Retinitis Pigmentosa: A Psychophysical Test of Explanations for Early Foveal Sensitivity Loss

Vivienne C. Greensrein, Donald C. Hood, Irwin M. Siegel, and Ronald E. Carr

A psychophysical procedure, the probe-flash paradigm, was used to test explanations of early foveal sensitivity loss in retinitis pigmentosa. The findings suggest that this loss may be due to a decreased responsiveness of retinal elements and not to a decrease in quantum catching ability of functioning photoreceptors. Invest Ophthalmol Vis Sci 25:118-120, 1984

Loss of rod system sensitivity in patients with retinitis pigmentosa (RP) is a well-documented finding. In recent years, psychophysical studies have demonstrated a loss of sensitivity in the foveal cone system. Various explanations for losses in both rod and cone system sensitivity have been suggested. One explanation attributes a major component of the sensitivity loss to a decrease in the quantum catching ability of the photoreceptors. Evidence for the latter comes from the results of psychophysical, retinal densitometric, and histopathological studies. Densitometry measurements provide evidence for reduced rod pigment content, and the results of psychophysical studies have been interpreted in terms of reduced cone pigment density. Histopathological studies of eyes with advanced or moderately advanced RP have demonstrated that the photoreceptors in peripheral and foveal retinal areas had outer segments, which were shortened, twisted, and/or distorted. Tilting or misalignment of the photoreceptors would result in a decrease in the effective intensity of a stimulus.

We have used a psychophysical procedure (the probe-flash paradigm) to test alternative explanations of changes in sensitivity caused by retinal disease. Here the procedure is used to test the hypothesis that the early loss of foveal sensitivity in RP is due to a decrease in the quantum catching ability of functioning photoreceptors. The probe-flash data we have obtained are not consistent with this hypothesis, and we suggest that the loss of foveal sensitivity in RP may be due to a decreased responsiveness of retinal elements rather than to a decrease in quantum catching ability of functioning photoreceptors.

Materials and Methods. Patients with retinitis pigmentosa. Table 1 lists the age, sex, corrected visual acuity, ERG findings, and mode of inheritance of the six patients examined. All patients complained of nightblindness. The diagnosis of RP was based on the results of fundus examination, electoretinography, dark adaptation studies, and retinal profiles. Patients were specifically selected with good visual acuity and sufficiently large visual fields so as to ensure good foveal fixation throughout the test period.

Unaffected observers. Five subjects with no known abnormality of the visual system comprised the control group. Two subjects were in their twenties, two in their thirties, and one in his early fifties. All had Snellen acuities in the tested eye of at least 20/20.

Apparatus. A projection system was combined with an adapted Goldman Weekers adaptometer to provide light stimulation. The final lens of the system projected circular images of the test and flash targets on a piece of frosted glass mounted in the sphere of the Goldman Weekers adaptometer. The luminance of the sphere was calibrated with a photometer and was recorded as 24 cd/m². Light intensity in the two channels was controlled by neutral density filters and by a two log unit neutral density wedge. All filters were calibrated in the apparatus. The temporal characteristics of the stimuli were controlled by electronic shutters.

Stimuli. The spatial and temporal paradigms are shown in Figure 1. The 500 msec flash was 1° in diameter and the 10 msec probe light was 23' in diameter. The probe light was presented simultaneously with the onset of the flash. Foveal fixation was aided by four small fixation points surrounding the stimuli. The...
Table 1. Clinical data for six patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Visual acuity tested eye</th>
<th>ERG</th>
<th>Mode of inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>51</td>
<td>F</td>
<td>20/30</td>
<td>Photopic and scotopic reduced 90%</td>
<td>Simplex</td>
</tr>
<tr>
<td>2</td>
<td>34</td>
<td>F</td>
<td>20/30</td>
<td>Photopic extinguished, scotopic reduced 90%</td>
<td>Simplex</td>
</tr>
<tr>
<td>3</td>
<td>31</td>
<td>F</td>
<td>20/20-</td>
<td>Photopic extinguished, scotopic reduced 70%</td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td>4</td>
<td>26</td>
<td>M</td>
<td>20/20-</td>
<td>Extinguished</td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td>5</td>
<td>21</td>
<td>M</td>
<td>20/30+</td>
<td>Extinguished</td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>F</td>
<td>20/20-</td>
<td>Photopic and scotopic reduced 50%</td>
<td>Autosomal recessive</td>
</tr>
</tbody>
</table>

flashes were “white” (unfiltered tungsten light) and the probe was red (this was obtained with a cut-off filter, which passed 10% of maximum at 600 nm and 1% at 598 nm).

