of serotonin may also reflect discrete effects at serotonin 1 or serotonin 2 receptors (Table 1). Synaptic excitation but not inhibition by iontophoretically applied serotonin is antagonized by drugs such as cyproheptadine, bromo-LSD, methysergide, and cinanserin, which are 40 to 400 times more potent at serotonin 2 than at serotonin 1 receptors. Lisuride, LSD, and metergoline, which influence iontophoretic serotonin inhibition, are 15 to 200 times more potent at serotonin 1 receptors than the peripheral serotonin antagonists, which fail to inhibit serotonin. Metergoline, which blocks both inhibition and excitation of serotonin, displays low nanomolar K_i values for both types of receptors. Since iontophoretic results are only qualitative, one cannot establish numerical correlations with drug affinities for receptor binding sites or behavioral potencies.

The data suggest that serotonin inhibition and excitation are mediated by serotonin 1 and serotonin 2 receptors, respectively. The excitatory actions of serotonin may reflect a facilitation of excitatory influences of other substances such as acetylcholine and glutamate (*22*). Since the serotonin behavioral syndrome appears to involve serotonin 2 receptors, it may reflect excitatory synaptic actions of central serotonin. The relationship between serotonin 1 receptors and both the serotonin cyclase and neural inhibition is less clear than the link of serotonin 2 sites and excitation. A major problem in evaluating serotonin 1 receptor binding, the serotonin-sensitive adenylate cyclase, and iontophoretic serotonin inhibition is the lack of specific, high-affinity antagonists. Whereas cyproheptadine has nanomolar affinity for serotonin 2 sites and a 500-fold predilection for serotonin 2 over serotonin 1 receptors, no such selective antagonist has yet been described for serotonin 1 receptors, the serotonin cyclase, or serotonin-mediated inhibition.

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11 August 1980; revised 21 October 1980

Rod-Cone Interaction in the Distal Human Retina

Abstract. *During the rod-isolated phase of dark adaptation, b-wave implicit time of the human cone electroretinogram increased exponentially with a time constant corresponding to that for the regeneration of rhodopsin. In the presence of different photopically equated short-wave backgrounds, cone b-wave implicit time varied inversely with the scotopic brightness of the background. Taking into account the origin of the b wave, these measurements support the idea of a rod effect on cone function in the distal human retina.*

Convergence of rod and cone signals in the human visual pathway has been suggested from both psychophysical and electrophysiological studies. For example, psychophysical measurements have shown that a background light that is above rod threshold, but below cone threshold, can raise cone increment threshold (*1*), elevate dark-adapted cone threshold (*2*), and reduce the brightness of cone-detected stimuli (*3*). Interaction between rod- and cone-generated signals has been observed electrophysiologically in single-unit recordings from ganglion cells and the optic nerve of the rhesus monkey (*4*) and presumably occurs also in human ganglion cells and optic nerves. Intracellular recordings from the cat have demonstrated that light stimulation of both rods and cones produces a greater hyperpolarization of cones (*5*), cone-type horizontal cells (*5, 6*), and cone bipolars (*7*) than does stimulation of cones alone. Electron microscopic studies have revealed gap junctions between rod spherules and cone pedicles in humans (*8, 9*) and macaque monkeys (*9, 10*), raising the possibility of functional confluence in the outer plexiform layer of the retina. The present study demonstrates that rod-cone interaction can be detected in the b wave of the human electroretinogram (ERG) and, therefore, originates in the retina distal to ganglion cells.

Fig. 1. Dark-adapted ERG's from a normal observer in response to the 640-nm stimulus and a photopically matched 500-nm flash. Each tracing begins at stimulus onset and is an average of 16 responses. The lower response is generated by cones alone, lacking the slow b-wave component of the upper response (arrow) characteristic of the rod system. A pure cone ERG to the 640-nm stimulus was seen also in a second normal observer. The three remaining normal subjects showed in addition a very late, small rod oscillation to this stimulus (*12*).

0036-8075/81/0515-0829$00.50/0

Cone ERG's were elicited from five normal observers by a 48°, 640-nm flash presented in Maxwellian view (*11*). Pilot studies in normal observers and in patients with congenital rod monochromatism, congenital stationary night blindness, and congenital dichromatism (*12*) indicated that this stimulus could be used to isolate a cone ERG generated predominantly by the long-wavelength cones (Fig. 1). Following a predominantly rod bleach (*13*), cone ERG's were recorded to this 640-nm stimulus subsequent to psychophysical cone dark adaptation (*14*). During this rod isolated phase of dark adaptation, implicit time (time to peak) of the cone b wave increased systematically (Fig. 2A). This increase in b-wave implicit time corresponded to an exponential function with a time constant of 7.5 minutes, which was comparable to that reported for the regeneration of rhodopsin as measured with retinal densitometry (*15*).

