Neural Mechanisms of Chromatic Adaptation in L-Type Cone Horizontal Cells of the Carp Retina

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Abstract When a background light is delivered, the responsiveness of horizontal cells to light stimulus initially lowers but subsequently recovers gradually as shown by the increase in response amplitude to test light. These changes of responsiveness are observed when white or close wavelengths are used for both the background and test lights. However, the response amplitude to blue-green test light was initially enhanced but decreased and reached a steady state after the onset of red background illumination. The mechanism causing such a change of test responses was studied in the luminosity-type cone horizontal cells. The initial response enhancement was accompanied by an increase of the slope of hyperpolarizing phase, while the subsequent decrease of response amplitude was caused by the advancement of the recovery phase. The advancement of the recovery phase was eliminated by γ-aminobutyric acid (GABA) or Co²⁺ (50 µM), which blocks GABA-induced currents in cone terminals. Dopamine, which inhibits GABA release from horizontal cells, stimulated the advancement of the recovery phase. The time course of the hyperpolarizing phase was not affected by these agents. The enhancement and the subsequent decrease of test responses were also observed in 6-hydroxydopamine-treated retinas. The results suggest that the GABAergic feedback pathway from horizontal cells to cones advances the recovery phase of response to test light. It appears, therefore, that the feedback modifies the responsiveness of horizontal cells to light stimulus under a red background illumination. The mechanism enhancing response amplitude will be also discussed.

Key words: chromatic adaptation, horizontal cell, GABA, dopamine, cobalt.

Luminosity type (L-type) horizontal cells are second-order neurons located in the most distal part of the inner nuclear layer of the retina (Mitarai et al., 1974; Hashimoto et al., 1976). It is widely assumed that horizontal cells play an important
role in forming the receptive field surround of retinal neurons (Werblin and Dowling, 1969; Baylor et al., 1971; Toyoda and Fujimoto, 1983) and of color opponency (Fuortes et al., 1973; Stell et al., 1975; Toyoda et al., 1982).

Horizontal cells respond with graded hyperpolarization to light stimuli, and the response amplitude becomes larger as the intensity of light stimulus increases (Svaetichin, 1956; Tomita, 1965). The responsiveness of horizontal cells to light stimuli is affected by background illumination. When the background light is turned on, the responsiveness of horizontal cells lowers as shown by the decrease of response amplitude to a test flash (Naka, 1969; Takizawa, 1970; Dowling and Ripps, 1971). During background illumination, however, horizontal cells become increasingly sensitive to light stimuli and the amplitude of the response to test flash increases. These effects of background illumination are seen when white or close wavelengths are used for both the background and test lights (Naka, 1969; Takizawa, 1970; Dowling and Ripps, 1971) (Fig. 2A in this paper).

We recently observed that the amplitude of responses of L-type horizontal cells to blue-green test lights is initially enhanced but subsequently decreases and reaches a steady state after the onset of red background illumination (Fig. 1). The change in response to test lights during the background illumination is opposite to the process of light adaptation mentioned above. In this paper, the decrease in response amplitude during background illumination was mainly studied. It will be shown that the decrease of response amplitudes to test lights is caused by the advancement of the initiation of recovery from hyperpolarizing responses, which includes the GABAergic feedback from L-type horizontal cells to cone photoreceptors. The mechanism underlying the enhancement of response to test flash after the introduction of background light will be also discussed. Some of these results have been published in abstract form (Umino and Watanabe, 1987).

MATERIALS AND METHODS

Preparation, photostimulator, and recording procedure. Carp (Cyprinus carpio) were kept in an aquarium under a natural daylight condition. After carp were decapitated, retinas were isolated from the pigment epithelium and mounted, receptor side up, on millipore filter paper. The preparation was placed in an acrylic plastic chamber (about 0.5 ml) and was continuously superfused with an oxygenated solution (1.2 ml/min). All experiments, except where noted, were performed on the luminosity-type cone horizontal cells. Recordings were made with glass microelectrodes filled with 3 M KCl and had resistances of 50–100 MΩ when measured in 3 M KCl solution. The reference electrode was an Ag-AgCl immersed in a chamber filled with 2 M KCl that was connected to the recording chamber with an agar bridge. A two-channel photostimulator equipped with grating monochromators (7 nm half-band width) was used. In most experiments reported here, a test light of 50 ms was first delivered in the dark and then the same light was given repeatedly at 1 or 2 s intervals 100 ms following the onset of background illumination.
light. Unless otherwise mentioned, diffuse light was used. For each experiment examining the effects of chemical substances, a new retinal preparation was used.

