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LASER FLASH EFFECTS: A NON-VISUAL PHENOMENON.(U)
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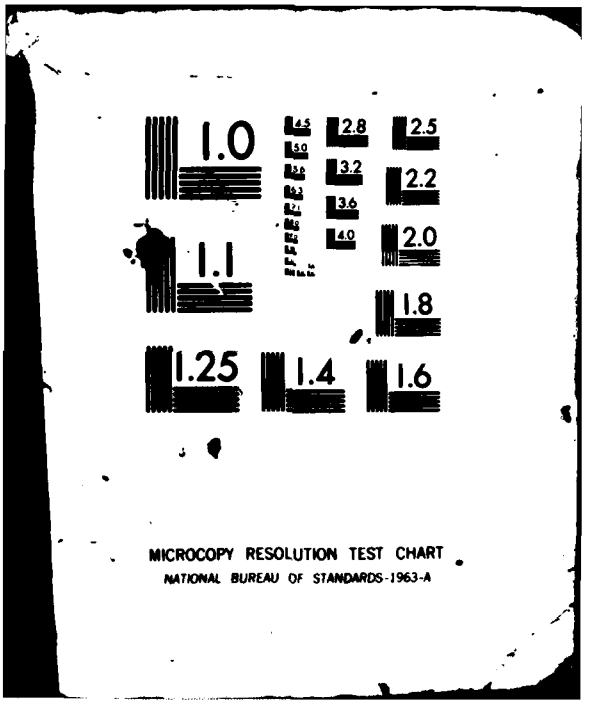
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RANDOLPH, SCHMEISSER & BEATRICE

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Laser Flash Effects: A Non-Visual Phenomenon? (U)

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Ruby and neodymium laser rangefinders, ground locator-designators and other devices which emit short (20 nsec) high energy flashes of laser radiation are currently being deployed to troop units in the field. Evidence of the effects of short laser pulses delivered in known quantities and spot sizes on the human retina has been limited to the treatment of proliferative diabetic retinopathy or other clinical states which involve abnormal ocular conditions(1). In these cases, the bulk of the laser energy is directed to the peripheral retina and, when necessary, to the capillary-free zone of the macula. No exposures are placed in the central fovea where visual acuity is best. The soldier using binoculars or other optical sighting devices in the combat environment would receive a laser flash directly in the fovea.

Research on flash effects with human subjects has been generally limited to white light, non-laser sources with large retinal spot sizes (2). The immediate effects upon the vision of individuals who receive foveal laser exposures (minimal spot size) is unknown. It is thus important to be able to predict accurately the biological and functional effects of these exposures, delineate the physical and physiological parameters and recommend a course of treatment for those thus exposed. Ultimately, these data should lead to techniques for preventing debilitating laser bioeffects.

Laser energy levels, wavelength, size of the affected area, pulse length, pulse repetition rate and other physical variables have been related to changes in the eye and skin since the mid 1960's (3,4)and have been primarily concerned with both gross and microscopic alterations in the tissue. Based upon these changes, inferences have been made about the functional effects, i.e. a lesion in the retina implied a loss of vision at that site.

In order to quantify the implied loss of vision, non-human primates

have been trained to respond to acuity criteria for high and low stimulus contrast targets. Robbins et al (5) reported immediate (within 2 min) high target contrast visual acuity decrements in the rhesus monkey following foveal exposure to 100 msec pulses of helium-neon (633 nm), krypton (647 nm) and argon (514 and 488 nm) laser lines. The spot sizes varied between 150 and 300 μ. Recovery occurred after approx. 5 minutes. Similarly, Zwick et al (6) found decrements in both the high and low contrast visual acuity of trained rhesus monkeys within the first 2 to 3 min following exposure of the foveal area to a 532 nm Q-switched pulse. The laser had a repetitive pulse rate of 10 to 20 Hz, and produced minimal (50 μ) foveal lesions. They reported acuity recovered in 5 to 15 minutes following exposure. Merigan et al(7) showed that destruction of the fovea resulted in the loss of fine acuity at high luminance levels in the rhesus monkey. At lower target luminosity and for larger targets, no decrease in performance was noted. In a series of experiments designed to determine the effects of flashblinding stimuli upon the ability of both humans and rhesus monkeys to maintain compensatory tracking, Callin et al (8) reported that for the stimulus conditions (100 msec tungsten halogen flash and 20.7 μJ/flash), the average recovery time for each species was approx. 3 sec. A second study by this group using green or white (multiwavelength) laser pulses found no consistent effect upon tracking performance. The average flash recovery in those animals showing some disruption was approximately 2 sec. This was attributed solely to startle responses of the animals. Another interpretation of these data is that the fast recovery times exhibited by their trained animals was the result of the animal's ability to use parafoveal cues in tracking. This thus negated the central field flash effect. One method of determining foveal flash effects is to measure indirectly the integrity of the central retinal area by evaluating the cortical response to a pattern visual stimulus before and after a foveal laser exposure.

