Contrast Sensitivity Deficits in Inferred Magnocellular and Parvocellular Pathways in Retinitis Pigmentosa

Kenneth R. Alexander, Claire S. Barnes, Gerald A. Fishman, Joel Pokorny, and Vivianne C. Smith

PURPOSE. To define the contrast sensitivity deficits of patients with retinitis pigmentosa (RP) under testing conditions designed to emphasize threshold mediation by either the magnocellular (MC) or parvocellular (PC) pathway.

METHOD. Contrast sensitivity was measured with spatially localized, narrow-band test patterns at peak spatial frequencies ranging from 0.25 to 8 cycles per degree (cpd), using a steady-pedestal paradigm (brief presentation of the test stimulus against a continuously presented luminance pedestal) and a pulsed-pedestal paradigm (simultaneous brief presentation of the test stimulus and luminance pedestal) to favor the MC and PC pathways, respectively. The contrast sensitivity functions of 12 patients with RP who had visual acuities ranging between 20/12.5 and 20/40 were compared to those of 10 visually normal, age-equivalent control observers.

RESULTS. Five of the patients with RP who had Snellen visual acuities better than 20/25 had contrast sensitivity functions that were within the normal limits at all spatial frequencies for both testing paradigms. The other seven patients with RP had reduced contrast sensitivities for both paradigms, with the greatest reduction in sensitivity occurring at the highest spatial frequency. Their contrast sensitivity deficits were equivalent for the steady- and pulsed-pedestal paradigms.

CONCLUSIONS. As observed in previous studies, the degree of contrast sensitivity loss shown by the patients with RP was greatest at the highest stimulus spatial frequency. However, in comparison to prior studies of contrast discrimination in patients with RP, there was no evidence of a preferential contrast sensitivity loss within the MC pathway. This apparent discrepancy is attributed to differences in the test targets and psychophysical judgments that were used in the studies, which emphasizes the importance of task characteristics in evaluating relative deficits within the MC and PC processing streams in visual disorders. (Invest Ophthalmol Vis Sci. 2004;45: 4510 – 4519) DOI:10.1167/iovs.04-0188

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Retinitis pigmentosa (RP) refers to a group of hereditary retinal degenerations that are characterized by night blindness, peripheral visual field depressions or scotomata, abnormal electroretinograms (ERGs) of both the rod and cone systems, intraretinal bone-spicule–like pigmentation, and narrowing of the retinal vessels. Because the integrity of the rod system is often severely compromised in patients with RP, the assessment of cone function is often the primary means of monitoring disease progression. The measurement of cone function is also likely to be an important outcome measure during trials of potential therapeutic interventions. Therefore, it is of considerable relevance to define the exact nature and extent of cone system dysfunction in RP, particularly of the foveal cone system, which can be affected less than the peripheral cone system, and therefore is more amenable to testing.

Clinically, the loss of foveal cone function in patients with RP is observed as a reduction in visual acuity. Patients with RP can also show a decrease in foveal spatial contrast sensitivity, as measured with grating stimuli1–5 and with letter optotypes. Typically, the contrast sensitivity deficits of patients with RP are greatest at high spatial frequencies, but patients’ performance also can be impaired at low spatial frequencies. The loss of contrast sensitivity that accompanies RP can be detrimental to patients’ mobility and can lead to difficulty in performing tasks of everyday life. Therefore, it is of interest to derive a better understanding of the deficits in contrast processing that can occur in such patients.

The encoding of contrast within the primate visual system is thought to be mediated by two processing streams with different response properties: the magnocellular (MC) and parvocellular (PC) streams. As characterized at the level of the retina and lateral geniculate nucleus (LGN), the MC pathway has a high contrast gain and saturates at relatively low levels of contrast, whereas the PC pathway has a more linear contrast-response function. It is presumed that the MC pathway is involved in the detection and discrimination of briefly presented, achromatic patterns of low contrast, whereas the primary roles of the PC pathway are thought to lie in visual resolution and chromatic processing (reviewed in Ref. 16).

Previous studies of contrast sensitivity deficits in patients with RP were not designed to determine whether contrast sensitivity was mediated by the MC or PC pathway. In those studies, contrast sensitivity typically was evaluated by using an extended viewing of printed charts. With long target durations, contrast thresholds can be equivalent for stimulus conditions that emphasize the MC and PC pathways. Consequently, either of the two pathways could have mediated the performance of the patients with RP.

