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Light- and Dopamine-Regulated Receptive Field Plasticity in Primate Horizontal Cells

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Abstract

Center-surround antagonistic receptive fields (CSARFs) are building blocks for spatial vision and contrast perception. Retinal horizontal cells (HCs) are the first lateral elements along the visual pathway, and are thought to contribute to receptive field surrounds of higher order neurons. Primate HC receptive fields have not been found to change with light, and dopaminergic modulation has not been investigated. Recording intracellularly from HCs in dark-adapted macaque retina, we found that H1-HCs had large receptive fields ($\lambda = 1,158 \pm 137 \mu\text{m}$) that were reduced by background light (–45%), gap junction closure (–53%), and D1 dopamine receptor activation (–48%). Tracer coupling was modulated in a correlative manner, suggesting that coupling resistance plays a dominant role in receptive field formation under low light conditions. The D1 antagonist SCH23390 increased the size of receptive fields (+13%), suggesting tonic dopamine release in the dark. Because light elevates dopamine release in primate retina, our results support a dopaminergic role in post-receptor light adaptation by decreasing HC receptive field diameters, which influences the center-surround receptive field organization of higher-order neurons and thereby spatial contrast sensitivity.

Keywords

horizontal cell; tracer coupling; retina; dopamine; center surround; electrophysiology

Neurons in the visual system detect light, and each visual neuron responds to light falling on its receptive field (Kuffler, 1953; Werblin and Dowling, 1969). Receptive fields of photoreceptors (first-order visual neurons) are small (Baylor et al., 1971; Verweij et al., 2003), and those of higher order neurons become larger and more complex. Their sizes are determined by convergent chemical synaptic signals from upstream neurons and lateral signal spread through electrical synapses. Primate retinal bipolar cells (Dacey et al., 2000) and ganglion cells (Gouras, 1967) have center-surround receptive fields, whereby the center response arises largely from the vertical flow of signals from photoreceptors, and the surround response, at least for many ganglion cells in light-adapted primate retina, is likely generated by horizontal cell (HC) feedback to cones (Verweij et al., 2003; McMahon et al., 2004).

For years, synaptic circuitry underlying receptive fields was considered “hard wired,” because synaptic structure and numbers in the mature visual system do not seem to change. However, recent evidence showed that the efficacies of synapses are regulated by physiological conditions via neuromodulators. In other animals, electrical coupling and HC

receptive field size vary with adaptation (Yang and Wu, 1989; Xin and Bloomfield, 1999), and dopamine and other neuromodulators can regulate photoreceptor and HC coupling (Tornqvist et al., 1988; Piccolino et al., 1989; He et al., 2000; Furukawa et al., 2002; Jouhou et al., 2007). It is not clear whether adaptation-and neuromodulator-induced changes in receptive field size and coupling occur in primate retina.

In humans and other primates, responses of higher order visual neurons, as well as visual perception, are altered in response to changes in light adaptation, and also during conditions that decrease retinal dopamine levels, as happens in Parkinson's disease patients (Harnois and Di Paolo, 1990). For example, contrast sensitivity decreases with dark adaptation, as well as in subjects with Parkinson's disease (Wink and Harris, 2000). These deficits arise at least partially in the retina, because changes are also found in the electroretinograms (ERGs) and pattern ERGs (PERGs) of Parkinson's disease patients (Langheinrich et al., 2000). It is unclear how lower dopamine levels alter retinal processing in primates. It has been proposed that ganglion cell receptive field surrounds are impaired, which could change the relationship between contrast sensitivity and spatial frequency (Bodis-Wollner, 1990), but this has not been tested.

Primate retina has two types of HCs, the H1 and H2 (Kolb et al., 1980; Boycott et al., 1987; Ahnelt and Kolb, 1994; Dacey et al., 1996), both of which are extensively, homologously coupled to neighboring HCs. Both receive mixed inputs from cones, but H2 HCs receive larger blue (S [short wavelength sensitive]) cone input (Ahnelt and Kolb, 1994; Dacey et al., 1996; Wässle et al., 2000; Packer and Dacey, 2002). It has been suggested that HC receptive fields in primates are narrower than those in other mammals (Verweij et al., 1999; Packer and Dacey, 2002), and it is not clear whether HC receptive fields are modulated by light or neuromodulators. We studied light responses, receptive field size, and dye coupling of HCs in dark-adapted primate retina. We also examined effects of background light, gap junction blockers, and D1 receptor ligands on these parameters. Our results suggest that a light/dopamine-dependent system exists in primate retina that regulates HC receptive field size and HC contributions to receptive field organizations of downstream visual neurons.

