Orientation-Specific Modulation of Rat Retinal Ganglion Cell Responses and Its Dependence on Relative Orientations of the Center and Surround Gratings

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Girman S. Lund R. Orientation-specific modulation of rat retinal ganglion cell responses and its dependence on relative orientations of the center and surround gratings. J Neurophysiol 104: 2951–2962, 2010. First published September 22, 2010; doi:10.1152/jn.00517.2010 In the primary visual cortex (V1), it has been shown that the neuronal response elicited by a grating patch in the receptive field (RF) center can be suppressed or facilitated by an annular grating presented in the RF surround area; the effect depends on the relative orientations of the two gratings. The effect is thought to play a role in figure-ground segregation. Here we have found that response modulation similar to that reported in cortical area V1 can also be found in all major classes of retinal ganglion cells (RGCs), including “concentric” cells. Orientation-specific response modulation of this kind cannot result from interactions of independent RF mechanisms; therefore more complex mechanism, which takes into account the relative orientations of the gratings in the RF center and surround, or sensing the borders between texture regions, has to be present in RFs of RGCs, even of the concentric type. This challenges the consensus notion that their responses to visual stimuli are governed entirely by a RF composed of separate mechanisms: center, antagonistic surround, and modulatory extraclassical surround. Our findings raise the question of whether initial stages of complex analysis of visual input, normally attributed to the visual cortex, can be achieved within the retina.

INTRODUCTION

A number of studies in the primary visual cortex (V1) in cats and monkey have documented that neuronal responses to a stimulus placed within the cell’s receptive field (RF) center can be strongly modulated by the simultaneous presentation of stimuli in the “silent” regions that surround the RF center (Cavanaugh et al. 2002; DeAngelis et al. 1994; Sceniak et al. 2001; Sengpiel et al. 1998). The presence of extraclassical RF surround has also been suggested in RGCs (Passaglia et al. 2001; Solomon et al. 2006). The most striking feature of center–surround interactions in V1 was shown by presenting a drifting grating patch in the RF center and an annular grating in the surround area. This latter stimulus, when presented alone, was ineffective in eliciting the cell’s response, but markedly influenced the neuron’s response when it was presented together with the center patch grating. The response magnitude depended on the relative orientations of these two grating stimuli: the response was maximal when the gratings were orthogonal, and was suppressed when the gratings were collinear, regardless of the orientation of the center grating and the orientation preference of the cell (Levitt and Lund 1997; Sillito et al. 1995). This character of response modulation shows contextual dependence of responses in V1: it cannot result from interaction of separate and independent effects elicited by the stimulus in the RF center and surround; rather, it implies a mechanism that has to take into account the relative orientations of the center and surround stimuli. This phenomenon has commonly been thought as playing a role in higher-level analysis of visual scenes, such as figure-ground segregation (Albright and Stoner 2002; Series et al. 2003).

Similar orientation-specific center–surround interactions have also been observed in area V1 in rats (Girman et al. 1999). Furthermore, when recording responses to grating stimuli in the most superficial layer (SGS1) of the rat superior colliculus, we (Girman and Lund 2007) found that many neurons displayed response modulation very similar to that found in area V1 as described above. We showed that these responses could not result from cortical feedback projections to the colliculus. This led us to question whether these properties were developed de novo in the colliculus in parallel to the cortex or whether they reflected properties already developed in the retina. This study was aimed at answering this question by exploring whether orientation-specific response modulation can be seen in the rat retina.

METHODS

Animal preparation

Long-Evans hooded rats (n = 18) were used in this study. All procedures were reviewed and approved by the OHSU Animal Care and Use Committee and were consistent with National Institutes of Health and Society for Neurosciences guidelines. Recordings were made with intraretinal microelectrode penetrations in vivo. Animal anesthesia and general preparations were described in our previous paper (Girman and Lund 2007). A neutral contact lens fixed in a metal ring was placed on the eyeball, with the ring attached to a stereotaxis frame. A satisfactory level of eye fixation was achieved because of natural adhesion of the eyeball to the lens. The microelectrode (tungsten-in-glass, tip length and diameter ~1–2 μm) was inserted obliquely into the eye through the microscopic sclera incision made ~0.5 mm behind the limbus. We isolated single units within the 40–60 μm after the microelectrode enters the retina. Our technique allowed stable recordings from single cells during the time necessary to complete ~10–15 tests, which could take up to 5 h. At the end of the recording session, the animal was recovered from the anesthesia, and the eye was treated with antibiotic ointment. The animal was rested for 5–10 days between subsequent, up to five, recording sessions. In subsequent sessions no signs of deterioration of the eye state or RGC responses were observed: the eye could not be distinguished by its appearance from an intact one (no inflammation, healed conjunctiva, normal pupil reflex); the multiunit activity, recorded when microelectrode approached the retina, was strongly modulated by visual stimuli; the maintained activity and responsiveness of isolated RGCs appeared normal.
Visual stimulation, data acquisition, and analysis