Test responses at high speed were obtained, if necessary, by subtracting the response to red background light alone from the test response recorded under background illumination.

**Solutions.** The normal solution contained (in mM) NaCl 100, NaHCO₃ 20, KCl 2, CaCl₂ 1, MgCl₂ 0.5, and glucose 20, continuously bubbled with 97% O₂ and 3% CO₂ (pH = 7.4). Substances tested were γ-aminobutyric acid (GABA; Sigma Chem. Co.), bicuculline methiodide (Pierce Chemical Co.), picrotoxin (Wako Pure Chem. Co.), dopamine (Nakarai Tesque Inc.), and Co²⁺. These substances were dissolved in the normal solution to a desired final concentration.

**Destruction of interplexiform cells.** To destroy dopaminergic cells, 6-hydroxydopamine (6-OHDA; 20 μg) and pargyline (20 μg) were injected into the vitreous body of one eye on two successive days about 2 weeks before eye enucleation (cf. NEGISHI et al. (1981)). Destruction of the dopaminergic interplexiform cells was confirmed by the disappearance of greenish fluorescent cells under a fluorescence microscope (NEGISHI et al., 1981).

**RESULTS**

**General properties**

As shown in Fig. 1, blue-green (480 nm) test flashes covering a large field produced a small hyperpolarizing response of about −5 mV (●) in an L-type horizontal cell. Blue-green (480 nm) test lights of 50 ms duration were applied to the retina in darkness (●) and repeated 15 times during red (690 nm) background illumination (▲ and subsequent responses). Both light stimuli were diffuse. When background light was turned on, the response to test light was initially enhanced (▲). The amplitude of the response gradually decreased with prolonged background illumination and reached a steady state. The similar experimental conditions, except otherwise noted, were used throughout the present study. Dark membrane potential: −25 mV. Test light: $7.0 \times 10^2$ photons/(s·μm²). Background light: $7.0 \times 10^4$ photons/(s·μm²).
horizontal cell. When red (690 nm) background light was applied to the retina, response to the same test light was greatly enhanced (▲). However, during application of the background illumination, the response amplitude to the test light decreased and reached a steady state. Similar experiments were performed with various wavelengths of test lights (Fig. 2). The response enhancement and the subsequent decrease of response amplitude were prominent for blue-green (490 nm), but not for red (670 nm) test light. Response amplitudes for 670 nm test flashes gradually increased during a prolonged exposure to the background light (see the trace labeled by the arrowhead). The wavelength-dependence of the change of test responses is more clearly demonstrated in the plots of Fig. 2B, in which the spectral...
response curves in darkness (thick line) and during red background light (thin lines) are plotted. This figure shows that the response peak shifted from approximately 610 nm (in darkness) to approximately 510 nm during the initial phase of red background illumination, and it returned to long-wavelength during prolonged adaptation. These results indicate that the enhancement and the subsequent decrease of responses to test lights are most apparent when a blue-green test light is used, and that the change of test responses greatly depends on the wavelength of test light. Therefore, long-wavelength input to horizontal cells would interact with short-wavelength input.

The response enhancement and the decrease of response amplitudes were observed in a wide range of test light intensity (Fig. 3). In the experiment of Fig. 3A, a red background light (690 nm) was first applied to the retina without test light and then blue-green test lights (480 nm) of various intensities were superimposed in a decreasing sequence on the background illumination. Gradual decline of response amplitude during background illumination occurred for responses evoked by test flashes of all intensities. The relationships between the response amplitude and the intensity of test light (response-intensity relation) are plotted in Fig. 3B. Immediately after the introduction of the red background illumination, the response-intensity relation shifted towards the left along the light intensity axis ("dark" curve to curve "0"). During the maintained background illumination the slope of the response-intensity relation became less steep, while the threshold remained unchanged.

The dependence of the decrease of response amplitudes on the intensity of the background light varied from cell to cell; for some cells the decrease of response amplitudes was most effective for dim background light, while for others it was most effective for moderate intensity background light. Similar enhancement and decrease of response amplitude were obtained with test flashes of long duration (500 ms). In about 15% of the retina preparations studied (n = 238), horizontal cells showed little or no change of responses to test light under red background illumination; in these preparations, response amplitudes were steadily enhanced or suppressed during background illumination. When red test flashes were applied over a blue-green background, there was no decrease of response amplitude during background illumination (n = 15).