The pattern visual evoked potential (VEP) is an electrical response to a shifting stimulus composed of alternating light and dark bars recorded at the cortex. This potential primarily reflects activity in the fovea and the immediately surrounding macular area while suppressing perimacular involvement by insuring constant retinal illumination. Regan (9) has shown that the response of the electroencephalogram (EEG) to an alternating stimulus is one of entrainment of this signal at the alternating frequency. This phenomenon requires several seconds to appear following the onset of the stimulus. One hypothesis for this phenomenon is a neural recruitment of the retinal elements at the cortical level. The cortical elements then become synchronized to the signal.

Differences between human psychophysical data and corresponding electrophysiological results have been noted; recovery of the VEP is much faster than psychophysical recovery after response suppression by adaptation in a contrast threshold task (10). However, direct comparison

of psychophysical and electrophysiological measures of contrast thresholds demonstrates a high correlation and indicates that the evoked potential can be an accurate reflection of perceptual experience (11 - 14).

The purpose of this study was twofold. First, determine if foveal flash effects could be identified and quantified by using an electrophysiological technique. Second, delineate those combinations of variables, such as spot size and energy level, which would yield immediate and short-term changes in the visual system.

METHODS

Subjects: Nine eyes of seven cynomolgus (Macaca fascicularis) monkeys were used in the present study. The animals were sedated by intramuscular injection of ketamine HCl (10 mg/kg) and premedicated with atropine (0.008 mg/kg). An intravenous catheter was established to administer and maintain the dose level of the paralytic agent pancuronium bromide. The animal was intubated and breathing was maintained by a small animal respirator. The breathing and the electrocardiogram were monitored on a single channel of the physiological amplifiers throughout the experimental session. The eye of interest was dilated with 2% cyclopentolate HCl and 10% phenylephrine HCl. The animal was placed on an animal holder whose plane of rotation was adjusted to be in the center of the cornea of the experimental eye. The head was fixed and a lid speculum installed. Corneal clarity was maintained by frequent washes of normal saline (approx. every 10 sec). The unused eye was kept closed throughout the procedure. At the conclusion of the experiment, the paralysis was reversed with neostigmine and atropine.

Apparatus: Figure 1A is a diagram of the system used in this study. A Holobeam Series 300 Q-switched Ruby laser operating at 694.3 nm with a pulse width of 20 nsec was coaxially aligned to the optics of a modified Zeiss fundus camera. Two spot sizes and two energy levels were chosen. The low dose level for minimal (50 μ: 0.2 degrees [°] visual angle) and large (500 μ: 2.0°) spot sizes were 18 and 178 μJ total interocular energy as measured at the cornea (TIE) respectively. At the higher dose level the TIE for the 50 and 500 μ retinal spot sizes were 39 and 422 μJ respectively. The fundus camera modification (Fig. 1B) consisted of a linear motion motor mounted on the side of the camera's optical system. The motor drove a high contrast square wave grating of either 1.6 or 2.8 cycles/degree visual angle in a square wave mode at 7 shifts/sec (3.5 Hz) in a focal plane conjunct with the retina. The normal field of view of the fundus camera is 30°. This was modified by the introduction of a field stop in the camera's final common path which reduced the projected grating to a stimulus diameter of 3.6° centered on the fovea. The VEP was recorded by a single subdermal needle electrode placed 1 cm superior to the inion and lateral to the midline referenced to linked ears. The

