Pharmacology Biochemistry and Behavior, Vol. 1, pp. 477–481. ANKHO International Inc., 1973. Printed in the U.S.A.

Drug-Induced Conditioned Aversion to Mouse-Killing in Rats[1]

DONALD E. CLODY AND JOHN R. VOGEL[2]

The Squibb Institute for Medical Research, Princeton, New Jersey 08540

(Received 3 January 1973)

CLODY, D. E. AND J. R. VOGEL. *Drug-induced conditioned aversion to mouse-killing in rats.* PHARMAC. BIOCHEM. BEHAV. 1(4) 477–481, 1973.–Posttrial administration of atropine methylnitrate (MA) to rats that kill mice resulted in a marked inhibition of mouse-killing behavior. This conditioned aversion to mouse-killing after treatment with MA was more readily produced in rats fed ad lib than in those on a restricted food regimen. Food-deprived rats demonstrated a greater incidence of predatory behavior (i.e., consumption of the prey) than did killer rats not deprived of food. Predatory behavior appeared more sensitive to this conditioned aversion procedure than did the act of killing.

Mouse killing Predatory behavior Conditioned aversion Atropine methylnitrate

RATS injected intraperitoneally (IP) with an anticholinergic drug after they have ingested a novel and preferred substance (sweetened condensed milk) subsequently demonstrate a strong aversion to that substance [1,9]. Presumably, the aversive effects of the drug are classically conditioned to the taste and ingestive properties of the novel substance. For this conditioned aversion phenomenon, it has been demonstrated that any of several classes of taste stimuli can serve as the conditioned stimulus, and that administration of any one of many drugs or of X-irradiation can function as the aversive unconditioned stimulus [7].

Predatory behavior can also be modified by the conditioned aversion procedure. The bluejay, for example, will attack and consume the monarch butterfly. If the butterfly has recently fed on plants containing cardiac glycosides, however, consumption of several butterflies will produce prolonged emesis in the bluejay [2]. The bluejay subsequently demonstrates a clear aversion to attacking and consuming the monarch butterfly or similarly marked insects.

Some laboratory rats, given the opportunity, will spontaneously attack and kill a mouse [4]. The present experiments were designed to examine conditioned aversion to mouse-killing behavior.

EXPERIMENT 1

Method

Male albino Hotzman rats (110–140 g) were placed on a limited feeding regimen (8–10 g of food/day and water ad lib) for 4 days prior to being tested. In each test session, a mouse was left in the rats' home cage for 3 min. Twelve rats that spontaneously attacked and killed mice were used in Experiment 1.

All mice, alive or dead, were removed from the home cages at the end of each test, and the rats were then given IP injections of either saline (SAL), 1 mg/kg (six rats) or atropine methylnitrate (MA), 1 mg/kg (six rats). All rats were switched to ad lib feeding after the fifth test, and treatments (MA or SAL) were reversed after the ninth test-session.

Results

As shown in Fig. 1, mouse-killing behavior in food-deprived rats was not consistently affected by posttrial injections of MA. After introduction of the ad lib feeding conditions, the mouse-killing behavior by rats in the MA-SAL group decreased precipitously, reaching a minimum by the sixth session. Introduction of the ad lib feeding conditions, however, did not affect the killing behavior of the SAL-MA animals, and rats in this group killed significantly more mice than did those in the MA-SAL group in Session 6 through 9 ($p<0.05$; Fisher's Exact Probability Test).

Figure 1 also shows the effects of reversing the drug treatment (Sessions 10 through 26). Five of six rats in the SAL-MA group stopped killing after several posttrial injections of MA (Session 21). Even after 17 sessions of saline treatment, however, there was no substantial recovery (Session 26) of mouse-killing behavior in the MA-SAL group.

Mouse-killing by rats is ordinarily a very predictable and stereotyped behavior: the mouse is seized and bitten at the servical or upper thoracic region of the spine, resulting in severance of the spinal cord and death. In many instances, the prey is consumed. After a few pairings of the mouse and an injection of methylatropine, the rats demonstrated clear approach-avoidance behavior to the mouse, and appeared to show a decreased tendency to consume it after it had been killed.

[1] This paper was presented in part at a meeting of the Behavioral Pharmacology Society, Bryn Mawr, 1971.
[2] Now at William H. Rorer, Inc., Fort Washington, Pennsylvania.

