Local Cone and Rod System Function in Patients with Retinitis Pigmentosa

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PURPOSE. To compare local cone and rod system function in patients with retinitis pigmentosa (RP) using electrophysiological and psychophysical techniques.

METHODS. Cone-mediated multifocal electroretinograms (M-ERGs), cone system threshold visual fields, rod-mediated M-ERGs, and rod system threshold visual fields were measured in seven patients with RP.

RESULTS. All the patients had normal cone system visual field thresholds and normal cone-mediated M-ERG implicit times within the central 5°. Both cone-mediated responses were abnormal at some peripheral retinal locations. There were significant correlations among cone system amplitude, timing, and visual field loss. All the patients had some retinal areas where the rod-mediated M-ERG amplitudes were not measurable. In areas where they were measurable, these rod-mediated M-ERG responses were often within normal limits for amplitude and timing. In contrast to the cone system data, there were no significant relationships between rod-mediated M-ERG measures and rod system threshold elevations. The cone and rod system psychophysical thresholds showed regional correspondence; the amplitude-scale and time-scale measures of the M-ERG did not.

CONCLUSIONS. The results indicate that there was better local correspondence between psychophysical and electrophysiological measures in the cone system than in the rod system in patients with RP. In addition, the psychophysical measures of cone and rod system function showed better correspondence than did the electrophysiological measures. (Invest Ophthalmol Vis Sci. 2001;42:779–788)

Retinitis pigmentosa (RP) is a group of degenerative retinal diseases that affect both dark- and light-adapted visual function.1 Typically, night vision is affected early in the disease and the dark-adapted full-field electroretinogram (ERG) reflects this loss of rod function. Visual function mediated by cones may be affected later in the disease, and the degree of cone impairment varies among patients with RP. Electrophysiologically, the cone system full-field ERG shows reductions in amplitude and delays in implicit time. In addition, psychophysical cone and rod system thresholds increase with disease progression.2,3 These deficits in both rod and cone function worsen as the disease progresses.

Although it is known that the rod and cone photoreceptors degenerate in RP, not much is known about the spatial distribution of the underlying electrophysiologic losses. Changes in the full-field ERG are well documented in patients with RP, but the full-field ERG reflects electrical activity summed across the entire retina and provides no information about local retinal activity. Recently, the development of the multifocal ERG (M-ERG) technique4 (see Hood5 for a review) has allowed researchers to gain information about localized cone-mediated electrical responses in patients with RP.5–9 These studies have shown that the cone-mediated responses of the midperipheral retina may not be recordable in patients with RP, or, in some patients, responses are reduced in amplitude and delayed. In the central retina, however, many patients are much less affected. Implicit times are often within normal limits, and amplitudes, although reduced, are still measurable. In addition, comparison of local cone-mediated electrophysiologic responses to local cone-mediated psychophysical sensitivity in patients with RP8 have indicated that retinal areas with normal implicit times typically have normal sensitivity.

There is much less information about local rod electrophysiologic activity in patients with RP. The rods are very sensitive to the effects of stray light at low light levels, and this sensitivity has made the development of techniques for assessing local rod function relatively difficult. Several investigators have measured rod responses for relatively local retinal areas.10–12 None of these techniques has allowed for the simultaneous recording of local rod function from a number of retinal areas, and none was used to gain topographic information about rod function. Recently, however, the M-ERG has been extended to record local dark-adapted rod-dominated M-ERG responses13 in control subjects. Application of this technique to the acquisition of local rod-mediated topography in patients with retinal diseases would increase our knowledge of the retinotopic distribution of rod system dysfunction in these diseases.

Recent evidence has suggested that in rod–cone retinal degenerative diseases, the degeneration of cones may be directly linked to and follow from the degeneration of rods.14–16 In fact, cone survival may directly depend on the preservation of spatially adjacent rods.16 Given this proposed relationship between cone and rod degeneration in RP, we were interested in comparing local cone and rod system electrophysiologic function in patients with RP to determine the spatial distribution of cone and rod system losses. To make this comparison, we applied the technique of recording rod-mediated M-ERG responses13 to patients with RP. In addition, we compared local cone-mediated and local rod-mediated M-ERG responses with psychophysically measured local cone and local rod system responses to determine how well these responses correspond in a group of patients with RP.

