Behavioral correlates of chemical stimulation in the cat thalamus

DAVID D. AVERY, *Colorado State University, Fort Collins, Colo. 80521*, and
DWIGHT M. NANCE,¹ *University of Houston, Houston, Tex. 77004*

The effects of adrenergic and cholinergic stimulation and blockage in the cat thalamus on food and water intake and operant responding were investigated. A facilitatory effect on responding with adrenergic stimulation and cholinergic blockage was observed. Cholinergic stimulation and adrenergic blockage lead to a deficit in response rate. Food intake increased with injections of nonadrenaline, and water consumption decreased with carbachol applications. Additionally, central applications of atropine sulfate reduced food intake.

Alterations of food and water behavior following intracranial injections of adrenergic and cholinergic substances have been extensively observed and documented for various subcortical structures in one particular species, the rat. For example, cholinergic stimulation in the hypothalamus (Grossman, 1962), hippocampus (Coury, 1967), anterior thalamus (Fisher & Coury, 1962), amygdala (Grossman, 1964a), and lateral and medial septum (Grossman, 1964b) induced drinking. In a reciprocal fashion, adrenergic applications to these same loci generally elicited eating.

Attempts to reproduce these chemically coded consummatory behaviors in other species, particularly cats, have for the most part been restricted to the hypothalamus and have not been successful. Even so, intracranial injections in species other than the rat were not without behavioral effects. Several investigators (Myers, 1964; Yamaguchi et al, 1964; MacPhail & Miller, 1968) have reported that injections of carbachol into the hypothalamus of the cat resulted in an affective defense reaction. In addition, there is some evidence for the chemical coding of the sleep-arousal continuum in the cat brain stem (Hernández-Peón et al, 1963; Velluti & Hernández-Peón, 1963).

In those investigations involving chemical injections into extrahypothalamic structures in the cat there have been no reports of altered food and water behavior

(Myers, 1964; MacPhail & Miller, 1968; Hamilton et al, 1968; Connor et al, 1966; Baxter, 1969). The present experiment explored the relationship between adrenergic and cholinergic mechanisms in loci outside the hypothalamus and appetitive behavior in the cat.

METHOD

Each of 18 mature mongrel cats, weighing between 6 and 9 lb at the beginning of the experiment, was implanted unilaterally with a double-wall cannula directed at the center median nucleus of the thalamus. Each animal was individually housed in a stainless steel cage located in a constantly illuminated, temperature-controlled ($22.0 \pm 1.0^\circ\text{C}$) room. The cannula assembly was attached via polyethylene tubing to a Hamilton microsyringe for injections.

Adrenergic stimulation and blockage were provided by 1-arterenol bitartrate (noradrenaline) (40 microG/microL) and ethobutamoxane (13.5 microG/microL), respectively. Carbamylcholine chloride (carbachol) (8 microG/microL) was the cholinergic stimulating substance and atropine sulfate (50 microG/microL), the cholinergic blocking agent. Each substance was dissolved in Locke-Ringer solution and all injections were in 2 microL quantities. The dosage levels were arrived at empirically after observing aversive effects at higher levels and no behavioral effects at lower concentrations.

Each animal was placed on a 23-h food and water deprivation schedule 2 days prior to the initiation of training. Thereafter, each S received ad lib food and water in his home cage for the first 30 min following each daily experimental session. Using .3 cc of milk as a reward, Ss were shaped to an FR-5 bar-pressing schedule.

The number of responses during the 30-min FR-5 operant period and quantities of food and water consumed during the 30-min ad lib sessions were recorded daily. Before chemical stimulation procedures were initiated, stable operant performance, food intake, and water intake were maintained by each S for 3 consecutive days. Subsequent stimulation was begun with at least one control day occurring before each stimulation session. There was no stimulation until the previous day's operant and consummatory measures were comparable to those of the initial criterion sessions. On control days, the procedure for handling animals was exactly the same as on experimental days except that no substance was injected.

RESULTS

Histology

Histological evaluation indicated that all placements were within ± 1.0 mm in the anterior-posterior and lateral planes and ± 5 mm in the horizontal plane of the intended Horsley-Clark stereotaxic coordinates for the center median nucleus. In view of Myer's (1966) data on spread of liquids injected intracerebrally, it was concluded that the locus of stimulation included most of the central medial thalamus.

Response Rate

The matched pair signed-rank test was used to test for statistical significance. Figure 1 shows the effects of adrenergic and cholinergic stimulation and blockage on FR-5 bar-pressing behavior, displayed in terms of the mean increase or decrease in number of responses as compared with the pre-injection baseline session. Adrenergic stimulation resulted in increased ($p < .01$) responding, whereas adrenergic blockage tended to decrease ($p < .10$) the number of responses. Conversely, injections of carbachol significantly decreased ($p < .01$) response rate and injections of atropine significantly raised ($p < .01$) the rate of responding.

Fig. 1. Mean increase or decrease in the number of responses from the pre-injection day for each injection condition.

