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Contributions of Dopamine Terminal Areas to Amphetamine-Induced Anorexia and Adipsia[1]

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CARR, G. D. AND N. M. WHITE. *Contributions of dopamine terminal areas to amphetamine-induced anorexia and adipsia.* PHARMACOL BIOCHEM BEHAV **25**(1) 17–22, 1986.—Systemic injections of amphetamine produce both anorexia and adipsia. Evidence suggests that it is the stimulation of activity by the drug in both noradrenergic and dopaminergic synapses that mediate these effects. The present study examined the contributions of dopamine terminal regions to these effects in rats by microinjecting amphetamine directly into one of six discrete sites (medial frontal cortex, nucleus accumbens, anteromedial caudate nucleus, ventrolateral caudate nucleus, amygdala, or the region surrounding the area postrema) and observing the effects of the injections on eating or drinking. The rats were mildly deprived of either food or water and following microinjection of either amphetamine or saline, were given access to food or water. Injections of amphetamine into either the nucleus accumbens or amygdala caused both anorexia and adipsia but no effects were observed from the other sites. It is suggested that amphetamine's action on these two sites contributes to the anorexia and adipsia that are observed after systemic injection of the drug. Possible behavioral mechanisms for the effects are discussed.

Amphetamine Anorexia Adipsia Dopamine Nucleus accumbens Amygdala Approach behavior

SOON after amphetamine was introduced into clinical practice, several articles appeared reporting that it had a powerful anorexic effect (e.g., [38]). Two decades later, Andersson and Larsson [3] reported that the drug also decreases drinking (adipsia). It was subsequently found that at very low doses, feeding and drinking could be stimulated by amphetamine [19,39]. In man, amphetamine produces both decreases in subjective ratings of hunger and decreases in food intake [35,36]. The pattern of reduced food intake in both man and rats includes an increase in the latency to begin eating and an increase in the rate of the eating that does occur [5,35].

A large body of evidence is accumulating to suggest that amphetamine's anorexic effect results from the drug's stimulation of activity in both dopaminergic and noradrenergic synapses (see [11,24] for reviews). Regarding noradrenaline, there are consistent findings that lesions of the noradrenergic system attenuate amphetamine-induced anorexia. Electrolytic lesions of the ventral noradrenergic bundle attenuate amphetamine anorexia as do more selective NE depletions using injections of the neurotoxin 6-hydroxydopamine (6-OHDA) into the vicinity of the bundle [1,2]. Radio frequency lesions of the brainstem noradrenergic cell bodies also attenuate amphetamine anorexia [7]. Leibowitz [29] has further demonstrated that amphetamine injections directly into the hypothalamus produce anorexia and that this can be blocked by including a beta-adrenergic blocker (propranolol) in the injection medium. Grossman [20] found that direct intra-hypothalamic injection of noradrenaline itself can stimulate feeding and that the effects could be blocked by a peripheral injection of an adrenergic blocker [21].

Dopamine also appears to be involved in amphetamine anorexia. A variety of dopaminergic antagonists has been used to attenuate amphetamine anorexia, including haloperidol, spiroperidol [22], flupenthixol and pimozide [6]. This is in contrast to the usual anorexic effects that dopaminergic blockers have on their own [37]. Heffner *et al.* [22] found that selective lesions of the dopamine system using 6-OHDA lesions (with NE protected by desipramine pretreatment) caused an attenuation of amphetamine's effects. Bilateral 6-OHDA lesions of the dopamine cell bodies in the substantia nigra also attenuate amphetamine anorexia [18]. Koob *et al.* [27] used 6-OHDA to produce a lesion which reduced dopamine levels in the nucleus accumbens, olfactory tubercle and frontal cortex (as well as NE in the frontal cortex) and found that this lesion did not affect the anorexia produced by amphetamine.

With regard to the amphetamine-induced adipsia, there

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do not appear to be any studies that have directly examined the contribution of dopamine and noradrenaline to the effect. In a review, Dourish [12] concludes that dopamine is not directly involved in the control of drinking. There are reports of both increased [14] and decreased [13,31] drinking produced by dopamine agonists. Dopamine antagonists have uniformly produced a decrease in drinking [12]. The lateral hypothalamus has been implicated in amphetamine adipsia by Leibowitz [28] who found adipsia following microinjection into the structure. However, there are two reports [8,18] that lesions of the lateral hypothalamus, while attenuating amphetamine anorexia, have no effect on amphetamine adipsia. The structure is therefore not critical for the effect. The site of action for amphetamine's adipsic effect remains unknown, although some insight may be gained from the observation that the adipsia is attenuated by a crude "prefrontal lobotomy" in dogs [3].