Recently, contrast-processing deficits have been evaluated in patients with RP by using testing paradigms that are designed specifically to target the MC and PC pathways. These studies did not measure contrast sensitivity per se, but assessed the ability of patients with RP to discriminate among test squares of differing contrast presented within the foveal region. In those studies, the patients with RP showed a greater functional deficit under testing conditions...
that favored the MC pathway. However, as just mentioned, patients with RP often show reduced visual acuity, and they tend to show greater contrast sensitivity losses at high spatial frequencies. These deficits imply that visual function within the PC pathway can also be impaired in RP, and further that the spatial frequency of the test stimulus may be a relevant factor in evaluating relative deficits within the MC and PC processing streams. Previous studies of contrast processing deficits in RP that specifically examined MC- and PC-pathway deficits18,19 used test stimuli that consisted of large test squares with a broad spatial frequency content. Therefore, the presence of any spatial-frequency-dependent deficits in MC- and PC-pathway function could not be evaluated.

The purpose of the present study was to evaluate the relative contrast sensitivity deficits of patients with RP as a function of spatial frequency, by using psychophysical paradigms that were introduced recently to emphasize contrast sensitivity within inferred MC and PC pathways.20 These paradigms were used successfully to characterize contrast sensitivity deficits in patients with melanoma-associated retinopathy (MAR).21 An additional goal of the present study was to determine the relationship between the contrast sensitivity deficits of patients with RP, as measured with the steady- and pulsed-pedestal paradigms, and their contrast sensitivity and visual acuity losses, as measured with letters on conventional vision charts.

The spatial contrast sensitivity functions of a group of patients with RP were measured using spatially localized, narrow-band test stimuli (sixth spatial derivatives of Gaussians or D6 patterns22) of different spatial frequencies. Two paradigms of stimulus presentation were used: a steady-pedestal paradigm intended to favor the MC pathway and a pulsed-pedestal paradigm, to favor the PC pathway. In the steady-pedestal paradigm, there is a brief presentation of a test stimulus and an adapting field (luminance pedestal). As discussed previously,20 this paradigm favors the MC pathway, at least at low to intermediate spatial frequencies, because the test target is presented only briefly. In the pulsed-pedestal paradigm, there is a simultaneous brief presentation of a test stimulus and an adapting field (luminance pedestal). This paradigm favors the PC pathway because the abrupt onset of the luminance pedestal saturates the MC pathway.20

**TABLE 1. Patient Characteristics**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (y)</th>
<th>Log MAR</th>
<th>Log LCS</th>
<th>Log VFA</th>
<th>PSC Grade</th>
<th>Fundus (macula)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>34</td>
<td>-0.16</td>
<td>1.88</td>
<td>4.05</td>
<td>0.0</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>40</td>
<td>-0.16</td>
<td>1.88</td>
<td>3.40</td>
<td>0.2</td>
<td>Epiretinal membrane</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>56</td>
<td>-0.06</td>
<td>1.70</td>
<td>3.21</td>
<td>0.5</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>26</td>
<td>-0.04</td>
<td>1.78</td>
<td>3.10</td>
<td>0.5</td>
<td>Normal</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>22</td>
<td>0.05</td>
<td>1.65</td>
<td>4.01</td>
<td>0.0</td>
<td>Epiretinal membrane</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>44</td>
<td>0.05</td>
<td>1.65</td>
<td>5.54</td>
<td>0.5</td>
<td>Bull’s-eye lesion</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>48</td>
<td>0.07</td>
<td>1.65</td>
<td>1.91</td>
<td>0.0</td>
<td>Normal</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>23</td>
<td>0.08</td>
<td>1.68</td>
<td>2.37</td>
<td>0.2</td>
<td>Bull’s-eye lesion</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>38</td>
<td>0.11</td>
<td>1.50</td>
<td>1.63</td>
<td>0.0</td>
<td>Normal</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>36</td>
<td>0.14</td>
<td>1.65</td>
<td>2.84</td>
<td>0.5</td>
<td>Epiretinal membrane</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>53</td>
<td>0.22</td>
<td>1.65</td>
<td>2.33</td>
<td>0.5</td>
<td>Normal</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>47</td>
<td>0.26</td>
<td>0.94</td>
<td>2.22</td>
<td>0.0</td>
<td>Bull’s-eye lesion</td>
</tr>
<tr>
<td>Control range</td>
<td></td>
<td>23–57</td>
<td>-0.27 -- -0.09</td>
<td>1.65-1.93</td>
<td>4.00-4.14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LCS, letter contrast sensitivity (Pelli-Robson chart); VFA, visual field area (log square degrees), with a Goldmann II/4e target; the control range is from Ref. 23; PSC, posterior subcapsular cataract, based on the grading scale of Ref. 24.