METHODS

Subjects

Seven patients with RP who were recruited from the practice of one of the authors (REC) participated in the study. The diagnosis of RP was
work of Sutter and Tran4 and has been described in detail elsewhere.8

Cone System Visual Fields. Threshold visual fields for the cone system were measured using a perimeter (Humphrey, San Leandro, CA). The standard program was modified to assess 103 points, including a central threshold point.6 Each test spot subtended 26 minutes of arc and was placed at the retinal location corresponding to the middle of each hexagon used for the cone-mediated M-ERG recording. The background luminance of the display was 10 candelas [cd]/m².

Cone System M-ERGs. After pupil dilation (1% tropicamide and 2.5% phenylephrine hydrochloride), cone-mediated M-ERGs were recorded. The M-ERG technique used in this study was based on the work of Sutter and Tran4 and has been described in detail elsewhere.8

Rod System Visual Fields. The subjects were dark adapted for 45 minutes before the measurement of the rod system measures. A computer program (written in Matlab; MathWorks, Natick, MA) was used to measure rod system dark-adapted thresholds as a function of retinal eccentricity. The stimulus display was viewed through a blue filter (Wratten 47B; Kodak, Rochester, NY). The display used was the same as for the rod M-ERG array, excluding the central hexagon, which contained a fixation spot. A method of limits was used to obtain individual thresholds for 60 hexagons. The hexagons were presented for approximately 50 msec.

Rod System M-ERGs. Rod-mediated M-ERGs were recorded using the method of Hood et al.13 The stimulus was an array of 61 equally sized hexagons. The stimulus display was viewed through a blue filter (Wratten 47B). At the viewing distance of 32 cm, the hexagon display subtended 42° horizontally and 38° vertically. A central X was used for fixation. The stimulus sequence was slowed with the insertion of three blank frames (3F). The rod-mediated M-ERG recording took 14 minutes to complete. The luminance of the hexagons was 0.125 cd/m² (bright) and 0.006 cd/m² (dim). A surround (0.28 cd/m²) was added to minimize the effects of stray light.13 The M-ERGs were recorded with a bipolar Burian-Allen electrode with the ipsilateral ear as the ground. The M-ERG signal was amplified (PS11 preamplifier Grass; 50,000), sampled at 1200 Hz, and band-pass filtered between 1 and 100 Hz.

Full-Field ERGs. Full-field ERGs were recorded using a photostimulator (Grass) with a Ganzfeld surround (see Table 1). ERGs were recorded with a bipolar contact lens electrode. The ipsilateral ear served as the ground. The signal was amplified (PS111 preamplifier Grass; 1000), sampled at 1000 Hz, and filtered (1–10,000). Dark-adapted mixed rod and cone system full-field ERGs were recorded to a bright white flash (S16 scotopic). For the majority of the patients, there was no recordable response to a dim (S1) blue flash. After 10 minutes of light adaptation to a Ganzfeld (3.5 log photopic troland [phot dl]), cone-mediated full-field ERG responses were recorded to 32-Hz flicker.

Analysis

For comparison, the cone and rod system visual field data were converted to log threshold elevation by calculating the difference between the patient’s log threshold and the averaged log threshold for the control group. Values more than 0.0 indicate elevated thresholds, whereas values less than 0.0 indicate thresholds better than the average control values.

The M-ERG responses were analyzed using programs written in Matlab (MathWorks).13 For the cone-mediated responses, the first 60 msec of the ERG trace for each hexagon was averaged across the control subjects to create 103 templates on a hexagon-by-hexagon basis, because previous work has demonstrated consistent shifts in waveform as a function of retinal position. We then fitted each control subject’s data to these templates to obtain individual esti-

### Table 1. Patients’ Clinical Characteristics

<table>
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<th>Patient</th>
<th>Type of RP</th>
<th>Sex</th>
<th>Age</th>
<th>Acuity (OD)</th>
<th>Full-Field ERG</th>
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Control ERG Norms: S16 scotopic mean = 363.7 ± 57.8 µV (SD); 44.9 ± 1.4 msec; photopic flicker mean = 128.2 ± 47.7 µV; 28.3 ± 3.1 msec.