We used the same technique of visual stimulation and data acquisition as described previously. In short, the visual stimuli were created with Neurophysiology software (Vision Research Graphics, Durham, NH) and presented in black and white on NEC FE 950 monitor (the screen size 360 × 270 mm, frame rate 120 Hz, resolution 800 × 600 pixels), positioned 40 cm from the animal’s eye. The monitor was windowed by a circular aperture (270 mm diam) in a wide black shield. The stimuli were the flashing circular spots or annuli centered on the RF or drifting sinusoidal grating patches and annuli of varying orientations and diameters. The grating spatial and temporal frequencies were set to optimal (typical values 0.1 c/° and 5 Hz, respectively), the mean grating brightness was 26 cd/m^2, same as background illumination, and Michelson contrast was ~80%. The brightness of flashing stimuli alternated from the background level to black (1.5 cd/m^2) or white (50 cd/m^2) for 0.67 s and switched back; the interstimulus intervals were 1.2 s. Ambient illumination was kept at ~0.5 cd/m^2.

The RF location, in most of the recorded RGCs, was invariantly (because of roughly the same orientation of the microelectrode relative to the eye coordinates) within an area ~30° in diameter, with the center located around 30° above the horizontal plane and 45° lateral to the median plane. This helped positioning the display in register with the RF. The RF was precisely centered on the display by adjusting the display position until the response to a circular concentric with the display screen, contrast-reversing bipartite field, oriented horizontally and then vertically, contained no or minimal component at the frequency of reversal. If the cell did not respond to this stimulus (only a minority of cells did not respond), the RF center was located by a maximal response to a flashing spot of a minimal diameter producing reliable responses. In a great majority of recordings, there was no need to correct the stimulus position during the whole experiment, but at any sign of RF displacement, we remapped its position.

In all cases, the recordings were made from well-isolated single cells, achieving the spike amplitude-to-noise ratio (the discharges of neighbor cells have been considered as a noise component) no less than 5, to accommodate the spike amplitude decrease often occurring during the phase of high-frequency responses and to avoid interference from the background noise. We periodically recorded the digitized samples of spike discharges and stored them together with the main experimental data, so that almost all recorded cells [except for those showing very short responses and no spontaneous activity (SA)] could be characterized by spike shape. To assure that recordings were made from single units, we programmed the software controlling the data acquisition to send a warning message if the interval between two consecutive spikes was less than the preset value, usually 1.5 ms. We made sure that no such events occurred before starting an experiment and discarded any data contaminated in such a way.

Neuronal activity was amplified, filtered (150- to 3,000-Hz bandwidth), and played over a loudspeaker. The spikes transformed into standard impulses by a window discriminator were passed, together with stimulus identification numbers from the stimulus presentation software, to a CED 1401 data acquisition device under control of Spike2 software (CED). Data analysis, first on-line and then more detailed off-line, was performed with the Spike2 script language program. The responses of stimuli composed of drifting gratings, the response was expressed as F0, F1, and F2 coefficients of the Fourier transform of the response peristimulus time histogram (PSTH), whose time span was equal to the period of the grating; each histogram accumulated 10 grating periods presented in a trial.