**METHODS**

**RP Patients and Control Observers**

Twelve patients (four women and eight men) with typical RP (age range, 22–56 years) participated in the study. Their characteristics are given in Table 1. In this table, patients are listed in order of increasing log MAR (logarithm of the minimum angle of resolution) or decreasing visual acuity. All patients had a best-corrected visual acuity that was better than 0.3 log MAR (20/40 Snellen equivalent) in the tested eye (which was chosen at random) and had minimal or no posterior subcapsular cataract. Three patients (2, 5, and 10) had mild epiretinal macular membranes in the tested eye, and three patients (6, 8, and 12) had a bull’s eye–like macular lesion, but no patient had an atrophic lesion or cysts within the fovea. With one exception (patient 8), all the patients were isolated cases, with no other known affected family member. The genetic type of patient 8 was uncertain, because X-linked transmission could not be excluded.

The spatial contrast sensitivity functions of the patients with RP were compared with those of 10 visually normal, age-equivalent control observers (age range, 23–57 years). The control observers had best corrected visual acuities that were better than 0.0 log MAR (20/20 Snellen equivalent) in the tested eye, clear ocular media, and normal-appearing fundi on ophthalmic examination. The study adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review board of the University of Illinois at Chicago. Informed consent was obtained from all observers after the nature and possible consequences of the study had been explained to them. All participants were remunerated for their participation.

**Stimuli and Equipment**

The test stimuli were identical to those used in a previous study21 and are illustrated in Figure 1. The test stimulus was a one-dimensional D6 pattern, which has a spatial frequency bandwidth of approximately one octave at half-height.22 The D6 pattern was defined by a sixth spatial derivative of a Gaussian in one direction and a Gaussian in the orthogonal direction. The space constant of the orthogonal Gaussian was a constant proportion of the peak spatial frequency of the D6 pattern and was chosen so that the test target was approximately circular.

The test target was presented in the center of a square luminance pedestal that subtended 7.6° on a side and had a luminance of 12.5 cd/m². The pedestal in turn was presented in the center of a steady adapting field that subtended 10.5° horizontally by 9.1° vertically and had a luminance of 25 cd/m². As illustrated in Figure 1, the pedestal produced a luminance decrement of 0.3 log unit, relative to the
The contrast sensitivity Chart (Haag-Streit, Köniz, Switzerland), using procedures described in a previous report.\textsuperscript{23} In a separate session, the visual fields of the patients with RP were obtained with a Goldmann perimeter, using II/4e and V/4e targets. All patients with RP had central visual field diameters for the V/4e target that were greater than 10°, with the exception of patient 9, whose central visual field diameter was 8°. The visual field data for the II/4e target were planimeterized to derive the total visual field area. As observed previously in patients with RP,\textsuperscript{24} there were significant inverse correlations between the patients’ log MAR values and their large-letter log contrast sensitivities ($r = -0.76$, $P < 0.01$), and between their log MAR values and log visual field areas ($r = -0.65$, $P < 0.05$). However, the correlation between log contrast sensitivity and log visual field area was not statistically significant ($r = -0.50$, $P = 0.10$).

The procedure for measuring contrast sensitivity for the D6 patterns was then explained and observers were given a brief practice series. Two testing paradigms were used. In the steady-pedestal paradigm (Fig. 1A), the luminance pedestal was presented continuously. During the test period, the D6 pattern was presented briefly against the luminance pedestal. In the pulsed-pedestal paradigm (Fig. 1B), the luminance pedestal and D6 pattern were presented briefly and simultaneously during the test period. For both paradigms, the test stimulus duration was 45 ms (three video frames).

A 50-second period of adaptation preceded each test condition. The observer initiated each trial by pressing a button on a response pad (GamePad; Gravis, San Mateo, CA). After a brief warning tone, the stimulus was presented. The observer’s task was to judge whether the D6 pattern was vertical or horizontal on that trial and to record the response by pressing the corresponding button on the response pad. The order of conditions was fixed at 1, 0.5, 2, 4, 0.25, and 8 cpd. Within each condition, the order of the steady- and pulsed-pedestal paradigms was randomized. Thus, there were 12 testing conditions within an experimental session (six spatial frequencies × two paradigms). In a pilot study, a spatial frequency of 16 cpd was also included, but no control observer was able to respond correctly at the highest contrast at this spatial frequency and duration. Additional testing showed that the difference between this result and that of a previous study,\textsuperscript{20} in which visually normal observers could detect a D6 pattern of 16 cpd, was due to the use of circular rather than elongated D6 patterns.