In the presence of backgrounds of different wavelength but equal photopic brightness (*16*), cone b-wave implicit time was least at 450 nm, increased toward 410 and 500 nm, and remained stable for background wavelengths greater than 500 nm (Fig. 2B). The variation in b-wave implicit time for background wavelengths less than 520 nm followed the variation in scotopic brightness of the background (*17*). For photopically matched backgrounds above 500 nm, the data approximated a horizontal line and showed an average b-wave implicit time shorter than that seen for complete dark adaptation (Fig. 2A), suggesting an adaptational effect on the cone b wave mediated by cones and not by rods (*18*). The shorter b-wave implicit times for backgrounds below 520 than for those above 500 nm (Fig. 2B) raises the possibility that rod and cone adaptational effects on cone b-wave implicit time are additive (*19*).

Computer analysis of the waveform change in the cone ERG during the rod phase of dark adaptation (Fig. 3A) revealed a subcomponent of the response whose amplitude depended on rod function. When the response to the 640-nm stimulus obtained at 2 minutes was subtracted from those obtained to the same stimulus at 4, 12, and 24 minutes, the "difference" waveform increased in amplitude but remained fixed in implicit time with time in the dark. Computer subtractions of the cone ERG obtained in the presence of the 450-nm background from those obtained in the presence of photopically matched backgrounds of longer wavelengths that were progressively dimmer for the rods (Fig. 3B) showed a similar result. These analyses indicated that these variations in cone b-wave implicit time were due to amplitude changes of a late subcomponent of the response.

The present studies demonstrate that rod function can influence cone function as monitored in the temporal aspects of the cone b wave. Since the b wave recorded at the cornea as a transretinal potential reflects current flow distal to the ganglion cell layer of the retina (*20*), the results support the idea that rod-cone interaction must exist in the distal human retina.

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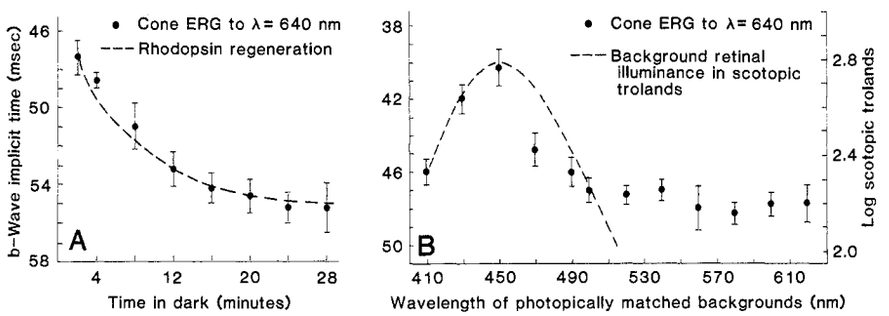

Fig. 2. (A) Means (filled circles) and standard errors based on five normal observers for cone b-wave implicit times during dark adaptation. Curve (dashed line) is an exponential function with a time constant of 7.5 minutes (*15*). (B) Means (filled circles) and standard errors based on four normal observers for cone b-wave implicit times as a function of background wavelength. A fifth observer showed the same trends but was not tested at all wavelengths. Curve (dashed lines) and right-hand ordinate identify the scotopic retinal illuminance of backgrounds of wavelength less than 520 nm (*17*). For the backgrounds above 500 nm, this dashed curve continues to fall (not illustrated).