AR, autosomal recessive; AD, autosomal dominant; OD, right eye; OS, left eye.

except on funduscopy and results from ERG (see Table 1), visual field, and dark-adapted sensitivity testing. These patients were chosen on the basis of good central vision, defined as visual acuity of 20/40 or better and central Goldmann visual fields (V4e) with diameters of 10° or greater. The patients had no evidence of cystoid macular edema, no clinically significant cataracts, and no other ocular or systemic diseases. The RP group had a mean age of 47.3 ± 13.3 years (SD; see Table 1). The control group consisted of eight age-similar observers with normal visual acuity and normal ophthalmic exams. The control group had a mean age of 45.6 ± 11.3 years. All subjects gave informed consent to participate after a full explanation of the procedure. Tenets of the Declaration of Helsinki were followed, informed consent was obtained after the nature and possible consequences of the study were explained, and the research was approved by the Institutional Board of Research Associates of New York University Medical Center and Bellevue Hospital.

### Apparatus and Procedure

In all subjects, the eye with the better visual acuity was tested. If visual acuity was equivalent in the two eyes, the right eye was tested. The contralateral eye was patched. For all data obtained with the left eye, the visual field and M-ERG locations were flipped so that retinal areas were comparable with the right eye data.

### Cone System Visual Fields

Threshold visual fields for the cone system were measured using a perimeter (Humphrey, San Leandro, CA). The standard program was modified to assess 103 points, including a central threshold point.6 Each test spot subtended 26 minutes of arc and was placed at the retinal location corresponding to the middle of each hexagon used for the cone-mediated M-ERG recording. The background luminance of the display was 10 candelas [cd]/m².

### Cone System M-ERGs

After pupil dilation (1% tropicamide and 2.5% phenylephrine hydrochloride), cone-mediated M-ERGs were recorded. The M-ERG technique used in this study was based on the work of Sutter and Tran4 and has been described in detail elsewhere.8 Briefly, the stimulus was an array of 103 hexagons that were scaled according to eccentricity. At the viewing distance of 32 cm, the hexagon display subtended 46° horizontally and 39° vertically. A central X was used for fixation. The stimulus sequence was set so each hexagon had a 50% probability of being white or black on each frame (0 F). The luminance of the white hexagons was 360 cd/m², the luminance of the black hexagons was 7 cd/m², and the surround luminance was 200 cd/m².

M-ERGs were recorded with a bipolar Burian-Allen electrode (Hansen Ophthalmic Development Laboratory, Iowa City, Iowa). The ipsilateral ear served as ground. The M-ERG signal was amplified (PS11 preamplifier; 100,000; Grass, Quincy, MA), sampled at 1200 Hz, and band-pass filtered between 10 and 300 Hz. Subjects wore best visual correction for the viewing distance and were light adapted to the ambient lighting conditions. Two recordings were obtained (3.6 minutes each) and averaged for analysis.
mates of variability for each hexagon. For each patient, the data for each hexagon were fitted to the corresponding template. The fit was achieved by varying two parameters. One parameter (amplitude-scale) scales the amplitude at each point to minimize the difference between response and template values. The second parameter (time-scale) is a multiplicative scaling of time that stretches the entire response waveform. For each hexagon, a least-squares fitting procedure yielded a value for the statistical fit. Based on previous results, the statistical fit levels were set at 0.75 for both the cone-mediated and rod-mediated M-ERGs.

For the rod-mediated responses, the data (VERIS; EDI, San Mateo, CA) were spatially averaged one time. The results for the first 140 msec obtained from the control subjects were averaged across hexagons, to obtain a single template measure for all 61 hexagons, because there was little local change in the rod-mediated responses as a function of retinal position for the control observers. For each patient, the data for each hexagon were fit to the template.

The amplitude results for each hexagon were plotted as amplitude-scale, which is the ratio of the amplitude of the patient response relative to the amplitude of the control template. Values smaller than 1.0 indicate that the amplitude of the patient responses were reduced, relative to the control responses. Likewise, implicit time values were converted to time-scales in the same manner, with values larger than 1.0 indicating delays in timing. The conversions to amplitude-scale and time-scale were performed so that results could be compared between cone-mediated and rod-mediated M-ERG data, for which the absolute amplitudes and implicit times were different. For each hexagon, the amplitude-scale and time-scale data were classified as abnormal if they were beyond the 95% confidence intervals of the mean fits of the control group.

