Contrast discrimination deficits in retinitis pigmentosa are greater for stimuli that favor the magnocellular pathway

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Abstract

Luminance contrast discrimination was measured in 14 patients with retinitis pigmentosa (RP) and 14 control observers with normal vision, using steady-pedestal and pulsed-pedestal paradigms [Pokorny, J., & Smith, V. C. (1997). Psychophysical signatures associated with magnocellular and parvocellular pathway contrast gain. Journal of the Optical Society of America A, 14, 2477–2486] to bias performance toward the magnocellular (MC) or parvocellular (PC) pathway, respectively. The aim was to determine the relative effects of retinal degeneration on MC- and PC-pathway function in RP. For five of the RP patients, contrast discrimination thresholds were within normal limits for both the steady-pedestal and pulsed-pedestal paradigms. The other nine RP patients showed threshold elevations for the steady-pedestal paradigm (presumed magnocellular mediation), whereas their thresholds for the pulsed-pedestal paradigm (presumed parvocellular mediation) were within normal limits for all but the two patients who had the most extreme threshold elevations using the steady-pedestal paradigm. A control experiment on four of the RP patients, using a greater number of pedestal contrasts, verified that the patients' thresholds for the pulsed-pedestal paradigm showed the pattern expected for contrast discrimination mediated by the PC pathway. The higher threshold elevations for the steady-pedestal paradigm than for the pulsed-pedestal paradigm indicate that the retinal degeneration that occurs in RP predominantly disrupts contrast discrimination under stimulus conditions that favor the MC pathway. © 2001 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Retinitis pigmentosa (RP) refers to a heterogeneous group of hereditary retinal degenerations that are characterized functionally by night blindness, peripheral visual field restrictions and/or scotomas, and abnormalities in the electroretinogram (ERG) of both rod and cone systems (Bird, 1995). In addition, patients with RP can show a reduction in foveal contrast sensitivity that extends across a broad range of spatial frequencies and/or letter sizes (Alexander, Derlacki, & Fishman, 1992a; Sucs & Uvijls, 1992). There is a high correlation between patients' letter contrast sensitivities at large letter sizes and their high-contrast visual acuities (Alexander, Derlacki, & Fishman, 1995a).

The exact explanation for the loss of contrast sensitivity in RP is uncertain at present. Nevertheless, recent studies have highlighted the significant relationship between contrast sensitivity and the performance of tasks of everyday life (e.g. Haymes, Guest, Heyes, & Johnston, 1996; Turano, Gurschat, Stahl, & Massof, 1999). Consequently, it is of interest to provide a better understanding of the nature of the deficits in contrast perception that are experienced by individuals with RP.

There is considerable evidence that contrast processing within the normal human visual system is mediated by two distinct pathways with different contrast response properties, (1) a magnocellular (MC) system

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that has a high contrast gain and saturates at relatively low contrasts; and (2) a parvocellular (PC) system that has a low contrast gain and a more linear contrast response function (reviewed by Kaplan, Lee, & Shapley, 1990; Merigan & Maunsell, 1993; Lee, 1996). The temporal properties of these two pathways also differ, in that the cut-off frequency for the achromatic temporal modulation transfer function is higher for cells within the MC pathway (Lee, Pokorny, Smith, Martin, & Valberg, 1990). Consequently, the MC pathway is more sensitive than the PC pathway in detecting a brief change in luminance. However, the MC pathway shows poor discrimination among luminance transients. The exact roles of these two pathways in vision remain controversial (e.g. Merigan & Maunsell). However, it is generally held that the MC pathway, which sums inputs from long-wavelength-sensitive (LWS) and middle-wavelength-sensitive (MWS) cones, is involved in the detection and discrimination of low-contrast achromatic patterns and in motion processing, whereas a primary role of the PC pathway, which shows spectral opponency for LWS and MWS cones, is in chromatic processing (reviewed by Pokorny & Smith, 1997).

As discussed by Swanson, Birch, and Anderson (1993), there is reason to expect that the disease process in RP might have a greater effect on the PC than on the MC pathway. Because the receptive field centers of foveal PC ganglion cells typically receive input from a single cone (Kaplan et al., 1990), damage to a random subpopulation of foveal cone photoreceptors would be very disruptive to the PC ganglion cells that receive input from those dysfunctional cones. Further, there is greater spatial as well as temporal summation within the PC pathway (Sun, Pokorny, & Smith, 1999), so that the functional loss of a fraction of PC cells could have a major impact on the response properties of the PC system, as discussed by Swanson, Pearson, and Fellman (1999). A selective loss of PC cell function might account for the reduced visual acuity of RP patients, given that lesions specific to the PC pathway have been shown to decrease the visual acuity of macaque monkeys (Lynch, Silveira, Perry, & Merigan, 1992). Such a selective loss of PC cell function might also account for the impaired chromatic discrimination that has been reported in patients with RP (Massof et al., 1979; Fishman, Young, Vasquez, & Lourenc¸o, 1981).

