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20 April 1971; revised 4 August 1971 ■

Prolonged Color Blindness Induced by Intense Spectral Lights in Rhesus Monkeys

Abstract. *Prolonged exposure of rhesus monkeys to intense blue light produces long-term changes which are consistent with loss of response of those cones that contain a photopigment with peak absorption at 445 nanometers. The 90 percent reduction of spectral sensitivity in the blue region has lasted more than 5 months. Reduced sensitivity to long wavelengths is produced by adaptation to light of 520 nanometers. This reduced sensitivity, which lasts no more than 30 days, is attributed to a temporary loss of response of the cones containing a photopigment with peak absorption at 535 nanometers.*

Studies on the effects of intense spectral light on the eye have been few, and have not dealt with recovery time of the eye after exposure. In an early study, Burch (*1*) created effects similar to hereditary color blindness in human subjects with "intense color adaptation." These effects lasted up to 1 hour. Burch exposed his subjects briefly to sunlight of unknown intensity filtered through broad-band filters. Auerbach and Wald (*2*) produced sizable but brief changes in photopic spectral sensitivity with 5-minute exposures to white light and to red, orange-red, orange, yellow, green, and blue light produced by broad-band filters. The retinal illuminances of these lights were up to 10^7 trolands. The subjects required 5 to 10 minutes to return to the initial state of adaptation to dark.

Brindley (*3*) exposed his own eye to retinal illuminances of 25,000 to 300,000 trolands for repeated 30-second periods. Using color matching as a measure, he found that the effects he produced were similar to hereditary dichromacy and in some instances to monochromacy. These effects lasted only 40 seconds, but Brindley also reported intense afterimages that lasted for 6 to 10 hours and a faint afterimage that lasted for 8 months. In other reports of duration of effects after exposure to intense light, subjects were exposed to intense but brief flashes of white light or broad-band light of an unspecified wavelength-energy distribution (*4*). In most studies (*4*), recovery of visual function was measured. In no instance, except Brindley's report of afterimages, has evidence been presented for long-term changes in visual thresholds in humans after brief exposures to radiant intensities below those which create gross pathology.

When rats have been exposed to intense white light for a long period, the rods of the eyes show microscopic degeneration of the membranes of the outer segments. This degeneration is not accompanied by gross retinal lesions (*5*). Recently, Kuwabara (*6*) found similar outer segment degeneration in cones of monkeys exposed to a high retinal irradiance, only 10 percent below that which produces gross thermal lesions.

These examples of rod and cone damage by white light led us to look for selective degeneration of different classes of cones caused by long exposure to intense light of different wavelengths. We exposed rhesus monkeys to intense blue and green lights for long periods, and measured spectral sensitivity before and after exposure.

Intense blue light caused a loss of short wavelength sensitivity that has persisted for more than 5 months. In contrast, we found a recovery time of 18 to 30 days for the changes in sensitivity to long wavelengths that followed exposure to green light. Using our model of spectral sensitivity (*7*), we relate the change effected by blue light to the cones that contain a photopigment with peak absorption at 445 nm; and the change caused by green light to the cones that contain a photopigment with peak absorption at 535 nm. Our results give us the hope of distinguishing between classes of color receptors by associating morphological changes of the type seen by Kuwabara and others (*5*, *6*) with the functional loss.

The optical system for both the spectral sensitivity measurements and for the spectral retinal irradiation consisted of three Maxwellian-view channels. (i) The white background channel produced a white background path of equal energy, which subtended a visual angle of 18 deg and produced retinal illuminance of 3400 trolands. All of the data are from increment-thresholds taken against this background. (ii) The test channel produced a 50-msec flash of 2-deg diameter, which was superimposed on the center of the white background. This channel used a 1600-watt compact xenon arc lamp, double monochromator, and counter-rotating neutral density wedges to reduce the flash to threshold. (iii) The spectral background channel used collimated light from the xenon arc lamp to produce a high intensity 18-deg spectral exposure path through narrow-band interference filters. The maximum radiant intensity, at the cornea, of the spectral exposure path was 10^{-4} watt/steradian, (*8*) which equals retinal power density of 10^{-3} watt/cm^2 (neglecting preretinal absorption). This is one-thousandth of the retinal power density for threshold retinal burns reported by Ham *et al.* (*9*) or for pigment epithelial damage reported by Friedman and Kuwabara (*10*).