Presenting moving or stationary flashing spots and annuli, we characterized the cell’s type (as ON, OFF, or ON-OFF, concentric, directional selective, local edge detector), defined the size of the RF center (as the diameter of the spot eliciting maximal response), and defined the extent of the RF classical surround (as the maximal inner diameter of the annulus still eliciting the cell’s responses; in this test, the outer annulus diameter was 270 mm). Applying the grating patch stimulus, we defined the optimal grating parameters (spatial and temporal frequencies, patch diameter, grating orientation). To evaluate the cell’s tuning for orientation, we calculated the orientation selectivity index (OSI)

\[ OSI = \frac{\sum_{i} R(\theta_{i}) \sin(2\theta_{i})^{2} + R(\theta_{i}) \cos(2\theta_{i})^{2}}{\sum_{i} R(\theta_{i})} \] (1)

where \( R(\theta_{i}) \) is the response (F1 component) at the orientation \( \theta_{i} \) of the grating patch.

To evaluate the effect of the annular grating of varying orientation on the response elicited from the RF center by the grating patch whose orientation was constant, we calculated the orientation selectivity index of modulation (mOSI) with Eq. 1, where \( R(\theta_{i}) \) is the response magnitude at the orientation \( \theta_{i} \) of the annular grating.

The magnitude of the modulation was evaluated by two indices

\[ nMax = \max[R(\theta_{i})]/Rc; \quad mMin = \min[R(\theta_{i})]/Rc \]

where \( R(\theta_{i}) \) is as indicated above, and \( Rc \) is the response to the center grating patch presented alone; \( nMax > 1 \) indicates response facilitation.

After recording the area-response curve presenting the center grating patch of varying diameter, we computed response suppression index (RSI). This was defined as

\[ RSI = 1 - \frac{R_{(\text{max diam})}}{R_{(\text{pref diam})}} \]

where \( R_{(\text{pref diam})} \) is a peak value of the area response curve, and \( R_{(\text{max diam})} \) is the response at the maximum size (20°). In the case of response asymptotic increase with the diameter, RSI = 0.

RESULTS

Applying stimuli and criteria commonly used to classify RGCs in other mammalian species, we identified all the main RGC types in the rat retina, as specified below. The cell types identified and the percentage of cells in each class are shown in Table 1. When stimulated with flashing spots centered on the cell’s RF, each cell class shows characteristic responses; their examples are presented in Fig. 1.

In each class, many cells responded well to a patch of drifting grating placed in the center of their RFs. We tested these cells further to see how the grating annuli presented in the RF periphery affected the center response. The results are presented separately for each cell type.

Concentric RGCs

These cells were identified as those responding with spike bursts to brightness changes in their RF center and periphery in an

<p>| TABLE 1. Cell types identified and the percentage of cells of each class |
|------------------------|-------------------|</p>
<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OFF BT</td>
<td>59 (26.9)</td>
</tr>
<tr>
<td>OFF BS</td>
<td>42 (19.2)</td>
</tr>
<tr>
<td>ON BT</td>
<td>48 (21.9)</td>
</tr>
<tr>
<td>ON BS</td>
<td>35 (16.0)</td>
</tr>
<tr>
<td>ON-OFF DS</td>
<td>8 (3.7)</td>
</tr>
<tr>
<td>ON DS</td>
<td>6 (2.7)</td>
</tr>
<tr>
<td>LED</td>
<td>7 (3.2)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>14 (6.4)</td>
</tr>
</tbody>
</table>

BT, brisk transient; BS, brisk sustained; DS, directionally selective; LED, local edge detector.
antagonistic manner. They were typified further as belonging to ON or OFF subclasses according to the brightness transition of the center spot eliciting the cell’s response. All these cells responded with spike bursts to the circular patch of drifting grating centered on the RF, and a majority of them showed some degree of response orientation tuning (OSI > 0.05).

We tested the concentric cells for center–surround interactions by presenting the following grating stimuli: 1) circular grating patch concentric with the RF, and 2) grating annuli with an outer diameter 20° and with the inner diameter equal to the diameter of the patch. During the test, the orientation of the center grating was constant, while the orientation of the grating annulus varied. About 40% of the cells (74 of 184) showed significant orientation-dependent modulation of the center response by the surround stimulation. We observed such modulation in ON- and OFF-cells of both brisk-sustained and brisk-transient cell subclasses.