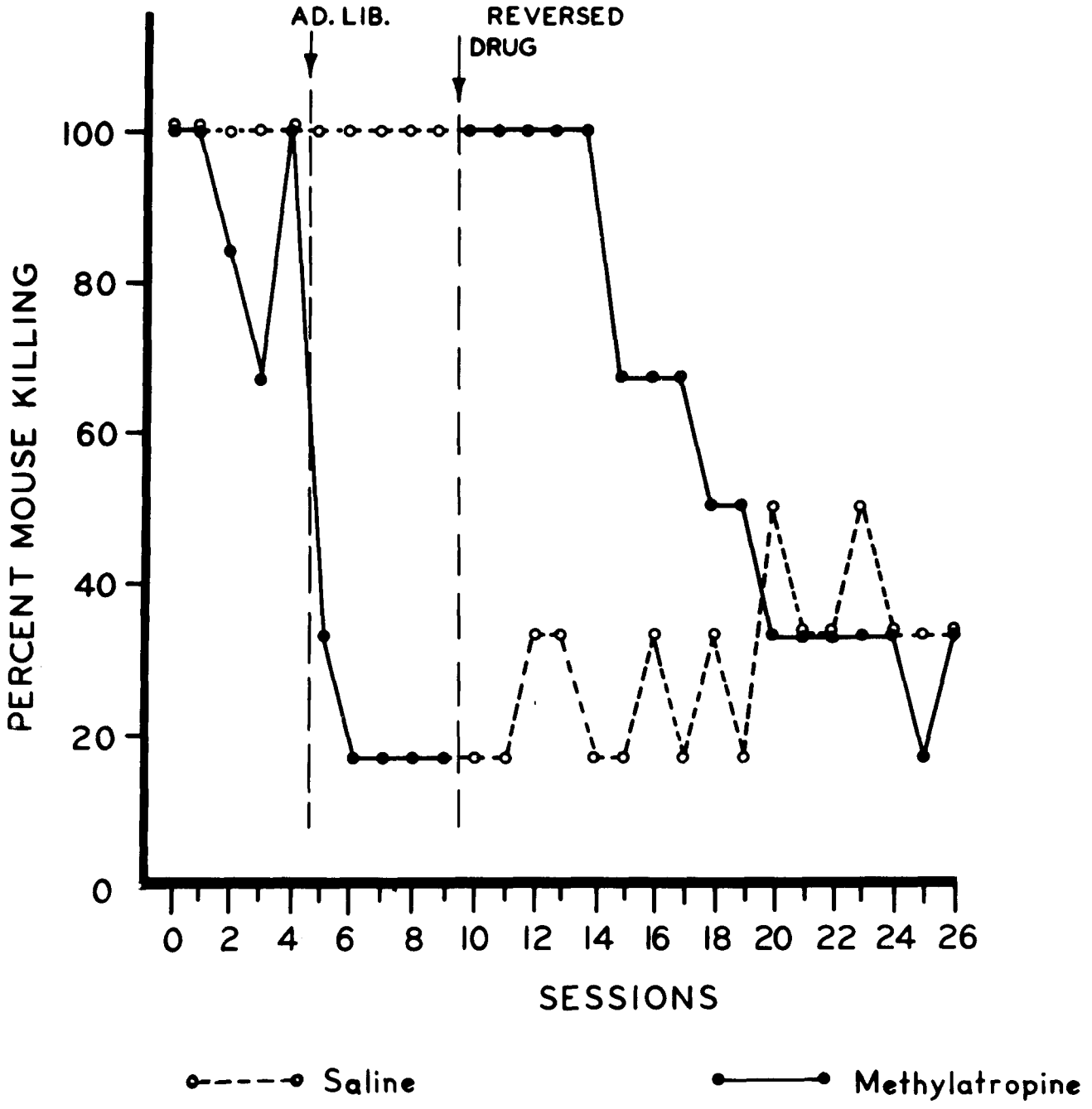

FIG. 1. The effects of posttrial injections of methylatropine (1 mg/kg) on the response of mouse-killing. All rats were placed on ad lib food and water prior to the fifth session; drug treatments were switched, beginning with Session 10.

EXPERIMENT 2

The results of Experiment 1 suggested that deprivation of food might interact with posttrial injections of MA in inhibiting mouse-killing behavior. It also appeared that treatment of killer rats with MA might lead, first, to an inhibition of consumption of the dead mouse and, later, to an inhibition of mouse-killing itself.

In Experiment 2, the effect of posttrial injections of MA on mouse-killing and on consumption of prey were studied in rats deprived of food and in others fed ad lib.