Subjects for the experiment were adolescent rhesus monkeys (*Macaca mulatta*) (*11*). The operant behavior procedure for increment-threshold measurements has been described (*12*, *13*). Threshold measurements were made at consecutive 10-nm intervals from 410 to 690 nm and then from 690 to 410 nm. The average of the two values was the threshold for that day.

The same operant behavior proce-

dure was used for retinal exposures to the intense spectral field. The chromatic channel was added to the white channel, and the animal was reinforced for responding to test flashes that were easily detected over the background. Each exposure session lasted 2½ to 3 hours, and repeated trials took 40 to 60 percent of each session. Although subjects' heads were not restrained, we are certain that they always looked into the exposure field during each trial, because they detected the test flashes, which occurred at random after the ready signal, with greater than 95 percent accuracy (*14*). Therefore, the minimum exposure period in each session was the total intratrial time, and we attempted to hold this period constant within an exposure series.

Figure 1 shows data from two experiments with 463-nm blue light of 6-nm half-bandwidth. In the first experiment (Fig. 1A) a radiant intensity of 3.9×10^{-4} watt/steradian at the cornea (1.1×10^{4} trolands) was applied in three series separated by 6-week intervals. Each series consisted of 80-minute daily exposures for seven consecutive days. The solid circles, data for the experimental eye before the first series, form a curve whose shape is characteristic of increment-threshold spectral sensitivity with high white background (*7*). The triangles are data for the animal's other eye a few weeks after the final exposure series. The circles with horizontal bars, data from 6 weeks after the first exposure series, show a reduction of 0.3 log unit in spectral sensitivity in the region from 410 to 480 nm (the blue peak). The circles with vertical bars, data from 6 weeks after the second exposure series, show an additional 0.3 log unit decrease in sensitivity in the blue region. The open circles, data from 6 weeks after the third series, show a further decline in the blue region. The total loss in the blue region after the third series is over 1 log unit, and there is almost no change in the green and red regions of the spectrum. The duration of the loss in the blue region can be seen from the crosses, data from five months after the final exposure series.

Figure 1B shows a slightly different experiment with a second monkey. The wavelength was the same as in Fig. 1A, but irradiance at the cornea was increased from 3.9×10^{-4} to 7.3×10^{-4} watt/steradian (2.3×10^{4} trolands). Exposure periods of 40 minutes, half as long as in Fig. 1A, were on seven consecutive days. Solid circles are data before the first exposure period, open circles are data from 2 weeks after the last exposure session, and crosses are data from 5 months after the exposure series. The triangles are the data for the animal's other eye 2½ weeks after the exposure series. The total loss of sensitivity over the region of the blue peak (410 to 480 nm) after 280 minute of exposure is the same as for the first monkey (Fig. 1A) after 60 hours of exposure.

Figure 2 shows data from experiments on two monkeys with intense green light. For the experiment in Fig. 2A we used a narrow-band filter with 520-nm peak and 6-nm half-bandwidth, which produced 8.6×10^{-4} watt/steradian (or 3.3×10^{5} trolands). The exposure series consisted of daily 55-minute sessions on ten consecutive days. For Fig. 2B we used a broad-band filter (510-nm nominal wavelength, 80-nm half-bandwidth) which produced $1.9 \times$