Contrast thresholds were measured with a two-alternative, forced-choice procedure based on an accelerated stochastic approximation.\textsuperscript{26} There were two randomly interleaved staircases: one for vertical and one for horizontal orientation of the D6 pattern. The staircase steps were defined by the relationship

$$X_{n+1} = X_n - \frac{c}{2 + m_{\text{sh}}} (Z_n - \phi), \quad n > 2,$$

where $X_n$ is the step size on trial $n$, $c$ is the initial contrast value, $m_{\text{sh}}$ is the cumulative number of reversals, $Z_n$ is the observer’s response (0 or 1), and $\phi$ is the percent correct value (80% in the present experiment). Each staircase was terminated after the 12th reversal. The threshold for each orientation was defined as the mean of all data points for that orientation beginning with the sixth reversal. There were no systematic differences between the contrast thresholds for the two stimulus orientations for any of the observers, so the results for the two orientations were averaged.

**RESULTS**

The mean contrast sensitivity functions of the control observers for the steady- and pulsed-pedestal paradigms are presented in Figure 2. As in previous reports,\textsuperscript{20, 21} the mean contrast sensitivity function for the steady-pedestal paradigm was low-pass in shape, whereas the function for the pulsed-pedestal paradigm had a band-pass shape. As a consequence, the greatest difference in contrast sensitivity occurred at the lowest
spatial frequency, and the functions tended to converge at the highest spatial frequency.

A repeated-measures analysis of variance (ANOVA) and post hoc t-tests with Bonferroni correction for multiple comparisons showed that there were statistically significant differences between the contrast sensitivities of the control observers for the two paradigms at all spatial frequencies ($t = 21.97, 17.83, 14.63, 8.96, 4.71, 2.52$; all $P < 0.05$; for 0.25, 0.5, 1, 2, 4, and 8 cd/p, respectively). The sensitivity difference between the steady- and pulsed-pedestal paradigms at the higher spatial frequencies was greater in the present study than in a previous report.20 Pilot testing indicated that this was due to the use of circular D6 patterns in the present study rather than elongated D6 patterns, which tend to favor the PC pathway.

In accordance with a previous study,20 the significant differences between the mean contrast sensitivities for the steady- and pulsed-pedestal paradigms are interpreted as indicating that, on average, the contrast sensitivities of the control observers were mediated by the MC pathway for the steady-pedestal paradigm and by the PC pathway for the pulsed-pedestal paradigm over this range of spatial frequencies. However, there was some overlap of the 95% confidence limits at the two highest spatial frequencies, indicating that, for some of the control observers, contrast sensitivities for both paradigms were mediated by the PC pathway at those frequencies.

The contrast sensitivity functions of the individual patients with RP are presented in Figures 3 and 4. For clarity, the patients’ results have been divided into two groups. Figure 3 presents the results for five patients with RP (patients 1, 2, 4, 5, and 6) whose contrast sensitivities were within or above the 95% confidence limits of the control observers (shaded regions) under all conditions. Figure 4 presents the data for seven patients with RP (3, 7, 8, 9, 10, 11, and 12) whose contrast sensitivities were below the 95% confidence limit of the control observers for more than one spatial frequency. In each figure, the contrast sensitivities for the steady-pedestal paradigm are plotted in the top graph, and the contrast sensitivities for the pulsed-pedestal paradigm are plotted in the bottom graph.

The separation of the patients’ data into Figures 3 and 4 tended to parallel their visual acuity reductions. That is, those patients with RP who had normal contrast sensitivity functions (Fig. 3) all had log MAR values that were $<0.1$ (better than 20/25 Snellen equivalent; Table 1). With one exception (patient 3), those patients with RP who had abnormal contrast sensitivity functions (Fig. 4) had worse visual acuities than those whose data are plotted in Figure 3. The seven patients with RP who had abnormal contrast sensitivity functions showed deficits for both the steady-pedestal paradigm (Fig. 4, top) and pulsed-pedestal paradigm (Fig. 4, bottom). Their contrast sensitivity deficits were particularly pronounced at the highest spatial frequency. That is, none of these seven patients...
had measurable contrast sensitivities at 8 cpd for the pulsed-pedestal paradigm (i.e., their contrast threshold exceeded the maximum available contrast of 0.97 [0.01 log contrast sensitivity]), and only three (patients 3, 9, and 10) had normal contrast sensitivity for the steady-pedestal paradigm at this spatial frequency.