The present study examined the effects of microinjections of amphetamine into several dopamine terminal regions on eating and drinking. The animals were mildly food or water deprived so that their undrugged consumption was well below the consumption of a more severely deprived animal. This allowed for the possibility that the drug injections would either increase or decrease consumption. The main forebrain dopamine terminal areas were examined (medial frontal cortex, nucleus accumbens, anterolateral caudate nucleus, ventrolateral caudate nucleus, and the amygdala) (see [15–17] for reviews describing dopamine terminal areas). In addition to these sites, the drug was also injected into the region subjacent to the area postrema which includes the nucleus of the solitary tract and the dorsal motor nucleus of the vagus. Both dopaminergic and noradrenergic neurons are present in the region [26,30]. In a previous study [10] it was shown that amphetamine microinjections into this region resulted in a conditioned taste aversion, as reflected by decreased consumption of a flavoured solution that had been previously paired with the injection.

METHOD

Subjects

The subjects were male hooded rats (Charles River Canada) weighing 300–325 g at the time of surgery. They were housed individually in suspended metal cages in a room with lights on between 7 a.m. and 7 p.m. The subjects in this study had been used previously in a study [10] in which they had received microinjections of saline and/or amphetamine. The amounts of food consumed by drug naive vs. amphetamine-experienced rats following the amphetamine injections on the first test day were 3.0 vs. 3.3 g. Therefore, the prior injections of amphetamine did not appear to affect the action of the injections on consumption in the present study. The rats were usually tested for feeding first and following resatiation were tested for drinking.

Surgery

Stereotaxic surgery was performed to implant stainless steel guide cannulae (0.7 mm outer diameter; Plastic Products Co.). Surgery was performed under 60 mg/kg sodium pentobarbital anesthesia and the implanted cannulae were anchored to the skull using screws and dental cement. The cannulae were aimed at one of six sites in each animal. Coordinates (below) were modifications (based on experience) of the atlas of Pellegrino *et al.* [32] and measured from bregma (anterior-posterior and lateral) with the depth determined by lowering a pre-cut cannula until the plastic sleeve touched the skull. Each rat was implanted bilaterally except for those in the midline area postrema region group which received a single cannula. The brain sites, their abbreviations used here, and the stereotaxic coordinates are:

Medial frontal cortex (MFC). Anterior (A): 4.5, lateral (L): 0.7, rotated 20° laterally from the midline to avoid the superior saggital sinus and lowered to the depth of a 4 mm cannula.

Nucleus accumbens (Accumbens). A: 3.6, L: 1.5, rotated 20° laterally to avoid the ventricles, and lowered to the depth of an 8 mm cannula.

Anteromedial caudate nucleus (Medial Caudate). A: 3.4, L: 1.9, rotated 15° laterally to avoid the ventricles, and lowered to the depth of a 5.5 mm cannula.

Ventrolateral caudate nucleus (Lateral Caudate). A: 2.0, L: 4.0, and lowered to the depth of a 7 mm cannula.

Amygdaloid complex (aimed at the central nucleus) (Amygdala). A: 0.0, L: 4.0, lowered to the depth of an 8.5 mm cannula.

Area postrema/nucleus of the solitary tract region (AP Region) (aimed for the region just below the area postrema in the surrounding NST). 11.6 posterior to bregma, L: 0.0, and lowered to the depth of a 10 mm cannula, with the posterior edge of the sleeve 2 mm from the skull (note that this placement is 1 mm anterior to where the atlas of Pellegrino *et al.* [32] places the area postrema).

Following surgery, a screw-on wire stylet was inserted into the guide cannula. This stylet, and the internal cannulae used for the injections (0.4 mm outer diameter), were cut so as to extend 0.5 mm from the tip of the guide cannula. An exception to this was the area postrema region placement, which was previously found to be sensitive to mechanical stimulation. This was avoided here by cutting the stylet to be flush with the guide cannula and recessing the internal injection cannula by 0.5 mm. Following surgery, the rats were given one to three injections of penicillin (Derapen) and were given a minimum of one week to recover before the experiment was started.