MATERIALS AND METHODS

These experiments were approved by the Baylor Animal Welfare Committee. Flat-mounted, isolated retinas of macaque monkey (*Macaca mulatta*) were used in this study. Eyes were harvested from 19 animals that were being euthanized for reasons not related to the eyes. Experiments were performed during the day, and animals were euthanized with overdoses of barbiturates prior to enucleation and hemisection of the eyes, after which eye-cups were only exposed to dim red light or infrared light. A piece of the eyecup (3–10 mm from the fovea) was placed over a hole in a piece of Millipore (Bedford, MA) filter secured in the superfusion chamber. The sclera and the pigment epithelium were removed from the retina. Procedures done under infrared illumination were visualized with dual Nitemare eyepieces (BE Meyers, Redmond, WA). Oxygenated Ames solution (pH 7.4) was introduced continuously to the recording chamber by a gravity superfusion system, and the medium was maintained at 34°C by a temperature control unit (TC 324B, Warner Instruments, Hamden, CT). All pharmacological agents were dissolved in Ames medium with a superfusion time of 45–60 seconds. The retina (photoreceptor side up) was viewed with a 32× objective lens modified for Hoffman modulation contrast optics (Hoffman Modulation Optics, Greenvale, NY).

Recording

Intracellular recordings were made with micropipettes drawn with a modified Livingston puller with Omega Dot tubing (1.0 mm o.d. and 0.5 mm i.d.; Friedrich & Dimmock,

Millville, NJ). Microelectrode tips were filled with 3% Neurobiotin (Vector, Burlingame, CA) in 50 mM Tris and backfilled with 3 M lithium chloride and had tip resistances of 100–600 M Ω . Horizontal cells were recorded with a microelectrode amplifier (Nihon Kohden, Foothill Ranch, CA). Impalement was facilitated by adjusting the negative capacitance in the head stage. Voltage traces were monitored with an oscilloscope and digitized, stored, and analyzed with a computer A-D system (p-clamp 8, Axon Instruments, Foster City, CA).

For receptive field measurements, voltage responses (V) to a light bar of width 2a (50 μ m) were measured as a function of position (x) relative to the receptive field center (where the light bar generates the maximum response, V_0), and these data were fitted with the following equation:

$$V_x = V_0 \sinh(a/\lambda) \exp(-|x/\lambda|) \quad |x| \geq a$$

derived for a network of coupled cells by Naka and Rushton (1967) and Lamb (1976) and used extensively to fit horizontal cell responses to a light bar (Nelson, 1977; Lankheet et al., 1990; Bloomfield et al., 1995; Xin and Bloomfield, 2000). The term λ in this equation is the space constant (length constant), where the response has declined to 1/e of the maximum, and has typically been used as an index for HC receptive field size in non-primate studies.

In this paper, the receptive field size was also measured as the width of the fitted slit response profile from 0.1 of the maximum response on one side of the central peak to 0.1 of the maximum on the other side in order to allow better comparison with previous primate HC studies (see Discussion). Therefore, we will use the term receptive field diameter to refer to the diameter of the fitted receptive field profile at 10% of the peak (V_0), and the term space constant to refer to λ in the fitted equation, which corresponds to the diameter of the receptive field profile at 1/e of the peak (both sides of the peak fit separately and added together). Averages are presented with $\pm$ standard deviation, and significance was determined by using a paired t test, with *P* values less than 0.05 considered significant.

Light source

The preparation was stimulated with a computerized dual-beam photostimulator (Shanghai Institute of Optical Instruments, Shanghai, China). Two independent light beams, whose intensity and wavelength could be adjusted by neutral-density filters and interference filters, were provided by quartz halogen sources. The light was projected to the preparation by way of a computer-driven moving mirror, and the spot diameter and moving light bars were adjusted automatically. The intensity of light sources was measured with a radiometric detector (United Detector Technology, Santa Monica, CA). The intensity of unattenuated 500-nm light ($\log I = 0$) was 1.78×10^5 photons $\mu\text{m}^{-2} \text{sec}^{-1}$.