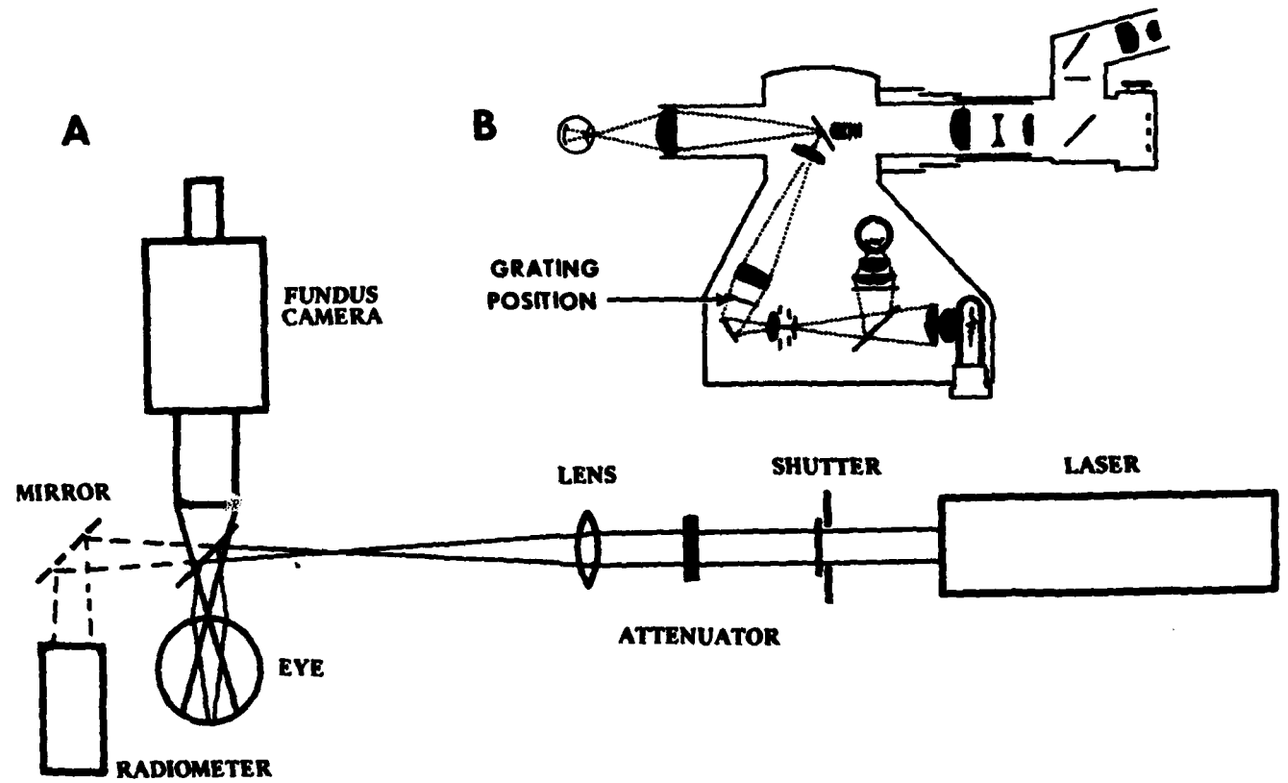

FIG. 1.A. Laser and stimulus system arrangement. B. Fundus camera diagram showing the position of the grating transparency.

signal was processed by a Grass 7P511 physiological amplifier. This signal was then recorded on FM magnetic tape while being analyzed on-line by a Nicolet MED-80 computer system and a PAR Vector Voltmeter. Off-line analysis was performed by playing back the taped signals into the MED-80 and/or Vector Voltmeter.