It is also plausible, however, that the disease process in RP could have a greater effect on the MC than on the PC pathway. The receptive field centers of ganglion cells within the MC pathway sum the input from a number of photoreceptors, and therefore, tend to be larger than the receptive field centers of PC ganglion cells (Croner & Kaplan, 1995). Further, MC ganglion cells are sparser than PC ganglion cells (Perry, Oehler, & Cowley, 1984), so that MC-pathway function is potentially more susceptible to disease processes owing to its reduced redundancy (Chauhan & Johnson, 1999). Suggestive evidence for an impairment within the MC pathway has been provided by observations that patients with RP can have difficulty with tasks that involve vernier acuity (Alexander, Derlacki, Fishman, & Szlyk, 1992b) and judgments of spatial displacements (Turano & Wang, 1992; Alexander, Derlacki, Xie, Fishman, & Szlyk, 1998), which are thought to be mediated by the MC pathway (Lee, Wehrhahn, Westheimer, & Kremers, 1993, 1995).

Based on a recent study (Pokorny & Smith, 1997), it should be possible to test whether there is a greater effect of photoreceptor degeneration on either the PC or MC pathway by using specific paradigms of contrast discrimination — the steady-pedestal and pulsed-pedestal paradigms. Data obtained with these paradigms have been found to have the contrast gain, spatiotemporal, and adaptational properties associated with the MC and PC pathways, respectively (Pokorny & Smith). These two stimulus paradigms are illustrated in Fig. 1. In the steady-pedestal paradigm (Fig. 1B), four squares (the pedestal) are presented continuously within a surrounding field. During the test trial, one square is incremented briefly in luminance. The task is to identify the location of the square that changed contrast. In the pulsed-pedestal paradigm (Fig. 1A), an adapting field is presented continuously. During the test trial, four squares (the pedestal) are presented briefly, with one square incremented in luminance from the other three. The task is to identify the location of the square that differed in contrast.

Fig. 1. Illustration of the stimulus display. (A) Stimulus sequence for the pulsed-pedestal paradigm. A black fixation dot was presented in the center of a homogeneous adapting field. During the test interval, a four-square pedestal array was presented briefly (30 ms), with one square incremented in luminance relative to the other three. (B) Stimulus sequence for the steady-pedestal paradigm. A black fixation dot was presented in the center of a four-square pedestal array that was shown continuously. During the test interval, one of the squares was incremented briefly (30 ms) in luminance.
The contrast discrimination functions for these two paradigms are quite different, and are illustrated in Fig. 2A, which presents the mean results for a group of eight control observers. In the steady-pedestal paradigm (open squares), discrimination thresholds increase monotonically with pedestal luminance, with a slope of unity (corresponding to Weber’s law). Thus, threshold data for pedestals that are darker than the surround luminance. The arrows on the x-axes indicate the surround luminance. (A) Mean thresholds for eight control observers for a range of pedestal luminances. Curves through the filled squares represent the least-squares best fit of Eq. (1). The diagonal line represents Weber’s law and passes through the grand mean of the steady-pedestal data. (B) Mean thresholds for 14 control observers for a subset of the pedestal luminances shown in (A). The dashed curves and diagonal line have been replotted from (A).

In comparison, the high contrast gain and saturation at low contrasts reported for the MC pathway can only be observed by using a pedestal-delta-pedestal paradigm (Pokorny & Smith, 1997), of which the steady-pedestal paradigm is the limiting case. In the pedestal-delta-pedestal paradigm, the pedestal squares are presented continuously, but they are all incremented or decremented in luminance by a small amount simultaneous with the presentation of the test square (in the steady-pedestal paradigm, the overall increment of the pedestal squares during a trial is zero). For the pedestal-delta-pedestal paradigm, the contrast discrimination threshold is elevated substantially when the overall pedestal is incremented or decremented from the steady value by only a small fraction of a log unit during the test trial. The magnitude of the threshold elevation above the steady-pedestal condition is consistent quantitatively with the high contrast gain reported for the MC pathway (Pokorny & Smith, 1997; Snippe, 1998).

In addition to these differences in contrast response properties, the steady-pedestal and pulsed-pedestal paradigms also differ in their temporal summation characteristics, as detailed in Pokorny and Smith (1997). Temporal summation extends to considerably longer durations for the pulsed-pedestal than for the steady-pedestal paradigm (i.e. 150–200 vs. 40–50 ms). Further, the temporal summation properties of the steady-pedestal and pulsed-pedestal paradigms are similar to those derived from temporal contrast sensitivity functions for purely luminance and purely chromatic modulation (Swanson, Ueno, Smith, & Pokorny, 1987).

In sum, the contrast gain, adaptational, and temporal summation properties of the steady-pedestal and pulsed-pedestal paradigms differ systematically and are consistent with those associated with the electrophysiologically described MC and PC pathways, respectively.
Therefore, in the present study, we used these two paradigms of luminance contrast discrimination in order to investigate whether there is a greater effect of the retinal degeneration process on either MC- or PC-pathway function in RP.