Dye injection and visualization

After some physiological experiments, dyes were injected with positive and negative currents (1–5 nA, 3 Hz, 30 minutes). Cells filled for less than 30 minutes were not used for tracer coupling measurements. Tissues were fixed with 4% paraformaldehyde for 2 hours and immuno-labeled with streptavidin-conjugated Cy-3. HC morphology and patterns of dye coupling were visualized with a confocal microscope (LSM510, Zeiss, Thornwood, NY). Images were acquired by using a 25 $\times$ or 40 $\times$ oil immersion objective, the 458-nm excitation line of an argon laser and a band-pass 505–525-nm emission filter for Lucifer yellow, and a 543 He-Ne laser and 570-nm long-pass filter for Cy3. Consecutive optical sections were stacked into a single image by using the Zeiss LSM-PC software and the stacked images were further processed in Adobe Photoshop 6.0 (San Jose, CA) to improve the contrast. The

diameter of the tracer coupled area was measured manually by visually determining where coupled cells could be distinguished from the background fluorescence.

RESULTS

Horizontal cell light responses under dark adapted conditions

Horizontal cells were identified based on their morphology as H1 or H2 cells (H1-HC, H2-HC) after recording and intracellular filling. H1-HCs had larger somas, thick primary dendrites, and extensive tracer coupling (Fig. 1a,b), whereas H2-HCs had smaller somas, thinner dendrites, and less extensive tracer coupling (Fig. 2a,b), as demonstrated previously (Kolb et al., 1980; Wässle et al., 2000). Under dark-adapted conditions, H1 cells filled with Neurobiotin revealed a large mosaic of coupled H1-HCs, typically over 900 H1 somas ($n = 12$) with a coupled field diameter greater than 1,200 μm , and filled H2-HCs typically stained over 70 H2 somas ($n = 3$), with a coupled field diameter over 350 μm .

We recorded voltage responses from horizontal cells under dark-adapted conditions and studied their receptive fields. H1 and H2 receptive fields in this study were localized over the soma, confirming results from Verweij et al. (1999) showing that recorded inputs came from HC dendrites and not the displaced axon terminals that receive inputs from rods and are probably electrically isolated from the soma (Kolb et al., 1980). Receptive field size under dark-adapted conditions was determined by recording voltage responses to a stepwise (120- μm steps) moving light bar (50 μm wide, 500 nm, -1 log attenuation) across the cell's receptive field. Receptive field diameters were 2,460 and 878 μm for the H1- and H2-HCs in Figures 1 and 2, respectively. From a total of 30 HCs recorded from 3–10-mm eccentricity, we found that the average ($\pm$ SD) receptive field diameter of the H1-HCs was $2,124 \pm 305$ μm ($n = 27$), and the average receptive field diameter of H2-HCs was 821 ± 57 μm ($n = 3$). Total space constants (λ) were $1,158 \pm 137$ μm and 427 ± 35 μm for these dark-adapted H1- and H2-HCs, respectively. In most cells, the space constant seemed to approximate the size of the tracer coupled area closer than the receptive field as defined in Materials and Methods.

Light modulation of HC receptive field

The effect of background light on the receptive field size of dark-adapted H1-HCs was assessed by measuring voltage responses to a moving light bar as described above, but with the addition of background illumination (500 nm/ -2.5 log attenuation [563 photons μm^{-2} sec^{-1}]) for at least 5 minutes prior to beginning receptive field measurements, and increased light bar intensity (0 attenuation) to maintain the same maximum response amplitude. An example is shown in Figure 3, in which the background light hyperpolarized the H1-HC by about 3 mV at onset, and then slowly depolarized the cell by 6 mV. At this mesopic level of background light, both rods and cones respond to light. The receptive field diameter of the H1-HC before, in the presence, and after the termination of background illumination was 2,056, 1,120, and 2,280 μm , respectively. The average receptive field diameter of H1-HCs was significantly reduced ($P < 0.01$) to $55 \pm 6\%$ of the dark-adapted values by steady background light ($n = 3$). The total space constant during background illumination averaged 622 μm . Tracer coupling in the presence of continuous background light was also reduced ($P < 0.01$, $n = 2$) to about 61% of that under control dark-adapted conditions (Fig. 4), suggesting that changes in coupling resistance play a determining role in decreased receptive field size.

