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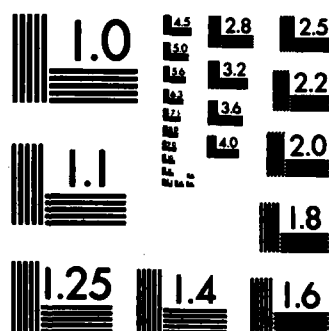
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Functional Assessment of Laser Irradiation

Annual Report

David O. Robbins, Ph.D.

March 1981

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Exposure of the retina in an awake, task-oriented animal to various duration flashes from an Argon laser produced immediate changes in visual acuity. The recovery from this exposure varied from several minutes to months depending upon the duration and energy of the flash as well as the extent of retina involved. The threshold for producing a permanent alteration in the animal's visual sensitivity was significantly below the MPE derived using morphological criteria alone.			

TABLE OF CONTENTS

	<u>PAGE</u>
INTRODUCTION	1
METHODS	5
RESULTS	9
DISCUSSION	15
REFERENCES	17

LIST OF ILLUSTRATIONS

FIGURE 1	Diagram of the optical system used to present image targets and the laser flash	6
FIGURE 2	Sample raw data of acuity immediately following laser exposure.....	9
FIGURE 3	Comparisons of the effects of exposure diameter on the magnitude and duration of the recovery function.....	10
FIGURE 4	Recovery functions for one subject following three single, 3.0 mW exposures on three separate days	12
FIGURE 5	Postexposure spectral sensitivity for one animal exposed over several sessions to 100 msec flashes of Argon (514.5 nm) light	14
FIGURE 6	Effects of flash duration on recovery from Argon laser exposure.....	15

INTRODUCTION

Intense light of sufficient power densities on the retina to produce ophthalmologically visible lesions not only seriously alter retinal morphology but also change the sensitivity of the system to light within the physiologic or safe operating range. The duration of the disruption in visual sensitivity has traditionally been considered to be permanent. The type of disruption will depend upon the region of the retina where maximum light adsorption and damage occurred. The extent of this region where damage will be evident will depend, in part, upon the wavelength and temporal characteristics of the exposure in addition to simply the total energy absorbed.(1).

Two different types of physical reactions can result from overstimulation of light energy: thermal and photochemical damage. In the case of photochemical alteration, the primary damage site has historically been reported to be in the pigment epithelium cells which surround and support the receptor cell. More recently rather subtle changes in cyclic AMP and calcium levels within the outer segments of the receptor have also been proposed as a possible mechanism for photochemical changes. Perhaps more important for vision is the observed reduction in the concentration of retinal, a form of Vitamin A, in the receptor cells within affected regions of the retina. Changes in the availability of retinal in either rods or cones will obviously reduce the number of active photopigments available in the region for catching light and hence change visual sensitivities. Depending upon the affected region, changes will occur in either one or all of the following visual functions: acuity, contrast, color or movement sensitivities. Photochemical alterations are usually associated with chronic exposures of the retina to relatively long duration pulses of low power densities. Particularly affective are exposure devices with short wavelength outputs.

In the case of thermal damage, on the other hand, it seems the rapid absorption of light energy by the pigment molecules within the outer segments of the receptor cells throughout the exposed retina leads to a rapid heating of the surrounding tissue. Elevations of retinal temperatures by as little as several degrees can be affective in causing cellular disruption although typically 10-15 degrees is usually considered threshold for this type of damage (1). The conversion of light to heat is typically associated with vaporization of the tissue fluid which leads to pressure waves which transverse the tissue.

A number of differences can be identified between thermal and photochemical damage. First, photochemical damage appears to be the result of some cumulative biochemical change occurring within the retina. Similar biochemical and/or mechanical cumulative mechanisms have been recognized as occurring in other sensory systems but have not traditionally been thought of occurring within the visual system. The paradigm used to study the chronic effects of low intensity light exposure on visual sensitivity is usually the exposure to diffuse, wide field stimulation over days, weeks or even months. The duration of individual exposure sessions can vary from one hour to twelve hours per day. Second, photochemical damage is more uniformly observed over the entire exposed

area whereas thermal burns are not as uniform and smaller in area. Photochemical damage also develops more slowly and is not immediately visible following exposure. Thermal damage, on the other hand, is visible fundoscopically immediately after exposure although the extent of the damage does grow with time (2). Typically photochemical changes are not visible fundoscopically for at least 48 hours and then the changes in retinal coloration are still only very slight. A final difference between these two types of damage mechanisms is that photochemical damage is independent of the size of the exposure on the retina whereas thermal damage thresholds are strongly dependent upon the exposure area as well as energy. Of the two possible alternatives for light-induced damage, photochemical damage if not too severe, is more likely to undergo repair. Thermal lesions are more likely to result in permanent scotomas within a smaller region of the area of involvement.

Historically, the maximum permissible exposure energy (MPE) to laser light has been based primarily on gross morphological criteria apparent immediately following exposure. Morphological assessments have included gross fundoscopic examination of the retina following acute exposure as well as more sophisticated examination of the cellular layers within isolated sections of exposed retina. Generally, lesser power densities are needed to demonstrate structural changes when ultrastructural components of the retina are observed with the electron microscope than when only fundoscopic examination of the intact retina is made (3).

Obviously morphological techniques have provided basic information as to the extent and site of the primary damage. The damage observed by these techniques have been widely used in determining safety standards for lasers. The usual paradigm for producing structural alterations has been single exposures of relatively long durations involving large and uniformly exposed areas of an immobilized retina. For histological convenience, the exposed area has traditionally been somewhere beyond the central fovea (4,5). While these exposure conditions may be necessary to facilitate visual verification of the induced structural alteration, they do not correspond well with the type of condition normally occurring in the field with accidental exposures to potentially damaging levels of laser light. Two different types of hazards will typically exist in the field. The first is either accidental or intentional exposure to an intense but brief laser beam, the source of which would presumably be some distance away. Associated with this type of exposure would be structural alterations in relatively small regions of the retina which might be difficult to depict morphologically. Depending upon the situation surrounding the exposure, ultrastructural changes might be in either the fovea or periphery. The second type of exposure might result from the intentional viewing and tracking of presumably safe and low energy level irradiation over relatively long periods of time; days, weeks or even months. Such prolonged exposures, if hazardous, would generally cause damage throughout the retina and produce a more gradual and uniform shift in visual sensitivity than would higher energy, point source exposures of an acute nature.