Method

Thirty male albino Holtzman rats (150–180 g) were placed on a limited feeding regimen (8–10 g of food/day and water ad lib) for 7 days prior to being tested. When the rats were tested for mouse-killing, 22 killed a mouse within 1 hr on each of two test days and within 5 min on the third test day. Following the third test, the rats were then injected intraperitoneally with either SAL or MA (see Experiment 1). Of these 22 animals, 10 were maintained on the food deprivation schedule and 12 were fed ad lib, starting

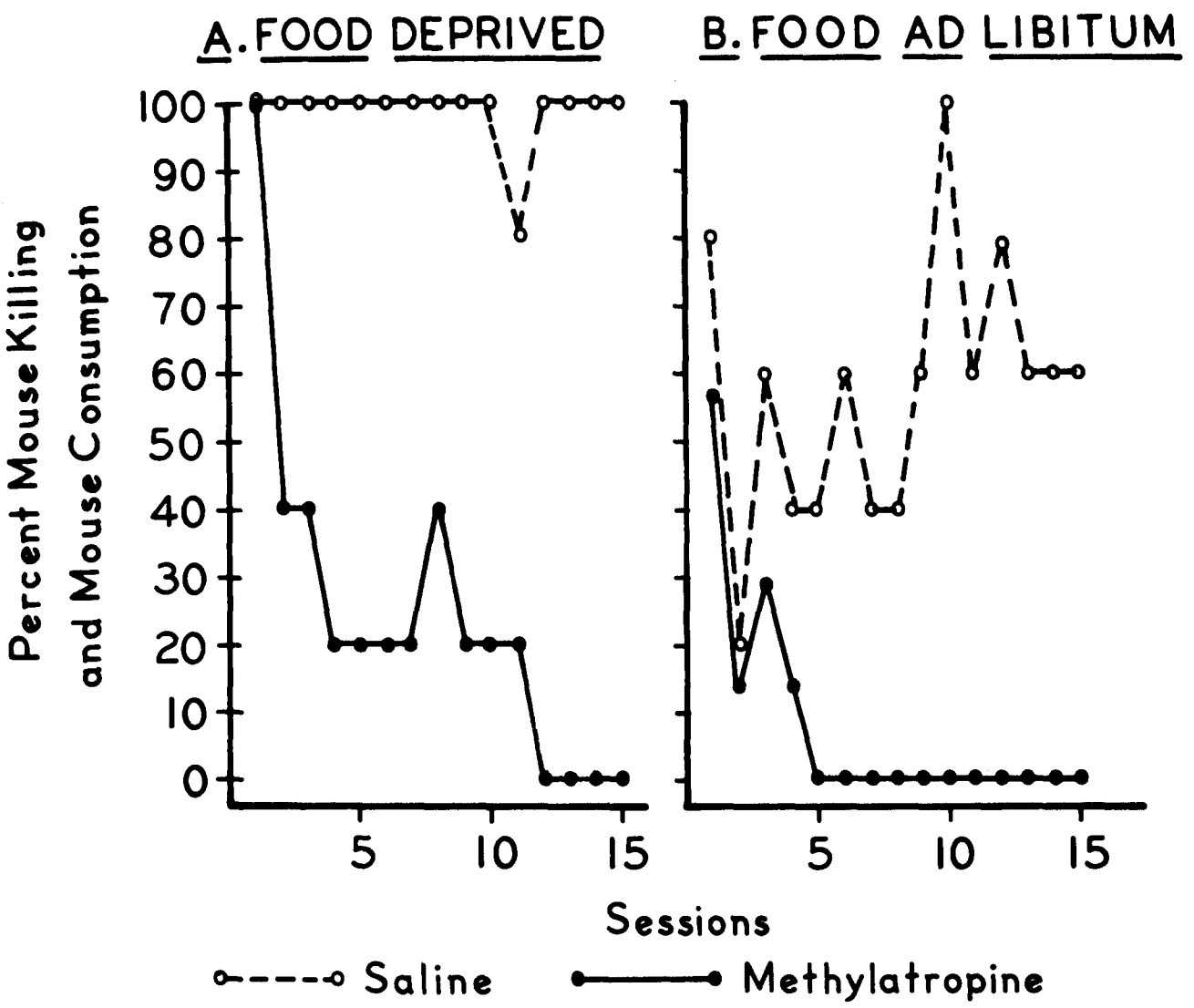

FIG. 2. The effects of posttrial administration of methylatropine (1 mg/kg) on mouse-killing by food deprived and nondeprived rats.

after the third test day. At least 1 day was allowed between sessions. In each test, a mouse was placed in the rat's home cage and the rat was allowed 5 min to kill it; and the latency to kill (in sec) was recorded. The dead mice were inspected for evidence of predation. Immediately after each test, the rats were given an injection of MA or SAL. There were five animals each in the MA-food-deprived and SAL-food-deprived group and in the SAL-food ad lib group. The MA-food ad lib group consisted of seven animals.