Because the light bar intensity was necessarily increased during the background light application, the response size approached 50% of the maximum. Correct calculation of the space constant (Lamb, 1976) stipulates that a small percentage of the maximum response be

used or else the space constant will be inflated. Therefore, the light-induced reduction in receptive field is likely underestimated.

Gap junction modulation of HC receptive field

Our results and those from other animals show that receptive field size can correlate with degree of tracer coupling, and that both parameters can be modulated by light (Bloomfield et al., 1995; Xin and Bloomfield, 1999). Because tracer coupling has been shown to be mediated by gap junctions (Mills and Massey, 1995), we examined the effect of a gap junction blocker, meclofenamic acid (Pan et al., 2007), on the receptive field of H1-HCs. Figure 5 shows that 200 μ M meclofenamic acid reduced the receptive field diameter of an H1-HC from 2,664 to 1,370 μ m. H1 receptive fields decreased in size significantly ($P < 0.01$) with meclofenamic acid, on average, by $53 \pm 4\%$ ($n = 3$) compared with control dark-adapted conditions. The average total space constant in the presence of the gap junction blocker was 597 μ m. The addition of meclofenamic acid also depolarized the dark-adapted H1-HCs by about 14 mV. The extent of dye-coupling between H1-HCs was reduced by 83% ($P < 0.01$, $n = 3$), on average, by meclofenamic acid (Fig. 4c). These results suggest that closing gap junctions has effects similar to those of increasing background light levels: both reduce HC receptive fields. Therefore, H1-HC receptive field size under dark-adapted conditions depends significantly on gap junction resistance along with other variables such as membrane resistance.

Dopaminergic modulation of HC receptive field

A potential link between background light levels and gap junction closure is the dopaminergic system, whereby dopamine is released from amacrine cells and acts to close gap junctions (Boelen et al., 1998; He et al., 2000; Ribelayga and Mangel, 2007). To investigate whether this pathway acts on H1-HCs, voltage responses were recorded in the presence of a dopamine antagonist or an agonist. In the presence of the D1 antagonist SCH23390, the H1-HC was hyperpolarized by about 21 mV (Fig. 6). H1-HC receptive field diameters measured from voltage responses to a moving light bar increased in the presence of SCH23390 by an average of $13 \pm 4\%$ ($n = 3$), a small but significant change ($P < 0.05$). The cell in Figure 6 increased to 1,980 μ m from the control value of 1,740 μ m. The total space constant averaged 1,242 μ m in the presence of the D1 antagonist. Figure 7 shows that SCH23390 can partially block the effect of background light on receptive field size, which would be expected if light-induced dopamine release played a role in decoupling and subsequent receptive field size reduction. After background light reduced the receptive field of this H1-HC from 1,546 to 474 μ m, addition of the D1 antagonist during background light application increased the receptive field size by about 15% to 543 μ m. The lack of complete block of the light induced effect by SCH23390 indicates that other mechanisms, in addition to the dopaminergic system, may be involved as well.

Figure 8 shows that the D1 receptor agonist SKF38393 reduced the receptive field diameter of an H1-HC from 2,076 to 1,008 μ m and depolarized it by about 8.3 mV. H1-HC receptive fields decreased significantly ($P < 0.02$) by about $48 \pm 6\%$ ($n = 2$) after application of the D1 agonist, similar to the effects of background light and blocking gap junctions. D1 stimulation decreased the space constant for H1 cells to 640 μ m. Similarly, the size of the field of dye-coupled cells was 67% smaller ($P < 0.01$, $n = 2$) in the presence of SKF38393 compared with control dark-adapted H1-HCs (Fig. 4d). These results, which are summarized in Figure 9, are consistent with a pathway whereby increased light levels cause elevated dopamine release, which acts to decrease HC-HC electrical coupling and plays a role in decreasing their receptive field size.