Procedure. Throughout the experiment the subject’s head was held in position by a chin rest and head rest. Subjects wore corrective lenses when necessary, the viewing distance of 30 cms being taken into account. The natural pupil was used since mydriasis combined with an artificial pupil did not alter the data obtained on unaffected observers. A method of limits procedure consisting of three to five up-and-down runs was used. The intensity of the probe was varied in 0.1 log unit steps with each intensity presented twice. Threshold for the probe alone (“no flash” condition) was obtained, then probe thresholds for seven flash intensities were measured; flash intensities covered a range of approximately 2.5 log units.

Results. The probe-flash data obtained on five unaffected observers are presented in Figure 1. The log of relative probe threshold is plotted against log luminance of the flash. The curve through the data is the best fitting curve obtained by eye through the median probe threshold data. The individual probe threshold values range from ±0.07 log unit around the median to ±0.28 log unit at the highest flash values. For all observers, probe threshold grows slowly at low flash values, then rises with increasing steepness.

Figures 2 and 3 show probe-flash data obtained on six patients with RP. The lower solid curve in each figure comes from the data for controls in Figure 1. For each patient, the threshold to the probe is increased for all flash intensities compared with the unaffected observers. The upper smooth curve is the normal curve shifted vertically for best fit for one patient in each figure. The probe-flash data can be fit reasonably well by a vertical shift of the template.

Discussion. All six of our patients exhibited a loss of foveal sensitivity. Let us suppose that this loss was due to a loss of quantum catching ability by otherwise normally functioning receptors. For example, cone outer segments could have a normal complement of pigment, but a reduced ability to absorb light due to tilting or misalignment of the receptors. Alternatively, the individual receptors may contain less pigment than normal due perhaps to a shortening of the outer seg-
ments. In either case, one consequence would be a decrease in the effective intensity of the stimulus. For example, halving the quantum catching ability is equivalent to decreasing the intensity of the probe and flash by a factor of 2. Since the effective intensity of both the probe and the flash are decreased by the same multiplicative factor, on a log-log plot the predicted probe-flash curve would be shifted up and over to the right by approximately equal amounts compared to the normal (see dashed curve A in Fig. 2).* Clearly, the probe-flash data we have obtained on six patients with RP do not resemble this prediction. There is no sign that the loss of sensitivity is due, even in part, to a decrease in the receptors' ability to absorb light.

One possible explanation for the changes we have observed in the probe-flash data is that RP causes a loss in the number of functioning photoreceptors. Histopathological studies have demonstrated a loss of photoreceptors both in peripheral and foveal retinal areas in eyes with advanced or moderately advanced RP,6-9 and the types of change in our probe-flash data are consistent with a loss of receptors (see Hood & Greenstein,10). Nevertheless, it seems unlikely in our patients with good visual acuities that the receptor populations in the fovea were so reduced as to produce the degrees of change that we obtained.

A second possibility is that in early RP all cones contain a reasonably normal complement of pigment and continue to function, but they exhibit a reduced responsiveness to light. This explanation of a reduced responsiveness to light is consistent with the type of probe-flash data we obtained (see Hood and Greenstein).11 In fact, there is an interesting resemblance between these results and those found on patients with diabetic retinopathy or macular degeneration.11 For the latter retinal diseases, a number of factors, such as anoxia, decreased metabolic activity, or a change in ionic environment, could cause changes in membrane potential and contribute to the decreased responsiveness of individual elements. It is possible that similar factors are contributing to the sensitivity loss demonstrated in this study.

Key words: retinitis pigmentosa, psychophysical procedure, foveal sensitivity loss


References


* The value of the multiplicative constant will be a function of the level of steady adaptation. In the dark, the constant will be equivalent to the factor by which the quantum catching ability is decreased. For a low background, such as the one used in this study, it will be slightly less.