Induction of mouse-killing in nonkiller rats by temporary chemical lesions in the medial hypothalamus

D. J. ALBERT

University of British Columbia, Vancouver, British Columbia, Canada

Male rats which could not be induced to kill a mouse by 120 h of food deprivation had bilateral cannulas implanted into the medial hypothalamus. All rats were tested for muricide 7 to 10 days later while part of the medial hypothalamus was made nonfunctional by an intracranial infusion of the local anesthetic, lidocaine (2% soln; infusion rate: 1 μ l/3 min to each side to a maximum of 3 μ l bilaterally). Fifty percent of the animals were induced to kill by the infusion. In a group of unselected animals, a similar proportion of animals were induced to kill by the infusion. It is suggested that the induction of muricide by medial hypothalamic infusions is not limited to the facilitation of muricide in animals with a substantial predisposition to kill.

Electrolytic or reversible chemical lesions of the medial hypothalamus can induce muricide. However, with electrolytic lesions, the proportion of killers is only about 25% (Eclancher & Karli, 1971; Panksepp, 1971a). With temporary chemical lesions, the percentage of killers is higher, about 70%, if only animals with cannulas in the most effective zone of the medial hypothalamus are considered (Albert & Wong, 1978).

The tendency to kill mice can also be influenced by behavioral manipulations. This is shown most dramatically by food depriving rats that are not spontaneous killers. In rats deprived of food for 48 to 72 h, the number of rats that kill a mouse put into its living cage is about 50% (Paul, 1972; Paul, Miley, & Mazzagatti, 1973; Thor & Ghiselli, 1975a, 1975b; Whalen & Fehr, 1964).

The reason why a higher proportion of animals cannot be induced to kill, particularly with the lesion procedures, is of interest. One possibility is that medial hypothalamic lesions or food deprivation may induce mouse-killing only in those animals that have a high likelihood of killing. Those that have a low propensity to kill may not be induced to kill with a medial hypothalamic lesion or when food deprived.

The object of the experiment reported here was to explore the possibility that temporary lesions in the medial hypothalamus produce mouse killing only in those animals with a high propensity to kill. To examine this, we first used a food-deprivation pro-

cedure in order to remove rats that could be induced to kill mice by a rather stringent behavioral procedure. Rats that did not kill mice under these conditions were considered to have a low propensity to kill, and they had bilateral cannulas implanted into the medial hypothalamus. Following recovery from surgery, temporary lesions were created in the medial hypothalamus by infusion of a local anesthetic. The tendency of each rat to kill mice was then observed.

METHOD

Subjects

The animals were 36 male hooded rats, weighing 300-400 g at the beginning of the experiment. They were obtained from the Canadian Breeding Farms and Laboratories (St. Constant, Quebec, Canada) and were housed in group cages prior to the beginning of the experiment.

Assessment of Killing Behavior

Twenty-four rats were each placed in an individual cage for several days and then deprived of food. After 96 h of food deprivation, a white albino mouse was left in each cage for 24 h, with the rat still food deprived. Those animals which did not kill a mouse (12 out of 24 tested) were designated as nonkillers. They were then returned to group cages and allowed ad-lib feeding for 2 weeks before being subjected to surgery.

For comparison purposes, an unselected group of 12 rats was set aside and subjected to the surgical implantation and subsequent muricide tests.

Surgical Procedure

The cannulas and surgical implantation technique have been described in detail previously (Albert & Wong, 1978). Cannulas and injection needles were made from 23- and 30-ga stainless steel tubing. The location of the implants is shown in Figure 1.

Behavioral Testing

Behavioral testing was done between 7 and 14 days postoperatively in a test chamber measuring 60 $\times$ 60 $\times$ 60 cm. The floor

Supported by a grant from the National Research Council of Canada (A0192). Reprint requests: D. J. Albert, Psychology Department, University of British Columbia, Vancouver, British Columbia V6T 1W5, Canada.

was covered with wood shavings and sprinkled with food pellets. The room was illuminated by low-intensity fluorescent lighting. While the animal was in the test situation, each injection needle was continuously connected to a control syringe (50 μ l, Hamilton) by 1 m of polyethylene tubing (P.E. 50, Intramedic).