2. Method

2.1. Subjects

Fourteen patients (6 women and 8 men) with typical RP or Type 2 Usher syndrome (age range, 28–53 years) participated in the study. The patients’ characteristics are presented in Table 1. All patients had 20/40 or better best-corrected visual acuity in the tested eye (which was chosen at random), and had minimal or no posterior subcapsular cataracts. Three patients (Nos. 2, 3, and 10) had mild epiretinal macular membranes in the tested eye; one patient (No. 7) had an atrophic-appearing macular lesion; and one patient (No. 12) had a bull’s eye-like macular lesion, but no patient had macular cysts. Four of these patients (Nos. 2, 5, 11, and 13) also participated in a control experiment that examined contrast discrimination with a greater number of pedestal contrasts. For patient No. 2, the contralateral eye (which showed a slightly greater visual acuity deficit) was tested in the second session. For the other three patients, the same eye was tested in both studies. A period of approximately 1 year elapsed between the two sets of measurements.

For the main part of the study, the contrast discrimination thresholds of the patients with RP were compared with those from 14 (9 women and 5 men) age-similar control observers with normal vision (age range, 24–60 years). In the second experiment using multiple pedestal contrasts, eight control observers with normal vision were tested (five women and three men; age range, 22–47 years). Two of these control observers also participated in the main study. The control observers had best-corrected visual acuities of 20/20 or better in the tested eye, clear ocular media, and normal-appearing fundi on ophthalmologic examination. Control observers were remunerated for their participation. Appropriate institutional review board approval was obtained, and all observers gave informed consent before testing.

2.2. Test stimuli

The test stimuli and procedure were based on those used by Pokorny and Smith (1997). Stimuli were generated by a Macintosh PowerPC 7500:100 and were presented on an Apple high-resolution gray-scale display that had a P4 phosphor, a vertical scan rate of 66.67 Hz, and a resolution of 640 × 480 pixels. As illustrated in Fig. 1, the stimulus was an array of four squares (the pedestal), with each square subtending 1° of visual angle, separated by 9.2 arcmin. The four squares were presented within a steady surround that subtended 12° horizontally by 9° vertically and filled the region between the squares. A black fixation dot 9.2

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<th>Age</th>
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<th>Genetic type‡</th>
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<th>log CS</th>
<th>log field area (deg²)†</th>
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*Based on the relative elevation of steady-pedestal and pulsed-pedestal thresholds (see text).

[1] Iso, isolated; Rec, autosomal recessive; Ind, genetic, indeterminate type; Ush 2, type 2 Usher syndrome; MAR, minimum angle of resolution; CS, Pelli–Robson contrast sensitivity.

[2] Visual fields were obtained with a Goldmann II/4e target. Control data are from the 21 observers of Ross, Fishman, Gilbert, and Anderson (1984).
arcmin in width was presented in the center of the display at all times.

Stimuli were viewed monocularly with the natural pupil through the best optical correction in a phoropter at a test distance of 1 m. A 10-bit video board (Radius ThunderPower 30/1600) and a linearized lookup table controlled the stimulus luminances. The surround luminance was held constant at 30 cd/m². For the main part of the study, the pedestal luminances were 15, 30, and 60 cd/m². For the control experiment, additional pedestal luminances of 19, 24, 38, and 47 cd/m² were included. Luminances were calibrated with a Minolta LS-110 photometer.

Two paradigms of contrast discrimination were used, as described in Section 1 and illustrated in Fig. 1. In the steady-pedestal paradigm, the four pedestal squares were presented continuously. During a test trial, the test square, chosen randomly, was incremented briefly in luminance following a warning tone. In the pulsed-pedestal paradigm, the four pedestal squares were presented only during the test trial, following a warning tone, with one square having a higher luminance than the other three. For both paradigms, the observer’s task was to identify the location of the square that differed in contrast from the other three.

The test stimulus duration was 30 ms (two video frames), which was brief enough to be within the range of temporal summation for both paradigms and thus provide the maximal threshold difference between steady-pedestal and pulsed-pedestal conditions, based on the temporal summation data of Pokorny and Smith (1997). This duration was also long enough to provide a sufficient working range of luminance in the case of elevated contrast discrimination thresholds. Stimulus durations were confirmed using a photocell and oscilloscope.

2.3. Procedure

The visual acuity of all observers was assessed with a Lighthouse Distance Visual Acuity Test and letter contrast sensitivity was measured with a Pelli–Robson Contrast Sensitivity Chart, using procedures described previously (Alexander et al., 1995a). In a separate session, the visual fields of the patients with RP were obtained with a Goldmann perimeter, using a II/4e target. Visual field data were planimeterized in order to derive the total visual field area.