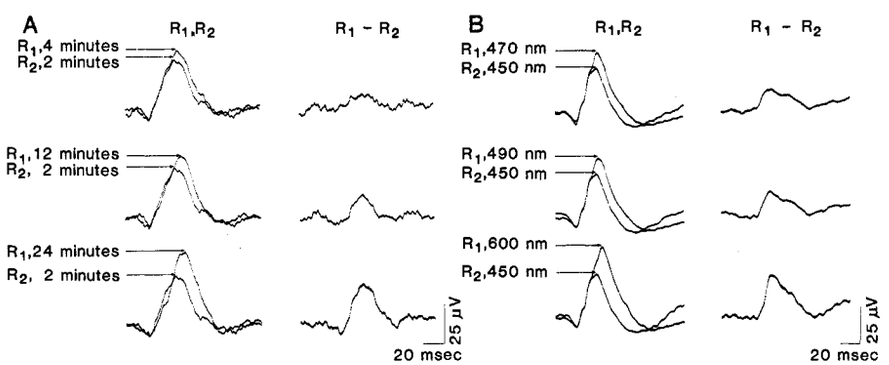

Fig. 3. (A) Cone ERG's to a 640-nm stimulus from a normal observer obtained at 2 minutes in the dark (R_2) either superimposed on (R_1, R_2) or subtracted from ($R_1 - R_2$) responses (R_1) obtained at later times in the dark. Each tracing begins at stimulus onset and is an average of eight responses. (B) Cone ERG's to a 640-nm stimulus from a normal observer obtained in the presence of a 450-nm background (R_2) either superimposed on or subtracted from responses (R_1) obtained in the presence of backgrounds of longer wavelength. Each tracing begins at stimulus onset and is an average of 64 responses.

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11. The stimulus, with a half bandwidth of 10 nm, was presented for 20 msec every 500 msec at a retinal illuminance of 250 photopic trolands and was centered on the fovea with the aid of a cross hair or dim red fixation point. Calibrations of retinal illuminance in photopic trolands were done with the aid of an electronic digital radiometer (United Detector Technology, model 10A) equipped with a photopic filter; adjustments were made with balanced cross-rotating Inconel-coated neutral density wedges. The eye to be tested was first dilated with a 0.5 percent tropicamide and dark-adapted for 45 minutes. ERG's were monitored with a contact lens electrode, differentially amplified, and summed with a signal-averaging computer.
12. Two congenital rod monochromats and three of the normal observers showed after 30 minutes of dark adaptation a small response that was 50 msec later than, and did not overlap with, the

cone b-wave responses of the normal observers or the ERG's of four patients with congenital stationary night blindness. With less than 20 minutes of dark adaptation or in the presence of background lights of less than 580 nm (Fig. 2), no response was obtained from the rod monochromats and no rod response from these normal observers. Testing of dichromatic observers with this stimulus indicated that 70 percent of the cone response was generated by long wavelength ("red") cones and about 30 percent by middle wavelength ("green") cones.

13. A 2-minute exposure to a 65°, 491-nm (40-nm half bandwidth) field of 2000 photopic trolands was used. This light was calculated to bleach approximately 27 percent of rod photopigment [W. A. H. Rushton, *J. Physiol. (London)* **156**, 166 (1961); E. Pugh, Jr., *ibid.* **248**, 393 (1975)] and 9 percent of cone photopigment [T. N. Cornsweet, *Visual Perception* (Academic Press, New York, 1970), p. 153].
14. In a pilot experiment with the 640-nm stimulus and the 491-nm bleach, dark-adaptation curves obtained psychophysically from three normal observers showed that the cone plateau (dark-adapted cone threshold) was reached at approximately 2 minutes in the dark and the rod plateau by 28 minutes in the dark.
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16. Backgrounds were photometrically equated at 25 photopic trolands. In addition to the photometric calibration, we observed that psychophysical increment thresholds for a 0.5°, 640-nm flash falling on the rod-free area of the fovea varied within 0.3 log unit over these backgrounds, confirming that they were matched with respect to cone light adaptation.
17. Conversion from photopic to scotopic trolands was calculated according to G. Wyszecki and W. S. Stiles [*Color Science, Concepts and Methods, Quantitative Data and Formulas* (Wiley, New York, 1967), p. 226].
18. An adaptational effect on the cone b wave not mediated by rods but presumably by cone function alone was shown also in the following way: the 600 nm background was increased stepwise from 25 to 500 photopic trolands and cone b-wave implicit time systematically decreased by 9 msec. But 500 photopic trolands is equivalent to 63 scotopic trolands, which is below the background level for a rod effect on the cone ERG under the present test conditions (Fig. 2B).
19. Patients with retinitis pigmentosa and night blindness have cone b-wave implicit times that are normal in the dark [M. A. Sandberg. E. L. Berson, M. H. Effron, *Invest. Ophthalmol. Visual Sci.* **19** (Suppl.), 259 (1980); E. L. Berson, *Vision Res.* **20**, 1179 (1980)], but delayed about 10 msec in the light [E. L. Berson, P. Gouras, M. Hoff, *Arch. Ophthalmol.* **81**, 207 (1969); E. L. Berson, *Trans. Am. Acad. Ophthalmol. Otolaryngol.* **81**, 659 (1976)]. These delays in the light could reflect a primary cone defect or, in view of this study, be secondary to diminished rod function, at least in part.
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21. Supported in part by National Eye Institute research grant EY00169 and in part by the National Retinitis Pigmentosa Foundation, Baltimore, Md., and the George Gund Foundation, Cleveland, Ohio.