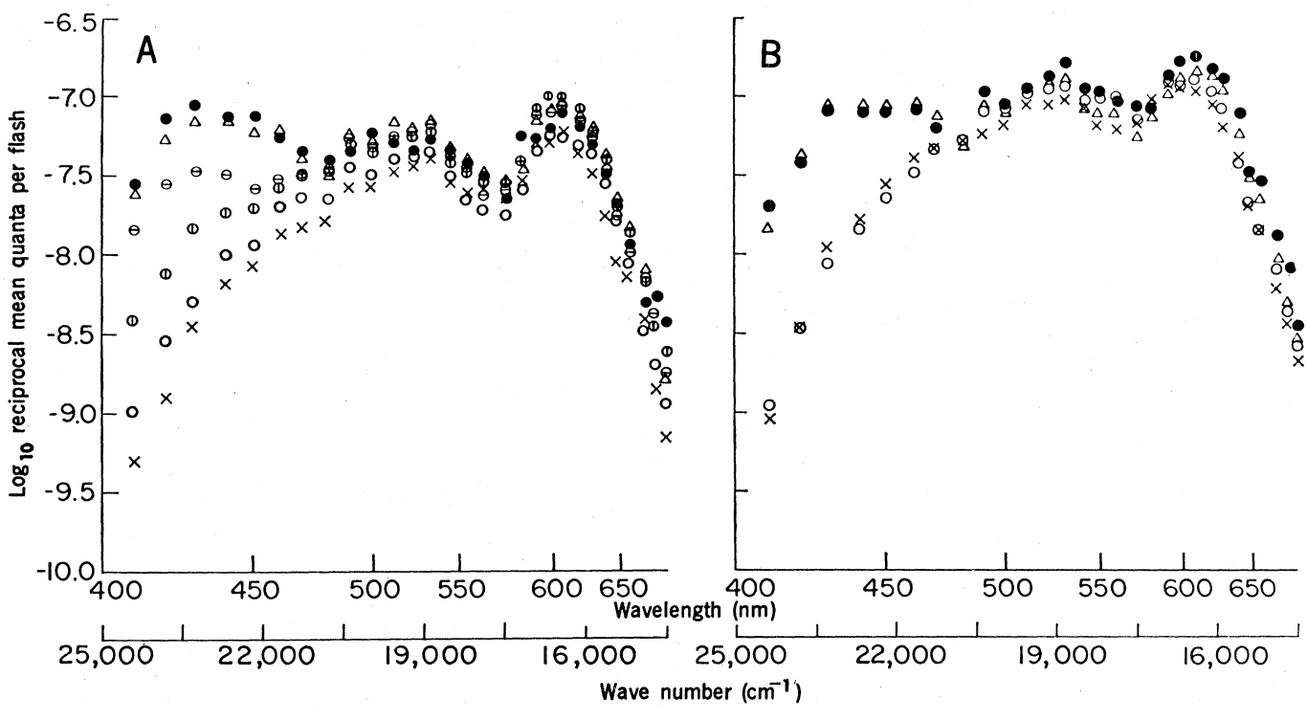

Fig. 1. Increment-threshold spectral sensitivity of two rhesus monkeys. In both experiments, the solid circles are data on the experimental eye before exposure, and open triangles are data on the unexposed eye 2½ weeks after the last exposure series. In (A) the eye was exposed to 463-nm light at radiant intensity of 3.9×10^{-4} watt/steradian at the cornea. Except where noted, measurements were made 6 weeks after the exposure time. Symbols and total exposure times are as follows: circles with horizontal bars, 560 minutes; circles with vertical bars, 1120 minutes; open circles, 1680 minutes; crosses, 1680 minutes (measured 5 months after exposure). In (B) the eye was exposed to 463-nm light for 280 minutes at 7.3×10^{-4} watt/steradian. Symbols are as follows: open circles, 2 weeks after exposure; crosses, 5 months after exposure.

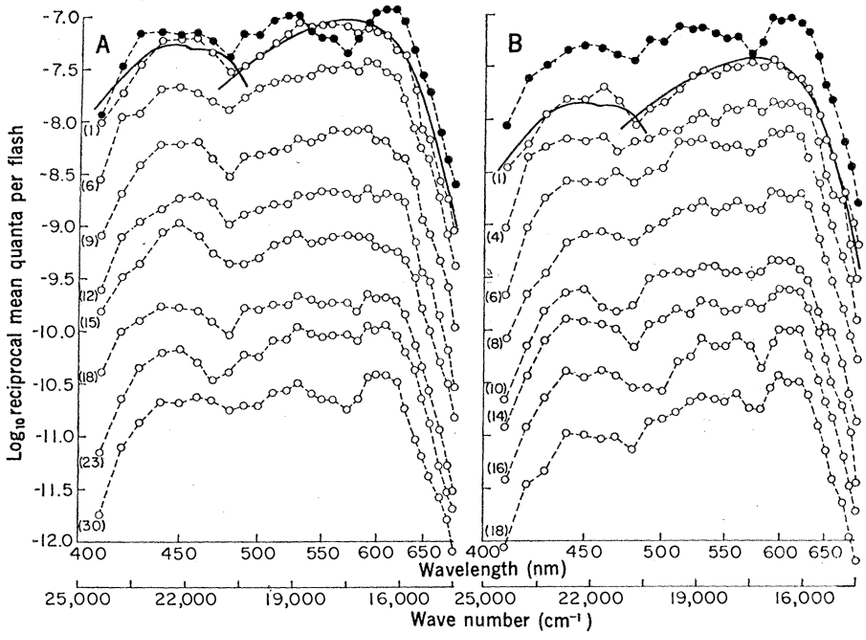

Fig. 2. Increment-threshold spectral sensitivity of two monkeys before and after exposure to green light. Solid circles are data before exposure. The open circles are data obtained at different days after exposure; the number to the left of each curve gives the number of days after exposure. The solid curves are the absorption spectra of the 575-nm and 535-nm cone photopigments. The data before exposure and 1 day after exposure are on the same scale; each successive day's measurements are displaced downward by 0.5 log unit for ease of viewing.