While these morphological data have greatly contributed to the development of the ANSI guideline, they provide no direct information about the degradation in visual performance following exposure to sources at or

above the MPE. Such information is critical when discussing the necessity of completing a visually-guided mission by a person exposed to an intense, short duration laser flash. Further, morphological criteria alone may not be the most sensitive criteria for determining MPE. As previously mentioned, minute enzyme and cyclic biochemical changes in the photoreceptor and associated structures may occur at levels where immediate morphological damage is not readily apparent. Such actinic insult may, however, adversely affect the overall functioning of the photoreceptor and thus produce changes in the electrophysiological response of the retina as well as its sensitivity to light.

For these reasons our research efforts have been directed toward the examination of functional changes in the visual system following laser exposure. In most behavioral studies, though, anesthesia has been required for the accurate placement of the exposure onto relatively small and predetermined areas of the retina. An exception has been those few behavioral studies where the subject is chronically exposed to diffuse, wide field laser light. In these cases ultrastructural alterations are usually spread throughout the retina and not isolated to foveal areas since eye position relative to the exposure source is not controlled. This type of exposure paradigm limits the ability to determine sensitivities of isolated retinal regions, especially the fovea.

If small and isolated regions of the retina are to be exposed with small diameter spots and examined behaviorally, the animal's eye movements must be eliminated during the time of exposure. In the past the primary means of accomplishing this immobilization has been with a general anesthesia to immobilize the entire animal. This procedure, however, virtually eliminated all possibilities of immediate postexposure behavioral testing and thereby eliminated the examination of the transitional point from temporary to permanent damage thresholds. Usually, postexposure assessments are delayed for a minimum of 24 hours until the animal fully recovers from the anesthesia (6, 7, 8). The immediate changes in visual performance are critical in determining how animals and personnel alike will be able to function within their specific mission once exposed. In addition, examination of the immediate consequences of individual exposures is important in exploring the question of adverse cumulative effects of repeated exposure on thresholds for retinal alteration.

In the initial stages of this effort, a behavioral procedure was designed and implemented which permitted accurate placement of small diameter exposures on the fovea in awake, task-oriented animals (9). This procedure, along with a modification of a rapid technique to measure rhesus visual acuity (10), has been used in the current support period to assess the immediate behavioral consequences of brief laser exposures both above and below the power densities necessary to produce long term deficits in either function or morphology. In subsequent efforts, various parameters of the exposure and testing conditions have been manipulated to more accurately simulate field conditions and to aid in the delineation of the damage mechanism.

In previous protocols, the behavioral effects of variations in the diameter of the exposure site on the retina were examined in several animals. As expected, as the size of retinal involvement increased, so did the magnitude of the initial deficit in visual acuity. The rationale

for the exposure of larger areas of retina (>300 microns) was to make the results of these functional explorations more compatible with other morphological and electrophysiological studies underway in other research laboratories. These efforts have traditionally used larger beam diameters to facilitate histological verification of the site of damage. The use of larger diameter exposure sites in our study has also provided the opportunity for histopathological examination of our animals' retinæ following completion of the behavioral portion of the study. Other advantages of the larger exposure area are to increase the probability of direct foveal involvement in any given exposure session and to elicit larger shifts in visual acuity following successful exposure. These advantages, however, are largely procedural and do not necessarily imply that larger diameter exposure sites are more appropriate or relevant than smaller ones in establishment of the MPE. In fact, the opposite might be expected. Smaller areas of retinal involvement should more closely simulate the type of exposure condition which might occur in the field following exposure to a laser beam originating from sources at great distances away. As a consequence we have begun exploring the effects of very small diameter beams producing less than 50 microns in diameter of involvement on the fovea. We have also begun exploring the temporal characteristics of the exposure on the magnitude and the duration of the deficit in visual acuity since in the field, exposures may vary from very transient durations to relatively long durations where subjects might voluntarily fixate on the laser beam.

In subsequent studies we have also begun to examine the sensitivity of our measuring devices by varying critical parameters of the stimulus used to follow the deficit in visual performance. In the initial studies, high contrast, white light targets were exclusively used to measure visual acuity before and after exposure. In the current experiment various monochromatic lights and luminance levels were used as backgrounds for the test targets during all phases of behavioral testing. We have, however, maintain the use of a Landolt ring discrimination task instead of transferring to sine wave or square wave gratings. The advantage of the Landolt ring over grating targets is that the break in the ring relates more specifically to small and more defined regions of the retina. Acuity has been measured by titrating the size of rings for different predetermined luminance and chromatic backgrounds. We have recently begun to expand the use of chromatic targets to assess visual sensitivity during and immediately following exposure. These chromatic tasks are more appropriate in determining changes in foveal sensitivity than are achromatic targets since it is the fovea where color vision predominates. We have also begun examining the effects of different contrast targets, chromatic and achromatic, on postexposure sensitivity. The use of lower contrast targets than those previously used in past studies will more accurately simulate adverse field conditions and hence more precisely predict the ability of exposed personnel to complete visually guided missions.

Over the course of several years we have also been comparing the effects of the wavelength of the laser beam on the derived changes in visual sensitivity. Exposure wavelength has been shown by our studies to be an important variable in determining the MPE for lasers. Functional thresholds for safe exposure levels as well as the type of shift in chromatic sensitivity following exposure has been shown to be dependent

upon the wavelength of the exposing source. Also, the examination of specific exposure wavelengths has helped in delineating the nature of the damage mechanism. At the present time we have examined the effects of three different spectral lines: 632.8 nm (HeNe), 647.1 nm (Krypton), and 514.5 nm (Argon).

The present progress report represents an interim support period of approximately seven months of effort. It represents a transitional period between two different contracts and had as its primary objectives:

1. continued postexposure testing of one subject exposed to repetitive 100 msec flashes of Argon during the previous support period. Daily measurements of spectral acuity and spectral sensitivity were performed to follow the animal's long term recovery process.
2. Following baseline measures of spectral and contrast sensitivity, expose a second animal to Argon flashes of different durations and beam diameters for comparisons of the effects of these parameters on visual recovery.
3. Begin training two additional animals in preparation for future exposures of these animals to laser irradiation in subsequent support periods.