The strongest effects of the annulus grating on center responses were observed in cells, which, when tested with center grating patches of increasing diameter, displayed considerable response suppression (RSI > 0.3; 22 of 59 cells). Typical examples of responses recorded in these cells are shown in Figs. 2 and 3. The diameter of the center grating patch (in a range of 6–9°) was set to elicit a maximal response. A striking characteristic of the center response modulation by the annular grating was the response dependence on relative orientations of the center and surround stimuli. When the annular grating was collinear with the grating of the center patch, the center response was most suppressed; in case of orthogonal orientations of the gratings, the response suppression was absent or much weaker. Often, response facilitation was even observed. Rotation of the center grating by 90° resulted in the 90° shift of the surround modulation pattern. The absolute orientation of the center grating affected to some degree the magnitude of the effect, but in every case, the response modulation depended on the relative orientations of the center and surround gratings as described.

This orientation-specific modulation was also observed in cells not tuned to the grating size. Their responses steadily rose and saturated with increasing diameter of the center patch or declined mildly after reaching the maximum (these cells are characterized by RSI < 0.15, n = 19). We tested the response modulation in these cells by applying a center patch of optimal diameter or of a diameter eliciting ~95% of the saturated response; typical values of diameters were in a range of 6–9°. The center responses were almost unaffected when the orientation of the annular grating was collinear to that of the center patch, in accordance with the cell’s area–response curve. However, many of these cells showed significant response facilitation when the grating orientations were orthogonal, as shown in the examples in Fig. 4. Again, the modulation profile depended on the relative grating orientations: rotation of the
Grating tests were located outside the classical RF outlined with the diameter of the aperture windowing the screen, inner diameter (the outer diameter of the annuli being equal to the diameter of the aperture). Observations were further tested by presenting flashing center spots. The orientation-specific modulation was independent of how the center grating patch exceeded an optimal value. Gratings spatial frequency (here and in all figures below) was 0.1 c/°; temporal frequency was 5 Hz. In each example show responses (solid curves, F1; dotted gray curves, when present, F0 Fourier components; mean ± SE) to drifting grating patches and annuli; SA, spontaneous activity. A–D: the plots of responses to the center grating patch and annulus presented together; orientation of the grating annulus varied (indicated at x-axis), whereas the orientation of the center patch was permanent; response to the center patch presented alone is shown at right (dashed line), its diameter and orientation are as indicated. A and B only differ by the orientation of the center grating patch. Note that changing its orientation results in the shift of modulation pattern by the same angle. C: responses to the annular grating of varying orientation presented alone (no responses in cell 1 example); the y-axis scale is the same as in the chart above. D: responses to the center grating patch of varying orientation presented alone; arrows indicated the center responses corresponding to these shown in A and B. E: area response curves plotted vs. the grating patch diameter; right to the curve, the response to the center patch of 20° in diameter is shown. Note that, in these examples, the cells displayed strong response decrease when the diameter of the center grating exceeded an optimal value. Gratings spatial frequency (here and in all figures below) was 0.1 c/°; temporal frequency was 5 Hz. In F, the charts show responses (500-ms average) to the flashing stimuli; responses are plotted against the diameter of the flashing center spots (solid curves, off-responses) or against the inner diameter of the annulus (dashed curves, on-responses); annulus outer diameter was equal to the diameter of visible screen. PSTH below each chart corresponds to the peak response in the chart.

The orientation-specific modulation was independent of how robustly the cell’s response was tuned to grating orientation: even the cells showing no orientation tuning displayed strong orientation-specific modulation of the center response, as shown in Fig. 3.

All the cells in which orientation-specific modulation was observed were further tested by presenting flashing center spots of light of varying diameter and flashing annuli with varying inner diameter (the outer diameter of the annuli being equal to the diameter of the aperture windowing the screen, ~36°). The goal was to check whether the grating annuli used in two-grating tests were located outside the classical RF outlined with the diameter of the aperture. We found that responses, antagonistic to those elicited by the center spot, were present in all cases when the inner diameter of the flashing annulus was considerably larger than the inner diameter of the grating annulus used in two-grating tests. Frequently, the inner diameter of the flashing annulus was even larger than the outer diameter of the annular grating (as shown in examples in Fig. 2). Thus the annular gratings lay entirely within the limits of the classical RF surround or extended beyond it; the gratings were never entirely outside the classical RF surround.