DISCUSSION

We studied receptive field size and tracer coupling of horizontal cells in dark-adapted macaque monkey retina. Cell morphology, soma distribution, and general patterns of coupling of the two types of HCs were similar to previous results (Wässle et al., 2000). In contrast to previous studies done largely under light-adapted conditions, we found that dark-adapted H1-HCs have large receptive fields that can be modulated by background light, gap junction blockers, and dopamine receptor activation. HC receptive fields from non-mammalian retina can be modulated pharmacologically and by light (Djamgoz et al., 1998; Pottek and Weiler, 2000), as can those in some mammalian retinas (Lankheet et al., 1996; Xin and Bloomfield, 1999; Reitsamer et al., 2006). Until now, there was no evidence for this phenomenon in primate retina, however. Earlier studies found that the receptive field diameter of light-adapted H1-HCs ranged from 122 to 600 μm (Packer and Dacey, 2002), measured at 10% of the peak along the receptive field sensitivity profile and using drifting sinusoidal gratings. We found that the receptive field diameter of dark-adapted H1-HCs from overlapping eccentricities averaged 2,124 μm when measured at 10% of the peak along the receptive field response profile ($\lambda = 1,158 \mu\text{m}$; see Materials and Methods), decreasing to about 1,200 μm ($\lambda = 622 \mu\text{m}$) in the presence of background light.

Because mesopic background illumination decreased H1-HC receptive field diameters to about half of the dark-adapted value, the smaller receptive fields in previous studies were likely due to higher light levels. Packer and Dacey (2002) used light typically at mid-photopic levels (1,000 trolands), but did go as low as 10 trolands. Because our brightest background light (563 photons $\mu\text{m}^{-2} \text{sec}^{-1}$, lower end of the mesopic range) was less than that, it is likely that most light-induced modulation occurs at the low end of the operating range of cones.

It must be acknowledged, however, that different techniques make exact comparisons of receptive field size difficult. Line weighting functions (moving light bar, or slit used here) or area summation functions (spot stimuli) and spatial frequency analysis (sinusoidally modulated gratings) should provide similar information (assuming a linear system) when characterizing receptive fields (Cleland et al., 1979; So and Shapley, 1981). Packer and Dacey (2002) found that spot and annuli stimuli gave similar estimates of receptive field size as drifting gratings. Although Lankheet et al. (1992) found cat HC receptive field estimates using slit stimuli to be larger than estimates using sinusoidal gratings, the slits were flashed only on a relatively dark background (when HC receptive fields should be larger), and the gratings presented under photopic luminance (when HC receptive fields are smaller). By using spot stimuli, Lankheet et al. (1996) confirmed that cat HC receptive fields increase in size with dark adaptation.

If we compare the space constants from our data, which estimate more conservatively the receptive field width at a narrower region of the sensitivity profile, receptive field sizes are still larger than those from previous primate studies. Another difference here is that isolated retina was used for recording, whereas other studies have used a retinal pigment epithelium attached preparation. It is unknown whether this would affect retinal dopamine concentration, because dopamine is released from amacrine cells in the inner retina, but if so then this could also affect HC receptive field size.

To investigate the mechanism by which background light alters receptive field size, we modulated gap junctions and dopamine receptors, both of which have been found to influence HC receptive fields in other species (Reitsamer et al., 2006). Under dark-adapted conditions, both gap junctions and D1 receptors modulated H1 receptive fields and tracer coupling. The gap junction blocker meclofenamic acid decreased their diameter by about

53%, suggesting that the receptive fields of dark-adapted H1-HCs are mediated, at least in part, by H1-H1 coupling. Even under light-adapted conditions, Packer and Dacey (2005) found that blocking H1-HC coupling with carbenoxolone decreased receptive field size. Tracer coupling results correlated directionally with receptive field results, as shown previously in rabbit retina (Xin and Bloomfield, 1999). Therefore, gap junction resistance plays a significant role in primate HC receptive field formation. Similar in effect to blocking gap junctions, the D1 dopamine receptor agonist reduced H1 receptive field size by 47% and tracer coupling by 67%. Although D1 receptor antagonist increased receptive field diameter by about 13%, we were not able to completely block the light-induced receptive field decrease with it, suggesting that other mechanisms in addition to dopamine may also be involved.