To determine whether the patients with RP showed a preferential deficit in contrast sensitivity under test conditions that favored either the MC or the PC pathway, we examined the log ratios of the contrast sensitivities for the steady- and pulsed-pedestal paradigms for each patient. These log ratios are plotted in Figure 5. The top graph presents the data of the five patients with RP who had normal contrast sensitivity functions. The bottom graph presents the results for the seven patients with RP who had abnormal contrast sensitivity functions.

To determine whether the patients with RP showed a preferential deficit in contrast sensitivity under test conditions that favored either the MC or the PC pathway, we examined the log ratios of the contrast sensitivities for the steady- and pulsed-pedestal paradigms for each patient. These log ratios are plotted in Figure 5. The top graph presents the data of the five patients with RP who had normal contrast sensitivity functions. The bottom graph presents the results for the seven patients with RP who had abnormal contrast sensitivity functions.

The data in Figure 5 represent the vertical distance between the log contrast sensitivity functions for the steady- and pulsed-pedestal paradigms. For the control observers (shaded region), the greatest vertical separation occurred at the lowest spatial frequency, and the difference decreased systematically with increasing spatial frequency (see Fig. 1). Log ratios near zero (Fig. 5, dashed line) indicate that the PC pathway mediated contrast sensitivity for both testing paradigms. Data points that lie below the shaded region represent a relatively greater sensitivity loss for the steady-pedestal paradigm (inferred greater sensitivity loss within the MC pathway), whereas data points above the shaded region represent a greater sensitivity loss for the pulsed-pedestal paradigm (inferred greater sensitivity loss within the PC pathway).

In the five patients with RP who had normal contrast sensitivity functions (Fig. 5, top), the log ratios fell generally within the normal region, as expected. This was also typically the case in the seven patients with RP who had abnormal contrast sensitivity functions (Fig. 5, bottom). Nevertheless, patients 11 and 12, who had the worst visual acuity and lowest letter contrast sensitivity, had log ratios that were slightly below the 95% confidence limit at intermediate spatial frequen-
cies, consistent with a slightly greater sensitivity deficit within the MC pathway.

There was generally good agreement between the contrast sensitivities of the 12 patients with RP as measured with D6 patterns and their contrast sensitivities and visual acuities for letter optotypes that were presented on conventional test charts. The correlations between these two sets of measurements are presented in Table 2 (correlations at 8 cpd were not included because of the small number of patients with RP who had measurable contrast sensitivities for the D6 target at this spatial frequency). There were statistically significant correlations between the patients’ log letter contrast sensitivities and their log contrast sensitivities for the steady- and pulsed-pedestal paradigms, except for the pulsed-pedestal paradigm at the lowest and highest spatial frequencies. The correlations with letter contrast sensitivity were highest for the steady-pedestal paradigm at intermediate spatial frequencies. There were also statistically significant correlations between the patients’ log MAR values and their log contrast sensitivities for the steady- and pulsed-pedestal paradigms at all spatial frequencies above 0.25 cpd. The correlations with log MAR were greatest at the highest spatial frequencies.

Representative scatterplots of these correlations are presented in Figures 6 and 7. Figure 6 provides an illustration of the relationship between log contrast sensitivity as obtained with the Pelli-Robson chart and log contrast sensitivity using the steady-pedestal paradigm. For this comparison, the spatial frequency of the D6 pattern was 1 cpd, which corresponds approximately to the peak spatial frequency of the letters on the Pelli-Robson chart (0.94 cpd, based on a stroke width of 32 arcmin at the testing distance of 1 m). Although the correlation between the two measures of contrast sensitivity was driven to a large extent by the data of patient 12, there remained a statistically significant correlation when the data of this patient were omitted from the analysis ($r = 0.70$, $P < 0.05$). Of note, eight of the patients with RP had contrast sensitivities that were within the 95% confidence limits of the data for the control observers (shaded region) for both the Pelli-Robson chart and the steady-pedestal paradigm. Only two (patients 9 and 12) had contrast sensitivities that were below the 95% confidence limits for both measures of contrast sensitivity. Two additional patients (7 and 10) had a reduced steady-pedestal contrast sensitivity for the D6 patterns but had a normal letter contrast sensitivity. The bivariate regression line in Figure 6 had a slope near unity (1.12), representing equivalent reductions in the two types of contrast sensitivities. However, the patients’ sensitivities were approximately 0.3 log units lower for the D6 patterns than for Pelli-Robson contrast sensitivity. This is probably due to the difference in the duration of stimulus presentation, which was 45 ms (and thus within the critical duration for temporal summation for the steady-pedestal paradigm) but was unlimited for the Pelli-Robson chart.