Procedure: The fovea was aligned with a reticle in the fundus camera field of view and the grating was focused onto the retina. Baseline VEPs were recorded in response to the oscillating grating. At this time, the aperture, if used, was introduced and further baseline data were obtained. During the stimulation, one or more single laser exposures was made to the fovea. Four measures of changes in the steady-state VEP were used, in addition to on-line observation of the averaged potential over short epochs. These measures were phase, magnitude, Pearson product moment correlation and the average standard deviation. Phase and magnitude traces were obtained by processing the VEP through the Vector Voltmeter synchronized with the 7 alteration/second grating stimulus. Changes in response phase reflect a change in the synchronization of the VEP and infer a loss of the ability of the visual system to follow the repetitive stimulus. The magnitude reflects the amplitude of the EEG component at the stimulation frequency. The Pearson correlation coefficient measure was obtained by comparing a pre-exposure averaged VEP (baseline) with sequential averaged VEPs (seven second epochs) recorded during the session. The correlation coefficient will theoretically approach 1.0 when the pre- and post-exposure VEP frequency elements show no difference in relative amplitude and phase. This measure is independent of absolute amplitude and ignores DC shifts. The average standard deviation measure is a mean variability estimate in relative units of the VEP processed in 11 sec bins (7 seconds averaging and 4 sec analysis time).

RESULTS

In the present study, under all of the stimulus and laser combinations: grating size (1.6 and 2.8 cycles/degree), field angular subtense (30° and 3.6°), high and low energy with large and small spot sizes, no immediate change in the VEP (i.e. within the first 5 sec) were observed. Neither were any long term effects noted for those conditions in which minimal spot, low or high energy flashes were combined with large stimulus field sizes (5 eyes). However, marked changes occurred in the VEP as the post-flash interval increased for those conditions in which the high energy, large spot size and/or small stimulating field was used (4 eyes).

Data are shown in Fig. 2 for four animals under four different sets of conditions. The first trace shows phase changes in the VEP of monkey B2. A 30° stimulus field produced a relatively stable phase locked response. The animal received a foveal exposure of 500 μ at 422 μJ, TIE.