It should be noted, however, that some studies have reported inconsistent actions of D1 antagonists in retina (Asare et al., 2005; Huppé-Gourgues et al., 2005; Pflug et al., 2008). Compared with dark-adapted conditions, therefore, background light, blocking gap junctions, and activating D1 receptors all are capable of significantly decreasing the receptive field size of H1-HCs, whereas inhibiting D1 receptors increases the size. These results suggest that: 1) dopamine uncouples H1-HCs via D1 receptors; 2) some endogenous dopamine is released in darkness, because blocking D1 receptors can still increase receptive field size; and 3) light increases the dark dopamine release, uncouples H1-HCs, and reduces their receptive field sizes.

The functional purpose of having smaller receptive fields under light-adapted conditions (Packer and Dacey, 2002) and larger receptive fields under dark-adapted conditions is poorly understood, both in other animals in which the phenomena has been studied for years and in primate retina as presented here. A possible function, based on the idea that HCs are integral to receptive field surround formation, involves adaptation-related changes to spatial vision, although this has been called into question (Dedek et al., 2008). McMahon et al. (2004) found that blocking gap junctional coupling attenuated the surround response of light-adapted large (parasol) ganglion cells, and they concluded that electrotonic HC feedback to cones is largely responsible for those ganglion cell surrounds. Because primate bipolar cells and even cones have a center-surround receptive field structure (Dacey et al., 2000; Verweij et al., 2003), it is plausible that HCs play a significant role in surround formation for some ganglion cells.

Packer and Dacey (2002, 2005) proposed that H1-HCs could be responsible for small (midget) ganglion cell surrounds due to their small receptive field size under photopic conditions, and the chromatic input to both H1-HCs and midget ganglion cell surrounds largely sums all of the overlying red and green cones (Diller et al., 2004; however, see Solomon et al., 2005). Similarly, it is possible that the larger H1-HC receptive fields reported here under dark-adapted conditions generate larger ganglion cell surrounds for lower spatial frequency vision that dominates at lower light levels.

Over the same range of eccentricities used in this study, midget and parasol ganglion cell surrounds range from 70 to 1,350 μm wide, with considerable overlap between the two types (Croner and Kaplan, 1995). Under low light conditions, when H1 receptive fields are larger (λ_{dark} 1,100 μm , $\lambda_{\text{bckgd light}} \approx 600 \mu\text{m}$), they would generate larger surrounds and shift ganglion cell spatial tuning toward lower spatial frequencies. The resulting loss of small surrounds would lower spatial contrast sensitivity for small ganglion cells, which is what happens to midget pathway neurons (Purpura et al., 1988), giving little response to spatial patterns in low light. Overall contrast sensitivity decreases with dark adaptation as well (Patel, 1966; Koenderink et al., 1978), and this has been proposed to be brought about by a weakening of the inhibitory surround (Gouras, 1967; Virsu, 1974). It has been known

for many years that ganglion cell surround responses decrease with dark adaptation (Barlow et al., 1957), and enlarged dark-adapted HC receptive fields may play a role in this adaptational change.

Insights into these adaptational differences may also be gleaned from considering the visual deficits of Parkinson's disease patients and animal models. The dopaminergic deficit of Parkinson's disease patients is systemic, including diminished retinal dopamine levels (Harnois and Di Paolo, 1990). Visual deficits associated with Parkinson's disease include decreased spatial contrast sensitivity (Bodis-Wollner, 1990; Wink and Harris, 2000; Langheinrich et al., 2000; Silva et al., 2005), with larger deficits at middle and higher spatial frequencies. Although some effect may originate in higher visual areas, many of these deficits arise in the retina, because significant differences are seen in flash and pattern ERGs (Langheinrich et al., 2000). In the context of our data, lower dopamine levels would be expected to increase H1-HC coupling and receptive field size at all adaptational states, thereby supporting larger than normal surrounds and shifting the spatial tuning of ganglion cells toward lower spatial frequencies and lowering spatial contrast sensitivity at higher spatial frequencies. Further evidence that dopamine can influence visual perception comes from Domenici et al. (1985), who found that dopamine agonists increased sensitivity to higher spatial frequencies in normal subjects. Therefore, the plasticity of primate HC receptive fields as presented here may help explain how adaptation-related changes as well as pathologic changes in the retina effect spatial contrast perception.

