Effects of hypothalamic and amygdaloid chemical stimulation on appetitive behavior in the cat

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Sixteen adult cats were chronically implanted unilaterally with cannulae in the preoptic and anterior hypothalamus and basolateral amygdala. Adrenergic and cholinergic drug stimulation with norepinephrine and carbachol, respectively, produced significant dose-dependent blockage of both food and water intakes. These data contrast with other studies which have reported that the cat does not show changes in patterns of feeding and drinking following hypothalamic and limbic chemical stimulation.

Adrenergic and cholinergic drug stimulation of various diencephalic and limbic structures have produced chemically coded ingestive responses in the rat (Grossman, 1962, 1964a, b; Fisher & Coury, 1962; Miller et al, 1964; Coury, 1967; Hutchinson & Renfrew, 1967). Typically, injections of adrenergic substances induce feeding, while applications of cholinergic substances at the same anatomical loci elicit drinking. Although efforts to reproduce chemically coded appetitive responses in other species have not been successful, chemical stimulation has evoked changes in patterns of feeding and drinking behavior following injections at hypothalamic sites in the rabbit (Sommer et al, 1967), at various diencephalic sites in the monkey (Myers & Sharpe, 1968; Sharpe, 1969), and at thalamic sites in the cat (Avery & Nance, 1970). Chemical stimulation of hypothalamic and limbic sites in the cat, however, has never been reported to produce changes in feeding and drinking

behavior (Hernandez-Peón et al, 1963; Myers, 1964; Connor et al, 1966; Macphail & Miller, 1968; Hamilton et al, 1968; Baxter, 1969). Instead, various autonomic and emotional reactions, which are drug specific and lack localization to any single brain site, have been observed.

The failure to find changes in feeding and drinking behavior following chemical stimulation of hypothalamic and limbic sites in the cat is unique among all mammals thus far tested. Since the relationship between neural chemical mechanisms and behaviors can be affected by a number of factors, such as the drug, drug dosage, and brain loci employed, the present experiment was designed to explore further the effects of hypothalamic and limbic chemical stimulation on ingestive behavior in the cat.

METHOD

Sixteen adult male and female mongrel and Siamese cats, which had an initial mean body weight of 3.1 ± 0.6 kg, served as experimental Ss. Lightweight double-walled stainless steel cannulae were chronically implanted unilaterally in the preoptic and anterior hypothalamus and in the basolateral amygdala by means of a Johnson stereotaxic instrument.

Stereotaxic coordinates were: preoptic hypothalamus (right hemisphere), 16.0 mm A-P, 2.0 mm L, -2.0 mm H; anterior hypothalamus (left hemisphere), 14.0 mm A-P, 3.0 mm L, -2.0 mm H; basolateral amygdala (right hemisphere), 11.0 mm A-P, 10.0 mm L, -5.0 mm H. After recovery from surgery, each animal was individually housed and tested in a stainless steel cage which measured 77 x 45 x 61 cm. All chemical injections were made using a Hamilton 100-microliter syringe and a vernier calibrated micrometer manipulator.

Adrenergic and cholinergic stimulation was produced by injections (2 μ l) of l-Arterenol bitartrate (norepinephrine) and Carbamylcholine chloride (carbachol), respectively. Drug doses in normal saline (0.9% sodium chloride) on a weight/volume basis were as follows: 20, 40, and 80 μ g/ μ l norepinephrine; and .05, .25, and .50 μ g/ μ l carbachol. Isotonic saline injections were employed as a control.

Brain areas and test chemicals were chosen randomly, with the restriction that no replication occur, and each injection was separated from the next by at least 48 h. On test days, food and water intakes were recorded for a 1-h preinjection baseline period and for a 1-h postinjection test period. Throughout the study, all animals were provided with Purina dry cat food and water ad lib. At the conclusion of the experiment, surviving animals were perfused and cannulae placements were histologically verified. Only data from cannula placements which were within ± 1.0 mm in the lateral, anterior-posterior, and horizontal planes of the intended Jasper & Ajmone-Marsan (1954) coordinates were included in the results.

RESULTS

Table 1 shows that direct intracranial adrenergic and cholinergic chemical stimulation of the preoptic and anterior hypothalamus and basolateral amygdala can elicit drug and dose-dependent blockage of ingestive behavior in the cat. Norepinephrine was the most potent drug in producing inhibition of feeding and drinking behavior.

Table 1
Percentage Change from Baseline in Food and Water Intakes Following Hypothalamic and Amygdaloid Drug Injections (2 μ L)

Brain Area		Saline	Norepinephrine			Carbachol		
			20 μ G/ μ L	40 μ G/ μ L	80 μ G/ μ L	.05 μ G/ μ L	.25 μ G/ μ L	.50 μ G/ μ L
Preoptic Hypothalamus	Food	-10 (16)	-18 (12)	-60 (7)**	-92 (7)**	+78 (9)	+8 (9)	-89 (7)**
	Water	+13 (16)	-45 (12)	-89 (7)**	-92 (7)**	-21 (9)	-29 (9)	-51 (7)
Anterior Hypothalamus	Food	+12 (15)	+84 (11)	+34 (8)	-91 (8)**	-49 (8)	-87 (7)*	-87 (9)*
	Water	-30 (15)	-47 (11)	-17 (8)	-89 (8)*	+1 (8)	-72 (7)**	-48 (9)
Basolateral Amygdala	Food	+41 (16)	+33 (8)	-70 (8)*	-72 (8)*	-33 (9)	-66 (9)*	-37 (9)
	Water	+46 (16)	-11 (8)	-36 (8)	-79 (8)**	+40 (9)	-15 (9)	+55 (9)

Note—Numbers in parentheses denote sample size. *Significant at the .05 level; **significant at the .01 level.