METHODS

A detailed description of the paradigm and experimental facilities has been reported elsewhere (9,11). Behavioral assessments of visual performance were measured in a light-tight, primate cubicle isolated from the programming equipment. Two such cubicles were used; one for training and the second for baseline sensitivity measures and exposure to the coherent light source. Both chambers were identical with exception to the addition of optics necessary to present the laser beam coaxial with the discrimination image on the screen. Except for the screen, the entire test chamber was dark and all test sessions were preceded by at least 15 minutes of dark adaptation.

A rear projection screen mounted on the far wall of each cubicle subtended 3 degrees at a distance of 1 m from the subject's pupil. Dark Landolt rings against a light background were projected onto the screen using a conventional carousel projector. Background luminance and wavelength were determined by neural density and interference filters placed in the path of the light. Monochromatic backgrounds varied from 420 nm to 700 nm and all filters were calibrated on a Carey spectrophotometer. All monochromatic backgrounds were standardized in terms of quantal irradiance at the 580 nm level. A second projector served as a source of diffuse

light onto the screen when different contrast levels were being examined. The overall luminance of the screen was kept constant by reductions in the intensity of the image projector; the proportion of light from each affecting the overall contrast level between the light background and "dark" figure.

The test patterns were conventional black Landolt rings. The thickness of the rings and the width of the gap that formed the critical detail was always $1/5$ of the diameter of the ring. The size of gap was varied from $0.25'$ to $30'$ visual angle in 20% steps. In one animal, square wave gratings were also used to measure spatial resolution and hence visual acuity. In this case, the horizontal grating was comparable to the Landolt ring ("C") while the vertical grating was made comparable to the gapless ring in the training paradigm.

The animal was aligned through a physical restraint device with the center of the viewing screen. The subject's head was kept stationary during testing and exposure by four Plexiglas head restraints mounted on the top of a standard primate chair. These restraints temporarily prevented movement in any direction. An opaque facemask and two 5.0 mm monocular iris diaphragms were aligned with the subject's pupils and viewing screen so that eye position could be well controlled during actual exposure to laser irradiation. All testing was done with monocular viewing. A diagram of the optical system is shown in Figure 1.

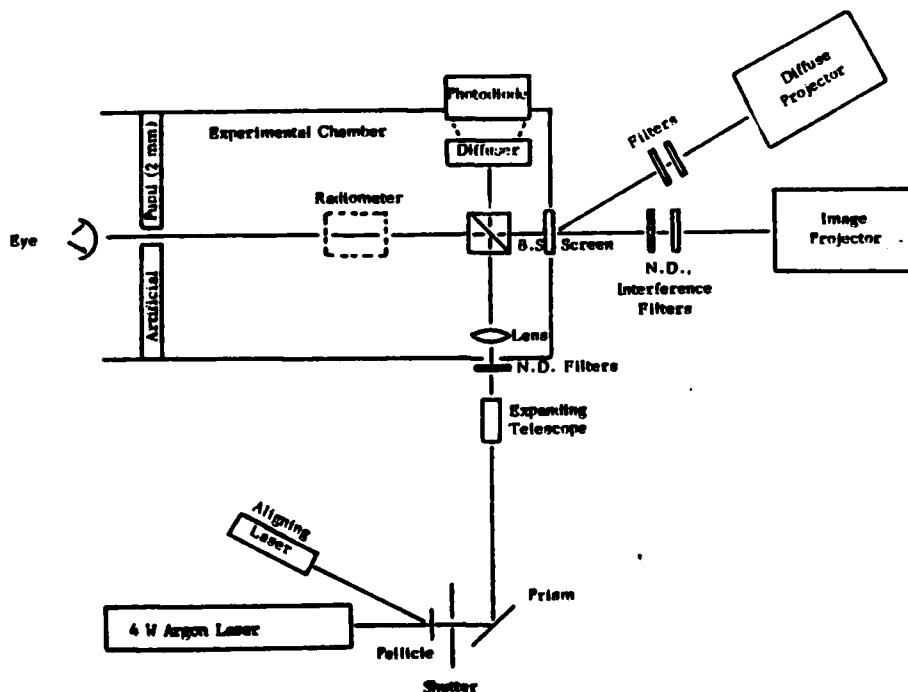


Figure 1. Optical system used to present image targets and the exposing laser irradiation.

Discrimination Task. The subjects were trained, using an avoidance paradigm, to depress a lever whenever a Landolt C (or horizontal square wave grating) was presented. Failure to depress the lever during the 3 second Landolt C trial was punished by a brief electrical shock. Lever responses during trials with completed rings (or vertical gratings) also initiated a brief shock on a fixed ratio reinforcement schedule. The test objects were presented in sets of four rings that were of equal diameter. Three rings in each set were gapless, while the fourth was a Landolt C that appeared in a random position within the set.

Threshold acuity measurements were obtained by an up and down, tracking method which allowed the animal to adjust in discrete steps the size of the test target about his own threshold level. The size of the gap in the Landolt C increased following incorrect "C" responses and decreased by correct "C" detections. Lever responses on completed ring trials did not affect the size of the gap to be presented on the next series of trials. Means and standard deviations of threshold visual acuity were obtained by the use of Dixon and Massey's (13) statistics for the up and down method. During recovery from laser irradiation, the average number of completed rings relative to Landolt C's was reduced from an average of four to two in order to more rapidly track transient changes in visual acuity as a function of time after exposure. Baseline mean levels or variability have not been affected by changes in the ratio of Landolt C's to completed ring trials. Also unaffected were the number of lever responses during completed ring trials which was always very small in our subjects.

Laser System. In the previous projects, one of three different laser systems were used as the adapting light source. In the earliest studies a standard 50 mW HeNe laser provided a beam diameter which produced an 150 micron spot on the retina. When larger diameter exposure sites were desired a second 4 W Argon laser with a Krypton plasma tube was capable of producing exposure diameters on the retina of from less than 50 microns (minimal spot) to greater than 500 microns. The output wavelength of the Argon laser with a Krypton tube was set at 647.1 nm and was very close to the primary 632.8 nm output wavelength of the HeNe laser. In this study the Krypton tube of the Argon laser was replaced with a Argon and the selected output wavelength of the laser was set at 514.5 nm. As with the Krypton plasma tube, sufficient power densities to produce retinal alterations were available from the Argon tube for beam diameter ranging from minimal spot to greater than 500 microns on the retina.