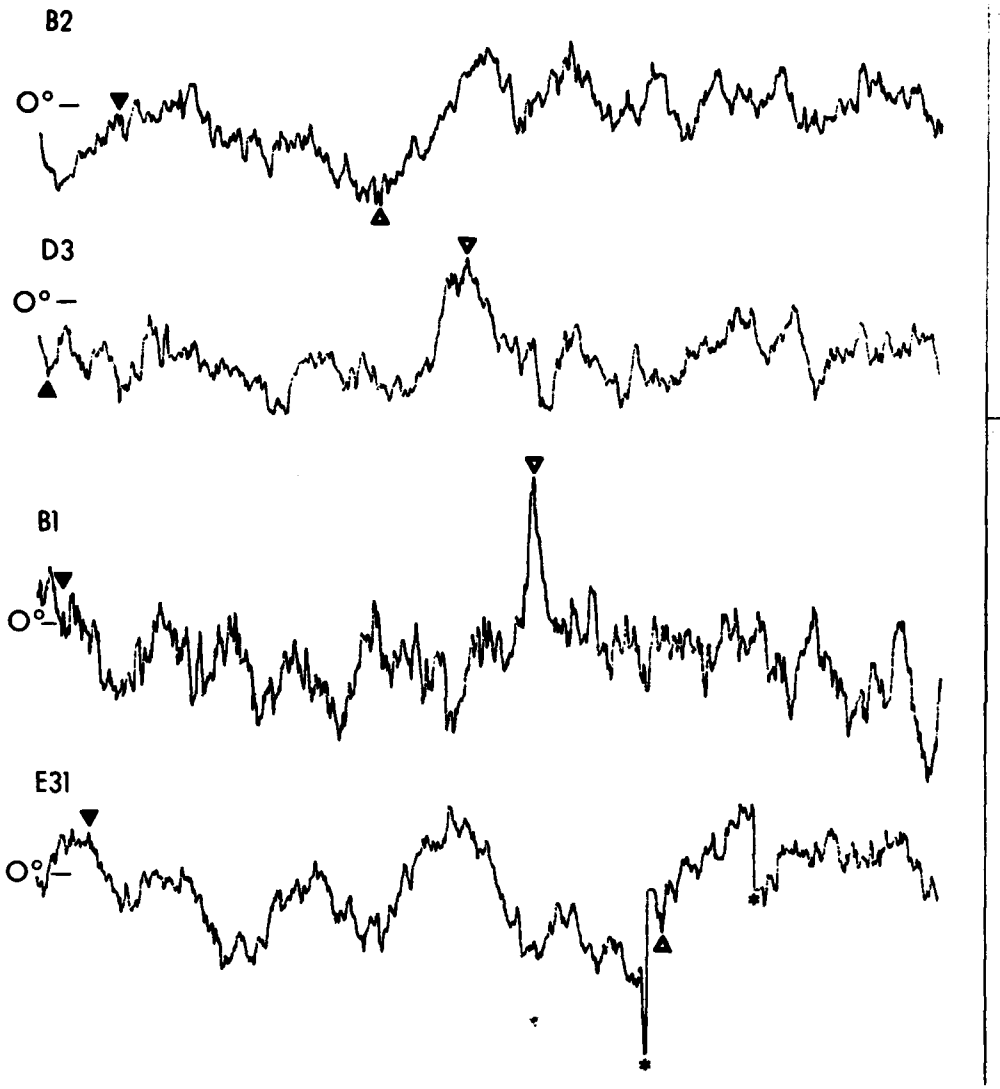

Fig. 2. Phase recordings from the vector voltmeter for 4 animals. Dark triangles indicate laser exposure; light triangles indicate response. Asterisks on trace E31 indicate manual shift into and out of the neighboring phase quadrant. Total time of traces is 204 sec. See text for description.

Little change in phase (digitized at 200 msec per point) was observed immediately after exposure. A later shift of 200° was noted which began approx. 45 sec after exposure and continued for 15 seconds. The second trace illustrates the response of monkey D3 to a Q-switched laser flash of low intensity (18 μJ) and minimal spot size (50 μ) with a test field of 3.6°. A large 90° phase shift occurred 90 seconds after the exposure. When the spot size of the laser exposure was increased to 500 μ (monkey B1) the 178 μJ T.I.E. flash produced a large sharp phase shift of approx. 180°, 106 seconds after the flash. The VEP quickly became resynchronized in this monkey and no further changes were observed. An increase in the laser energy to 422 μJ for the 500 μ spot size, 3.6° stimulus field condition produced a very large (approx. 250°) phase shift, 130 sec after the exposure (monkey E31). The asterisks in this trace mark the manual repositioning of the trace.

In addition to phase, three other measures of the changes in the VEP were recorded. These are shown in Fig. 3 for monkey D3. The first trace is a measure of the relative magnitude of the stimulus locked component of the VEP recorded simultaneously with the phase, phi (amplified from D3, Fig. 2). The point at which the magnitude approaches zero corresponds to the maximum of the phase shift. Line 3 shows the Pearson correlation coefficients for this epoch of data. A large decorrelation can be noted at the same time as the phase and magnitude shifts. The line marked sigma in Fig. 3 represents the variability of the VEP expressed as the mean of the standard deviations of the time-locked VEP 7 sec bin. The increased variability coincided with the shifts in magnitude, phase and correlation indices.

DISCUSSION

In the present study, little or no immediate flash effects were seen under any of the conditions used in this experiment. We have assumed that the VEP represents an ongoing, entrained response of the visual system to foveal events. Since we produced a visible change in the fovea with a Q-switched pulse, we would have expected to observe an immediate change in the VEP. This observation plus the fact that we observed a delayed change in the VEP leads to several possibilities. First, as Callin (8) has pointed out in his three studies of compensatory tracking performance, the flashes of laser light produced a momentary (2-3 sec) startle effect followed by a return to normal tracking behavior. In the curarized animal, this startle response would be absent. In Callin's (8) experiments, the animal's total tracking time was only 45 sec whereas in the present study, the effects did not appear until after 45 sec had passed. In addition, the data in the present study, as shown in Figs. 2 and 3, were recorded with time constants of sufficient length so as to mask a short 2-3 sec transient event.