10^6 trolands. In this experiment the exposure series consisted of six daily 90-minute sessions. In both graphs, the solid circles are data before exposure, and each point is the average of three daily determinations. Each of the lower curves (open circles) shows spectral sensitivity data for a single day (day number given at left of each curve) after the exposure series. The data for the first day after the exposure series are on a true scale with respect to the control data, but each successive curve is displaced downward by 0.5 log unit for ease of viewing. These data show that the two monkeys experienced a sizable loss in sensitivity (except near 575 nm in the yellow region), and recovered gradually. Complete recovery had occurred by the 30th day for the animal in Fig. 1A and by the 18th day for the animal in Fig. 1B. The two solid curves superimposed upon the data for the first day after exposure are the absorption functions of the two cone photopigments with maximum absorption at 445 nm and 575 nm, derived from the absorption spectra of single cones (*7*). The animals were reduced to deuteranopia (absence of cone photopigment with maximum absorption at 535 nm) for periods lasting at least 24 hours for the monkey in Fig. 2B and at least 6 days for the monkey in Fig. 2A. The narrow peaks at 535 nm and at 610 nm are gone. They are replaced by the single broad peak at 575 nm which is fitted by a single photopigment absorption function. This is the same function that has been obtained above 500 nm on congenital deuteranopes (*15*). This result strongly supports our previous finding (*7*) that the 610-nm peak is the result of inhibitory interaction of the responses of cones with maximum absorptions at 535 nm and 575 nm.

These experiments demonstrate long-term loss of spectral sensitivity—lasting days or months rather than seconds or minutes—over different regions of the spectrum after prolonged exposure to intense light of different wavelengths. The nature of that loss is consistent with the statement that blue light eliminates the response of only those cones containing the 445-nm photopigment and that green light, while it reduces sensitivity elsewhere, eliminates the response of the cones containing the 535-nm photopigment. The effect of green light is temporary, and the 535-nm and 610-nm peaks gradually reappear over a period of weeks.

The time course of the recovery of these two peaks, hence of the cones containing a 535-nm photopigment, is similar to that shown in autoradiographic studies by Young (*16*) for the regeneration cycle of rod outer segments. Kroll and Machemer (*17*) have shown definite but incomplete regeneration of monkey cone outer segments in the month period after retinal detachment. Kuwabara (*6*) has observed regeneration of cone outer segments in monkeys in the 2 weeks after intense light exposure.

Intense exposure to blue light eliminates the peak at 445 nm, which is fitted by the absorption spectrum of cones containing a photopigment with maximum absorption at 445 nm. Intense exposure to green light does not affect the 445-nm peak, but it temporarily suppresses the peaks associated with the cones containing a photopigment with maximum absorption at 535 nm. Thus, for the first time, two kinds of prolonged dichromacy have been induced by intense spectral lights. The period of induced dichromacy was sufficiently long to imply spectrally selective tissue damage to different classes of cones, caused by selective absorption of energy in the cone photopigments. This is a new kind of lesion. It is different from the thermal lesion which is accounted for by energy absorption in the nonselective pigment epithelium of the retina.

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12 April 1971; revised 14 July 1971

Sensory Neglect Produced by Lateral Hypothalamic Damage

Abstract. *Unilateral lateral hypothalamic lesions in rats produce deficits in orientation to contralateral visual, olfactory, whisker-touch, and somatosensory stimuli. This syndrome of sensory neglect appears to be involved in some of the deficits in feeding and attack which follow bilateral lateral hypothalamic lesions.*

The lateral hypothalamus is important in both feeding and attack behavior. Electrical stimulation of this region can produce overeating (*1*) and stimulation-bound killing (*2*). Lateral hypothalamic lesions produce deficits in both behaviors (*3*). MacDonnell and Flynn (*4*) found that touching the contralateral upper or lower lip of a cat during unilateral hypothalamic stimulation elicited reflexive mouth opening. Furthermore, touching a discrete area in the contralateral maxillary snout region of the cat elicited reflexive head turning toward the stimulus. These reflexes, head turning and mouth opening, are involved in the cat's integrated biting attack on a rat. Increasing the intensity of lateral hypothalamic stimulation enlarged the effective sensory field around the mouth. In the absence of any hypothalamic excitation, touch around the mouth did not elicit the attack reflexes. MacDonnell and Flynn therefore suggested that lateral hypothalamic control over attack behavior may act partly through sensory systems, since hypothalamic excitation facilitates the action of sensory stimuli involved in eliciting such behavior.