The entire laser system, with exception of a focusing lens and beam splitter was mounted outside the experimental chamber. The "raw" beam passed first through a manual safety shutter and then a electronic shutter. The shutter was preprogrammed to produced a calibrated exposure duration of 100 msec. The beam was then attenuated by neutral density filters before being diverted by a 4.5 cm diameter front surface mirror. The diverted beam entered a beam expanding telescope which produced a collimated beam of adjustable size. Removal of the expanding telescope produced a minimal diameter beam of less than 50 microns on the retina. The collimated beam then passed into the experimental chamber and through a 1.25 diopter lens placed 85 cm in front of the subject's pupil. A 5 x 10 cm coated pellicle beam splitter was placed 5 cm in front of the 1.25 diopter lens and at the intersection of the diverging laser beam and the image beam from the carousel projector. Coaxial alignment with the line of

sight was verified by noting that the reflected beam also passed through a 2 mm aperture and onto the critical feature of the target on the screen. Mounted on the opposite side of the beam splitter was a diffuser and ultrafast photodiode (HPA-4203). The output of this detector was displayed on a memory oscilloscope and was regularly calibrated against an EFF Model 580 Radiometer placed at the corneal plane. The power and pulse width of each irradiation was measured and recorded. Exposures of 100 msec duration were made at various corneal power levels, beginning with the lowest power level.

Laser exposure. Prior to any laser exposures, stable baseline acuity levels were established for each subject using both monochromatic and white light targets of several different contrast levels. Initially, a criterion of, at minimum, 14 consecutive sessions of white light threshold measurements were used to establish a baseline mean and standard deviation for each subject. Following the determination of a stable, white light threshold, the animal's spectral sensitivity (using an acuity criteria) was determined before exposure sessions began. Prior to each exposure, a 15 minute baseline session was completed and the mean for this pre-exposure testing was determined. The number of completed rings relative to incomplete rings (Landolt "C") was then reduced and comparisons made to assure a stable baseline. Failure of the subject to obtain mean acuity within one standard deviation of his pre-determined baseline level on either reinforcement schedule, aborted the session. Session variability which exceeded baseline variability also aborted the session.

Exposures were made during threshold measurements after the above performance criteria were met. The laser flash (100 msec duration) was triggered by the animal's correct detection of his threshold Landolt ring which most often corresponded to gap sizes of between 1.0 and 0.5 minutes of visual angle. The electronic shutter was immediately triggered by a microswitch on the response key. Somewhat causal observations of numerous animals working under these conditions imply that subjects maintain fixation during their response period. The results of this study thus far have shown that triggering the onset of the exposure to the subject's response elicited significant deficits in visual sensitivity characteristic of inactivation of more central regions of the retina. Voluntary eye movements or blinking during exposure were eliminated by the use of a 100 msec exposure duration. Exposures were made over power levels increasing in energy from 0.5 mW to greater than 11 mW. No more than one exposure was made per day and exposures were never made either following incorrect detections of Landolt C's or following correct detection during the last 1 second of the trial.

Immediately after exposure, recovery was measured until the subject returned to baseline acuity levels or in the case of a permanent or semipermanent alteration until either the degree of deficit stabilized or 45 minutes whichever came first. The entire test session lasted approximately 2 hours. If acuity did not recover within a given session, further exposures were discontinued until evidence of recovery at all spectral points was achieved. The laser exposure level at which this recovery criterion failed to be achieved defined the transitional zone between temporary and permanent acuity loss measured in these experiments.

RESULTS

Sample data of threshold acuity using the tracking technique are shown in Figure 2. This record is taken from a strip chart recorder which was programmed to follow the mechanical movements of a traditional Kodak carousel projector. In this particular session the subject was exposed to a 7 mW, HeNe flash of 100 msec duration. The exposure site was calculated to be 150 microns in retinal diameter. Similar recovery functions have been observed using different laser systems and power densities but were not graphically represented in this manner because the raw data is now automatically processed and stored in our computer rather than being displayed on a strip chart recorder. In this figure, the occurrence of the exposure is indicated by an arrow at time zero. The ordinate indicates various sizes of gaps in presented Landolt ring and is

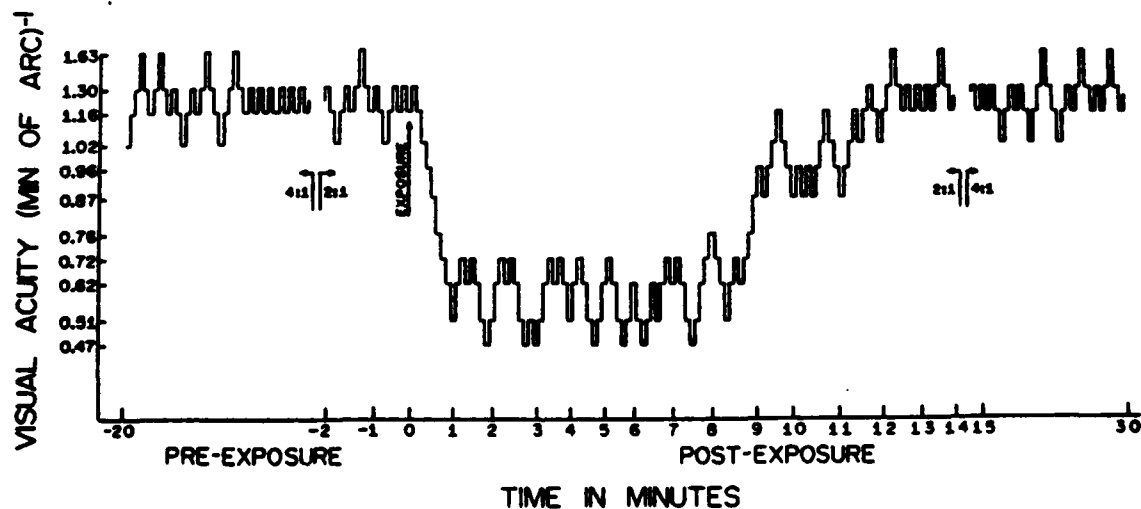


Figure 2. Sample raw data of acuity following laser exposure.

plotted in reciprocal minutes of arc. Horizontal excursions on the chart represent the presentation of these targets. The abscissa represents corresponding times in minutes. The presentation of gapless rings is indicated by vertical excursions between the horizontal excursions. The order of presentation of the slides in terms of their diameters was entirely dependent upon the animal's response on Landolt ring trials. Incorrect detection of the Landolt ring caused the recorder to plot downward and corresponded to the presentation of larger diameter rings.