Because it was not feasible to test all of the RP patients on the extended set of conditions shown in Fig. 2A, we chose a limited set of conditions that were judged most likely to differentiate between MC and PC pathway dysfunction. To that end, we used pedestals that differed in luminance from the surround by 0.3 log units in both positive and negative directions. We also included a condition in which the pedestal luminance equaled the surround luminance, and measured the contrast threshold for each pedestal square separately. The purpose was to determine whether there might be scotomas in the region of the visual field corresponding to the stimulus array.

Prior to testing, the contrast discrimination procedure was explained and observers were given a practice series. A 1-min period of adaptation preceded each test condition. The observer initiated each trial by pressing a button on a response pad (Gravis Gamepad). Following the test stimulus presentation, a black cross appeared in the center of the display, and the observer pressed the appropriate diagonal portion of a joystick button to move the cross to the outer corner of the chosen square. The observer then pressed a response button to confirm the choice, and pressed the same button again to initiate the next trial.

Thresholds were measured using a four-alternative forced-choice adaptive staircase procedure with no feedback. The initial staircase step was set at a fixed contrast level that was easily visible to all observers, based on pilot work. The step size was then halved until a criterion size of 1.56% of the initial step size was reached, and then it remained fixed for the remainder of the staircase. A ‘2-down, 1-up’ decision rule was used, in which two successive correct responses were required to reduce the contrast, whereas a single incorrect response increased the contrast. This decision rule corresponds to the 71% correct point on a psychometric function (regardless of the number of stimulus alternatives; Levitt, 1971). The staircase was continued until ten reversals had occurred at the criterion step size.

The first test condition was one in which the pedestal luminance equaled the surround luminance. This is a measure of detection, which is a special case of contrast discrimination (Pokorny & Smith, 1997). For this condition, thresholds were measured separately for each of the four squares using four interleaved staircases. The purpose was to determine whether any of the squares fell on scotomatous regions. The other four test conditions were then presented in random order. For each condition, the first two reversals in each staircase were discarded, and the threshold was defined as the mean of the last eight staircase reversals. For the ‘pedestal equals surround’ condition, the threshold was defined as the mean of the individual staircase estimates for each of the four squares. Pilot data indicated that the thresholds derived in this way were equivalent to those obtained with a single staircase.

In a subsequent experiment, using a greater number of pedestal luminances, the procedure was modified in order to obtain a full set of thresholds within a single testing session of reasonable duration. Specifically, the adaptation interval at the beginning of each condition was shortened to 30 s, and the number of staircase reversals at the criterion step size was reduced to seven,
3. Results

3.1. Contrast discrimination using steady-pedestal and pulsed-pedestal paradigms

Thresholds for the individual pedestal squares under the ‘pedestal equals surround’ condition are shown in Fig. 3. Data for the control observers are shown in the bottom panel and data for the individual patients with RP are shown in the top panel. For comparison, the shaded region in the top panel represents the 95% confidence limits for the control observers. The thresholds were analyzed by a repeated-measures analysis of variance. According to the Tukey test for multiple comparisons, there were no significant threshold differences among the individual squares for the control observers ($P > 0.05$). The maximum threshold difference across squares for the control observers was 0.24 log unit.

The patients with RP (top panel) showed a range of overall threshold elevations. The Tukey test indicated that there was a significant threshold difference between the squares at the upper right and lower right locations ($P < 0.01$), but no other comparisons were significant ($P > 0.05$). The significant threshold difference between these two squares was due primarily to the four patients who had the highest overall thresholds. Of these four patients, Nos. 13 and 14 had a maximum threshold difference among the squares that was near the upper limit of normal (0.22 and 0.26 log unit, respectively), and the other two patients (Nos. 11 and 12) had intersquare threshold differences of 0.34 and 0.42 log unit, respectively. The latter patient was the one who had a bull’s eye-like macular lesion.

Inspection of the staircases for these four patients indicated that the differences in intersquare thresholds represented systematic differences in sensitivity at these visual field locations (most likely resulting from local nonuniformities in the retinal disease process), because the staircases showed small but consistent differences in the thresholds for the four patches. However, these small differences in sensitivity are not likely to have affected performance on the single-staircase conditions, based on the fact that the standard error of the staircase estimates were not systematically higher for these four patients than for the other patients with RP.

The mean contrast discrimination thresholds for the control observers under the five standard test conditions are shown in Fig. 2B. The error bars in this figure indicate the 95% confidence limits, and the dashed lines correspond to the solid lines from Fig. 2A, replotted for comparison. It is apparent that the results were similar for both groups of control observers. For the steady-pedestal paradigm (open triangles in Fig. 2B), thresholds increased systematically with pedestal luminance in accordance with Weber’s law, as in Fig. 2A. For the pulsed-pedestal paradigm (filled triangles in Fig. 2B), thresholds were substantially higher than those for the steady-pedestal paradigm, and were above the ‘pedestal equals surround’ condition for both decrements and increments, equivalent to the results shown in Fig. 2A.

