

## THE EFFECT OF OPHTHALMECTOMY UPON RESPONSES OF THE RAT TO RADIATION AND TASTE STIMULI<sup>1</sup>

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A nonlethal dose of ionizing radiation can serve as an unconditioned stimulus for rats to produce spatial avoidance of a distinctive radiation compartment (2), and to establish a conditioned aversion toward a normally preferred saccharin solution (4). It has been observed that X irradiation of the eye in dark-adapted humans produces a phosphene which has been described as a homogeneous, luminous glow completely covering the visual field (5, 9). Lipetz (8), in his recent review on the X-ray and radium phosphenes, cites earlier experiments which demonstrate that positively phototropic insects and crustaceans in a dark compartment move toward an area exposed to X rays. Blinded animals did not respond in a similar manner, and the conclusion was drawn that a sensation of light was produced which elicited the behavior.

Since visible light has been used to motivate rats in avoidance-conditioning experiments (7), it seems plausible that a visible stimulus could explain the avoidance behavior observed in rats following radiation exposure. The studies reported upon here were conducted with ophthalmectomized rats in order to test the hypothesis that a radiation phosphene, acting in a manner similar to a strong light, established the avoidance responses. The ophthalmectomy per se produced interesting effects upon the rat's response to taste stimuli, radiation exposure, and confinement which were reflected in the fluid-consumption scores.

### METHOD

Sprague-Dawley male rats bred in the colony at this laboratory were employed in this study. The animals were maintained in individual cages under constant illumination, and were 70 days of age at the time of the ophthalmectomy. Litters were represented proportionately in both operated and normal groups.

<sup>1</sup> The opinions or assertions contained herein are the private ones of the authors, and are not to be construed as reflecting the official views of the Defense Department. A short discussion of Experiment B was presented at the 1956 APA Convention.

The ophthalmectomy was performed on rats under ether anesthesia and the entire eye excised by severing the muscles and nerves posterior to the sclera. The normal animals were anesthetized as a sham treatment.

Experiment A was conducted to determine the consumption level for food, water, and saccharin solution following ophthalmectomy. Daily food and water consumption was measured for 35 days following the operation in both blind and normal animals. Following these measurements, saccharin consumption of both groups was measured in a series of 12, 4-hr. tests conducted on an irregular schedule. For this test, the home-cage water bottle was replaced by a bottle containing a solution of 1 gm. of saccharin per liter of water, and the consumption was measured over a 4-hr. period from 1000 to 1400 hr.

Experiment B was conducted to test the radiation-phosphene hypothesis. Six weeks after enucleation a group of ophthalmectomized animals was irradiated concurrently with a group of normal animals. For radiation exposure the animals were confined individually for 6 hr. (0900 to 1500 hr.) in Lucite chambers arranged at isodose distances around a cobalt-60 point source described in a previous paper (3). Total doses of 30 r. and 60 r., measured in air by Victoreen chambers, were administered simultaneously by placing the two groups of animals at different distances from the radiation source for the 6-hr. exposure period. The non-irradiated ophthalmectomized and normal controls were confined to Lucite chambers behind a lead shield which reduced the radiation to background-level in one quadrant of the field. The Lucite chambers were 7 $\frac{3}{4}$  by 4 $\frac{1}{3}$  by 3 $\frac{1}{8}$  in., and were equipped with a plastic water bottle which provided the saccharin solution to the animal during exposure.

In Experiment B, the test for saccharin preference consisted of measuring the saccharin-solution consumption from a single bottle in the home cage over a 6-hr. period between 0900 and 1500 hr. The animals were tested one day prior to irradiation and 2, 5, 8, and 13 days after irradiation.

Deprivation was not employed at any time during either experiment. The groups and numbers of animals used in both experiments are given in Table 1.

### RESULTS

The data from Experiment A indicate that ophthalmectomized animals tend to drink more water than normal rats (Fig. 1). Thirty-five days after the operation they were drinking approximately 20 per cent more than their littermate controls. There were no differences in food consumption between the two groups during this period.

The results of the 4-hr. saccharin-solution consumption tests which followed the 35 days of food- and water-intake measurements are illustrated in Figure 2. With repeated testing the saccharin consumption of blind animals is markedly increased, and in later tests the blind animals drank 50 per cent more of the saccharin solution than the normal animals consumed.

