Spatial and temporal vision of macaques after central retinal lesions

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Spatial contrast and temporal modulation sensitivity of two macaque monkeys were measured at three luminance levels before and after binocular laser coagulation of the fovea. The radius of the lesions ranged from 1.6 to 2.2 deg from the center of the fovea. After placement of the lesions, the visibility of high spatial frequencies was greatly reduced, although sensitivity at middle and low spatial frequencies was unaffected. No loss of spatial resolution was found at the lowest luminance tested. When temporal modulation sensitivity was tested with 4 deg targets, foveal lesions had no effect at any temporal frequency or luminance. However, with a 0.57 deg target, sensitivity to lower temporal frequencies was impaired. Thus visual loss after destruction of the fovea is limited to high luminance, small targets, and the resolution of fine detail.

Key words: fovea, spatial contrast sensitivity, temporal modulation sensitivity, central scotoma, macaques

The primate fovea is a unique portion of the retina both structurally and functionally. Its anatomical specializations include an absence of blood vessels and nerve fibers of passage, dense packing of ganglion cells and cone photoreceptors (but a scarcity of rods), and a disproportionate representation in geniculate and cortical projections. Physiologically, the foveal area is characterized by small receptive fields with high spatial resolution. These specializations suggest unusual psychophysical properties for foveal vision, and indeed primate visual capacities have been shown to change dramatically with eccentricity from the fovea. This nonhomogeneity has been studied primarily in human subjects by means of controlled fixation to place test stimuli at various locations in the visual field. Although extremely informative, the controlled fixation technique is limited by the following inherent constraints. The reduction of eye movements by fixation can alter the visibility of certain test stimuli. Precise fixation is difficult to achieve during the testing of scotopic vision. Finally, mapping visual nonhomogeneity with spatially extended stimuli is problematic because large stimuli simultaneously test a range of eccentricities. On the other hand, the exclusive use of small stimuli is not an adequate solution, since many visual thresholds vary inversely with target size.

A complementary approach to the study of foveal vision that avoids some of these limitations is the study of residual visual capacities...
after experimental or clinically observed damage to the fovea. Weiskrantz and Cowey used this technique to relate the residual visual acuity of macaques to the size of central retinal lesions produced by photocoagulation. In a more recent example, Hess et al. have described the impairment of photopic spatial contrast sensitivity in a patient with a small uniocular central scotoma.

We have used the lesion technique to study the foveal contribution to vision over a wide range of stimulus conditions. Visual sensitivity of two macaques was examined as a function of spatial and temporal frequency of stimulation, luminance, and target size both before and after the placement of foveal lesions. Spatial vision as a function of luminance was evaluated by measurement of spatial contrast sensitivity at three luminances. The roles of luminance and spatial summation in the temporal vision of the fovea were examined with modulation sensitivity measures at high and low luminance and with large and small stimuli. Our results indicate that visual impairment after loss of the fovea is confined to high luminance, small targets, and the resolution of fine details.

Methods

Subjects. Two feral, adult female pigtail monkeys (Macaca nemestrina) were obtained from Primate Imports, Port Washington, N. Y. The monkeys were tested 5 days each week and had been water-deprived for 22 hr at the time of testing. Streak retinoscopy showed that monkey 602 was 1.25 D myopic in both eyes and that monkey 605 was emmetropic.

Apparatus. Stimuli were presented on two Tektronix 606 oscilloscopes (P-31 phosphor) by conventional techniques. The centers of the two displays were 30 cm apart, and each screen was bordered by a white surround that extended out 24 cm. A filter holder was mounted on the face of each oscilloscope to permit attenuation of the display luminance. The monkeys sat in an acrylic chair that restrained the animals at the neck. The chair was placed in front of a response panel inside a sound-attenuating enclosure 86 cm long, 73 cm wide, and 88 cm high. The response panel had a central juice-dispensing tube that extended to the monkeys' mouths and had two pushbuttons 6 cm to the right and left of the tube. The interior of the enclosure was painted flat white, and a masking noise was continuously present. The experiment was controlled by an on-line computer in an adjoining room.