The contrast discrimination thresholds for the individual patients with RP under these five standard test conditions are presented in Fig. 4A–D. For clarity of presentation, the patients’ results have been separated into four sets, based on the overall pattern of results. However, as will be seen in Fig. 6, the patients’ results actually represent a continuum of dysfunction in terms of which the last six were averaged to obtain the threshold contrast. The 13 test conditions were presented in a random order.
of contrast discrimination. For the first set of five RP patients, shown in Fig. 4A, contrast discrimination thresholds were within normal limits for all of the test conditions. Normal limits are defined as the 95% confidence limits for the control observers and are indicated by the shaded regions in the plots. These confidence limits have been replotted from Fig. 2B.

The other nine patients with RP had various degrees of threshold elevation. The second set of five RP patients, shown in Fig. 4B, had mildly elevated thresholds for the steady-pedestal paradigm (open symbols), but had thresholds for the pulsed-pedestal paradigm (filled symbols) that were within the normal limits or at the upper limit of normal. Set 3 (Fig. 4C) consisted of two patients who had a marked elevation of contrast discrimination thresholds for the steady-pedestal condition, but whose pulsed-pedestal results were within normal limits. The threshold elevation for the steady-pedestal paradigm for these two patients was approximately 0.4 log unit above the upper limit of normal and 0.6 log unit above the normal mean. Set 4 (Fig. 4D) consisted of two RP patients whose contrast discrimination thresholds were elevated for both the steady-pedestal and the pulsed-pedestal paradigms, but were more elevated for the steady-pedestal paradigm. Their thresholds were approximately 0.7 log unit above the upper limit of normal (0.9 log unit above the normal mean) for the steady-pedestal paradigm, but only 0.2 log unit above the upper limit of normal (0.5 log unit above the normal mean) for the pulsed-pedestal paradigm. It is apparent, then, that for the nine RP patients who showed some degree of impairment in contrast discrimination, thresholds were more elevated for the steady-pedestal than for the pulsed-pedestal paradigm.

For three of the four RP patients who had the highest threshold elevations in the steady-pedestal paradigm (Nos. 11, 13, and 14; Fig. 4C and D), the threshold functions tended to flatten at the lowest pedestal luminance. It is possible that this might have been due to intraocular light scattered from the surround, given that RP patients can have increases in intraocular straylight even in the absence of clinically observable lens opacities (Alexander, Fishman, & Derlacki, 1996). To determine whether this might be the case, we tested one of the patients (No. 14) under two additional conditions, (1) using a surround luminance that was equal to the decrement pedestal luminance (15 cd/m²); and (2) using a surround of 30 cd/m² that extended only 9.2 arcmin beyond the pedestal squares. This patient’s thresholds were equivalent under the three conditions, indicating that light scatter was not likely to have been the primary factor for the deviation from Weber’s law at the lower pedestal luminance. A more likely explanation is considered in Section 4.3.

3.2. Contrast discrimination at multiple pedestal luminances

![Fig. 4. Contrast discrimination thresholds for the 14 patients with RP for the steady-pedestal (open symbols) and pulsed-pedestal (filled symbols) paradigms. The inset in each plot indicates the relationship between the symbols and patient numbers from Table 1. The shaded regions represent the 95% confidence limits for 14 control observers, replotted from Fig. 2B, with the darker shaded regions indicating the results for the pulsed-pedestal paradigm. The arrows on the x-axes indicate the luminance of the surround. (A) Patients within set 1, whose thresholds all fell within normal limits. (B) Patients within set 2, whose thresholds were mildly elevated for the steady-pedestal paradigm, but were within normal limits or at the upper limit of normal for the pulsed-pedestal paradigm. (C) Patients within set 3, whose thresholds in the steady-pedestal paradigm were elevated substantially, but whose thresholds in the pulsed-pedestal paradigm were within normal limits. (D) Patients within set 4, whose thresholds were elevated for both paradigms, but more so for the steady-pedestal paradigm.

It is possible that patients’ contrast discrimination thresholds in the pulsed-pedestal paradigm might have been abnormal at low pedestal contrasts despite being within normal limits at the higher contrasts shown in Fig. 4. This could occur, for example, if there was an increase in $C_{sat}$ within the PC pathway, which would have the effect of flattening as well as elevating the Y-shaped contrast discrimination functions normally obtained in the pulsed-pedestal paradigm. To examine this possibility, we measured contrast discrimination in
a subset of four of the RP patients, using a range of pedestal contrasts. The patients’ thresholds were measured in both the pulsed-pedestal and steady-pedestal paradigms, and results were compared with those of a group of eight control observers.

The results for the control observers are shown in Fig. 2A and were described in Section 1. To summarize these control results, thresholds in the steady-pedestal paradigm (open squares) increased with increasing pedestal luminance in accordance with Weber’s law (solid line). Thresholds in the pulsed-pedestal paradigm increased in a V-shaped pattern as the pedestal luminance was increased or decreased from the surround luminance, in a manner consistent with the contrast gain properties of the PC pathway (represented by the curves through the filled squares).