The magnitude of the initial deficit in visual acuity immediately following exposure was independent of exposure power or wavelength of the exposing source. The duration of the initial deficit as well as the total

time required for full recovery was, however, systematically related to the energy of the exposure. Typically, as the energy density of the flash was increased, both the duration of the initial maximum deficit as well as the total time for full recovery increased. For very low power densities, full recovery was complete in less than 4 minutes and was difficult to follow due to the inherent time required for our equipment to track the initial stages of a continuously changing deficit. As reported elsewhere (3), some slight differences were also seen when different test targets and backgrounds were used to follow the immediate recovery from laser irradiation. The effects of changes in the diameter of the retinal exposure on the magnitude and duration of the recovery process is shown in Figure 3. In this figure, per cent deficit in visual acuity is plotted against time after exposure for three different exposure diameters. The energy of the exposure was kept constant at 1.0 mW and acuity was followed using the same white light, high contrast background. Per cent deficit in visual acuity was defined as the magnitude of the deficit relative to the animal's average pre-exposure baseline. For a 150 micron spot, the animal's initial sensitivity following exposure was approximately 50% of

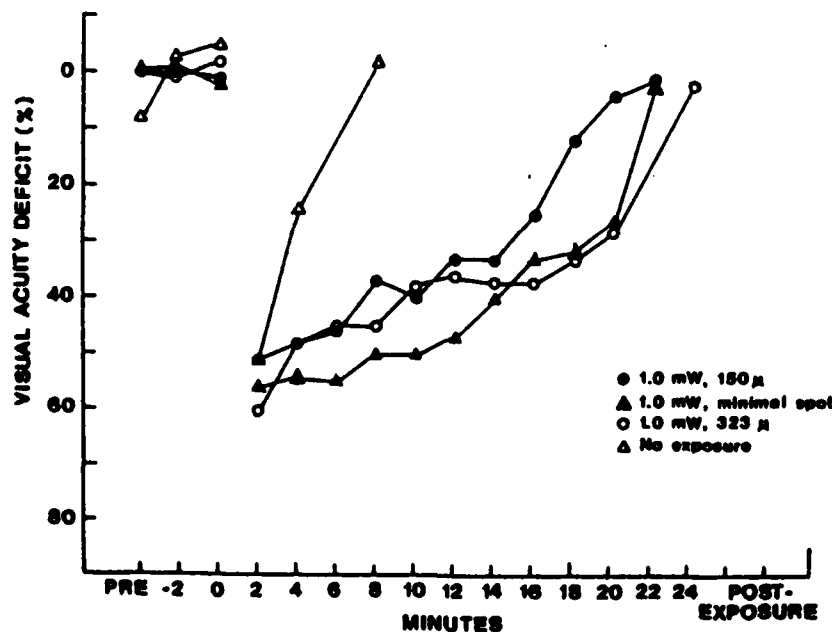


Figure 3. Comparisons of the effects of exposure diameter on the magnitude and duration of the recovery function.

its pre-exposure sensitivity. Full recovery from this flash was complete in approximately 20 to 22 minutes. At this particular power level, the initial maximum deficit in sensitivity quickly began to recover. With more intense power densities the initial deficit remained depressed for a longer time before recovery gradually occurred. With a 323 micron spot size, the initial deficit was significantly larger and represented a decrease in postexposure sensitivity of approximately 65%. Here again with this particular power level, the recovery in sensitivity was rather gradual with full recovery in approximately 24 minutes and no maintained initial deficit evident. The recovery to a flash which exposed only very small area of retina (less than 50 microns) produced a surprisingly large

initial deficit of approximately 55% of pre-exposure acuity and a relatively long time for total recovery, approximately 22 minutes. The "no exposure" or sham exposure condition, shown in this figure, represents the time required for the animal to return to baseline following an artificial increase in the size of the target to a level near the acuity level typically observed immediately following laser exposure. This particular curve represents the time required for the program to reverse itself and present slides of increasing smaller diameters as the animal correctly detects suprathreshold targets.

As previously reported (4), one subject during the last year was exposed to brief pulses of 514.5 nm (Argon) coherent light in a manner described above. The beam was expanded and represented a 323 micron spot on the retinal surface. During the current period we continued to follow this subject's long term deficit to check for any recover in function over time. This animal's exposure history included a number of exposures at and below 3 mW. For each exposure, recovery was complete within the 2 hour test session. Especially for low energies at 1 mW or beyond, recovery was quite rapid. No more than one exposure was made per session (day) and often exposures were separated by several days. In total this animal received over several dozen exposures of increasing power densities before a permanent functional alteration was noted. A permanent deficit in visual sensitivity was noted following the third consecutive exposure to a 3 mW, 100 msec flash from an Argon laser. In Figure 4 the recovery functions for the three exposures are presented. Recovery was plotted as the per cent visual acuity deficit as a function of time following exposure. The background luminances and contrasts of the test targets were the same in each case. The upper plot represents the recovery function for the first 3.0 mW exposure and recovery began almost immediately following exposure. For this exposure full recovery was complete within 4 to 6 minutes. Recoveries of this magnitude in the past were often considered so rapid as to possibly represent a "miss" in terms of influencing foveal activity. In the middle plot, the recovery for the second 514.5 nm exposure is shown and this exposure occurred 4 days after the first exposure. In this case, again, recovery was rapid but not quite as rapid as in the case of the first exposure. Full recovery occurred in approximately eight minutes but here again the initial deficit showed no long lasted affect. In the third and final exposure shown in the bottom plot, the initial decrease in sensitivity was prolonged several minutes before recovery eventually occurred. Twenty four hours later, however, a significant deficit in both achromatic and chromatic was noted. This deficit was followed during the course of the current project and to date full recovery is still not complete.

Postexposure spectral responses curves derived over the first five days following the last 3.0 mW exposure showed a generally uniform depression in sensitivity across the entire visible spectrum and extended for achromatic targets as well. Within two weeks of the last exposure, recovery to pre-exposure baseline sensitivities were noted for achromatic targets and on a lesser basis for targets with backgrounds in the middle and long wavelength end of the visible spectrum. No significant recovery to short wavelength targets was observed during the first month after exposure. Almost two months after exposure spectral acuity in the exposed eye, relative to the control or unexposed eye, was still significantly depressed in the short wavelength region.