Lateral hypothalamic control of sensory mechanisms has also been suggested by Turner's unpublished observations. Turner found that unilateral lesions in the amygdalo-lateral hypothalamic system of rats produced contralateral deficits in responding to visual and somatosensory stimuli. This experiment was undertaken, therefore, in order to extend Turner's observations and to determine the extent to which sensory deficits might contribute to the syndromes of aphagia and loss of attack.

Twelve female Sprague-Dawley albino and two male hooded rats were used. All rats were housed individually. Water in Richter tubes and food pellets on the cage floor were available at all times. Most rats received the tests described below for at least 1 week preoperatively. This provided a baseline against which to measure the effect of lateral hypothalamic damage. Rats were then anesthetized with Equithesin or Nembutal and placed in a stereotaxic instrument (David Kopf Instruments) with the skull level. Unilateral or bilateral lesions were made by passing 1 to 2 ma of direct current for 10 to 30 seconds through an insulated stainless steel anodal electrode (0-0 insect pin), bared to a 0.5-mm conical tip (*5*). All animals were tested on the day after the operation to evaluate initial deficits. Thereafter, the animals were tested two or three times per week in order to assess recovery of function.

Three sets of tests were used to measure sensory and motor functions. The first set measured head orientation to sensory stimuli. A normal rat investigates a stimulus by orienting its head toward it. As shown in Fig. 1, this natural response was used to determine the responsivity of rats before and after lateral hypothalamic damage. For example, to test vision on each side of the body, a 2 by 2 inch (5 by 5 cm) piece of white or yellow cardboard was moved in front of each eye. Normal

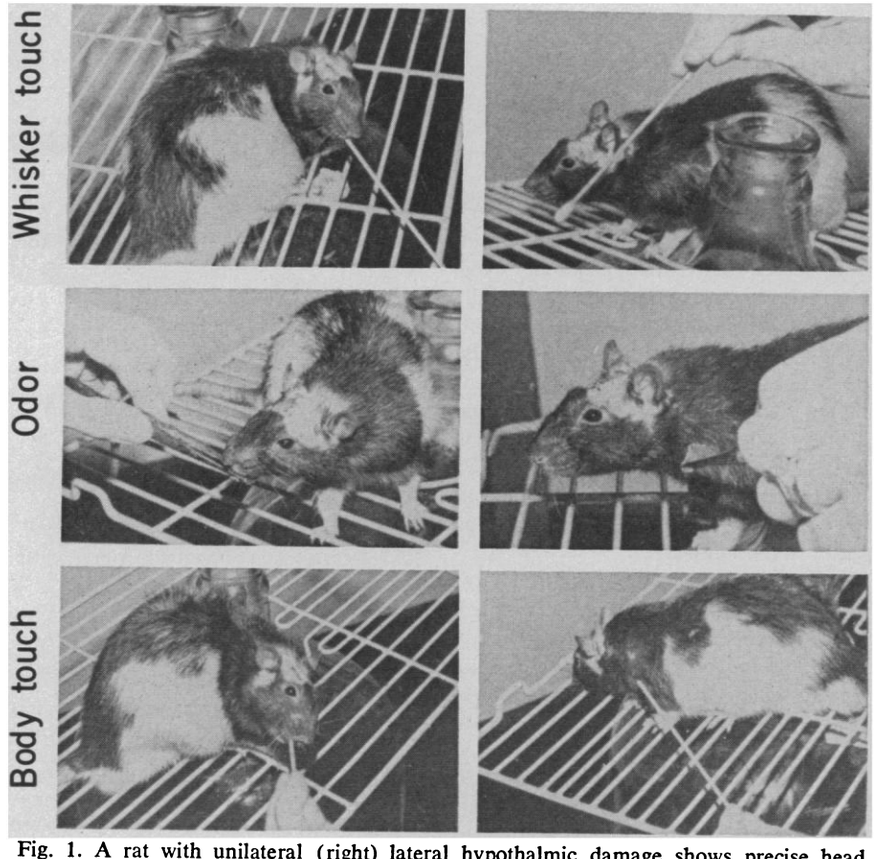

Fig. 1. A rat with unilateral (right) lateral hypothalmic damage shows precise head orientation and biting to various kinds of stimuli (whisker touch, odor, body touch) on the ipsilateral side (pictures at left) while neglecting the same stimuli presented contralaterally (pictures at right).