**RESULTS**

Figure 1 shows M-ERGs recorded from a control observer. The top panels show the hexagonal arrays used for the cone-mediated and rod-mediated M-ERGs, and the bottom panels show the filtered cone-mediated and rod-mediated trace arrays. There were differences in waveshape, timing, and absolute amplitude between the cone-mediated and rod-mediated trace arrays. Although the full-field rod-mediated ERG is larger in amplitude than the full-field cone-mediated ERG, the opposite was true for the M-ERG (see Hood et al.13 for a discussion).

**Cone System Data**

Figures 2A and 2B show the results for two patients with relatively good cone-mediated function. In these figures, the visual field results are shown at top right. The numbers inside each hexagon represent log threshold elevation for that hexagon. The hexagons with X's represent the optic disc. The M-ERG results are at top left. At bottom left are the amplitude-scale data and at bottom right the time-scale data obtained from the fit of the control template to the M-ERG data. In these figures, psychophysical values more than 0.0 indicate threshold elevations, amplitude-scale values less than 1.0 indicate reductions in amplitude, and time-scale values greater than 1.0 indicate delays in implicit time.

The results from these two patients show findings that were typical for the group of patients with RP. With respect to cone system psychophysical sensitivity, all seven patients had normal psychophysical thresholds within the central retinal areas.
In addition, five of the patients had normal sensitivity in some peripheral areas, ranging from 30% of the field to 70% of the field. The M-ERG responses were also less impaired for the central 5° than for more peripheral regions. All the patients had responses with normal timing within the central 5°, and four of the patients also had areas with normal amplitude within the central 5°. For five of the patients, the number of hexagons with normal timing was larger than the number of hexagons with normal amplitude (but see the results for patient P7).
The next series of figures shows the relationship between the psychophysical and M-ERG results for all conditions. Figure 3A shows the cone-mediated plot of time-scale versus amplitude-scale. The majority (61.2%) of the responses were abnormal for both amplitude-scale and time-scale (top right). There were more areas with normal timing (35%) than areas with normal amplitude (10.5%). There was a significant negative relationship between these two variables, as shown by the Spearman correlation coefficient. However, a few (3.7%) responses with normal or near amplitudes were delayed (top left), and some (28.2%) responses with normal timing were reduced in amplitude (bottom right).

Figure 4A shows the relationship between the cone-mediated amplitude-scale and psychophysical threshold elevation. Again, there was a significant negative relationship between these two variables, in that smaller amplitudes were associated with increasing visual field elevation, and the majority of responses (56.2%) were abnormal for both measures. There was some variability between the measures, however, and small amplitudes could be associated with varying amounts of field loss.

Figure 5A shows the relationship between the cone-mediated time-scale and psychophysical threshold elevation in the same manner. The correlation between the psychophysical measure and time-scale was higher than the correlation between the psychophysical measure and amplitude-scale.
tween the psychophysical measure and the amplitude-scale. For these measures, the majority of the responses were either normal for both measures (28.8%) or abnormal for both measures (51.2%). For the responses that were abnormal, as field elevation increased, time-scale also increased. However, at higher amounts of threshold elevation (>1.0 log unit), many of the time-scales for each patient reached asymptomatic levels and did not increase beyond that level. The results for cone-mediated function in patients with RP are consistent with previously published results from our laboratory.8

**Rod System Data**

Figures 6A and 6B show the rod system results for the same two patients whose cone system results are shown in Figures 2A and 2B. In general, in both these patients, the rod-mediated psychophysical thresholds (top right) were normal in areas of the visual field that correspond to areas where cone-mediated psychophysical thresholds were also within normal limits. Within the group of patients, five had rod system thresholds within normal limits for some portion of the visual field area. In contrast to the cone system results, however, not all the rod system sparing included the central areas. Two of the patients had rod system thresholds within normal limits only at more peripheral locations.

In general, the rod-mediated M-ERG responses in this group of patients were low in amplitude. The trace arrays for patient P5 (Fig. 6A, top left) show the best rod-mediated M-ERG recording obtained in this group of patients. The results for patient P7 (Fig. 6B, top left) show essentially nonrecordable rod-mediated M-ERGs, despite the relatively large-amplitude cone-mediated M-ERG responses generated by this patient (see Fig. 2B).