Temporal modulation thresholds. Details of training and testing of the monkeys have been described elsewhere. For each monkey, the temporal modulation sensitivity function was measured with large unpatterned flickering stimuli (4.6 by 5.7 deg visual subtense) at two levels of mean target luminance (16 and 0.0016 cd/m²). Modulation sensitivity was also tested at the higher (16 cd/m²) luminance with small flickering targets (0.57 by 0.57 deg). All temporal thresholds were obtained with the displays located 1 m from the monkey's eyes.

In each daily session of 200 trials, sensitivity was measured at a single flicker frequency, luminance, and target size. On each trial, a flickering stimulus appeared on one of the two displays according to a random sequence of positions. Two seconds later, onset of a tone signaled that the response buttons were activated. A response on the pushbutton corresponding to the flickering display was rewarded with a small amount of fruit juice. Incorrect responses were punished by a 10 sec delay period signaled by a beeping tone. Trials were separated by a 5 sec interval.

The modulation depth of the flickering stimulus was defined as (Lmax - Lmin/Lmax + Lmin) where Lmax was the highest luminance and Lmin the lowest luminance reached by the flickering stimulus. In each session, modulation depth was initially set above threshold and then varied in 1.6 dB steps according to a staircase (or titrating) procedure. Modulation depth increased one step after errors and decreased with probability 0.3 after correct responses. This ratio ensured that approximately 75% of responses would be rewarded. A psychometric function relating modulation depth to the percentage of correct responding was plotted for each session, and modulation threshold was taken at 75% correct. The different frequencies, luminances, and target sizes were interleaved in the testing sequence to minimize order effects.

During occasional sessions, flicker-fusion thresholds were measured rather than modulation sensitivity. In these sessions, modulation depth, luminance, and target size were held constant while flicker frequency was varied in 0.18 octave steps under the staircase procedure to determine the flicker-fusion threshold.

Spatial contrast sensitivity. The spatial contrast sensitivity of each monkey was measured at three levels of target luminance (16, 0.16, and 0.0016 cd/m²). The stimuli were stationary, vertical grating patterns with a sinusoidal luminance profile in
Fig. 1. Location and extent of the retinal lesions derived from fundus photographs taken before, immediately after, and several months after laser treatment.

Table 1. Radial size of lesions (deg)

<table>
<thead>
<tr>
<th>Eye</th>
<th>Monkey 602</th>
<th>Monkey 605</th>
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<tr>
<td>Right eye</td>
<td>1.7</td>
<td>1.6</td>
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<td>Left eye</td>
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Retinal lesions. The monkeys were sedated with an injection of ketamine HCl (12 mg/kg). Additional injections were given if necessary to maintain sedation. Mydriasis was achieved by topical instillation of cyclopentolate (Cyclogyl 1%; Alcon Laboratories, Inc., Fort Worth, Tex.). A single lesion was centered on the foveola of each eye. The lesions were made under direct visualization through a slit-lamp biomicroscope with an argon laser photoagulator. The treatment was carried out through a fundus examination corneal contact lens and consisted of a single 1000 μm exposure of 2 W for 0.05 sec.

Reconstruction of lesions. The location and extent of the lesions were determined from multiple fundus photographs of each eye taken prior to treatment, immediately after photoagulation, and several months thereafter. Quantitative measurements of lesion dimensions were made by...
Fig. 2. Spatial contrast sensitivity of the two monkeys measured at three levels of stimulus luminance. Contrast sensitivity (reciprocal of contrast threshold) is plotted as a function of the spatial frequency of the test grating. (---), Sensitivity before the lesion; (o and ●), sensitivity after the lesion; (●), visual acuity (highest resolvable spatial frequency) measured at 55% contrast. Sensitivity loss (in dB) after the foveal lesions is plotted below each contrast sensitivity function. Grating stimuli each subtended 5 deg by 4 deg visual angle.