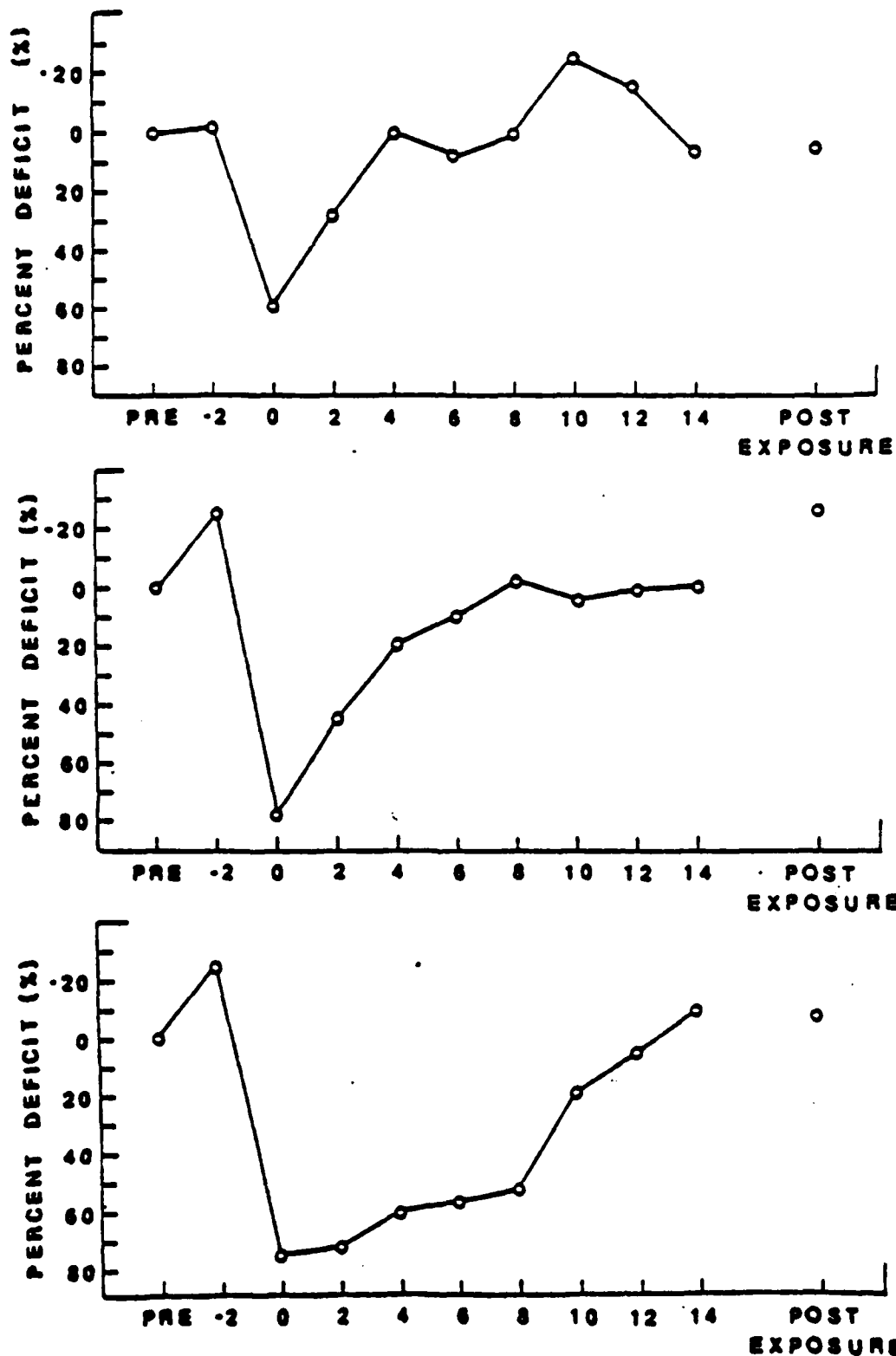


Figure 4. Recovery functions for one subject following three single, 3.0 mW exposures on days 2, 6, and 9. Each exposure was a single 100 msec pulse of 514.5 nm laser light which produced a retinal spot size of approximately 323 microns. The backgrounds of the test targets used to measure visual sensitivity were the same and were high contrast, achromatic fields which elicited maximum photopic visual acuity.

The spectral sensitivity curves shown in Figure 5 for this same animal were derived beginning the fourth month after the final 3.0 mW exposure. Similar curves were found six and nine months later. The solid line in each figure represents the spectral sensitivity of the exposed eye while the dashed line represents the sensitivity of the unexposed or control eye. The standard Landolt ring acuity task was used to derive these curves and three different criterion acuity curves are shown in this figure. The different criterion curves (1.11, .76 and .52) were derived from intensity-acuity functions at various spectral points across the visible spectrum. Initially, no significant differences existed between the sensitivity of the control (unexposed) eye and the pre-exposure spectral sensitivity of the experimental eye. Likewise, the baseline sensitivity of the control eye remain consistent over a period of one year following exposure. For all selected criteria, spectral sensitivity in the exposed eye was most depressed in the very long (beyond 600 nm) and very short (below 460 nm) regions of the spectrum. Sensitivity was also greatly reduced in the region of the spectrum near the output wavelength (514.5 nm) of the laser; this mid-spectrum insensitivity was especially pronounced when high criterion responses (high acuity targets) were selected. Standard deviations for each spectral point have been calculated for both within and between sessions. The data points in Figure 5 represent the extrapolated criterion values derived from least squares equations of the mean data points of at least four different test sessions over a minimum 5 log unit intensity range measured every 0.5 O.D.

Calculated standard deviations for each spectral point were excluded from the graph for reasons of clarity but do show that the differences between the exposed and unexposed eyes in the extremely short and long wavelength regions of the spectrum were statistically significant. We have continued to follow this animal's spectral sensitivity and more recently there has been some slight recovery in the very long and short wavelengths regions although some depressions in these spectral regions still exist some 9 months after the final 3.0 mW Argon exposure.