Figure 5B shows the relationship between the rod-mediated measures of M-ERG amplitude-scale and time-scale. When these results were compared with the cone-mediated data (Fig. 3A), several points were apparent. First, there were fewer data points for the rod system results. Averaged across the seven patients, only 43% of the hexagons yielded measurable rod-mediated M-ERG amplitudes using our goodness of fit criterion. This is in contrast to the cone-mediated M-ERGs in these patients, in which 93% of the hexagons had recordable responses using the same goodness of fit criterion. Nonetheless, all the patients had measurable rod-mediated M-ERG responses in some areas of the retina, and the majority (65.8%) of these hexagons had responses that were within normal limits. Consistent with the cone findings, for all the hexagons with measurable rod-mediated M-ERG responses, the time-scale measure was within normal limits more frequently (95.1%) than was the amplitude-scale measure (68.0%). Finally, there was a significant negative correlation between the measures of time-scale and amplitude-scale, although there was clearly quite a bit of scatter in the amplitude-scale measure that appeared unrelated to changes in time-scale.

As shown in Figures 4B and 5B, for the rod system, the correlations between the M-ERG measures and threshold elevation were poorer than for the cone system. Neither amplitude-scale nor time-scale showed a significant relationship with threshold elevation and, in fact, the correlation coefficients for these measures approached 0. Although the patients showed a reasonable range of amplitude-scale values, the changes in amplitude are unrelated to the degree of threshold elevation (Fig. 4B). In areas where there were measurable responses, the rod-mediated timing tended to be within normal limits (Fig. 5B). In contrast to the cone-mediated results, it was not possible to measure large delays in rod-mediated time-scale.

**Cone and Rod System Comparisons**

To compare the results of the rod and cone protocols, the 103 points for the cone system conditions were collapsed into 61 points corresponding to the array used for the rod system conditions. Correlations were obtained between cone and rod system threshold field data, between cone and rod system amplitude-scale values, and between cone and rod system time-scale values. Figure 7 shows the relationship between cone- and rod-mediated threshold elevation in the seven patients. The majority of responses (59.4%) were abnormal for both psychophysical measures. There was a significant positive relationship between these two measures. Increases in cone-mediated thresholds were associated with increases in rod-mediated thresholds.
There were no statistically significant correlations between the cone-mediated and rod-mediated M-ERG results. Figure 8 shows the relationship between the cone and rod amplitude-scales and Figure 9 shows the relationship between the cone and rod time-scales. As shown in these figures, there was no consistent pattern between either of these M-ERG measures.

**DISCUSSION**

**Cone System Results**

In the present study, we examined local cone system function using both psychophysical and electrophysiological techniques. We examined a group of patients with visual acuity of...
20/40 or better and Goldmann central fields of 10° or larger. The results confirm our previous comparisons of cone-mediated M-ERG responses and psychophysical measures of sensitivity in a similar group of patients with RP.8 As expected, our patients had thresholds within normal limits for the central areas (from the fovea to approximately 10°) on the threshold field test (Humphrey). In addition, five of the patients had areas with thresholds within normal limits at more peripheral locations. For the cone-mediated M-ERG, we found a similar pattern of results. Within the central hexagons (from the fovea to approximately 7.5°), many of the responses were within normal limits. This was true more often for time-scale (74% of the hexagons within normal limits) than for amplitude-scale (34% within normal limits). In addition, five of the patients had responses from peripheral retinal areas that were also within normal limits. This finding of normal electrophysiological timing in the central 5° to 10° in patients with RP agrees with previously published studies using focal ERG recordings18–22 and M-ERG recordings.6–9

When we examined the cone-mediated M-ERGs across all 103 hexagons, we found that the relationship between the cone-mediated M-ERG measures of amplitude-scale and time-scale was not the same in all the patients. Within the central hexagons (from the fovea to approximately 7.5°), the time-scale measures for the majority of the hexagons were normal, whereas the amplitude-scale values ranged from 20% to 100% of normal. At more peripheral locations, areas with normal time-scale measures were more extensive than were areas with normal amplitude-scale measures. In five of the patients, losses in cone-mediated M-ERG amplitude-scale occurred in areas with normal M-ERG time-scale. However, two of the patients had a different pattern of loss, with peripheral areas with reasonable amplitude-scales and delayed time-scales (e.g., patient P7). Therefore, for these peripheral locations, losses in M-ERG amplitude-scale do not always occur in areas with normal M-ERG time-scales, making it difficult to understand the relationship between changes in amplitude and changes in timing as a function of retinal eccentricity in these patients.