Background illumination induced a remarkable change in response waveform of horizontal cells to identical test flashes (Fig. 4). As shown in Fig. 4A, the hyperpolarizing phase becomes steeper after the introduction of background light, which results in enhancing response amplitude. The change of test responses during background illumination is twofold (Fig. 4B): gradual decline in response amplitude, and gradual shortening of response duration. The shortening of response duration is brought about by an early return of membrane potential to the dark level and not by a change in the hyperpolarizing phase. Thus, the decrease of response amplitude to test light seen in the red background is produced by a gradual advancement of the recovery phase of each response.

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Effects of the spatial pattern of light stimulus

To study the mechanism causing changes in responses to test lights, we first examined whether direct interaction between cones of different types contribute to these changes by using light of various spatial patterns.

The enhancement and the subsequent decrease of response amplitude were produced even when the test light and the background light were applied on different parts of the retinal surface. In the experiment of Fig. 5A, blue-green annulus lights (inner diameter = 3.0 mm; outer diameter is large enough to cover the whole retina) were flashed while red spot (2.25 mm diameter) was given as a background light. As this figure shows, the response to test flashes was initially enhanced by the introduction of background light, but subsequently began to decrease gradually. Since the test and adapting lights are separated by a 0.75 mm gap, a distance much longer than that of cone-cone interaction (BAYLOR et al., 1971), it seems unlikely that direct interaction between cones (see NORMANN et al. (1984)) is responsible for the enhancement and subsequent decrease of response amplitude. Similar results were obtained in all cells tested (n = 5).

In the experiment of Fig. 5B, a small spot (diameter = 0.5 mm) was used as a test stimulus and a diffuse test light as a background light. Under these experimental conditions, direct interaction between cones can occur within the retinal area illuminated by the test light. The decrease of response amplitude, however, did not occur during background illumination (n = 4). Comparison of the kinetics of responses indicates that the amplitude of the response labeled 19 is larger and faster than that of the response labeled 1. The results of Fig. 5, thus, suggest that more proximal neurons contribute greatly to the change of test responses in the background.

Effects of GABA

GABA has been suggested as a neurotransmitter involved in the feedback pathway from L-type horizontal cells to cones (LAM and STEINMAN, 1971; MURAKAMI et al. 1982a, b; TACHIBANA and KANEKO, 1984). Under our experimental conditions, 0.5 mM GABA eliminated the depolarizing responses in chromaticity (R/G)-type
horizontal cells, which are believed to be caused by the feedback activity from L-type horizontal cells (not shown, see MURAKAMI et al. (1982b)).

Application of GABA (0.5 mM) blocked the advancement of the recovery phase (Fig. 6). When GABA was applied to the superfusate, the dark membrane potential

Fig. 4. Responses to each test flash in a flash train displayed with an expanded time scale. A: superimposed records of responses to test flashes in the dark (dark) and immediately after the introduction of background (0). B: superimposed records of responses to test flashes during background illumination. Numbers (0 through 14) indicate the elapsed time (s) after the onset of the background light (see Fig. 2A). Test light: 490 nm, $3.5 \times 10^3$ photons/(s·µm²). Background light: 680 nm, $3.5 \times 10^3$ photons/(s·µm²).
Fig. 5. Effect of size and form of illumination on L-type horizontal cell response. A: annular test light (490 nm; i.d., 3 mm; o.d., larger than the whole retina; $7.0 \times 10^3$ photons/(s·µm²)) was applied repeatedly during a steady spot (680 nm; diam., 2.25 mm; $3.5 \times 10^3$ photons/(s·µm²)). Note that the inner diameter of the annulus is larger than the adapting spot. B: small spot test lights (490 nm; diam., 0.5 mm; $7.0 \times 10^2$ photons/(s·µm²)) were applied under diffuse background light (680 nm, $7.0 \times 10^2$ photons/(s·µm²)). Two responses, recorded 1 and 19 s after the onset of background, are displayed in a higher gain and with a faster time scale. When diffuse test lights were applied repeatedly, the cell showed a decrease of response amplitudes, similar to those of Fig. 1.