A summary of quantitative characterization of the center response modulation by the annular gratings presented in the RF surround is presented in Fig. 5. We characterized the strength of modulation by two indices: mMax and mMin (Eq. 2). The plot of indices calculated for 74 cells in which the modulation was...
significant (by a criterion \( m_{\text{Max}} - m_{\text{Min}} > 0.2 \)), and the histogram of modulation depth \( (m_{\text{Max}} - m_{\text{Min}}) \) in these cells showed that, in a majority of these cells, a facilitation of the center response by a simultaneous presentation of the annular grating occurs; the effect of the annular grating was strong: modulation depth exceeded 0.6 in 56 of 74 cells (Fig. 5, A and B). We calculated the correlation between the orientation selectivity indices OSI and mOSI in 59 concentric RGCs, which displayed the modulatory effect of the surround stimulation and in which both indices were measured. Results are presented in Fig. 5C; the two indices show rather weak correlation. Analysis of correlation between the degree of the cell’s area response tuning (RSI) and the mOSI index showed that they correlate strongly (Fig. 5D).

**ON-OFF and ON-directional RGCs**

These cells showed responses to the spot of light moving in the preferred direction and no or very weak responses to movement in the opposite direction. Occasionally, we also encountered bidirectional units (of on-type) showing optimal responses for movement in both directions along the axis of the preferred orientation. The direction-tuned cells of both types also displayed a strong increase in the mean spike rate and a robust modulated response at the fundamental grating frequency (F1) when stimulated with the center patch of the drifting grating. The cell responses were tuned for the patch size and for the drift direction, but not, in case of uni-directional cells, for the grating orientation: the grating drifting in the preferred direction elicited maximal response, whereas the grating of the same orientation but drifting in the opposite direction (i.e., whose orientation differed by 180° with respect to the first) elicited no or minimal response, as shown in the examples in Figs. 6 and 7. When tested with a center grating patch and grating annuli placed in the RF surround, all cells tested (ON-OFF, \( n = 8 \); ON, \( n = 6 \)) displayed strong modulation of the center response by the peripheral annular grating, which itself was
ineffective in eliciting the cell’s response. The orientation dependence of modulation was very similar to that reported in the previous section: regardless of absolute orientations of the center grating patch and of the grating annulus, the strongest response suppression was observed when the gratings presented in the RF center and surround were collinear; the maximal response corresponded to the orthogonal grating orientations, and frequently, this response was stronger than those elicited by the center stimulation alone.

Local edge detectors

These cells were encountered infrequently and were characterized by ON-OFF responses and small RF size (typically in a range of 3–5°); overall we encountered five cells of this type. The cells responded moderately but reliably to the center grating patch and showed some response dependence on the grating orientation. They also showed responses to moving spots but no directional selectivity. When tested in two-grating experiments, these cells showed very strong modulation of the center response by the annular grating, which, when presented alone, induced no responses. Representative examples of their responses are shown in Fig. 8. The magnitudes of the center response suppression or facilitation by the annular grating varied somewhat depending on its absolute orientation, but in every case, the center response modulation profile was dependent on the relative orientations of the center grating patch and the annular grating in the RF surround: the center response was maximally suppressed when the gratings were collinear, and the response was maximal when the gratings were orthogonal. When the orientation of the center grating was changed, the modulation pattern shifted correspondingly. In some cells, the center response was strongly facilitated by the annular grating orthogonal to the center grating (example of Fig. 8, cell 2).

**DISCUSSION**

Our data showed that the properties of rat RGCs, described using traditional analysis, conform to standard classifications, including the classical center–surround relationship in concentric RGCs. However, we uncovered evidence of more complex RF properties. We showed that, in a majority of rat RGCs, a modulation of the center response by the surround depends on the relative orientations of the two grating stimuli. The effect was observed in all major RGC types but was strongest in nonstandard cells, directional RGCs, and the local edge detectors. Approximately 40% of concentric RGCs also showed this kind of response modulation. The RGCs of the concentric type are the most common RGCs in the mammalian retina and were most frequently encountered in our recordings; the properties

**FIG. 4.** Examples of orientation-specific modulation of the center response by an annular grating presented in the RF surround. In each example, A shows, in the same way as in Fig. 2, the center response modulation by annular gratings presented in the RF surround. Note the shift of the modulation pattern when the orientation of the center patch grating is changed. B: top: the area response curves; note that responses of these cells increased monotonically or decreased only slightly after reaching the maximum. Bottom: plotted responses vs. the orientation of the center patch of grating. PSTHs show responses to the flashing stimuli as described in Fig. 2.
of orientation-specific modulation in these cells are the main focus of our study.