During the course of this effort the temporal effects of laser irradiation were examined. Using a minimal diameter spot (less than 50 microns), various duration exposures were presented and the changes in visual sensitivities examined. The effects of exposure duration for a 1.0 mW CW flash of Argon light is shown in Figure 6. In this figure as in past figures, visual recovery is plotted in per cent deficit from the animal's pre-exposure baseline sensitivity level. With each different exposure, the background parameters of the test target were held constant. The test targets were projected against a high contrast, white light background. Exposure durations in excess of 100 msec were avoided to eliminate any possibilities of confounding eye movements which would have the effect of smearing the exposure over large and undefinable regions of the retina. For very short durations of 50 msec or less the recovery functions were reminiscent of those seen in Figure 3 for sham exposures. Above 50 msec, exposures produced a longer lasting effect before the animal regained his pre-exposure sensitivity. That a real deficit did exist for even the shortest durations was demonstrated by the animal's inability to maintain his pre-exposure acuity level when the projector was not manually reverse to an approximated postexposure sensitivity level.

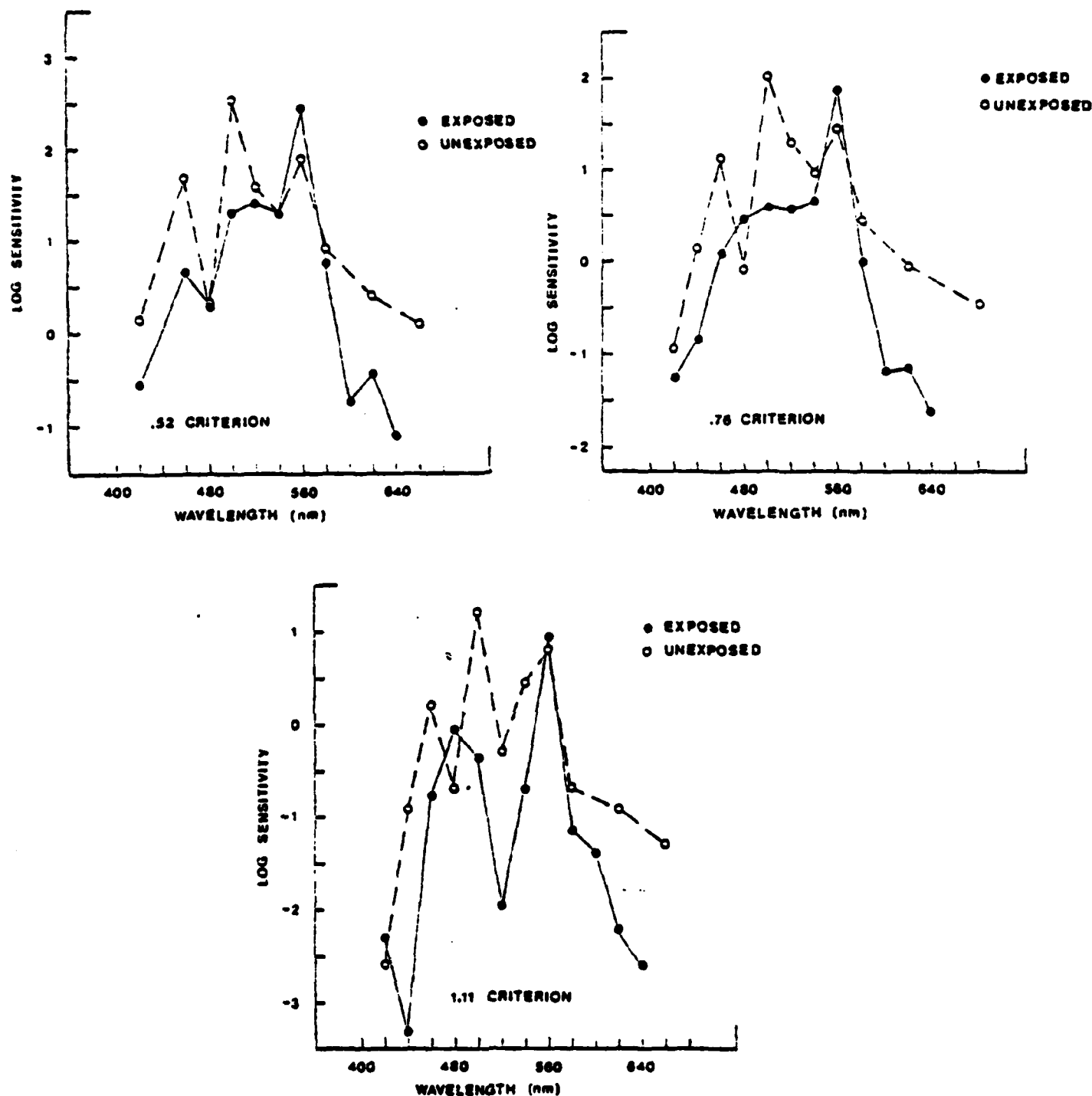


Figure 5. Spectral sensitivity curves for one animal repeatedly exposed over many sessions to 100 msec flashes of Argon (514.5 nm) light. The diameter of the exposures on the retina were 323 microns. Individual spectral sensitivity curves were derived from interpolated intensity acuity functions at each spectral point and represent the mean of at least four different test sessions. The criterion selected (0.52, 0.76, and 1.11) represents the reciprocal of the energy necessary to elicit a criterion acuity of this magnitude at each spectral point.