The results for the four patients with RP are shown in Fig. 5A-D. The shaded regions in these plots represent the 95% confidence limits for the control observers, replotted from Fig. 2A. The thresholds of the RP patients in the steady-pedestal paradigm (open symbols) showed varying degrees of threshold elevation, ranging from none (Fig. 5A), to mild (Fig. 5B), moderate (Fig. 5C), and extensive (Fig. 5D). These steady-pedestal thresholds generally conformed to Weber’s law, shown as the diagonal lines in Fig. 5, which have a slope of 1 and pass through the grand mean of the steady-pedestal thresholds. For two patients (Nos. 11 and 13), the threshold functions showed a flattening at low pedestal luminances, consistent with the results in Fig. 4. For these patients, the Weber functions were only fit to those thresholds that were beyond the initial horizontal portion, as indicated by the truncation of the diagonal line, which only extends through those data points that were included in the fit.

For all four patients with RP, the pulsed-pedestal thresholds (filled symbols in Fig. 5) conformed to the V-shaped function that characterizes contrast discrimination mediated by the PC pathway. Further, there was no evidence for a selective threshold elevation at low pedestal contrasts that would indicate an increase in $C_{sat}$ within the PC pathway. This is illustrated by the good fit of the curves through the filled data points. These curves represent the least-squares best fits of Eq. (1), with $C_{sat}$ fixed at unity as for the control observers, and only $R_{max}$ and $K$ as free parameters, with a simultaneous fit to both positive and negative contrasts. For patient No. 5, all pulsed-pedestal thresholds were included in the fit. For the other three patients, the thresholds for the steady-pedestal paradigm were so elevated that they approached those for the pulsed-pedestal paradigm at low contrasts, making it difficult to discern whether these thresholds were mediated by the MC or PC pathway. Therefore, for these patients, Eq. (1) was fit only to the pulsed-pedestal thresholds that clearly were above those for the steady-pedestal paradigm. This is indicated by the truncation of the fitted functions, which pass through only the data points included in the fits. For patient 13, who showed a clear separation between steady-pedestal and pulsed-pedestal thresholds for only four pedestal luminances, both $C_{sat}$ and $K$ were fixed, and only $R_{max}$ was varied.

For all four patients, the curves provide a reasonable fit to the pulsed-pedestal thresholds. In addition, for the three RP patients who had pulsed-pedestal thresholds that were within or near the normal limits (Nos. 2, 5, and 11), the derived values of $R_{max}$ were within the normal range described by Pokorny and Smith (1997). These results confirm, then, that contrast discrimination
thresholds can remain normal in shape and value for the pulsed-pedestal paradigm in patients with RP, despite elevated thresholds within the steady-pedestal paradigm, indicating that there is a greater functional impairment within the MC than within the PC pathway.

3.3. Relationship between contrast discrimination and other measures of foveal function

The correlations among the contrast discrimination thresholds of the 14 RP patients and the other measures of their visual function are presented in Table 2. For this table, contrast thresholds were converted to contrast sensitivities. All of the correlations were statistically significant except for the correlation between visual acuity and contrast sensitivity in the decrement pulsed-pedestal condition. In addition, the correlation between visual acuity and contrast sensitivity in the increment pulsed-pedestal condition was weak, although statistically significant. The implication of this low degree of correlation is considered in Section 4.2. Of note, there were high and statistically significant correlations between the patients’ log visual field areas and the various measures of foveal visual function. This implies that there is a diffuse, progressive component in RP that affects both peripheral and foveal cone function, as suggested by Massof et al. (1979).

Of particular interest are the high, statistically significant correlations between the patients’ contrast sensitivities derived from the steady-pedestal paradigm (presumed MC-pathway mediation) and their letter contrast sensitivities, given that contrast sensitivity at low spatial frequencies (large letter sizes) is thought to be mediated by the MC pathway (e.g. Wilson, 1997). Fig. 6 illustrates the relationship between contrast sensitivity derived from the ‘pedestal equals surround’ condition and Pelli–Robson letter contrast sensitivity for the individual patients with RP. Contrast sensitivities were higher overall for the Pelli–Robson chart than for the ‘pedestal equals surround’ condition. This is likely due to the difference in target duration, which was within the limits of temporal summation for the steady-pedestal paradigm but was unlimited for the Pelli–Robson chart, as per the testing instructions. Nevertheless, the patients’ data tended to cluster along the line in Fig. 6, which has a slope of 1 and passes through the normal mean, representing equal deficits in both measures. The high degree of correlation between these two measures of contrast sensitivity would be expected if both tasks are mediated by the same underlying mechanism.