It is well documented in the literature that concentric RGCs display many effects that cannot be simply attributed to their classical RFs. Examples are 1) the shift-effect elicited by a sudden change in contrast or by a continuously moving texture in the far periphery of the RF (Barlow et al. 1977; Fischer and Kruger 1980; McIlwain 1966); 2) an increase or decrease, depending on the spatial and temporal structure of the stimulus, induced in the continuous discharge rate by remote moving patterns (Passaglia et al. 2001); and 3) suppression of responses to brief probes by simultaneous changes in surrounding patterns (Solomon et al. 2006). These effects are attributed to a separate RF mechanism, termed the far (extraclassical, modulatory) surround.

Novel in our study is a demonstration that modulation of the center responses by surround in RGCs is orientation specific and depends on the relative orientations of the center and surround gratings. The common notion is that the response modulation dependent on relative grating orientations described above is a context-dependent phenomenon that cannot be explained in the terms of the classical RF (Albright and Stoner 2002; Levitt and Lund 1997; Series et al. 2001, 2003; Sillito et al. 1995). First discovered in the VI, the phenomenon is considered as revealing an initial stage of context-dependent transformation of image into perception that starts in the visual cortex. Thus it is surprising to find such a complexity of response properties at the retinal level.

In the cortex, the contextual effects are thought to be mediated by cortico-cortical feedback from higher cortical areas and by long-range horizontal connections within V1; a network model of the center-surround modulation based on interconnections between neurons at different locations in the cortical orientation map has been proposed (Series et al. 2001).
FIG. 6. Examples of responses of ON-OFF directional cells to different stimuli. A–C: responses to grating stimuli presented in the same way as in Fig. 2 (responses to the annulus grating alone are shown below the chart C or B). D: responses to the spot of 4° in diameter brighter than background plotted vs. the direction of its movement through the RF center. E: responses to the center patch of drifting grating plotted vs. the grating orientation. The PSTHs show responses to the center flashing spot; the time scales are the same as in the histograms of Fig. 1 and elsewhere.
FIG. 7. Examples of responses of ON directional cells to different stimuli. A and B: responses to grating patches and annuli are shown in the same way as in the previous figures. C: responses to the moving 5° spot plotted vs. the movement direction. D: responses to the center patch of drifting grating plotted vs. the grating orientation. PSTHs show, in the same way as in Fig. 6, responses to the center flashing spot.
FIG. 8. Examples of responses recorded in ON-OFF local edge detectors. A and B show, in the same way as in previous figures, the center response modulation by the annular grating presented in the RF surround. C: responses to the spot of light moving through RF center. D: responses to the center patch of drifting grating plotted vs. the grating orientation. PSTHs show responses to the center flashing spot of light similar to those shown in the previous figures.
Orientation tuning of cortical neuronal responses is their major property and is suggested to play an important role in mechanisms underlying the orientation-specific modulation of the center responses from the RF far surround (for review, see Series et al. 2003). In the retina, there is no evidence that neuronal mechanisms specifically tuned for grating orientation are present (but see Shou et al. 2000). Orientation bias of responses shown in many RGCs is thought to reflect elongated profiles of their RFs (Passaglia et al. 2002; Soodak et al. 1987). Moreover, orientation selectivity perhaps plays no role in the orientation-specific modulation we uncovered in the retina: 1) the modulation was well expressed even in cells showing no orientation tuning of the center response and 2) population data show that the mOSI correlates weakly with the OSI. Perhaps the modulation effect of the RF surround we described in the retina may have more in common with the cortical mechanism related to the perceptual “pop-out” effect of the borders between texture regions.

Response modulation dependent on relative orientations of the grating patch and annulus, besides VI, have previously been seen in the rat superior colliculus (Girman and Lund 2007). There are controversial data on whether the effect of the surround stimulation in the lateral geniculate nucleus is tuned for grating orientation: whereas some studies found no preference for orientation of the surround effects (Bonin et al. 2005; Camp et al. 2009; Solomon et al. 2002), others showed its dependence on the relative orientations of the two gratings (Naito et al. 2007) or more complex relations (Sun et al. 2004).