Results

Lesion reconstructions. Ophthalmoscopic reconstructions of the retinal lesions are shown for both monkeys in Fig. 1. The optic disc and a portion of the arteriolar bed are included in the drawings as landmarks. The spot near the center of each lesion represents the location of the foveola before photocoagulation. The white region immediately around the foveola shows the area of funduscopically visible atrophy of the retina. This region showed complete destruction of the pigment epithelial pattern and an absence of blood vessels; it was partially translucent, with scattered clumps of pigment. The stippled area represents a ring of pigment hyperplasia surrounding the central atrophic area.

We have expressed lesion size as the radial distance from the center of the foveola to the nearest nonnecrotic region of the retina. Angular subtense of the lesions was determined with the horizontal and vertical dimensions of the disc and the distance from the foveola to

Post-lesion testing. Psychophysical testing resumed 2 days after the lesions were placed. Visual acuity was measured first, then high luminance spatial contrast sensitivity, then the other measures in mixed order. Testing continued until reliable redeterminations were made of all prelesion thresholds. This required approximately 8 months.
Spatial, temporal vision after retinal lesions

Fig. 3. Temporal modulation sensitivity of the two monkeys measured with large (5.7 deg by 4.6 deg) and small (0.57 deg by 0.57 deg) flickering stimuli. Modulation thresholds are plotted as a function of the temporal frequency of sinusoidal flicker. Large targets: solid curve, threshold before the lesions; Δ, results after lesions. Small targets: (···), thresholds before lesions; ○, results after the lesions. Filled symbols, Flicker-fusion thresholds (highest resolvable flicker rate) measured at 55% modulation depth. Sensitivity loss (in dB) after retinal lesions is shown below the modulation sensitivity data.

Psychophysical results. Spatial contrast sensitivity measures before and after the lesions are shown in Fig. 2. Prelesion data are similar to those reported previously for macaques. At the highest luminance there was a dramatic loss of sensitivity to high spatial frequencies for both monkeys. The extent of this loss increased with spatial frequency, reaching about 30 dB at the highest frequencies tested. The limit of spatial resolution (grating acuity) can be obtained by extrapolating the high frequency limb of the contrast sensitivity function to 100% contrast. This analysis showed that the acuity of monkeys 602 and 605 decreased from 34 to 15 and from 45 to 23 cy/deg, respectively, after placement of the lesions.

The two monkeys also showed some loss of high-frequency sensitivity at the middle luminance. Visual acuities decreased from 13 to 9.5 cy/deg for monkey 602 and from 23 to 15 for monkey 605. There was no evidence of sensitivity loss for low spatial frequencies at any of the three luminances or at any frequency at the lowest luminance. Moreover, we found a slight and unexpected increase in sensitivity for monkey 605 at the lowest luminance.

Temporal modulation sensitivity results for both large and small high-luminance targets are presented in Fig. 3. The lesions resulted in no changes in sensitivity measured with large flickering targets. However, when the targets subtended 0.57 deg visual angle, the retinal lesions produced a consistent decrease in sensitivity at middle and low rates of temporal modulation. The magnitude of this loss clustered in the range of about 4 to 8 dB.

Finally, Fig. 4 shows temporal modulation sensitivity measured with large targets (4.5 by 5.7 deg) at high and low luminance. Data for high luminance in this figure are identical to those shown in Fig. 3. Central retinal lesions caused no disturbances of either high-or low-luminance temporal modulation sensitivity.

Discussion

Central retinal lesions caused a profound impairment of some aspects of the spatial and temporal vision of the two macaques. Grating acuity and sensitivity to high spatial fre-
Fig. 4. Temporal modulation sensitivity of the two monkeys measured with high (16 cd/m²) and low (0.0016 cd/m²) luminance stimuli. The stimuli subtended 5.7 deg by 4.6 deg of visual angle. High luminance data: solid curve and ○ are the same as shown in Fig. 3; low luminance: (·····), thresholds before lesions; D, thresholds after placement of the lesions.