The Wilcoxon matched-pairs signed-ranks test (Siegel, 1956) was employed to evaluate statistical significance. Significant blockage of both food and water intake was observed at all brain sites following injections of the highest test concentration (80 $\mu\text{g}/\mu\text{l}$) of norepinephrine. At this concentration, many Ss showed no measurable food or water intake. Blockage of both feeding and drinking was also observed after injections of 40 $\mu\text{g}/\mu\text{l}$ of norepinephrine in the preoptic area. While a marked increase in food intake was observed following injections of the lowest test concentration (20 $\mu\text{g}/\mu\text{l}$) of norepinephrine in the anterior hypothalamus, the increase was found to be insignificant. Injections of carbachol, at the highest test concentration (50 $\mu\text{g}/\mu\text{l}$), were also effective in producing significant inhibition of feeding at both sites in the hypothalamus. In contrast, significant blockage of drinking occurred only after injections of .25 $\mu\text{g}/\mu\text{l}$ of carbachol in the basolateral amygdala.

DISCUSSION

The present data indicate that intracranial adrenergic and cholinergic chemical stimulation can produce depression of both feeding and drinking behavior in the cat. Injections of norepinephrine and carbachol elicit dose-response curves which generally show a decrease in ingestion as test dosage increases. Similar ingestive depression effects following injections of carbachol, but not norepinephrine, have been observed in the monkey (Sharpe, 1969). Further, it appears that the cat, unlike the rat, does not have adrenergic and cholinergic chemically coded neural systems which facilitate feeding and drinking, respectively; however, the data remain inconclusive. The nonsignificant, but facilitating, trend effects observed in some brain loci following injections of the lowest test concentration of both drugs suggest the need for additional dose-response information.

The observed appetitive depression effects contrast with results from other investigations which report that hypothalamic and limbic chemical stimulation produces no changes in ingestive behavior in the cat. It is suggested that the different findings may be due, in part, to variation in experimental procedures, such as employment of different drugs, drug concentrations, and brain loci. Further, it is possible that in similar chemical-stimulation cat studies reported in the literature, the authors were anticipating facilitation of ingestive behavior, not blockage; and, in most instances, the authors were studying other behaviors, such as sleep

and emotionality, and, subsequently, may have overlooked ingestive depression effects.

With respect to the nature of the drug's inhibitory effects on feeding and drinking behavior, at least two explanations are possible. Either test drugs acted specifically on satiation or they evoked other reactions (e.g., autonomic and emotional) which were antagonistic to ingestive behavior.

REFERENCES

- EVERY, D. D., & NANCE, D. M. Behavioral correlates of chemical stimulation in the cat thalamus. *Psychonomic Science*, 1970, 19, 7-8.
- 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. C., 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. E., & 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.
- 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.
- HERNANDEZ-PEON, R., CHAVEZ-IBARRA, G., MORGANE, P. J., & TIMO-IARIA, C. Limbic cholinergic pathways involved in sleep and emotional behavior. *Experimental Neurology*, 1963, 8, 93-111.
- HUTCHINSON, R. R., & RENFREW, J. W. Modification of eating and drinking: Interactions between chemical agent, deprivation state and site of stimulation. *Journal of Comparative & Physiological Psychology*, 1967, 63, 408-416.
- JASPER, H., & AJMONE-MARSAN, C. A stereotaxic atlas of the diencephalon of the cat. Ottawa: National Research Council of Canada, 1954.
- MacPHAIL, E. M., & MILLER, N. E. Cholinergic brain stimulation in cats: Failure to obtain sleep. *Journal of Comparative & Physiological Psychology*, 1968, 65, 499-503.
- MILLER, N. E., GOTTESMAN, K. S., & BERRY, N. Dose response to carbachol and norepinephrine in the rat hypothalamus. *American Journal of Physiology*, 1964, 206, 1384-1388.
- MYERS, R. D. Emotional and autonomic responses following hypothalamic chemical stimulation. *Canadian Journal of Psychology*, 1964, 18, 6-14.
- MYERS, R. D., & SHARPE, L. G. Chemical activation of ingestive and other hypothalamic regulatory mechanisms. *Physiology & Behavior*, 1968, 3, 987-995.
- SHARPE, L. G. Chemical stimulation of the diencephalon of the rhesus monkey (*Macaca mulatta*). Unpublished PhD thesis, Purdue University, 1969.
- SIEGEL, S. *Nonparametric statistics for the behavioral sciences*. New York: McGraw-Hill, 1956.
- SOMMER, S. R., NOVIN, D., & LEVINE, M. Food and water intake after intrahypothalamic injections of carbachol in the rabbit. *Science*, 1967, 156, 983-984.

Hypothalamic anticholinergic inhibition of eating and drinking in the cat

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Preoptic and anterior hypothalamic injections of three concentrations of atropine sulfate in the cat resulted in a dose-related decrease in food and water intake. Water intake was more effectively inhibited by atropine than was food intake, which was suppressed only at the highest concentration employed. Results were interpreted as being consistent with behavioral effects of hypothalamic lesions and somewhat less related to "chemically coded" behaviors in the cat.

Drinking has been elicited in water-sated rats following cholinergic injections in the hypothalamus (Grossman, 1962; Fisher & Coury, 1962). In contrast, intrahypothalamic injections of cholinergic drugs have resulted in autonomic and emotional

reactions and inhibition of eating and drinking in monkeys (Myers & Sharpe, 1968; Sharpe, 1969) and in cats (Milner et al, 1970; Milner, 1970). Intrahypothalamic injections of anticholinergic drugs have been observed to inhibit drinking in the rat (Khavari, 1969; Block & Fisher, 1970), but comparable data has not been reported for the cat. Thus, the present investigation tested whether or

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