The relationship between log MAR and log contrast sensitivity for the pulsed-pedestal paradigm at 4 cpd is presented in Figure 7. This plot illustrates the range of the visual acuities of the patients who were tested in this study. This particular correlation was chosen because 4 cpd was the highest spatial frequency for which data were available for the majority of patients with RP, and, further, it is likely that both pulsed-pedestal contrast sensitivity and log MAR were governed by the PC pathway. Only three of the patients in Figure 7 had log MAR values and log contrast sensitivities for the pulsed-pedestal paradigm that were within the 95% confidence limits of the control observers. The other nine patients had log MAR values that were beyond the 95% confidence limits, and six of these patients also had log contrast sensitivities for the pulsed-pedestal paradigm at 4 cpd that were lower than the 95% confidence limits. In comparison, only four of the patients with RP whose data are plotted in Figure 6 had contrast sensitivities for both measures that were outside the 95% confidence limits of the control subjects. This comparison of Figures 6 and 7 suggests that the patients with RP were more abnormal when the test conditions involved stimuli of high spatial frequency.

**Table 2.** Correlations Between Log Contrast Sensitivity for D6 Patterns, Log MAR, and log LCS of the Patients with RP

<table>
<thead>
<tr>
<th>Spatial Frequency (cpd)</th>
<th>0.25 ($n = 12$)</th>
<th>0.5 ($n = 12$)</th>
<th>1.0 ($n = 12$)</th>
<th>2.0 ($n = 12$)</th>
<th>4.0 ($n = 11$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Steady-pedestal paradigm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>log LCS</td>
<td>0.62*</td>
<td>0.92***</td>
<td>0.92***</td>
<td>0.86***</td>
<td>0.61*</td>
</tr>
<tr>
<td>log MAR</td>
<td>-0.40</td>
<td>-0.69*</td>
<td>-0.69*</td>
<td>-0.86***</td>
<td>-0.84**</td>
</tr>
<tr>
<td><strong>Pulsed-pedestal paradigm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>log LCS</td>
<td>0.53</td>
<td>0.75**</td>
<td>0.76**</td>
<td>0.80**</td>
<td>0.57</td>
</tr>
<tr>
<td>log MAR</td>
<td>-0.57</td>
<td>-0.74**</td>
<td>-0.69*</td>
<td>-0.85***</td>
<td>-0.81**</td>
</tr>
</tbody>
</table>

LCS, letter contrast sensitivity. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. 

![Figure 6](https://example.com/figure6.png)

**Figure 6.** Relationship between log contrast sensitivity for a D6 pattern of 1 cpd, presented in the steady-pedestal paradigm, and log contrast sensitivity as measured with a Pelli-Robson chart. **Symbols:** results for the individual patients with RP; **shaded region:** 95% confidence limits for the data of the control observers. **Solid line:** bivariate regression line fit to the data of the patients with RP.
The indication of a greater sensitivity loss at high spatial frequencies is borne out by an examination of the patients' visuograms, which are presented in Figures 8 and 9. These graphs plot the log threshold ratio between the data of each patient with RP and the mean of the control observers at that spatial frequency (the mean control values are represented by the horizontal dashed line in each plot). As in Figures 3 and 4, the data have been plotted separately for the two groups of RP patients: those who had contrast sensitivities within the 95% confidence limits of the control observers (Fig. 8), and those with contrast sensitivities that were lower than these limits for more than one spatial frequency (Fig. 9).

The five patients with RP whose data are plotted in Figure 8 had log sensitivity ratios that were within the 95% confidence limits of the control observers (shaded region) for both the steady- and pulsed-pedestal paradigms, as expected. Nevertheless, these patients tended to show a greater sensitivity loss at the highest spatial frequency for both paradigms. For the steady-pedestal paradigm, for example, the patients’ data points were at or above the dashed line (representing the mean control values) at 0.25 cpd, but the data points for four of the five patients were below the dashed line at 8 cpd. Similarly, for the pulsed-pedestal paradigm, the three patients who had the worst visual acuity (patients 4, 5, and 6) were well within the 95% confidence limits for the control observers at 0.25 cpd but were at the lower limit of normal at 8 cpd. This trend of a greater contrast sensitivity loss at high spatial frequencies was more apparent for the seven patients with RP whose data are presented in Figure 9. None of these seven patients had measurable contrast sensitivities at 8 cpd for the pulsed-pedestal paradigm, and four had unmeasurable contrast sensitivities for the steady-pedestal paradigm at this spatial frequency.