Temporal frequencies were greatly reduced at the highest luminance tested. This loss was luminance-dependent, however, and little deficit was apparent at the middle luminance, and none at the lowest. Temporal modulation sensitivity declined after placement of the lesions for targets of small angular subtense, modulated at low temporal frequencies. Other aspects of spatial and temporal vision were unaffected by the lesions; this included spatial vision at low spatial frequencies and low luminance and all temporal visual thresholds measured with large (5 deg) stimuli. These results show that a foveal contribution is not essential for the detection of such stimuli. The great consistency of the unaffected thresholds before and after the lesions were placed suggests that those deficits we found cannot be attributed to a general disruption of responding or a change in the detection strategy of our monkeys.

The possible role of pupil size, eye movements, fixation locus, and binocular viewing in our study should be considered before our findings are compared to those of previous studies. We measured pupil size while the monkeys were exposed to the highest adapting luminance used in this study (16 cd/m²) to see the effect of retinal lesions. Pupil diameters of monkeys 602 and 605 were 5.1 and 6.0 mm, respectively, which is close to the mean of five normal monkeys, 4.7 mm. Thus it is unlikely that the threshold changes we found were due in part to altered pupil sizes.

Our procedure encouraged eye movements during viewing, since fixation locus was not controlled, and the two displays were widely separated. The postlesion eye movements of monkey 605 were observed during acuity testing by means of a high resolution video camera (RCA TC 1005 U01) and infrared illumination. During most trials, the monkey glanced briefly at the right display, then at the left display, then responded, a pattern similar to that of other nonlesioned monkeys. The response latency of monkey 605 averaged 1.6 sec. On occasional long latency trials, the monkey shifted gaze several times between the two displays. We also observed that this monkey could steadily and reliably fixate a small spot of light that dimmed occasionally to signal the availability of juice. These observations suggest that the visual loss of monkey 605 was not due to a gross abnormality of eye movements.

We also tested the acuity of monkey 605 monocularly with an opaque contact lens to cover the untested eye. The monocular acuity of the left eye was equal to the binocular acuity whereas that of the right eye was less than 15% lower. This suggests that some of the postlesion thresholds described above may reflect the performance of the more sensitive eye. We did not measure the postlesion fixation locus of the two monkeys. In the following discussion, we assume that the locus of their fixations was optimal for detecting each test stimulus.
Photopic spatial contrast sensitivity. Three previous studies have reported the effects of central scotoma on photopic spatial vision. Weiskrantz and Cowey studied the effect of central retinal lesions on the visual acuity of macaques. They found that acuity loss was directly proportional to the radial dimensions of their circular lesions. Acuity decreased by a factor of 2 for lesions of 2 deg radius. Our acuity results at 16 cd/m² were almost identical to theirs. Lesions of about 2 deg radius reduced the resolution of high spatial frequencies twofold (34 to 15 cy/deg for monkey 602 and 45 to 23 cy/deg for monkey 605).

More recently, Kelly has examined the effect on spatial contrast sensitivity of blocking the central 3 deg of the macula by a stabilized obscuring stripe. His results are similar to ours at frequencies above 5 cy/deg. However, across all lower frequencies he found a twofold loss of sensitivity, whereas the sensitivity of the monkeys at low frequency was not reduced by foveal lesions.

A recent clinical study reported that a central scotoma caused impairment of a patient's photopic contrast sensitivity that was similar to what we report here for monkeys. The sensitivity of the patient's normal eye was compared to ours at frequencies above 5 cy/deg. However, across all lower frequencies he found a twofold loss of sensitivity, whereas the sensitivity of the monkeys at low frequency was not reduced by foveal lesions.