4 November 1980

Color and Luminance: Independent Frequency Shifts

Abstract. *Simultaneous opposite spatial frequency shifts can be obtained in chrominance and luminance channels. The chrominance shift cannot be transferred interocularly. Chrominance and luminance channels seem to perform similar but independent spatial frequency analyses.*

One task in vision research is that of determining to what extent visual dimensions such as spatial frequency, luminance, and color are processed in the same or in separate channels. We report that a spatial frequency shift (*1*) can be induced with chromatically defined gratings and that this shift can occur independently of a luminance-induced shift; this result implies that spatial frequency is analyzed separately in chrominance and luminance channels.

Investigations of color channels have shown that some effects can be obtained with chromatically defined stimuli, whereas others cannot (*2*, *3*). While it is known that color information can be used in spatial frequency analysis, chrominance and luminance channels have never been clearly dissociated. Virsu and Haapsalo (*4*) induced color-based spatial frequency shifts, but their gratings contained both luminance and chrominance differences, and so the effect may have been mediated by a channel in which the two are linked. Such a linkage appears possible as some form-color effects require both luminance and chrominance contrast (*5*). Stromeyer *et al.* (*6*) showed that exposure to sinusoidal violet gratings elevates the threshold for violet but not red gratings, again showing that color can be used in spatial frequency analysis, but not conclusively showing independence of color from luminance.

Much previous work has shown that color-related effects do not transfer interocularly, thus implying that chrominance channels are driven monocularly (*7*). However, there is some indication that the relation between chrominance channels and ocular dominance is complex (*8*). We examine this problem with respect to the chromatic spatial frequency shift.

In the two experiments, observers were exposed to red-green or black-white square-wave gratings like those used by Blakemore and Sutton (*1*) to induce a spatial frequency shift. The stimuli were generated by computer on a color television monitor (*9*).

We used red-green gratings in order to eliminate the operation of luminance channels and thereby isolate chrominance channels. This aim can be achieved only indirectly, however, and there is no general agreement as to the appropriate psychophysical technique (*10*). Some researchers opt for luminance matching by heterochromatic flicker photometry or the minimal distinct border technique; others use brightness matching. We used a combination of these techniques to approximately equate red and green (*11*). Because we could not be certain that we were not activating luminance channels, we used an opposing aftereffects paradigm to ensure that no residual luminance differences in the color stimuli could mediate a frequency shift in a luminance channel.

Accordingly, observers were adapted to alternate presentations of red-green and black-white gratings in which the former were arranged so that the upper grating was of higher spatial frequency than the lower, and the reverse was true for the latter (Fig. 1). Thus, if there is a residual luminance difference in the chromatic gratings, any resulting luminance-based frequency shift with the chromatic test would be overwhelmed by the shift in the opposite direction generated by the achromatic gratings. A color-based frequency shift is therefore direct evidence of an independent chrominance channel.

Observers sat 2.5 m from the display,

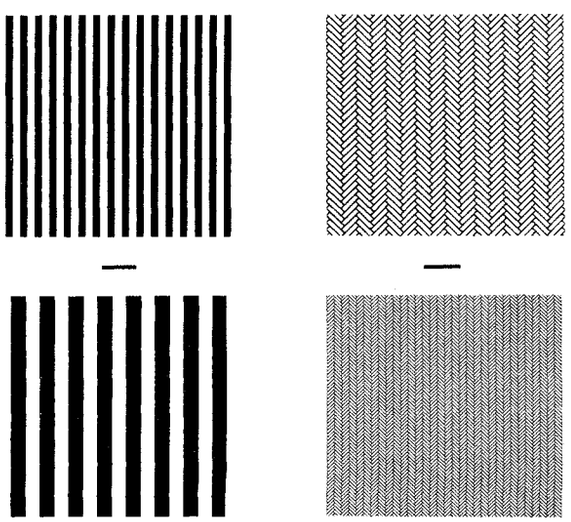

Fig. 1. Schematic representation of the adapting stimuli used in experiments 1 and 2. The black-white gratings are represented on the left, and the red-green gratings on the right. The relative locations of high and low spatial frequencies are reversed. The test gratings were of intermediate equal frequencies, similarly arranged above and below a central fixation point.

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