Intracranial Injections

Injections were made via internal cannula which were connected to 5 μl Hamilton syringes by polyethylene tubing. For the bilateral injections, two syringes were attached together and two separate lengths of tubing connected them to the left and right internal cannulae. The injections were done simultaneously, infusing the fluid over a one minute period (50 seconds for injection plus 10 seconds for diffusion). Each injection consisted of 10 μg of d-amphetamine sulphate (Smith, Kline and French, Canada) dissolved in 0.5 μl of physiological saline solution, or the saline vehicle alone, injected bilaterally. For the one-cannula area postrema region injections, the 20 μg was dissolved in distilled water. The concentration of this solution is approximately iso-osmotic with serum and the saline control injections [33]. The AP region injections were done over one minute with thirty additional seconds of diffusion time to compensate for the recessed injection cannula.

At the end of the experiment, the animals were anesthetized with an overdose of chloral hydrate and perfused intracardially with physiological saline, followed by 10% formalin. Their brains were removed and frozen sections were cut at 100 micron intervals for histological examination.

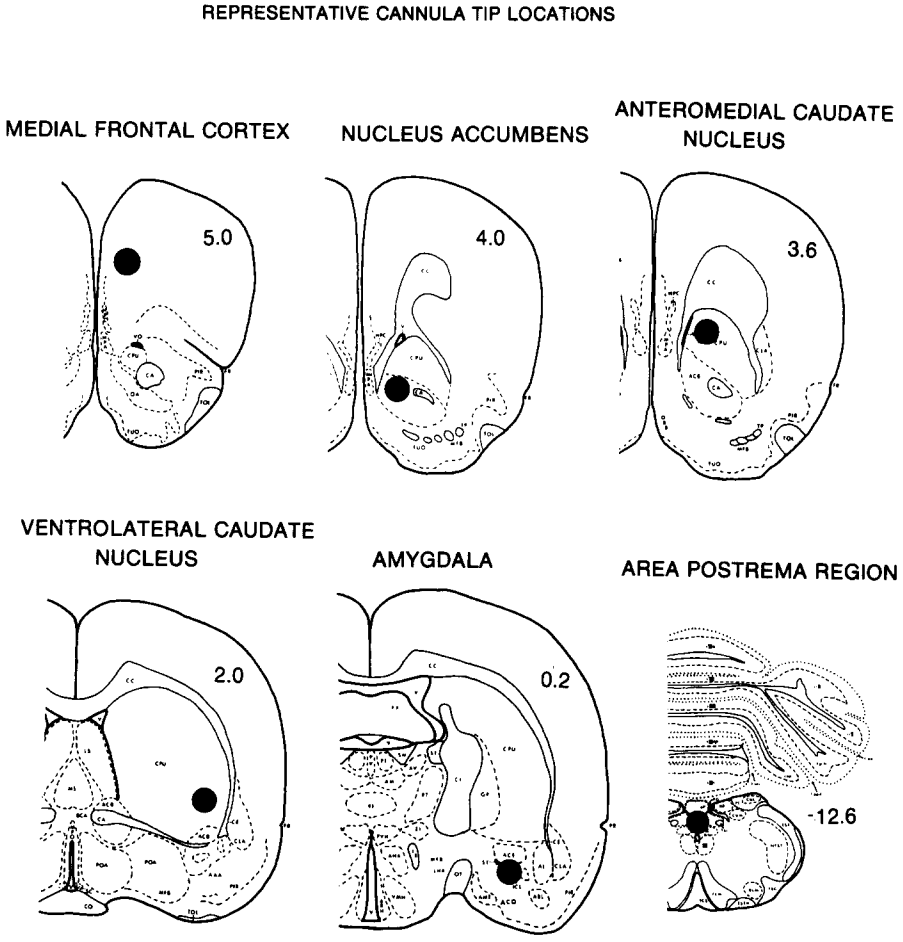

FIG. 1. Representative cannula tip locations for each of the six brain sites. The cross sections are from the atlas of Pellegrino *et al.* [32].