Many studies have used controlled fixation to compare foveal and extrafoveal spatial vision. Among these, the greatest attention has been directed to the variation in visual acuity with retinal location. There is general agreement among mapping studies using controlled fixation that human visual acuity decreases linearly with eccentricity from the fovea. Studies employing Snellen letters, Landolt rings, and gratings have found that acuity decreases by approximately 50% at 2 deg eccentricity. Our results show that macaque spatial resolution drops by an equivalent amount after placement of lesions extending to about 2 deg.

The variation of acuity with eccentricity is of particular interest because of its proportionality to ganglion cell density and cortical magnification factor in humans. In addition, the density of cone photoreceptors also decreases with eccentricity, although this does not appear to parallel changes in acuity. Comparison of our acuity data with results from controlled fixation studies in humans suggests that the anatomical organization of the fovea must be quite similar in macaques and man. Indeed, this appears to be the case for cone density, ganglion cell density, and cortical magnification factor.

The regional variation in human photopic contrast sensitivity has also been studied, and several of these investigations have used parameters that permit comparison with the present findings. In these experiments, contrast sensitivity was measured at the fovea and at eccentricities between 2 and 4 deg. Visual subtense of the test gratings ranged from 2.5 to 5 deg, and temporal parameters included no modulation, 2 Hz modulation, and 0.5 sec pulse presentation. In each case, the high-frequency portion of the contrast sensitivity function showed reduced sensitivity with eccentric viewing. Although this is qualitatively similar to our results, a quantitative comparison is precluded by the great variation in the magnitude of this effect in the above studies. The twofold reduction in grating acuity that we found is in agreement with the contrast sensitivity data in two of the above studies.

At lower spatial frequencies, each of the above studies found reduced sensitivity at eccentricities of 2 to 4 deg. Our failure to find this effect is a major difference in outcome between the present results and the clinical study of Hess et al. on the one hand, and both controlled fixation and stabilized scotoma experiments on the other. Although grating size is clearly important in determining the amount of low-frequency loss with eccentricity, this does not appear to be the crucial difference between our study and previous ones. In two of the above studies, low-frequency loss was found with targets of the same visual subtense (5 deg) as those in the present study.
It is more likely that differences in eye movements explain the different findings at low frequencies. Kelly\textsuperscript{19} has shown that increased target velocity greatly improves the visibility of low spatial frequencies. Although the controlled fixation technique severely restricts image motion, our monkeys may have produced some of the effects of stimulus motion by alternately viewing the two displays.

**Middle- and low-luminance spatial vision.**

The data in Fig. 2 indicate a dramatic luminance dependence in the foveal contribution to spatial vision. At 0.16 cd/m\(^2\) the resolution loss after lesion placement is considerably less than at higher luminance, and at 0.0016 cd/m\(^2\) no loss was seen. The slight improvement of monkey 605 at the lowest luminance may be due simply to additional training or might represent increased sensitivity due to eccentric viewing after placement of the lesions.\textsuperscript{33} The luminance dependence may involve both the retinal distribution of photoreceptors and changes in receptive field properties with dark adaptation. With increasing dark adaptation there is a reduction in the contrast sensitivity and spatial resolution of retinal, lateral geniculate, and cortical neurons, and these changes may be proportionally greater for receptive fields tuned to higher spatial frequencies.\textsuperscript{2} Such changes may contribute to the reduced slope of the acuity-eccentricity function (and thus the relative contribution of the fovea) for stimuli of lower luminance.\textsuperscript{33} In addition, only rod vision is involved at the lowest luminance we tested, and the lack of a foveal contribution is consistent with the distribution of rods in the macaque retina. Crawford\textsuperscript{4} has demonstrated a central rod-free area in macaques with rod density increasing gradually from about 0.5 to more than 5 deg eccentricity. A similar increase in rod density, though with a different profile, was described by Osterberg\textsuperscript{26} in the human retina. Consistent with the distribution of rods is Sloan's finding\textsuperscript{33} that the scotopic acuity of humans increases with eccentricity from the fovea, peaking at about 4 to 7 deg.

