Schneck, & Haegerstrom-Portnoy, 2003). For example, if the dark-adapted cone response can be removed from the mixed rod and cone ERG response recorded to a brief flash under dark-adapted conditions, the isolated rod response can be obtained. As summarized by Verdon et al. (2003), previous approaches to estimating the dark-adapted cone ERG waveform have included: (1) a double subtraction method involving the ERG responses to short- and long-wavelength test stimuli obtained under dark-adapted conditions, (2) the measurement of the light-adapted ERG, and (3) a "paired-flash" technique in which a first flash desensitizes the rod system and then the response to a second flash is recorded in the absence of an adapting field. However, each of these techniques has potential drawbacks (Verdon et al., 2003). An alternative method described recently is to record the brief-flash ERG shortly after the termination of a rod-desensitizing adapting field (Robson, Saszik, Ahmed, & Frishman, 2003). This procedure was used in that study to derive the properties of the dark-adapted cone photoreceptor response, under the assumption that the cone system recovers from the effects of light adaptation while the rod system remains desensitized.

However, it is possible that this latter procedure does not capture the entire fully dark-adapted cone ERG response. For example, it has been reported that two different adaptational processes influence the amplitude of the cone ERG following a sudden change in adapting field luminance (Peachey et al., 1992b). One process, which has a rapid time course, serves to reposition the luminance-response function along the luminance axis following the adapting field change. The other process, which is relatively slow, reduces response amplitude by the same proportion at all stimulus luminances following the adapting field change. It is possible that the cone ERG measured shortly after the offset of an adapting field may not represent the actual dark-adapted cone ERG response because there may be insufficient time for the slower-acting adaptational process to be completed. To investigate this possibility, we compared the time course of changes in the parameters of cone phototransduction with the growth of the *a*- and *b*-waves when brief-flash ERG responses were obtained following a temporary cessation of an otherwise continuously presented adapting field.

2. Method

2.1. Subjects

Five visually normal female subjects, ages 25 (S_1), 28 (S_2), 36 (S_3), 53 (S_4), and 60 (S_5) years, participated in the study. The subjects had best-corrected visual acuities of 20/20 or better in the tested eye, refractive errors no greater than 5 D of myopia, clear ocular media, and normal-appearing fundi on ophthalmologic examination. Appropriate institutional review board approval was obtained, and the experiments were undertaken with the understanding and written consent of each subject.

2.2. Stimuli and recording system

The full-field test stimuli were presented in an Espion ColorDome desktop Ganzfeld controlled by an Espion electrophysiology console (Diagnosys LLC, Littleton, MA). ERGs were recorded with a Burian-Allen bipolar contact lens electrode, grounded with an earclip electrode. Responses were acquired with the Espion console. Amplifier bandpass settings were 0.15–500 Hz and the sampling frequency was 2 kHz.

Full-field ERGs were recorded in response to achromatic flashes of 2.8 and 4.0 log td-s (assuming a dilated pupil diameter of 8 mm) that were generated by a xenon strobe in combination with a UV-absorbing filter. Stimulus flashes were presented against an achromatic, rod-desensitizing