The contrast sensitivity deficits of the patients in Figure 9 at the highest spatial frequencies were greater than would be predicted from an overall loss of contrast sensitivity (i.e., if there were a uniform downward shift of the corresponding contrast sensitivity functions of the control subjects). A uniform downward shift would produce a log sensitivity ratio that was constant across spatial frequencies, and this was typically not the case. This was particularly evident for the two patients who had the worst visual acuities (patients 11 and 12). The visuograms of these two patients showed a consistent decline in relative contrast sensitivity across spatial frequencies. This trend toward a greater loss of contrast sensitivity at high spatial frequencies was confirmed by a repeated-measures ANOVA in which the contrast sensitivities of the six patients with RP who had the worst visual acuities (patients 7–12; Fig. 7, rightmost filled symbols) were compared to those of the control observers, collapsed across testing paradigms. There was a statistically significant group-by-spatial frequency interaction in this analysis ($F = 2.41, P < 0.05$), although this interaction was not statistically significant when patients with RP who had lesser degrees of visual acuity loss were included in the ANOVA. By this analysis, then, the contrast sensitivity deficits of the patients with RP who had the worst visual acuities were not uniform across spatial frequencies, but were greater at high spatial frequencies.

**DISCUSSION**

In this study, we evaluated the contrast sensitivity deficits of a group of patients with RP within the framework of the MC and PC contrast-processing streams. The patients showed losses of
It is likely that this apparent disparity between studies is related to key differences in the stimulus configurations and psychophysical tasks involved. The previous studies of contrast discrimination required observers to identify the location of a pedestal square that differed in contrast from three other pedestal squares, all of which were relatively large (1° in width). A recent study of the spatial summation properties of contrast discrimination in visually normal observers indicated that contrast discrimination within the pulsed-pedestal paradigm under these conditions is based on the luminance contrast at the edges of the targets. Further, according to this study, there is considerable spatial summation of such edge information, presumably at a cortical level. As a result, even if there were a substantial loss of receptive fields within the PC pathway in RP, the availability of abundant edge information in the pedestal squares of the previous studies may have led to an underestimation of the loss of PC-pathway sensitivity. By comparison, the one-dimensional D6 patterns that were used in the current study, which were circular in shape, contained little edge information that could have contributed to detection. Thus, circular D6 patterns appear to provide a more sensitive measure of dysfunction within the PC pathway than do the large pedestal squares that were used in previous studies of contrast discrimination in patients with RP. Consistent with this conclusion is our observation that the patients with RP showed significant correlations between their contrast sensitivities, as measured with D6 patterns, and their visual acuities and contrast sensitivities, as measured with letter optotypes.

For both the steady- and pulsed-pedestal paradigms, the patients' contrast sensitivity losses occurred across a range of spatial frequencies, but the losses were most pronounced at the highest spatial frequency (8 cpd). This predominant loss of contrast sensitivity at high spatial frequencies is consistent with previous studies that did not use test conditions that were designed to emphasize selectively the MC and PC pathways. Further, our results are in agreement with the previous observation that the contrast sensitivity functions of patients with RP are not simply shifted uniformly downward from normal.

It is presently uncertain why patients with RP show a greater loss of contrast sensitivity at high spatial frequencies. A reduced quantal catch by foveal cone photoreceptors, which has been described as a "dark-glasses" model of RP, does not appear to be an adequate explanation. Studies in which retinal densitometry and color matching have been employed have shown evidence of a reduced optical density of foveal cone photopigment in patients with RP (although Swanson and Fish found no evidence of reduced foveal cone optical density in patients with RP whose visual acuities were within the range of the patients in the present study). However, a reduced cone photopigment optical density would effectively decrease the mean retinal illuminance of the stimulus display but would not alter the stimulus contrast. Therefore, under adapting conditions for which Weber's law holds, such as in the present study, a decreased retinal illuminance would not be expected to produce a contrast sensitivity loss at high spatial frequencies. This was confirmed in a pilot investigation in a control observer. Further, previous studies have concluded that a dark-glasses model of RP does not account for various aspects of foveal vision loss in these patients, including abnormalities in temporal contrast sensitivity, increment thresholds, probe-on-flash thresholds, motion perception, and symmetry discrimination. Consequently, it seems unlikely that a decreased quantal catch due to a reduced foveal cone optical density accounts for the high-spatial-frequency deficits shown by patients with RP.