![Fig. 6. Contrast sensitivity derived from the ‘pedestal equals surround’ condition vs. Pelli–Robson letter contrast sensitivity for the individual patients with RP (filled symbols). Data points for the RP patients are plotted by set, as indicated in the inset. The number next to each symbol refers to the patient number from Table 1. The solid line has a slope of 1 and passes through the mean of the control observers (open circle). Error bars represent the 95% confidence limits for the control observers.](image-url)
4. Discussion

4.1. Nature of contrast discrimination deficits in RP

The aim of this study was to examine the relative effects of the retinal degenerative process on MC- and PC-pathway function in patients with RP. This issue was evaluated by measuring thresholds for contrast discrimination using steady-pedestal and pulsed-pedestal paradigms in order to favor the MC and PC pathways, respectively (Pokorny & Smith, 1997). Threshold elevations were greater for the steady-pedestal than for the pulsed-pedestal paradigm for the nine RP patients who showed some degree of impairment in contrast discrimination in the main part of the study (Fig. 4). Further, thresholds for the pulsed-pedestal paradigm were within normal limits for all patients except the two who had marked elevations of their steady-pedestal thresholds. A control experiment on a subset of four of the RP patients confirmed that thresholds for the pulsed-pedestal paradigm had the V-shaped function expected for contrast discrimination mediated by the PC pathway, and that there was no selective threshold elevation at low pedestal contrasts that would indicate an increase in $C_{sat}$.

These results indicate, then, that there was a greater functional deficit within the MC than within the PC pathway in these patients with RP. The elevated thresholds shown by the RP patients in the steady-pedestal paradigm could represent either a decrease in $R_{max}$ or an increase in $C_{sat}$ within the MC pathway. To distinguish between these two possibilities would require use of the pedestal-delta-pedestal paradigm, which is difficult even for visually normal observers to perform and was beyond the scope of the present study. For the two patients out of the 14 who had elevated pulsed-pedestal thresholds (Nos. 13 and 14), the results from patient No. 13 (Fig. 5D) suggest that the threshold elevations are likely due to a decrease in $R_{max}$ within the PC pathway. If there had been an increase in $C_{sat}$, then this patient’s thresholds for the pulsed-pedestal paradigm would have been substantially higher than those for the steady-pedestal paradigm at low positive contrasts, and this was not the case.

An impairment in MC-pathway function is consistent with the deficits in high-frequency flicker sensitivity (Tyler, Ernst, & Lyness, 1984; Dagnelie & Massof, 1993), in vernier acuity (Alexander et al., 1992b), and in motion perception (Turano & Wang, 1992; Alexander et al., 1998) that have been reported previously in patients with RP. These are tasks that are presumed to be mediated by the MC pathway (Lee et al., 1993; Lee et al., 1995). The significant correlations between contrast sensitivity derived from the steady-pedestal paradigm and large-letter contrast sensitivity (Table 2) are also consistent with dysfunction of the MC pathway. A greater impairment in MC- than in PC-pathway function is in agreement with the previous observation that patients’ deficits in chromatic discrimination involving the LWS and MWS cone system (presumed to be mediated by the PC pathway; Pokorny & Smith, 1997) occur predominantly in those RP patients whose visual acuities are worse than 20/30 (Fishman et al., 1981). In our study, only two RP patients (Nos. 13 and 14), both with visual acuities of 20/40, showed elevated thresholds for contrast discrimination using the pulsed-pedestal paradigm, indicating an impairment within the PC pathway.

As described in Section 1, a likely explanation for the predominant deficit within the MC pathway is a reduced cone photoreceptor input to the receptive field centers of MC ganglion cells as a consequence of a loss of cone photoreceptors. Histologic studies have shown evidence of a reduced foveal cone spatial density in RP, even in patients with good visual acuity (Flannery, Farber, Bird, & Bok, 1989; Stone, Barlow, Humayun, de Juan, & Milam, 1992). And as discussed by Kaplan et al. (1990), a reduction in the number of photoreceptors that provide input to the receptive field centers of MC ganglion cells would effectively decrease the contrast sensitivity of those ganglion cells. If this is the explanation for the present results, then the large threshold elevations for steady-pedestal contrast discrimination seen in those patients with 20/30 to 20/40 visual acuity (nearly 1 log unit above the normal mean, Fig. 4D and Fig. 5D) indicate that there must be a considerable reduction in the cone photoreceptor input to the MC pathway within the foveal region.

4.2. Relationship between contrast discrimination and visual acuity deficits in RP

It might be expected that a large reduction in the number of foveal cone photoreceptors, as implied by our results, would have a greater effect on patients’ visual acuities than is seen in this group of RP patients, whose visual acuities were no worse than 20/40 (Table 1). However, studies of the effect of spatial sampling on visual performance have provided evidence that visual acuity should be little affected by undersampling by the foveal cone photoreceptor lattice, due in large part to the redundancy inherent in the visual stimuli (Geller, Sieving, & Green, 1992; Alexander, Xie, Derlacki, & Szlyk, 1995; Seiple, Holopigian, Szlyk, & Greenstein, 1995). As a result, visual acuity can theoretically be relatively preserved despite large losses of cone photoreceptor cells.