In the cortical literature, orientation-specific center–surround response modulation is considered to arise from the salient far surround, spatially separated from the neuron’s classical RF. Our data cast doubts on whether the same notion can be applied to RGCs. First, we found a strong correlation of mOSI with the degree of response tuning to the stimulus size (Fig. 5). The descending branch of the area response curve in RGCs is commonly attributed to response suppression form the classical RF surround, whose involvement increases with the stimulus diameter increase. Second, in our experiments, the annular gratings were not in the far RF surround but in the classical RF surround. This was shown by presenting a uniform flashing annulus even in the more remote RF periphery: the annulus elicited a classical surround response, antagonistic to those elicited from the RF center. Thus geometrically, the annulus gratings were within the limits of the classical RF, but the stimulus strength was subthreshold for eliciting significant, if any, spike responses. Our results suggest that the classical RF mechanism and the mechanism underlying the orientation-specific modulation may originate from the same RF area. A similar conclusion was made regarding the extent of the extraclassical RF surround in the lateral geniculate nucleus of the cat and monkey (Bonin et al. 2005; Camp et al. 2009).

A majority of the cells that show orientation-specific modulation exhibits marked response facilitation when the center and surround gratings are orthogonal. In RGCs tuned to grating orientation, we observed a facilitation of the center response even in cases when the center grating patch was in a nonpreferred orientation. A similar type of response facilitation was reported previously in V1 (Sillito 1995), although this finding was not confirmed in other laboratories. One explanation for the facilitatory effect noted in this study is that facilitation was observed in tests where the surround grating abutted the center grating and thereby partly stimulated the center mechanism, so that the excitation of the classical RF center by the optimally oriented grating annulus summed with the response to the center grating patch (Angelucci and Bressloff 2006; Cavanaugh et al. 2002). Our data do not support this classical explanation of facilitation of responses to the center grating patch of nonpreferred orientation: 1) in some RGCs tuned for orientation, we observed facilitation of the response (to the center grating patch of an optimal diameter) with both preferred and orthogonal to that (nonpreferred), orientations of the annular grating, when the latter was orthogonal to the center grating; and 2) facilitation was observed even in the cells showing none orientation selectivity at all. Obviously, the facilitatory effect of modulation in these cases cannot be explained in terms of the classical RF mechanism and have to result from the orientation-specific center–surround modulation whose mechanism remains to be identified.

Whether the orientation-dependent surround effect in the retina is specific to rat is not clear: it has not been examined in the retinas of more heavily studied animals, such as the rabbit, cat, and monkey. However, a study in monkey retina (Solomon et al. 2006) showed a modulatory effect (while its orientation specificity has not been examined) of surround on center response, where stimulation of the surround alone had little effect on the cell’s response. This effect was mainly observed in magnocellular cells, a characteristic of which is a strong tuning to the size of the center grating. In line with this finding, our data showed a very reliable correlation between the mOSI and the degree of the response tuning to the size of the center grating (RSI index). It should be noted, however, that the monkey studies were using a different stimulation condition and were not specifically addressing the issue of orientation-specific surround effects on responses to center stimulation.

Although, following the cortical literature, we interpret our data as indicating that high-order visual processing can start in the retina, we cannot rule out that response dependence on relative orientations of the center and surround gratings might simply be a property of the classical RF described by the difference-of-Gaussians (DOG) model. From general considerations only, that seems improbable but must be proved. We can refer to a mathematical solution of response of the DOG model to circular grating patches concentric with the RF (Einevoll and Plesser 2005). Results showed that, in some conditions, expansion of the patch into the strong classical antagonistic surround results not in response suppression but in its facilitation; that seems very unexpected. Mathematical tools described in the referred paper allow as well finding response of the DOG model to the grating patch presented together with the annular grating. However, finding the solution is not a trivial task, which can constitute a goal of a separate study and is beyond the scope of our paper.

In conclusion, our findings suggest that initial stages of complex analysis of visual input, normally attributed to the visual cortex, can be achieved within the retina.

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GRANTS

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DISCLOSURES

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