Procedures (Feeding)

The animals were given ad lib access to water but food, in the form of their standard rat chow pellets, was only available for restricted periods. For the first two days the subjects were given access to food pellets placed on the floors of their cages for one hour periods. The next day (Test No. 1) they were given 20 minutes of free access to food pellets on the floors of their cages in the morning. A minimum of three hours later, they were given microinjections of either amphetamine or saline (random assignment). Five minutes after the injections they were again given twenty minutes of free access to food pellets. Their consumption was measured by subtracting the weight of the food remaining at the end of the twenty minute period from the weight of the food initially placed into the cage and then subtracting the weight of the crumbs that had fallen through the cage and collected on blotter paper (method accurate to within 0.1 g in most cases). The next day (Test No. 2), the procedures of the first day were repeated except that the treatments were reversed so that Test No. 1 saline rats received amphetamine, and vice versa.

Procedures (Drinking)

Following the feeding experiment, the rats were resatiated with ad lib food and water for a minimum of two days, and water was then removed from their cages. For the next two days, the rats were given access to water for two 15 minute periods per day, a minimum of three hours apart. Water was presented at room temperature in drinking tubes with ball-bearing spouts. On the next day (Test No. 1), the subjects were given free access to water tubes for 15 minutes in the morning. A minimum of three hours later, they were given microinjections of either amphetamine or saline (random assignment). Five minutes after their injections they were again given 15 minutes of free access to the water and their consumption was recorded to the nearest 0.5 ml. The next day (Test No. 2), the procedure of the first test was repeated except that each rat's treatment (saline vs. amphetamine) was reversed.

RESULTS

The results of the histological examination are presented as representative placements for each brain site group in Fig. 1. For a detailed illustration of each individual cannula placement the reader is referred to Carr and White [10].

The results of the feeding experiment are presented in Fig. 2. A two-way analysis of variance with one repeated measure (treatment) showed significant effects of site,

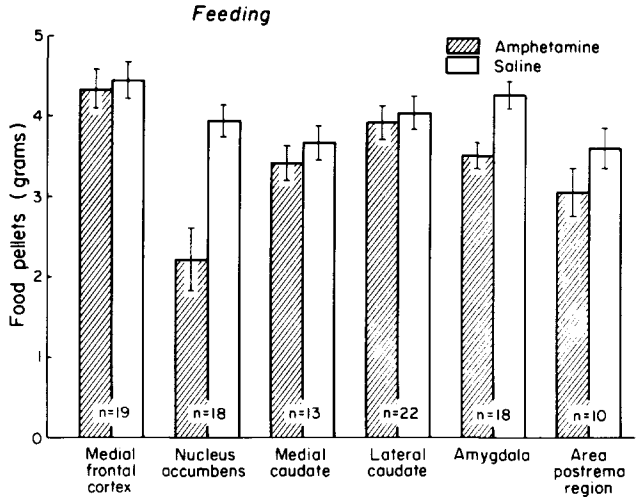

FIG. 2. Amount of food consumed during the test period by rats representing each brain site after receiving microinjection of either amphetamine or saline. Significant effects were obtained for the accumbens ($p<0.001$) and amygdala ($p<0.005$) groups. The vertical line on each bar represents the standard error of the mean.

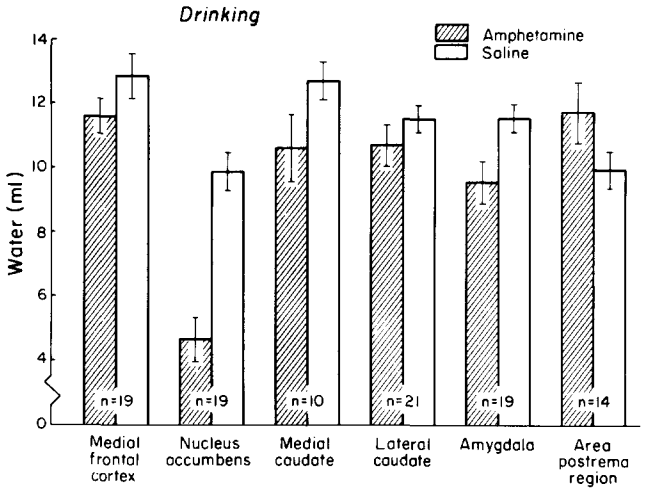

FIG. 3. Amount of water consumed during the test period by rats representing each brain site after receiving microinjection of either amphetamine or saline. Significant effects were obtained for the accumbens ($p<0.001$) and amygdala ($p<0.05$) groups. The vertical line on each bar represents the standard error of the mean.