Results

Figure 2 illustrates the effects of posttrial injections of either methylatropine or saline on mouse-killing behavior in food-deprived and fed killer rats. After only four injections of MA ($p<0.05$), rats fed ad lib showed a significant reduction in mouse-killing as compared with control rats. Food-deprived rats did not demonstrate a significant decrease in mouse-killing until after 11 pairings of mice and MA.

Figure 3 shows the percentage of rats that killed and consumed mice. Posttrial administration of methylatropine to food-deprived animals significantly inhibited consumption of the prey ($p<0.05$) by the fourth trial, but there was no decrease in killing behavior at this time (cf., Fig. 2).

In rats fed ad lib, consumption of dead mice was highly variable, and no significant differences were observed until there was also a marked reduction in killing. Most of the rats killed mice within 20 sec. There were no consistent differences in latencies between groups except that the latencies for the SAL-food ad lib group tended to be longer (but not significantly) than those for the SAL-food deprived group.

DISCUSSION

Mouse-killing behavior by rats was inhibited by posttrial injections of methylatropine nitrate. One difference between this conditioned aversion procedure and others reported in the literature is that methylatropine does not produce overt malaise, as do apomorphine [3], cyclo-

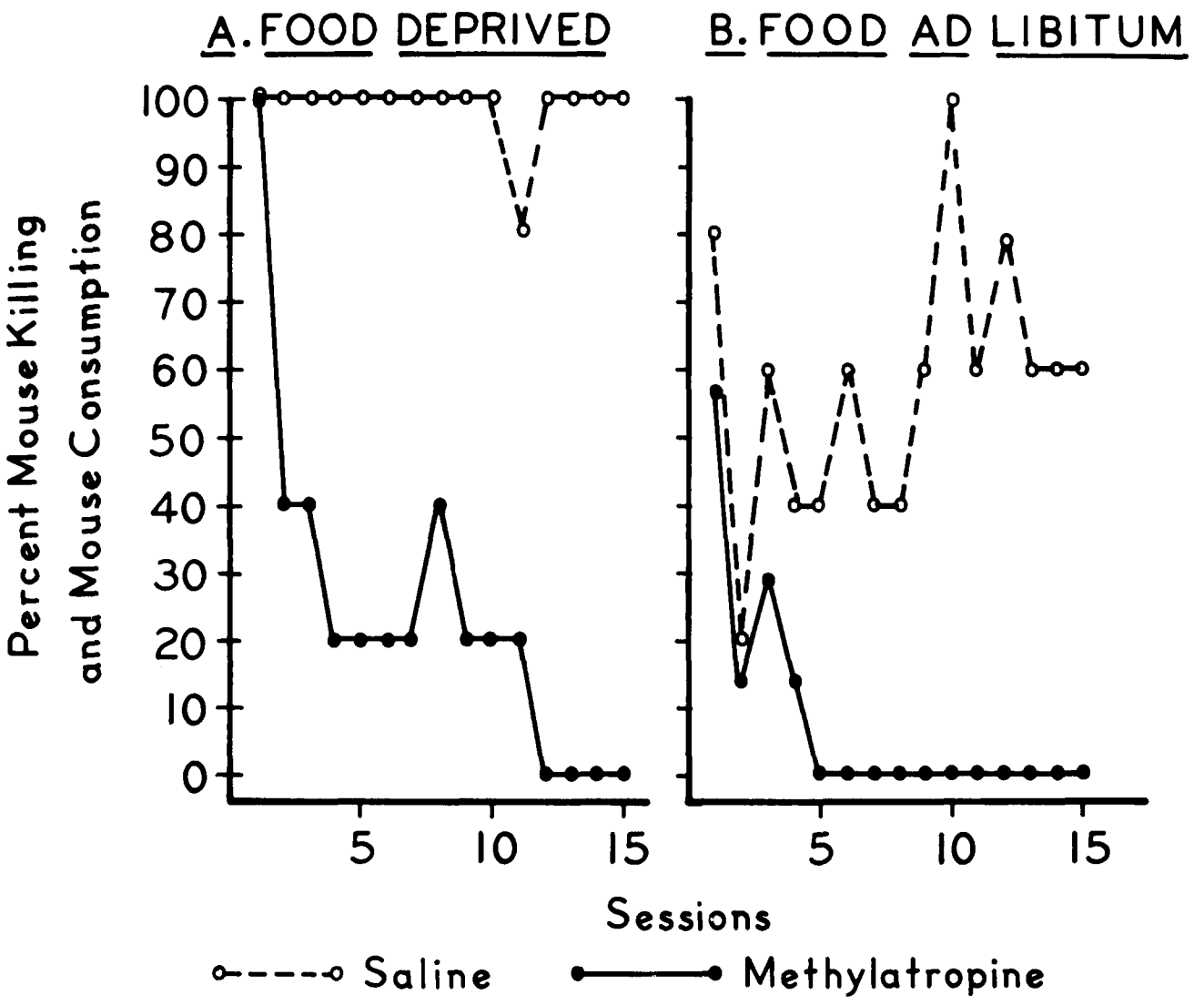

FIG. 3. The effects of posttrial administration of methylatropine (1 mg/kg) on the response of mouse-killing and consumption of the prey by food-deprived and nondeprived rats.

phosphamides [11] and X-irradiation [8].

The results also suggest something about the motivational components of mouse-killing. Paul *et al.* [6] demonstrated that depriving rats of food and water does not influence the maintenance of mouse-killing. Their finding, at first, appears to have been confirmed in the present study; saline-treated animals showed no changes in mouse-killing behavior as a result of deprivation. However, posttrial injections of MA immediately inhibited mouse-killing in nondeprived animals, but not in deprived animals. In this respect, at least, deprivation may be said to influence mouse-killing behavior.

When shock is administered to a killer rat for attacking a mouse, the attacking and killing behavior gradually declines, but is recovered within 24 hr after shock has been discontinued [5]. In other paradigms of aversive conditioning, in which footshock is associated with ingestion of a novel substance, subsequent tests for aversion demonstrate relatively weak effects, as compared with those observed when a drug is associated with the ingestion of that same substance [1]. The