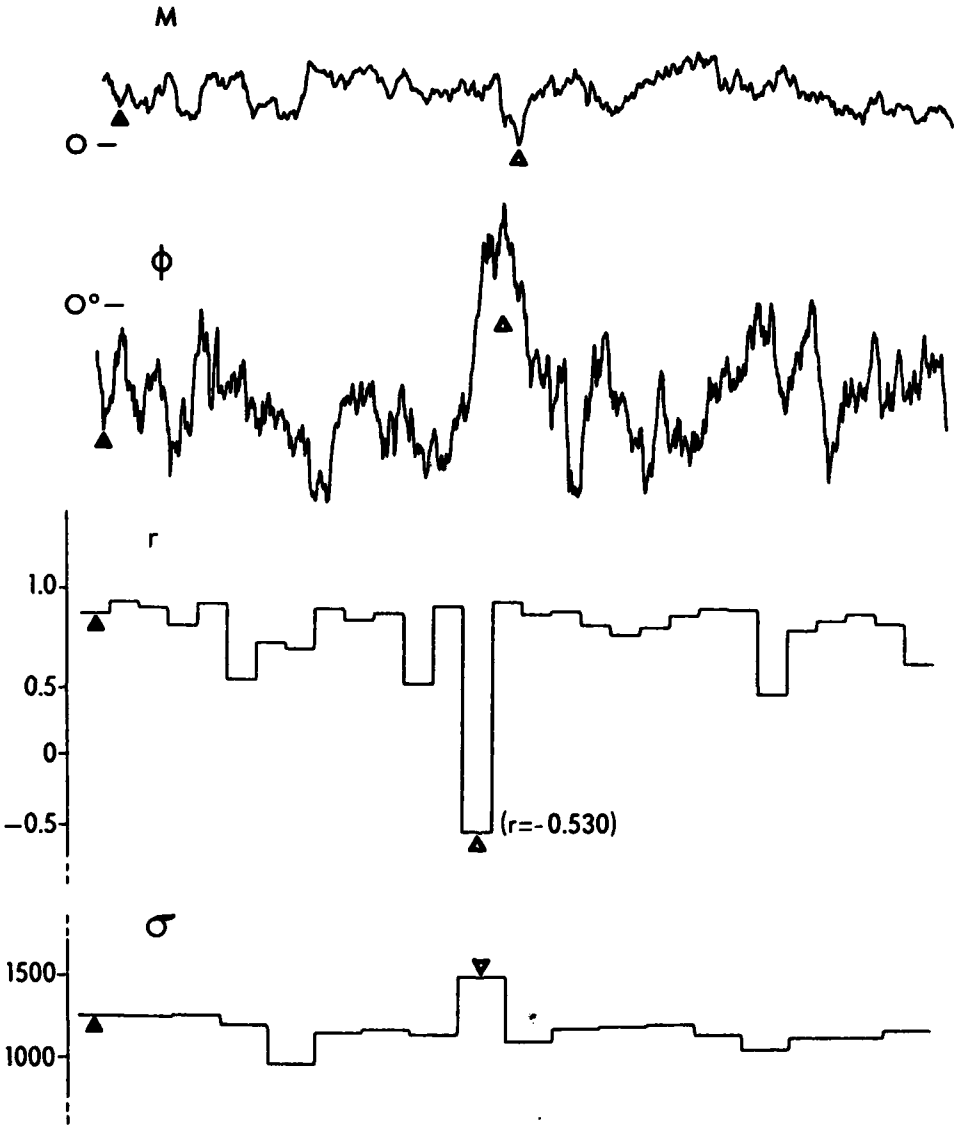

Fig.3. Analysis of animal D3 VEP. Magnitude (M), phase (phi), Pearson correlation coefficient (r) and average standard deviation (sigma) are shown. Dark triangles indicate laser exposure; light triangles indicate response. Total time of trace is 204 sec. See text for description.

Second, Zwick et al (6) showed data in which retinal lesions were produced by flashes resulting in visual acuity loss for considerable periods of time. Their immediate post exposure measures were the average of the first 2-3 min post flash acuity data and thus do not reflect the nearer term continuous monitoring of the retino-cortical response system. The perturbation reported in this paper may thus reflect the neurologic beginning of the phenomenon which was observed as an acuity decrement.

Third, the short Q-switched pulse may not have been sufficiently long to produce a measurable flash response. In the earlier studies (5,6,8), longer (100 msec) single pulses were placed in the fovea. In another study (7) the Q-switched 20 nsec pulses were delivered in a 120 msec train at a rate of 10 to 20 Hz. While a VEP response to the flash itself may have been present, it may not have been of sufficient duration or persistence to be detected.