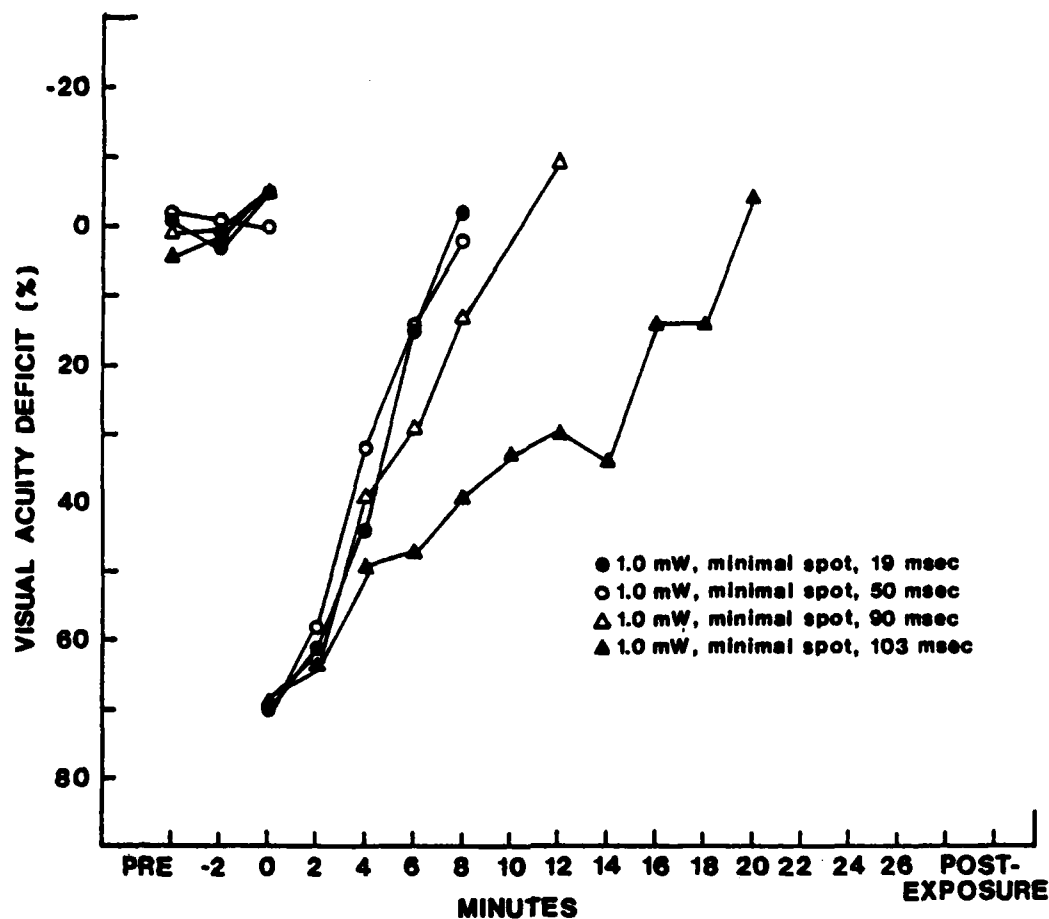


Figure 6. Effects of flash duration on recovery from laser exposure. All exposures were made with an Argon laser which produced a minimal diameter spot on the retina.

Discussion

The results of the current projects support and extend the conclusions of previous reports. We have found that relatively long lasting deficits in visual sensitivities have been produced by exposure to laser sources at corneal irradiances below those typically reported using gross fundoscopic or fine histological criteria. These results suggest that the functional criteria for assessment of laser effects are extremely sensitive and may reflect subtle changes in receptor action that currently are not readily visible by morphological or histological techniques.

In the course of these investigations we have expanded the number of stimulus and exposure parameters for two reasons. First, the use of

additional behavioral assessments have been used to simulate the type of field conditions under which persons may be accidentally exposed to a laser beam. The attempt to simulate field conditions is directed toward a better understanding of what kinds of decrements in visual performance might be expected from persons exposed. This information is necessary to judge the ability of these persons, once exposed, to continue to carry out their specific visual-motor task and is somewhat independent of the problem of permanent vs temporary induced effects. Second, the expansion of exposure parameters has been directed not only at an attempt to simulate the various types of possible field exposures but also to understand the underlying mechanisms in any type of laser induced damage.

In comparison to long wavelength laser sources we have tested in our laboratory, the threshold for permanent functional alterations in visual sensitivity was significantly lower for Argon (514.5 nm) irradiation than for either HeNe or Krypton irradiation. This might be expected since the rhesus fovea might have fewer long wavelength receptors than intermediate and short wavelength receptors (12) making the absorption of long wavelength light less probable than short or intermediate light. Less absorption should be associated with higher thresholds for damage. Our data would appear to support the notion that specific spectral lines of coherent light at low levels selectively alter specific foveal cone processes and the use of chromatic acuity targets best delineate these rather subtle, but important, effects

In all of the results we have reported to date, the transition from temporary flash blindness effects to permanent functional alterations occurred after a succession of exposures at the same corneal irradiance level and not after the first exposure at the next higher energy level. This phenomenon occurred in spite of the fact that individual exposures were never presented in the same session and were separated from each other by a minimum of 24 hours. These results are therefore strongly suggestive of some cumulative mechanism occurring in the eye which is capable of summing brief pulses (100 msec) over relatively long periods of time. The time course and degree of additivity remain unknown. A similar cumulative effect for low level laser irradiation has been observed by Zwick, et al. (13) using a chronic exposure paradigm quite different from the exposure conditions employed in our studies. Only recently have vision researchers begun to consider the possibilities of some long term cumulative mechanism occurring for damage thresholds in the visual system even though both temporary (TTS) and permanent shifts in auditory thresholds as a result of repeated low level stimulation have been long recognized. No distinct long-term chemical process has yet been implicated within the eye in which changes of this nature and time course could be explained. The exploration of disc shedding and reformations in both rods and cones and the effects of light stimulation on this renewal process may, however, provide some explanation for our effects.

In relation to the effects of exposure diameter on visual sensitivity, one might have expected that exposure of the central fovea to increasing larger diameter spots of high energy light would elicit larger and larger initial deficits in visual acuity. These larger initial deficits should approximate the spatial resolution abilities of uninvolved retinal areas outside the fovea. Such was the case with relatively large diameter beams but clearly was not true when a minimal spot was produced on the retina.

The brief flashes of this type should have produced very localized disruptions in function which the animal should have rather easily been able to avoid by moving his eye only very slightly to fixate the target on a secondary area of the fovea unaltered by the flash and of somewhat equal spatial resolution ability. Flash durations of less than 100 msec should have reduced the smearing effect of both involuntary and voluntary eye movements and produced rather discrete punctate lesions. Our preliminary data using a minimal diameter spot do not support the above assumptions. The data suggest that exposure of the retina to brief flashes which represent less than 50 micron spots on the retina produce rather significant shifts in spatial resolution abilities and are as effective in disrupting visual performance as our much larger diameter spots. We do not believe these exposures were solely disruption to the behavior or attention of the subject since our subjects were well trained to avoid errors and were accustomed to the occurrence various kinds of potentially disruptive stimuli during the course of their testing. The data instead suggest the possibility of some neural or photochemical process occurring which might affect the sensitivities of surrounding areas in much the same way as direct light absorption.

Our results continue to demonstrate the importance of functional analyses in the determination of the MPE. This method continues to provide a more sensitive criterion than either the morphological or electrophysiological approach and provides additional information regarding the degradation of visual sensitivity following exposure.

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