Fig. 6. Effect of GABA on responses to blue-green test lights under red background illumination. A: after the effect of red background light was examined in normal solution, 0.5 mM GABA was applied (between arrows) and the same light stimuli were repeated. The right trace was obtained after GABA was washed. B, C: test responses superimposed with an expanded time scale (■ control; △, □ in GABA) show that the recovery phase did not start earlier in the solution containing GABA. Both light stimuli were diffuse. Test light: 490 nm, $1.4 \times 10^3$ photons/(s·µm²). Background light: 700 nm, $1.0 \times 10^4$ photons/(s·µm²).
was depolarized by about 10 mV (Fig. 6A). Contrary to the control responses (before GABA application), the amplitude of responses to 490 nm test flashes was almost constant during the background illumination. The waveform of responses to test lights during the background light was almost invariant; i.e., the recovery phase did not start earlier in the presence of GABA (Fig. 6C). Furthermore, the time course of the hyperpolarizing phase was the same as that of the recovery phase except near the peak and dark levels.

The effect of GABA on the dark membrane potential was variable; some cells showed depolarization, as shown in Fig. 6, but others showed hyperpolarization (see HANKINS and RUDDOCK (1984)). However, the effects of GABA on test responses were consistent in all cells tested (n = 28).

Contrary to our expectation, changes of responses to test lights under red background light were not affected by GABA antagonists, bicuculline (n = 8; 100, 250, 500 µM) and picrotoxin (n = 3; 250, 500 µM). These two GABA antagonists also failed to block the depolarizing response of chromaticity (R/G)-type horizontal cells (n = 42 for bicuculline, n = 5 for picrotoxin; but see MURAKAMI et al. (1982b)). Perhaps these agents did not reach the cone-horizontal synaptic region under the present experimental conditions.

The enhancement and subsequent decrease of responses to test lights were also seen in the 6-OHDA-treated retina (n = 7). As seen in the control session of Fig. 7, response to blue-green test light was initially enhanced by red background
illuminated but decreased as the background was maintained. These observations are identical to those seen in the untreated retina (Fig. 1), indicating that dopaminergic interplexiform cells are unnecessary for causing the enhancement and subsequent decrease of response amplitude. The effects of GABA on dopamine-deprived retina were identical to those of the untreated retina. These observations eliminate the possibility that the action of GABA on responses is mediated by interplexiform cells.

**Effect of Co**

It has been shown recently that low concentration of Co\(^{2+}\) blocks the GABA-induced current in isolated cones of the turtle (Kaneko and Tachibana, 1986b). The effective concentration of Co\(^{2+}\) is much lower than that needed to suppress the Ca\(^{2+}\) influx. Antagonistic effect of Co\(^{2+}\) to GABA was confirmed in the experiment using whole retina of carp (Fig. 8A). Application of 50 µM Co\(^{2+}\) depolarized the dark membrane potential and eliminated the depolarizing responses of chromaticity (R/G)-type horizontal cells (n = 3, Fig. 8A, also see Murakami et al. (1982b)).

With these preliminary results, we next examined the effects of 50 µM Co\(^{2+}\) on responses to test lights in L-type horizontal cells (Fig. 8B). Application of Co\(^{2+}\) almost inhibited the decrease of responses to test lights; the responses did not change very much during background illumination (lower right record), and the advancement of the recovery phase was suppressed (n = 6, upper superimposed
Effect of dopamine

Dopamine may be the transmitter released from interplexiform cells (DOWLING and EHINGER, 1978). As already demonstrated, interplexiform cells are probably not involved in the mechanism producing the decrease of response amplitude. However, it is important to examine the effect of dopamine on responses to test lights because dopamine inhibits the release of GABA from horizontal cells (YAZULLA and KLEINSCHMIDT, 1982; O'BRIEN and DOWLING, 1985).

Figure 9 shows an experiment in which 250 µM dopamine was applied to the retina. The lower traces show that the responses to test lights under red background light were strongly suppressed by the application of dopamine. Superimposed responses at a faster time scale (upper records) showed that the recovery phase started earlier in dopamine-containing solution, while the slope of the hyperpolarizing phase was identical. Similar results were obtained in all preparations examined (n = 5).

As shown in Fig. 9, the hyperpolarizing phase, related to the response enhancement (see Fig. 4), was hardly affected by dopamine.