Regarding the relationship between visual field loss and M-ERG timing, retinal areas with normal time-scales tended to have normal sensitivity, and areas with delayed time-scales showed corresponding increases in visual field deficits. Although it was possible to find a few retinal areas with normal visual field sensitivity but with delayed time-scales, the areas typically bordered the edges of the normal portion of the visual field. In the present study, the correlation between cone-mediated M-ERG time-scale measures and cone system threshold visual fields accounted for more of the variance than the correlation between cone-mediated M-ERG time-scale and amplitude-scale. Because the visual field and M-ERG measures are obtained under different conditions (e.g., threshold versus suprathreshold, different levels of retinal adaptation) and the two M-ERG measures are derived from the same data set, the correlations between the two M-ERG measures could be expected to be higher. However, even though the amplitude-scale and time-scale measures are obtained from the same data measurements, they may reflect different disease mechanisms. The changes in M-ERG amplitude-scale may reflect losses in the number of cone photoreceptors, whereas sensitivity and time-scale changes may reflect changes in the functioning of these receptors, such as loss of visual pigment and shortening and/or misalignment of cone outer segments. Both of these changes

**Figure 7.** The correlation between cone and rod system psychophysical threshold elevation. Data, 95% confidence intervals, percentage of hexagons in each quadrant, Spearman rank order correlation coefficient, and statistical significance are as in Figure 3.

**Figure 8.** The correlation between cone- and rod-mediated M-ERG amplitude-scale. Data, 95% confidence intervals, percentage of hexagons in each quadrant, Spearman rank order correlation coefficient, and statistical significance are as in Figure 3.

**Figure 9.** Correlation between cone- and rod-mediated M-ERG time-scale. Data, 95% confidence intervals, percentage of hexagons in each quadrant, Spearman rank order correlation coefficient, and statistical significance are as in Figure 3.
have been documented at autopsy in eyes of patients with degenerative retinal diseases.\(^{23-25}\)

Several previous studies have examined the relationship between visual field loss and full-field ERG changes in patients with RP. These studies have demonstrated a significant relationship between visual field area and full-field cone-mediated ERG amplitude.\(^{20-27}\) and between cone system visual field threshold measures and full-field cone-mediated ERG amplitude.\(^{28}\) The relationship between visual field size and ERG timing was either not examined.\(^ {27-29}\) or no significant relationship was observed.\(^ {20}\) These studies differ from the present study because these correlations were obtained from a single measure of ERG amplitude, whereas in the present study, the relationship between local psychophysical and electrophysiological activity was examined.

**Rod System Results**

One of our goals was to record local rod-mediated M-ERGs in patients with RP. We were able to record local rod-mediated responses successfully in some retinal areas in all seven patients. The patients examined in this study had relatively mild disease, defined as a visual acuity of 20/40 or better and measurable full-field ERGs. In general, the local rod-mediated M-ERG responses in the patients were more likely to be nonmeasurable (i.e., fail to fit the criterion statistical level) than were local cone-mediated M-ERG responses. Because these patients were all classified as having rod–cone degeneration, the finding of more nonrecordable rod-mediated M-ERG responses than cone-mediated M-ERG responses is not surprising.\(^ {29}\)

Within the retinal areas where rod-mediated M-ERG responses were measurable, the responses were often normal in amplitude-scale and time-scale. Regarding time-scale, we found very few measurable rod-mediated responses that were delayed in these patients. This finding was somewhat surprising, because we were able to identify delayed cone-mediated M-ERG responses. These delayed responses were typically found adjacent to areas with normal time-scale values. There are several possible explanations for the normal timing of the rod-mediated M-ERG responses. Because the rod-mediated M-ERG responses are broad, low-frequency potentials, there is more variability in measuring time-scale than in the sharper, higher frequency cone-mediated M-ERG responses. Therefore, responses with small changes in time-scale (e.g., 3 msec) could fall into the abnormal range for the cone system recordings but fail to be significantly different from normal for the rod-mediated recordings. In addition, the rod-mediated M-ERG responses are presumably more affected than the cone-mediated M-ERG responses in these patients, and it is possible that once timing became delayed, the responses were no longer recordable. Another possibility is that the death of the rod photoreceptors occurs more rapidly than that of the cone photoreceptors, making it difficult to detect local delayed responses.