It is noteworthy that a luminance-dependent deficit in spatial vision, similar to that of our monkeys, has been reported for human strabismic amblyopes.\textsuperscript{10} The nature of this deficit may be related to the fact that the visual abnormality of strabismic amblyopes is frequently confined to the central portion of the visual field.\textsuperscript{12, 16} In fact, Hess et al.\textsuperscript{9} predict that "it should be possible to mimic the strabismics' results using a normal subject with a simulated central scotoma." (p. 302). The luminance-dependent effect on the spatial vision of our monkeys appears to bear out that prediction.

**Temporal vision.** It is clear from our results that the fovea is not crucial to flicker sensitivity for 5 deg targets at either high or low luminance. However, low temporal frequency detection with a 0.57 deg target is strongly dependent on the fovea. Although comparable data have not been reported for human subjects, flicker fusion (the high frequency limit of temporal resolution) has been examined as a function of eccentricity and target size. Most studies (e.g., refs. 7 and 15) have shown that flicker-fusion frequency increases with eccentricity for large targets (>3 deg) whereas for small targets (e.g., 0.5 deg) it decreases with eccentricity from a peak at the fovea. In addition, flicker sensitivity at very low luminances is greater extrafoveally than in the fovea.\textsuperscript{8} These results are in agreement with our data for large-target and low-luminance temporal resolution. However, one earlier study\textsuperscript{15} suggests that we should have found a slight decrease in temporal resolution for the 0.57 deg target. Such an effect would be small (~4 Hz) and might not be apparent in our data.

The decrease we found in low frequency sensitivity for small but not large targets apparently reflects an involved spatio-temporal interaction. Kelly\textsuperscript{17} has pointed out that the high spatial frequencies present in the sharp edges of flickering targets can greatly enhance the visibility of low-frequency flicker. To study this "edge effect" Kelly blurred the boundaries of targets by defocussing the oscilloscope beam to a 0.5 deg spot. This removed spatial frequencies above 2 cy/deg from the display and resulted in a dramatic loss of modulation sensitivity at low but not high temporal frequencies. Kelly also found that increases in target size increased mod-
ulation sensitivity at all frequencies but that this "area effect" appeared independent of the "edge effect."

Kelly's area effect can be seen in the pre-lesion data of our monkeys with 5 deg and 0.57 deg targets. Although sensitivity was greater at all frequencies for the 5 deg target, the greatest increment was at high temporal frequencies. The effect of foveal lesions on the small target modulation sensitivity is quite similar to Kelly's edge effect. This similarity suggests that the twofold loss of spatial resolution produced by the lesions had the same effect as Kelly's defocusing the edges of his display. Our failure to find an edge effect with 5 deg targets is not inconsistent with Kelly's results, since the magnitude of defocus he used was so much greater than the resolution loss after placement of our lesions. The difference between our results for the 0.57 and 5 deg stimuli does indicate that the contribution of high spatial frequencies to the detection of low temporal frequencies is more pronounced for small target sizes.

In summary, we have measured the effects of foveal lesions on a wide variety of visual thresholds. Many of the functions we have studied (e.g., low-luminance contrast sensitivity) have not previously been examined at different visual field locations. The results of these parametric studies show that luminance, target size, and spatial frequency content are major determinants of the foveal contribution to macaque vision. There are, on the other hand, many investigations with human subjects that parallel our studies of photopic acuity and contrast sensitivity. The close correspondence of such human data with those of our monkeys suggests a great similarity in the organization of macaque and human central vision. Thus retinal lesions in macaques, in addition to providing convergent evidence on the properties of primate vision, may also prove valuable in understanding the loss of visual capacities that accompanies clinically observed field defects.

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