Fig. 9. Effect of dopamine on L-type horizontal cell responses to blue-green test light under red background illumination. The response amplitude evoked by test light under the background illumination was decreased in the presence of dopamine (250 µM). Upper traces are superimposed test responses (▲, ■ control; △, □ in dopamine) with an expanded time scale. Test light: 490 nm, 3.5 x 10³ photons/(s µm²). Background light: 680 nm, 1.0 x 10³ photons/(s µm²).
DISCUSSION

We demonstrated that the amplitude of responses of L-type horizontal cells to blue-green test lights is initially enhanced by red background light but subsequently decreases and reaches a steady state. As shown in Fig. 10, many factors, in addition to inputs from cone photoreceptors, affect L-type horizontal cells' response. Based on the present experimental results, the underlying mechanism causing the response enhancement to test light and the decrease of response amplitude will be discussed.

Initial enhancement of responses. MAKSIMOVA et al. (1966) were the first to show that the responses of horizontal cells in the perch retina to green light were amplified by red background light. BYZOV et al. (1977) attributed this response amplification to the resistance increase of a nonsynaptic membrane of horizontal cells. YANG et al. (1983) suggested the involvement of the feedback from horizontal cells to cones based on experimental results using two successive light flashes of

![Diagram](image)

Fig. 10. A schematic drawing of factors affecting L-type horizontal cells, and neurotransmitter candidates related to these factors. Red-sensitive cones provide a dominant input to L-type horizontal cells. L-type horizontal cells also receive two other inputs, one from short-wavelength-sensitive cones (probably green-sensitive cones), and a second from interplexiform cells. Cones employ glutamate as their neurotransmitter while interplexiform cells release dopamine. Furthermore, abundant evidence suggests that L-type horizontal cells are GABAergic and send their signals back to cones through a negative feedback pathway (thick arrows). In addition, cones are coupled to neighboring cones through fine processes called telodendria, and horizontal cells are electrically coupled with neighboring horizontal cells through gap junctions. GABAergic amacrine cells probably input to interplexiform cells. For references see text.
different colors. Also, Negishi (1971) and Laufer and Negishi (1978) reported that a combination of central spot and annulus illumination resulted in enhanced response.

In our experiments, response enhancement was observed when different monochromatic lights were used for test and background lights and was not observed when lights of close wavelengths were used (see Fig. 2). Because L-type horizontal cells receive synaptic inputs from red and short-wavelength-sensitive cones (Fig. 10) (Orlov and Maksimova, 1965; Fukurotani et al., 1979; Yang et al., 1983), it is reasonable to assume that the response enhancement results from an interaction between these inputs to horizontal cells. Since response enhancement was seen even when the test and background lights were placed spatially separated on the retina, direct interaction between different types of cones (Normann et al., 1984) is unlikely. GABA and Co²⁺, which blocks the GABA-induced current at cone terminals (Kaneko and Tachibana, 1986b), did not affect the response enhancement (Figs. 6–8), indicating that the GABAergic feedback is unnecessary for the response enhancement. Response enhancement was also seen in horizontal cells of 6-OHDA-treated retina implying that the dopaminergic interplexiform cells are unnecessary for this phenomenon to occur. Although the origin of response enhancement was not directly revealed by the present experiment, there is a possibility that the membrane properties of horizontal cells are involved (in the process). As mentioned above, the voltage-dependence of nonsynaptic membrane is able to enhance the response (Byzov et al., 1977). Furthermore, Tachibana (1985) demonstrated that membrane conductance of horizontal cells produced by glutamate, a putative transmitter of cones (see Fig. 10; for review see Kaneko (1987)), also depends on the membrane potential.

Decrease of response amplitude to test lights. Response amplitudes to blue-green test lights decreased and reached a steady state during prolonged red background illumination. The decrease of response amplitudes was observed even when blue-green flashes and prolonged red light were applied to different parts of the receptive field. Such a decrease was not seen when a small blue-green spot was superimposed on the red background. These results imply that direct interactions between cones (Normann et al., 1984) are not involved in the decrease of response amplitudes.

Comparison of the kinetics of responses indicates that the decrease of response amplitude is produced by a gradual advancement of the initiation of the recovery phase of successive responses.

As shown in Fig. 10, GABA receptors locate on cones and interplexiform cells (Lam and Steinman, 1971; Murakami et al., 1982a,b; Tachibana and Kaneko, 1984; Negishi et al., 1983). When GABA was applied to the 6-OHDA-treated retina, the advancement of the recovery phase of responses to test flashes was eliminated. Since, among factors affecting the horizontal cells’ response in the treated retina, GABA probably affects only the feedback pathway from horizontal cells to cones (Fig. 10), the experimental results indicate that the feedback pathway from
horizontal cells (thick arrows in Fig. 10) is involved in the regulation of the onset of the recovery phase.