In Experiment B the ophthalmectomized animals drank significantly less ( $p < .01$ ) than their shielded controls during the period of radiation exposure (Fig. 3); this effect of radiation was not significant in the normal animals. Furthermore, sham-irradiation of the controls, which involved only confinement to the irradiation chamber, produced a decrement in the consumption level of the operated controls but had little or no effect upon the normal controls.

There was a marked decrement in saccharin consumption following irradiation of the ophthalmectomized rats. The operated animals which drank saccharin-flavored water

TABLE 1

Tabulation of Experimental Groups, Treatments, and Numbers of Animals for Both Experiments

Experiment	Radiation (r.)	Number of Animals ophthalmectomized	Normal
A	(none)	13	12
B	0	9	7
	30	10	7
	60	10	7

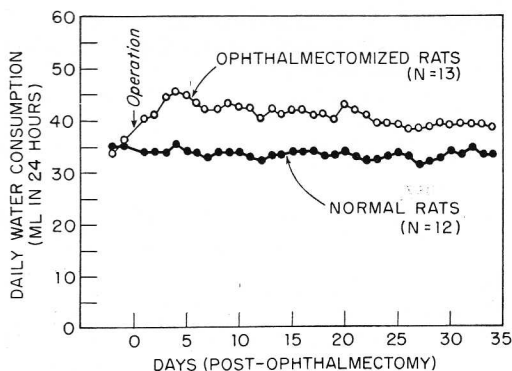


FIG. 1. Mean daily water consumption (24 hr.) of ophthalmectomized rats and littermate controls for 35 days following the operation (Experiment A).

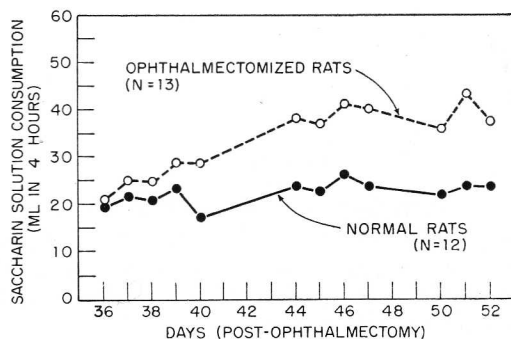


FIG. 2. Mean consumption of saccharin solution (4 hr.) of ophthalmectomized and normal rats obtained in a series of 12 tests conducted in the home cages, 36 days following the operation (Experiment A).

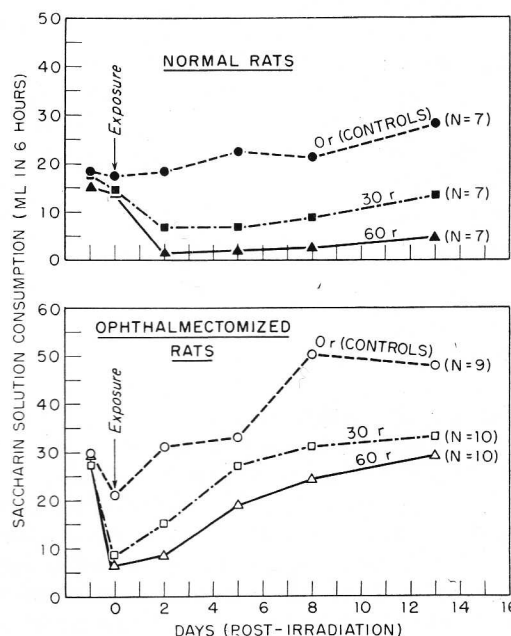


FIG. 3. Mean consumption of saccharin solution (6 hr.) of normal and ophthalmectomized rats during: (a) the preirradiation test in the home cage, (b) confinement to the irradiation chamber, (c) four postirradiation tests in the home cage.

during exposure to radiation showed a significant decrease ( $p < .01$ ) in consumption of the fluid during the first postirradiation test when compared with their sham-irradiated littermates (Fig. 3). The decrement in consumption was apparent in all the subsequent tests conducted in the home cages during the two weeks following exposure, although the ophthalmectomized animals progressively increased their consumption with repeated

testing, as was noted in Experiment A. The change in saccharin consumption following irradiation is also evident in the normal animals (Fig. 3).