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Figure 1.

H1 horizontal cells. **a,b:** Confocal micrographs of the inner nuclear layer of dark-adapted flat-mounted macaque retina showing the mosaic of H1 somas stained by neurobiotin injection. **c:** Voltage responses of the H1-HC to a stepwise (120-μm steps) moving light bar (50 μm wide, -1 log attenuation) across the cell's receptive field. The receptive field diameter of this H1-HC is 2,460 μm, measured as the width of the receptive field profile at 10% of the maximum response. Scale bar = 100 μm in a; 20 μm in b.

Figure 2.

H2 horizontal cells. **a,b:** Confocal micrographs of the INL of dark-adapted flat-mounted monkey retina showing the mosaic of H2 somas stained by neurobiotin injection. **c:** Voltage responses of the H2-HC to a stepwise (120-μm steps) moving light bar (50 μm wide, -1 log attenuation) across the cell's receptive field. The receptive field diameter of this H2-HC is 878 μm. Scale bar = 100 μm in a; 20 μm in b.

Figure 3.

Effect of background light. Voltage responses of an H1-HC to a stepwise (120- μm steps) moving light bar (50 μm wide, 0 attenuation) across the cell's receptive field before (a), in the presence (b), and after the termination (c) of steady background illumination (500 nm/-2.5). The receptive field diameters of this H1-HC before, in the presence, and after the termination of background illumination are 2,056, 1,120, and 2,280 μm , respectively.

Figure 4. H1-HC tracer coupling. Examples of tracer coupling fields of H1-HCs comparing control dark-adapted conditions (**a**), continuous background light ($\sim 2.5/500$ nm) adaptation (**b**), gap junction block by meclofenamic acid (**c**) and D1 agonist SKF38393 (**d**). Scale bar = $100\ \mu\text{m}$ in **a** (applies to **a**–**d**).

Figure 5.

Effect of blocking gap junctions. Voltage responses of a dark-adapted H1-HC to a stepwise (120-μm steps) moving light bar (50 μm wide, -1 log attenuation) across the cell's receptive field before (a) and in the presence (b) of 200 μm meclofenamic acid. The receptive field diameters of this H1-HC before and in the presence of meclofenamic acid are 2,664 and 1,370 μm, respectively. Responses in b have been shifted on the graph only to fit all of the smaller responses on the graph.

Figure 6. Effect of D1 antagonist. Voltage responses of a dark-adapted H1-HC to a stepwise (120-μm steps) moving light bar (50 μm wide, -1 log attenuation) across the cell's receptive field in control (**a**) and in the presence (**b**) of the D1 receptor antagonist SCH23390 (10 μm). The receptive field diameters of this H1-HC in control and in the presence of SCH23390 are 1,740 and 1,980 μm, respectively.

Figure 7.

Effect of background light (500 nm, -3.1) + D1 antagonist. Voltage responses of a H1-HC to a moving light bar in control (**a**), in the presence of background light (**b**), in the presence of background light + the D1 antagonist SCH23390 (10 μM) (**c**), and with SCH23390 after the background light was turned off (**d**). The receptive field diameters of this H1-HC under each condition were 1,546 μm (**a**), 474 μm (**b**), 543 μm (**c**), and 1,782 μm (**d**).

Figure 8.

Effect of D1 agonist. Voltage responses of a dark-adapted H1-HC to a stepwise (120-μm steps) moving light bar (50 μm wide, -1 log attenuation) across the cell's receptive field in control (**a**) and in the presence (**b**) of the D1 receptor agonist SKF38393 (10 μM). The receptive field diameters of this H1-HC in control and in the presence SKF38393 were 2,076 and 1,008 μm, respectively.

Figure 9.

Summary of results showing average H1-HC receptive field size ($\pm$ SD) for control conditions (dark-adapted, no drug: light gray) and during experimental treatment (dark gray). Background light ($P = 0.002$), meclofenamic acid ($P = 0.001$), and the D1 agonist SKF38393 ($P = 0.01$) significantly decreased receptive field size by about half, and the D1 antagonist slightly but significantly ($P = 0.04$) increased receptive field size.