Further, the weak (and, in one case, non-significant) correlations between the RP patients’ visual acuities and their contrast discrimination thresholds within the pulsed-pedestal paradigm (Table 2) suggest that the
patients’ visual acuity deficits are not related directly to dysfunction of the PC pathway. In fact, the exact relationship between visual acuity deficits and PC pathway function remains equivocal (Lee, 1996). As indicated in the Introduction, lesions of the PC pathway have been shown to reduce the visual acuity of macaque monkeys (Lynch et al., 1992). However, the resolution capabilities of PC and MC ganglion cells are not dissimilar (Kaplan et al., 1990), and it has been hypothesized that the MC pathway plays a significant role in a luminance channel for spatial vision (Lee). As further support for this hypothesis, we found relatively high correlations between RP patients’ visual acuities and their thresholds within the steady-pedestal paradigm (Table 2). These significant correlations suggest that a major source of their visual acuity loss is a reduced contrast response within the MC pathway. This is consistent with the previous observation that RP patients can have an overall reduction in letter contrast sensitivity that extends across letter sizes (Alexander et al., 1992a), and that their visual acuity loss is correlated significantly with the loss of contrast sensitivity at large letter sizes (Alexander et al., 1995a). It is also consistent with a significant correlation reported previously (Alexander et al., 1992b) between patients’ deficits in vernier acuity (presumed to be mediated by the MC pathway, Lee et al., 1995) and their deficits in letter acuity.

4.3. Adapational properties of steady-pedestal contrast discrimination in RP

Four of the patients with RP had a greater threshold elevation in the steady-pedestal paradigm when the pedestal luminance was low (Fig. 4C and D, Fig. 5C and D). A control experiment indicated that this was not due to light scattered from the surround into the pedestal. Instead, it is more likely that this deviation from Weber’s law at the low pedestal luminance is related to the fact that the discrimination threshold began to approach the pedestal luminance itself for those patients with the greatest threshold elevations. That is, the steady pedestal would have had a lower effective value for the patients than for the control observers. As a consequence, the steady-pedestal threshold functions of those patients with RP (Fig. 4C and D, Fig. 5C and D) were effectively shifted rightward relative to those of the control observers.

However, it is also the case that their threshold functions were displaced vertically from those of the control observers, by an amount that was greater than the horizontal shift. This is indicated by the fact that the steady-pedestal functions for the patients and controls did not approach convergence at the higher pedestal luminances, as would be the case if there were a 45° translation of the patients’ functions. Our steady-pedestal results are consistent with previous reports of foveal increment thresholds in patients with RP (e.g. Sandberg & Berson, 1977; Alexander et al., 1991; Greenstein & Hood, 1992; Seiple, Holopigian, Greenstein, & Hood, 1993), in which patients showed greater vertical than horizontal shifts of their increment threshold functions. It has been suggested that these properties of the patients’ foveal increment threshold functions could be accounted for by a reduced foveal cone spatial density together with normal response properties of the remaining cone photoreceptors (Alexander et al., 1991; Seiple et al., 1993). The present results indicate further that the patients’ abnormal increment threshold functions are likely to represent the impact of cone photoreceptor loss on the adaptational properties of the MC pathway.

We note that our results for the steady-pedestal paradigm are inconsistent with a reduced quantal catch or ‘dark glasses’ model of foveal vision loss in RP that has been explored previously and generally discounted as an explanation for dysfunction of the foveal cone system in RP. There is evidence for a reduced foveal cone optical density in some RP patients within the visual acuity range included in our study (van Meel & van Norren, 1983; Elsner, Burns, & Lobes, 1987; but see Swanson & Fish, 1995). However, several previous studies have concluded that a dark glasses model does not account for many aspects of foveal vision loss in RP, including temporal contrast sensitivity (Tyler et al., 1984), probe-flash thresholds (Greenstein & Hood, 1986), motion perception (Turano & Wang, 1992), and foveal increment thresholds (Alexander et al., 1991; Seiple et al., 1993). Our present results are in agreement with that conclusion. A dark-glasses model predicts a 45° translation of the steady-pedestal threshold function, because the effective luminance of both the pedestal and the test stimulus would be reduced in equal proportion. This was not observed.

5. Conclusion

The patients with RP examined in this study showed greater deficits in contrast discrimination under stimulus conditions that are thought to represent the response properties of the MC pathway. These results suggest that the most sensitive tests for monitoring foveal function in patients with RP are likely to be those that involve the MC rather than the PC pathway (e.g. use of low-contrast stimuli, motion perception). The pathway-specific nature of the deficit in contrast discrimination in these patients indicates that RP may provide a means for exploring further the roles of the MC and PC pathways in visual processing.
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