present studies have demonstrated that the act of mouse-killing can be attenuated and, in some cases, virtually eliminated, by association of it with a presumably aversive internal event produced by a drug. These effects are qualitatively similar to those reported with footshock [5], but the aversion to mouse-killing based on association with MA is much stronger, i.e., there is no substantial recovery of the behavior after the drug treatment has been discontinued.

An alternative explanation for these data is that MA has some proactive effect on subsequent tests for mouse-killing. It was demonstrated that this is not the case; pretest administration of methylatropine did not block the mouse-killing response [9].

The behavioral repertoire of mouse-killing that is observed in laboratory rats is apparently similar to other appetitive-consummatory behaviors, in that the act of mouse-killing was able to assume aversive qualities when

subjected to a conditioned aversion procedure. In the present studies, this aversive conditioning of mouse-killing followed an orderly pattern. The last member of the behavioral chain, the consummatory response, was suppressed before the attacking and killing responses were inhibited.

REFERENCES

1. Berger, B. D. Conditioning of food aversions by injections of psychoactive drugs. *J. comp. physiol. Psychol.* **81**: 21–26, 1972.
2. Brower, L. P. Ecological chemistry. *Sci. Amer.* **220**: 22–29, 1969.
3. Garcia, J., F. R. Ervin and R. A. Koelling. Learning with a prolonged delay of reinforcement. *Psychon. Sci.* **5**: 121–122, 1966.
4. Karli, P. The Norway rat's killing response to the white mouse: an experimental analysis. *Behaviour* **10**: 81–103, 1956.
5. Myer, J. S. and R. Baenninger. Some effects of punishment and stress on mouse-killing by rats. *J. comp. physiol. Psychol.* **62**: 292–297, 1966.
6. Paul, L., W. M. Miley and R. Baenninger. Mouse-killing by rats: role of hunger and thirst in its initiation and maintenance. *J. comp. physiol. Psychol.* **76**: 242–249, 1971.
7. Rozin, P. and J. W. Kalat. Specific hungers and poison avoidance as adaptive specializations of learning. *Psychol. Rev.* **78**: 459–486, 1971.
8. Smith, J. C. and D. L. Roll. Trace conditioning with X-rays as an aversive stimulus. *Psychon. Sci.* **9**: 11–12, 1967.
9. Vogel, J. R. and D. E. Clody. Habituation and conditioned food aversion. *Psychon. Sci.* **28**: 275–276, 1972.
10. Vogel, J. R. and R. C. Leaf. Initiation of mouse-killing in "non-killer" rats by repeated pilocarpine treatment. *Physiol. Behav.* **8**: 421–424, 1972.
11. Wilcoxin, H. C., W. B. Dragoin and P. A. Kral. Illness-induced aversion in rat and quail: relative salience of visual and gustatory cues. *Science* **171**: 826–828, 1972.