It can be speculated that the light response of horizontal cells is produced as follows. When the light is turned on, cone photoreceptor cells begin to hyperpolarize and the rate of transmitter release decreases, causing hyperpolarization of horizontal cells (hyperpolarizing phase; for review see Kaneko (1978)). Thus, the hyperpolarizing phase is attributed to the signal transmission from cones to horizontal cells. The horizontal cells' hyperpolarization then decreases the GABA release from horizontal cells (Miller and Schwartz, 1983; Yazulla, 1983), which in turn causes depolarization in cones (Cervetto and MacNichol, 1972). The depolarization of cones increases the transmitter release from cones, which results in the depolarization of horizontal cells (recovery phase). Therefore, the recovery phase involves a pathway which includes feedback from horizontal cells to cones. This suggests that the recovery phase is adjusted by the depolarizing action of the feedback.

Maksimova and Maksimov (1969) and Tauchi et al. (1984) reported that L-type horizontal cells show a depolarizing response to light stimulus under red background illumination. Although such a depolarizing response was not recorded in the present study, the depolarizing response observed by these investigators may be produced by the similar feedback mechanism.

Applied GABA might increase GABA-induced current by binding to GABA receptors at cone terminals. On the other hand, desensitizing action of GABA at cone terminals was reported by Kaneko and Tachibana (1986a); the responses of solitary cones to the applied GABA are suppressed when GABA is bath-applied. Thus, bath-applied GABA in our experiments might cause desensitization at cone terminals. In another report (Kaneko and Tachibana, 1986b), these investigators demonstrated that a small amount of Co\(^{2+}\) reduces the GABA-induced current at cone terminals in a way similar to GABA; the maximum amplitude of dose-response curve is decreased by Co\(^{2+}\) or GABA (see also Kaneko and Tachibana (1986a)). Therefore, the inhibition of the depolarizing effect of the feedback with applied GABA (probably due to saturation and/or desensitization) or with Co\(^{2+}\) (due to blocking) might result in elimination of the advancement of the recovery phase in responses to test light (also see Murakami et al. (1982b)).

Dopamine receptors are present on horizontal cells (Fig. 10) (Dowling and Ehinger, 1978). In contrast to the effect of GABA and Co\(^{2+}\), dopamine enhanced the advancement of the recovery phase (Fig. 9). Since the decrease of response amplitude to test light was also observed in 6-OHDA-treated retina, it seems reasonable to suppose that dopamine affects the onset of the recovery phase indirectly by affecting GABA release from horizontal cells (see Yazulla and Kleinschmidt (1982) and O'Brien and Dowling (1985)). Decoupling effect of dopamine on gap junctions between horizontal cells (Teranishi et al., 1983) is not involved in the change of responses to test light because the change was seen for the full-field light. Dopamine is reported to enhance the excitatory amino acid-gated conductance in
cultured horizontal cells (Knapp and Dowling, 1987). However, because the hyperpolarizing phase of responses was not affected by dopamine (Fig. 9), perhaps such an effect of dopamine is not involved under our experimental condition.

The present study is not sufficient to explain how the onset of recovery phase was advanced by the negative feedback during red background. Only speculation can be made. L-type horizontal cells probably release GABA tonically (Ayoub and Lam, 1984) (also see Kaneko and Tachibana (1986a)). Because cones are desensitized to GABA in the presence of GABA in the medium (Kaneko and Tachibana, 1986a), applied dopamine might sensitize the cone terminals to GABA by inhibiting the tonic release of GABA from horizontal cells (Yazulla and Kleinschmidt, 1982; O'Brien and Dowling, 1985). Because the sensitization at cones stimulates the feedback action, applied dopamine enhances the depolarizing action of the feedback which might stimulate the advancement of the recovery phase of test responses. This discussion, together with the results of GABA and Co²⁺ experiments, raises one possible idea that feedback becoming more effective during red background illumination might cause the advancement of the onset of the recovery phase of responses to test light.

In contrast, the decrease of response amplitudes to test lights was not seen when red flashes were superimposed on blue-green background light. Therefore, the nature of the feedback pathway to red cones may be different from that to short-wavelength-sensitive cones; the problem remains to be studied in more detail.

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