A reduced responsiveness of the foveal cone photoreceptors, which has been examined in previous studies as a potential explanation for foveal abnormalities in RP, also does not appear to be an adequate explanation for the predominant loss of contrast sensitivity at high spatial frequencies. Reduced cone photoreceptor responsiveness would be expected to result in a uniform loss of contrast sensitivity across spatial frequencies, but this was not observed. Further, in these studies of a possible reduced photoreceptor responsiveness in patients with RP, a probe-on-flash paradigm was used, which is similar to the pulsed-pedestal paradigm used in the present study. This paradigm is thought to favor the PC pathway. As a consequence, any reductions in maximum response amplitude (R_{max}) observed in studies of probe-on-flash thresholds may have represented the impact of cone photoreceptor degeneration on the response properties of the PC pathway, rather than the response properties of the cone photoreceptors per se. For example, one way in which a reduction in R_{max} could occur is through a dropout of foveal cone photorecepto-
tors from a summation pool within the PC pathway. Therefore, a reduced responsiveness of the foveal cone photoreceptors does not appear to be a satisfactory explanation for the loss of contrast sensitivity at high spatial frequencies shown by these patients with RP.

A reduction in the spatial density of foveal cone photoreceptors owing to cone photoreceptor cell death seems a likely explanation for the predominant contrast sensitivity loss at high spatial frequencies in RP. Histologic studies have reported a reduced number of foveal cone photoreceptors in RP donor eyes, even in those eyes that had relatively good visual acuity. Nevertheless, simulations of spatial sampling deficits that have been performed in visually normal observers have led to the conclusion that a random loss of foveal cone photoreceptors is not likely to be the major determinant of patients’ performance deficits at high spatial frequencies. For example, the visual acuity of control observers is relatively well-preserved despite a substantial decrease in the number of visual samples, intended to mimic a loss of cone photoreceptors. Further, a study of the effect of spatial undersampling on contrast sensitivity for D6 patterns in control observers, in which random portions of the target were replaced by the background, found that contrast sensitivity was reduced equivalently at all spatial frequencies, rather than predominantly at high spatial frequencies. In addition, another form of undersampling produced by static visual noise that was presented simultaneously with a D6 test target (analogous to the pulsed-sampling produced by static visual noise that was presented alentely at all spatial frequencies, rather than predominantly at background, found that contrast sensitivity was reduced equivalently at all spatial frequencies, rather than predominantly at high spatial frequencies. In addition, another form of undersampling produced by static visual noise that was presented simultaneously with a D6 test target (analogous to the pulsed-pedestal paradigm used in this study) resulted in a greater contrast sensitivity deficit at low than at high spatial frequencies in control observers, contrary to the results of the present study. Thus, none of these various sampling paradigms predicts the relatively greater contrast sensitivity loss at high spatial frequencies observed in patients with RP. However, the extent to which these sampling paradigms accurately mimic a random loss of foveal cone photoreceptors remains to be determined.

On a practical note, it is often assumed that visual acuity that is better than 20/40 (0.3 log MAR), as seen in the patients with RP in the present study, provides a viable degree of visual function. For example, visual acuity of 20/40 or better is the criterion for a driver’s license in most U.S. states. However, in individuals with retinal disease, our results emphasize that there can be a substantial reduction in sensitivity to contrast at these presumably modest levels of visual acuity loss. As an example, RP patient 12, whose Snellen visual acuity was slightly better than 20/40 (Table 1), had an approximately 10-fold reduction in contrast sensitivity for the steady-pedestal paradigm at moderate to high spatial frequencies (Fig. 4) as well as a similar reduction in letter contrast sensitivity (Fig. 6).

In conclusion, the patients with RP in this study showed equivalent contrast sensitivity deficits under testing conditions that targeted the MC and PC pathways. These results are in apparent disagreement with previous studies of contrast discrimination in RP in which greater deficits were found under conditions that favored the MC pathway. This apparent discrepancy is likely to be due to the nature of the testing conditions that were used in the various studies. That is, contrast discrimination among large test stimuli, used in the prior studies, may not be as sensitive to damage to the PC pathway as is orientation discrimination of a spatially band-limited stimulus, used in the present study. Consistent with previous studies of contrast sensitivity in RP that did not specifically target the MC and PC pathways, we observed a greater loss of contrast sensitivity at high spatial frequencies in this group of patients with RP. The exact explanation for the high-spatial-frequency deficits in contrast sensitivity in patients with RP remains to be resolved, although a reduction in the spatial density of the foveal cone photoreceptors may be a major contributor.

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References