A fourth consideration is the effect of the wavelength of the flash upon the response. The Q-switched ruby laser pulse produces a 694.3 nm pulse which is near the spectral perceptual limit of the primate visual system. Randolph (15) has shown that flash blindness production was far inferior for a red (620 nm) source than for blue, green or white light flashes of equivalent energy. The studies previously cited used visible wavelength flashes closer to the peak of visual sensitivity. Thus the wavelength of the flash source may have contributed significantly to the lack of any immediate response.

Fifth, while the higher energy laser flashes at both the 50 and 500 μ spot sizes produced visible alteration at the exposure site, the changes observed may have been limited to the non-visual cell layer, the retinal pigment epithelium, with little accompanying effect upon vision as measured by the VEP.

While all of the aforementioned factors may have contributed to the finding of no immediate VEP response differences, the nature of the delayed response is such as to suggest a dual mechanism. Initially, edema develops at the site of the laser injury and extends laterally. The delayed effects noted in this study may reflect the disentrainment or desynchronization of the cortical response due to the mechanical displacement of the retina by edema. The subsequent recovery of the response indices may reflect the re-entrainment of the cortical elements due to recruitment among surviving retinal elements and may be independent of possible changes in visual acuity i.e. a non-visual phenomenon.

CONCLUSIONS

The 20 nsec Q-switched ruby laser exposures centered on the fovea produced no immediate changes in the grating visual evoked potential for

50 and 500 micron spot sizes at two energy levels even when visible changes occurred at these sites.

The findings may have been the result of the ruby laser wavelength, which was near the visual sensitivity limit of the eye, or of the single Q-switched pulse which may have occurred too quickly to produce an immediate and/or sustained change in the cortical response.

The observed delayed effects and subsequent apparent recovery of the VEP may reflect the development of edema at the laser exposure site resulting in the desynchronization of the response for a period of time. This is followed by apparent recovery which was interpreted as recruitment of the spared retinal elements with subsequent neural re-entrainment at the cortical level.

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In conducting the research described in this report, the investigation adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care, Insitute of Laboratory Animal Resources, National Research Council.

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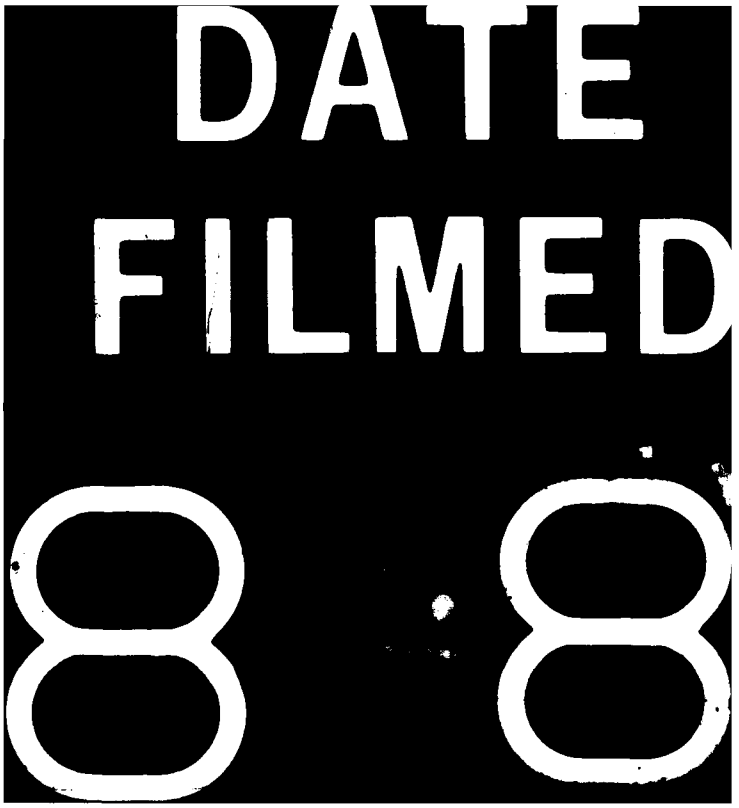
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