Table 1
Mean Increase or Decrease, as Compared with Preinjection Measures, in Food Intake and Water Intake After Each Injection Condition

Chemical	Food (g)	Water (cc)
Noradrenaline (N = 10)	+11.73**	-15.50
Ethobutanol (N = 8)	-14.90	+1.6
Carbachol (N = 9)	-6.30	-21.40**
Atropine sulfate (N = 9)	-22.6*	-12.6

* $p < .05$

** $p < .01$

Food and Water Intake

The mean increases or decreases in food and water intake as compared with the pre-injection baseline day, are listed in Table 1 for each stimulation condition. Injections of noradrenaline produced increased food consumption ($p < .01$) without significantly affecting water intake. Carbachol significantly lowered ($p < .01$) water consumption without altering food intake. A significant decrease ($p < .05$) in food intake was observed with injections of atropine sulfate, whereas ethobutanol had no reliable effect on consummatory behavior.

DISCUSSION

The observed stimulation effects on simple operant responding are consistent with the notion of overlapping neural pathways, each selectively sensitive to different modes of neurohumoral action. Both cholinergic stimulation and adrenergic blockage resulted in a decreased rate of responding. Reciprocally, adrenergic stimulation and cholinergic blockage lead to an increase in response rate. Similar reciprocally inhibitory relationships have been observed in the rat. Increased locomotor activity was observed with cholinergic stimulation and adrenergic blockage of the midbrain reticular formation, whereas adrenergic stimulation and cholinergic blockage reduced locomotor activity (Grossman, 1968).

In view of the results in the present experiment regarding the effects of chemical stimulation and blockage on food and water intake, it would appear that, contrary to the rat, a reciprocal inhibitory relationship between adrenergic and

cholinergic systems regulating consummatory behavior may not be present in the cat. Injections of noradrenaline was found to increase food intake reliably, whereas carbachol was shown to reduce water consumption. However, applications of atropine sulfate significantly reduced food consumption without affecting water intake, while ethobutanol had no significant effect on food and water behavior. It is possible that selective alterations in behavior may be more dependent upon the particular concentration of drug injected. Possibly, changes in simple operant behavior as a result of stimulation represent a more general facilitation or inhibition of ongoing behavior and are less dose-related than is the case with specific consummatory responses. Thus, until specific dose-response curves are derived for the cat regarding consummatory, as well as performance variables, it is difficult to come to any definite conclusions about chemical coding of behavior in the cat.

REFERENCES

- BAXTER, B. L. Induction of both emotional behavior and a novel form of REM sleep by chemical stimulation applied to cat mesencephalon. *Experimental Neurology*, 1969, 23, 220-229.
- CONNOR, J. D., ROSSI, G. V., & BAKER, W. W. Analysis of the tremor induced by injection of cholinergic agents into the caudate nucleus. *International Journal of Neuropharmacology*, 1966, 5, 207-216.

- COURY, J. N. Neural correlates of food and water intake in the rat. *Science*, 1967, 156, 1763-1765.
- FISHER, A. A., & COURY, J. N. Cholinergic tracing of a central neural circuit underlying the thirst drive. *Science*, 1962, 138, 691-693.
- GROSSMAN, S. P. Direct adrenergic and cholinergic stimulation of hypothalamic mechanisms. *American Journal of Physiology*, 1962, 202, 872-882.
- GROSSMAN, S. P. Behavioral effects of chemical stimulation of the ventral amygdala. *Journal of Comparative & Physiological Psychology*, 1964a, 57, 29-36.
- GROSSMAN, S. P. Effects of chemical stimulation of the septal area on motivation. *Journal of Comparative & Physiological Psychology*, 1964b, 58, 194-200.
- GROSSMAN, S. P. Behavioral and electroencephalographic effects of micro-injections of neurohumors into the midbrain reticular formation. *Physiology & Behavior*, 1968, 3, 777-786.
- HAMILTON, L. W., McCLEARY, R. A., & GROSSMAN, S. P. Behavioral effects of cholinergic septal blockade in the cat. *Journal of Comparative & Physiological Psychology*, 1968, 66, 563-568.
- HERNÁNDEZ-PEÓN, R., CHAVEZ-IBARRA, G., MORGANE, P. J., & TIMO-IARRA, C. Limbic cholinergic pathways involved in sleep and emotional behavior. *Experimental Neurology*, 1963, 8, 93-111.
- MacPHAIL, E. M., & MILLER, N. E. Cholinergic brain stimulation in cats: Failure to obtain sleep. *Journal of Comparative & Physiological Psychology*, 1968, 65, 499-503.
- MYERS, R. D. Emotional and autonomic responses following hypothalamic chemical stimulation. *Canadian Journal of Psychology*, 1964, 18, 6-14.
- MYERS, R. D. Injection of solutions into cerebral tissue: Relation between volume and diffusion. *Physiology & Behavior*, 1966, 1, 171-174.
- VELLUTI, R., & HERNÁNDEZ-PEÓN, R. Atropine blockage within a cholinergic hypnogenic circuit. *Experimental Neurology*, 1963, 8, 20-29.
- YAMAGUCHI, N., LING, G. M., & MARCZYNSKI, T. J. The effects of chemical stimulation of the preoptic region, nucleus centralis medialis, or brain stem reticular formation with regard to sleep and wakefulness. In J. Wortis (Ed.), *Recent advances in biological psychiatry*. Vol. 16. New York: Plenum Press, 1964. Pp. 9-20.

NOTE

1. Now a postdoctoral fellow in the Neuropsychology Laboratory, Department of Psychology, University of Houston, Houston, Tex. 77004.