When we examined the distribution of rod system loss, we found that the correspondence between amplitude-scale and time-scale and field elevation was much poorer than for the cone system. Although there was a relationship between rod-mediated amplitude-scale and time-scale, the degree of visual field elevation did not consistently agree with either of these local M-ERG measures. This finding is consistent with the pattern of results seen in our study of patients with progressive cone dystrophy\(^ {30}\) in which rod-mediated M-ERG time-scale responses also showed lower correlations to changes in rod system sensitivity.

Previous studies have examined the relationship between rod system psychophysical and electrophysiological measures in patients with RP. Again, these studies differed from the current one, in that single measures of full-field ERG responses were examined across a group of patients. The results from these studies have been equivocal. Consistent with our findings, Massof et al.\(^ {31}\) found no significant correlation between dark-adapted b-wave \(R_{\text{max}}\) values and Goldmann visual field area. Arden et al.\(^ {32}\) also found poor correspondence between full-field scotopic ERG amplitudes and visual field thresholds in a group of patients with RP. However, other investigators found good correspondence between ERG scotopic maximum amplitude parameters and visual field measures in patients with RP.\(^ {28,53-55}\) Hood et al.\(^ {54}\) and Shady et al.\(^ {55}\) used data from simulated retinas and patients with RP to develop a model to relate threshold visual fields to maximum amplitude and sensitivity parameters derived from the full-field ERG. They found a positive relationship between the change in the \(V_{\text{max}}\) parameter derived from the b-wave and the degree of visual field loss in their group of patients.

**Cone and Rod System Comparisons**

In the present study, we were able to compare local psychophysical and electrophysiological results obtained under cone- and rod-mediated conditions in our group of patients. For the cone and rod system visual field thresholds, there was good local correspondence between our two measures. This result is consistent with the findings of Massof and Finkelstein\(^ {26}\) and Cideciyan et al.\(^ {37}\) who found concomitant psychophysical cone and rod system sensitivity losses in patients with RP. Despite the correspondence between our local psychophysical measures, we were not able to detect any relationship between the local electrophysiological measures of cone- and rod-mediated function. In the present study, we attempted to optimize the recording conditions for the rod system, based on previous work.\(^ {53}\) In addition, the patients included in this study had relatively mild disease, as assessed by visual acuity and Goldmann fields.

Although we had difficulty obtaining measurable rod-mediated responses in these patients, probably due to a paucity of rod receptors, we were still able to record M-ERG responses. Our failure to detect a pattern of local correspondence between the cone-mediated and rod-mediated M-ERG recordings may reflect differences in the pattern of photoreceptor loss in RP. Our results suggest that, although there is evidence that the loss of rod photoreceptors may directly cause the loss of cone photoreceptors in RP,\(^ {14-16}\) these events may occur separately in time and at different retinal locations. This type of photoreceptor loss need not be inconsistent with the finding of good correspondence between cone and rod system psychophysical thresholds, because psychophysical sensitivity may depend on the most sensitive mechanism mediating detection.

Although there were differences in the spatial distribution of cone and rod system abnormalities in the M-ERG responses, one consistent pattern emerged. Under both cone- and rod-mediated conditions, M-ERG implicit times were less affected than were amplitudes. All the patients had local retinal areas with normal timing but significantly reduced amplitude. This local sparing of implicit time but not amplitude has been previously documented for the cone system in patients with RP.\(^ {5-9,18-22}\) but this is the first demonstration of regional differences in rod-mediated ERG amplitude and timing in patients with RP. Taken together, our electrophysiological results indicate that although the degeneration of cone and rod photoreceptors in RP do not show local correspondence, they appear to follow the same pattern of amplitude loss preceding timing changes.

In summary, we were able to record local cone- and rod-mediated electrophysiological responses in patients with RP. Although our measures of cone-mediated psychophysical and electrophysiological responses showed good regional corre-
spondence, we were unable to demonstrate local correspondence between our rod-mediated measures. In addition, we were unable to demonstrate local correspondence between our cone- and rod-mediated electrophysiological measures. Our results indicate that cone and rod system changes may occur independently in some patients with RP.

References