The rat was allowed to explore the test box for 5 to 10 min before testing began. Prior to any injections, each rat was tested for muricide by having an adult albino mouse placed next to it for about 30 sec. The use of a short exposure period for the muricide test was based upon previous results showing that the infusion induces very strong behavioral effects and that if muricide is induced by the injection it occurs very quickly (Albert & Wong, 1978).

After this behavioral baseline was established, the infusion of lidocaine (Xylocaine, 2%, Astra) began. The rat was infused with 1 μ l (to each hemisphere) every 5 min up to a total of 3 μ l (bilaterally). The infusion rate was 1 μ l/3 min and was controlled automatically by a modified Sage infusion pump (Model 341). Behavioral observations of muricide began approximately 1 min following each 1- μ l infusion. The infusion was stopped during the time behavioral testing was taking place to ensure that any mechanical action of the infusion process did not influence the behavioral results. Ten to 15 min following the entire infusion, muricide was examined again to confirm that it had disappeared as the effects of lidocaine dissipated.

Two or 3 days following the lidocaine infusion, all animals were again tested. The procedure was identical to that at the first test session, except that the animals were infused with .9% NaCl at the second session.

Following behavioral testing, the animals were killed with CO₂. Their brains were removed, placed in 10% formol-saline and later sectioned on a cryostat.

RESULTS

Rats that could not be induced to kill mice by starvation were induced to kill by infusion of the local anesthetic, lidocaine. Of the 12 animals designated as nonkillers by the starvation selection procedure, 6 were induced to kill by infusion of lidocaine into the medial hypothalamus. Of the 12 randomly selected animals, 6 were also induced to kill. None of the rats in either group killed at the preinfusion baseline assessment or at the final postinfusion test.

With saline infusions, muricide did not occur in any rats of either group. This is reliably less than the 50% frequency obtained with lidocaine ($\chi^2 = 8.0$, $p < .01$).

Additional Observations

Data on latency to kill were not gathered in the present experiment. Latency to kill is of limited value in this situation because the mouse and rat are both moving about freely over a rather large chamber. Most rats that would kill did so within a few seconds of orienting to the mouse. Each rat was allowed to kill only one mouse at each session because previous observations have shown that allowing repeated kills decreases the probability that the rat will stop killing at the postinjection test. Muricide was typically accomplished by a bite on the back, usually toward the neck.

Histology

The infusion sites were concentrated in the region

which we have previously found effective for producing muricide (Figure 1). This includes the tissue immediately adjacent to the fornix and the region between the fornix and the ventromedial nucleus.

DISCUSSION

Fifty percent of rats in which muricide was not elicited by 120 h of food deprivation were induced to kill mice by infusion of a local anesthetic into the medial hypothalamus. This result suggests that temporary chemical lesions in the medial hypothalamus can induce muricide in animals that otherwise have a very low predisposition to kill.

That killing did not occur in all animals with similar cannula implants is a perplexing problem. In view of the similar muricide rate in the nonkillers and unselected animals, it seems unlikely that the variability within groups is primarily due to interanimal differences in predisposition to kill. As an alternative, we tentatively infer that there may be considerable variation in the precise pattern of neural activity being influenced by the infusion. This variation may be the prime determinant of whether or not the activity of the system inhibiting aggression is affected strongly enough to induce muricide. A significant aspect of this variation may be the extent to which the immediately adjacent lateral hypothalamic area is affected by the infusion. There is evidence that parts of this area increase reactivity and aggression when activated (Panksepp, 1971b; Woodworth, 1971). We would infer that variations of size and extent also influence the frequency with which electrolytic lesions induce muricide (Eclancher & Karli, 1971; Panksepp, 1971a). An adequate test of this inference will require more control and analysis of lesion size and placement than has been accomplished previously (Eclancher & Karli, 1971; Panksepp, 1971a).