#### DISCUSSION

Previous studies (1, 4) have demonstrated that decrement in consumption is dependent upon the association of radiation exposure and saccharin consumption in a conditioning paradigm rather than adipsia in animals suffering from radiation sickness. It is apparent from the present study that the avoidance conditioning is not established through action of radiation upon the retina. Although ophthalmectomized animals differ from normal rats in their pattern of responses, the effect of the single 6-hr. association of radiation and saccharin upon their consumption scores is no less obvious. An alternative hypothesis to account for the avoidance behavior has been discussed previously (1, 2); it was suggested that radiation exposure produced prompt effects in autonomic function with attendant gastrointestinal disturbances.

The blinded animals appeared to be more responsive to the influence of radiation during the actual exposure period while manifesting a milder aversion for the test fluid during the postirradiation period. This apparently greater extinction rate may be related to two factors: the reduced consumption during exposure, which made the conditioning less effective, and/or, perhaps more important, the reward value of saccharin may be higher for the operated animals. The progressive increase in saccharin intake by the blind animals with repeated tests indicated that they learned to drink large quantities of the solution during the limited periods of availability. Since this progressive change was small in the normal groups, it follows that saccharin is a greater incentive for the blind animals.

The increased ingestion of the nonnutritive saccharin solution is difficult to explain except in terms of compensation for the effect of the ophthalmectomy. One effect of this operation is obviously the reduction in the avenues of sensory stimulation. Hebb (6) has emphasized that organisms manifest an "exploratory curiosity-manipulatory drive, which essen-

tially comes down to a tendency to seek stimulation." In the home-cage tests, the operated rats in the present studies appear to seek more taste stimuli through drinking the saccharin-flavored water; however, *under the novel environmental conditions* of confinement and/or irradiation, they show a decrement in consumption of the fluid. If this hypothesis is true, then ophthalmectomized animals should demonstrate this stimulus-seeking behavior through other modalities. Some evidence for this view has already been obtained by Rhodes and Wyers (10), who recently reported that blind animals tended to show a higher manipulatory behavior with a clicker device placed in their home cage.

#### SUMMARY

Ophthalmectomized rats, as well as normal controls, were exposed to radiation and simultaneously drank saccharin-flavored water. Both blind and normal animals exhibited a subsequent decrement in consumption of the solution in postirradiation tests; therefore, the hypothesis that the avoidance behavior was established through the action of radiation upon the retina (radiation phosphene) was rejected. Blind animals progressively increased their intake of the saccharin solution with repeated testing in the home cage, and drank significantly more of the fluid compared with normal controls. It was suggested that this increased ingestion of the nonnutritive solution may be a compensatory reaction to the ophthalmectomy.

#### REFERENCES

1. GARCIA, J., & KIMELDORF, D. J. Temporal relationships within the conditioning of a saccharin aversion through radiation exposure. *J. comp. physiol. Psychol.*, 1957, **50**, 180-183.
2. GARCIA, J., KIMELDORF, D. J., & HUNT, E. L. Spatial avoidance behavior in the rat as a result of exposure to ionizing radiation. *Brit. J. Radiol.*, 1957, **30**, 318-321.
3. GARCIA, J., KIMELDORF, D. J., HUNT, E. L., & DAVIES, B. P. Food and water consumption during exposure to gamma radiation. *Radiation Res.*, 1956, **4**, 33-41.
4. GARCIA, J., KIMELDORF, D. J., & KOELLING, R. A. A conditioned aversion towards saccharin resulting from exposure to gamma radiation. *Science*, 1955, **122**, 157-158.
5. GODFREY, E. W., SHENK, H. P., & SILCOX, L. E.

- Response of the retina to the direct roentgen beam. *Radiology*, 1945, **44**, 229-236.
6. HEBB, D. O. Drives and the CNS (conceptual nervous system). *Psychol. Rev.*, 1955, **62**, 243-254.
  7. KELLER, F. S. Light-aversion in the white rat. *Psychol. Rec.*, 1941, **4**, 235-250.
  8. LIPETZ, L. E. The X-ray and radium phosphenes. *Brit. J. Ophthal.*, 1955, **39**, 577-597.
  9. NEWELL, R. R., & BORLEY, W. E. Roentgen measurement of visual acuity in cataractous eyes. *Radiology*, 1941, **37**, 54-61.
  10. RHODES, J. M., & WYERS, E. J. Effect of blindness on saccharin intake and manipulatory activity in rats. *Amer. Psychologist*, 1956, **11**, 445. (Abstract)

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