Figure 1. The location of injection sites in the hypothalamus. Squares represent placements in the nonkiller group; circles show the injection sites in the unselected group. In either case, filled figures are sites in animals where the infusion induced killing; empty figures are sites in animals in which killing was not induced. Brain sections are from Pellegrino and Cushman (1967).

In the present experiment, food pellets (Purina Lab Chow) were available on the floor of the testing box at the time the injections were made and notes were kept to indicate whether each rat was observed to eat any food pellets. Some eating was observed in 8 of the 24 animals during the lidocaine infusion. However, only 3 of the animals that ate also killed mice. In none of the animals was the eating continuous or sustained. This observation is consistent with the apparent anatomical overlap in the medial hypothalamus of sites concerned with feeding and muricide. The fact that the identical sites are not consistently associated with both behaviors is congruent with similar observations made using permanent lesions (Eclancher & Karli, 1971).

It should be noted, that the present experiment was not intended to delimit the region of the medial hypothalamus that is involved in the modulation of reactivity and aggression. This has been done previously (Albert & Wong, 1978). It has also been shown that injections into the ventricles do not induce increased reactivity or muricide (Albert & Richmond, 1976; Albert & Wong, 1978).

REFERENCES

- ALBERT, D. J., & RICHMOND, S. E. Hyperreactivity and aggression following infusion of local anesthetic into the lateral septum or adjacent areas. *Behavioral Biology*, 1976, **18**, 211-226.
- ALBERT, D. J., & WONG, R. C. K. Irritability, muricide, and intraspecific aggression in the rat produced by infusion of local anesthetic into the medial hypothalamus. *Physiology & Behavior*, 1978, **20**, 755-761.
- ECLANCHER, F., & KARLI, P. Comportement d'agression interspécifique et comportement alimentaire du rat: Effets de lésions des noyaux ventromédians de l'hypothalamus. *Brain Research*, 1971, **26**, 71-79.
- PANKSEPP, J. Effects of hypothalamic lesions on mouse-killing and shock-induced fighting in rats. *Physiology & Behavior*, 1971, **6**, 311-316. (a)
- PANKSEPP, J. Aggression elicited by stimulation of the hypothalamus in albino rats. *Physiology & Behavior*, 1971, **6**, 321-329. (b)
- PAUL, L. Predatory attack by rats: Its relationship to feeding and type of prey. *Journal of Comparative and Physiological Psychology*, 1972, **78**, 69-76.
- PAUL, L., MILEY, W. M., & MAZZAGATTI, N. Social facilitation and inhibition of hunger-induced killing by rats. *Journal of Comparative and Physiological Psychology*, 1973, **84**, 162-168.
- PELLEGRINO, L. J., & CUSHMAN, A. J. *A stereotaxic atlas of the rat brain*. New York: Appleton-Century-Crofts, 1967.
- THOR, D. H., & GHISELLI, W. B. Mouse-killing by devibrissae and facially anesthetized rats. *Psychological Reports*, 1975, **37**, 15-20. (a)
- THOR, D. H., & GHISELLI, W. B. Suppression of mouse-killing and apomorphine induced social aggression in rats by local anesthesia of the mystacial vibrissae. *Journal of Comparative and Physiological Psychology*, 1975, **88**, 40-46. (b)
- WHALEN, R. E., & FEHR, H. The development of the mouse-killing response in rats. *Psychonomic Science*, 1964, **1**, 77-78.
- WOODWORTH, C. H. Attack elicited in rats by electrical stimulation of the lateral hypothalamus. *Physiology & Behavior*, 1971, **6**, 345-353.

(Received for publication October 2, 1978;
revision accepted November 15, 1978.)