$F(5,94)=5.03$, $p<0.001$, and treatment, $F(1,94)=26.73$, $p<0.001$), and a significant site × treatment interaction, $F(5,94)=5.07$, $p<0.001$. Simple main effects tests showed that the amphetamine-injected nucleus accumbens group ate significantly less than the saline-injected group ($p<0.001$). A significant reduction was also produced by the intra-amygdala amphetamine injections ($p<0.005$). No other treatment effects approaching significance were observed for any other site ($p>0.1$).

The results of the drinking experiment are presented in Fig. 3. A two-way analysis of variance with one repeated measure (treatment) showed significant effects of site, $F(5,96)=11.17$, $p<0.001$, and treatment, $F(1,96)=15.29$, $p<0.001$, and a significant site × treatment interaction, $F(5,96)=5.30$, $p<0.001$. The simple main effects tests showed that the amphetamine-injected nucleus accumbens group drank significantly less than the saline-injected group ($p<0.001$). A significant reduction of drinking was also produced by the intra-amygdala amphetamine injections ($p<0.05$). No significant treatment effects were obtained from any other group ($p>0.05$).

DISCUSSION

Microinjections of amphetamine into either the accumbens or the amygdala resulted in both anorexia and adipsia. These observations contrast with the findings of Leibowitz [29], who found anorexia from lateral hypothalamic amphetamine injections, but failed to find it from the accumbens or the amygdala. It is possible that differences in procedure could account for this discrepancy. Relative to the present study, Leibowitz used unilateral injections (same total dose), a more severe food deprivation schedule, a longer test period, and repeated testing. Although it is not possible to determine if one of these factors accounts for the different results in the two studies, or if some other factor was involved, our early pilot data suggest that deprivation level may be an important factor. It is possible that the paradigm used by Leibowitz [29] is a more stringent test of anorexia (perhaps due to more severe food deprivation) and that the contributions of the accumbens and amygdala, being relatively weaker than that of the lateral hypothalamus, are not apparent under those conditions. However, the present study demonstrates that the anorexia produced from these other sites, particularly the accumbens, can be substantial. It is noteworthy that the amygdala placement of Leibowitz was slightly more medial than the one used here and this may account for the discrepant findings at this site. Although our data diverge from those of Leibowitz on the accumbens and amygdala, the two studies concur on the finding of no anorexia from the caudate. The fact that Leibowitz finds strong anorexia from lateral hypothalamic injections in the absence of effects from the accumbens or amygdala suggests that the hypothalamus is likely the primary mediator of the anorexia observed after systemic injections. That the accumbens is not critical for this anorexia is suggested by the findings of Koob *et al.* [27] that 6-OHDA lesions of the accumbens dopamine system did not significantly affect the anorexia produced by systemic injections. We therefore tentatively suggest that amphetamine anorexia is mediated primarily by the lateral hypothalamus with relatively smaller contributions from the accumbens and amygdala.

The presence of anorexia following amphetamine injections into these three sites parallels the findings of Heffner *et al.* [23] who found that when food deprived rats were given access to food, the concentrations of a dopamine metabolite (DOPAC) were increased (suggesting increased dopamine release) in the accumbens, amygdala and hypothalamus, but not in other dopaminergic areas. The commonality of active sites for dopamine release and amphetamine-induced anorexia suggests that the drug may suppress feeding by stimulating the brain mechanisms that normally mediate the animal's response to food. Regarding the amygdala, Heffner *et al.* [23] found that dopamine release could also be produced by tube feeding or intragastric injections of saline. It therefore appears that amygdaloid dopamine may mediate

a satiety signal related to gastric distension, and perhaps intra-amygdala amphetamine decreased eating by mimicking this signal.

Berger *et al.* [4] reported that rats tested in a stimulus-rich environment (after habituation) ate much less following amphetamine than did rats habituated and tested in a barren environment. They interpreted these data as suggesting that amphetamine's anorexic effects may be due to its potentiation of the secondary rewarding value of external stimuli. This notion provides a possible mechanism for the anorexia and adipsia produced by accumbens amphetamine injections that is consistent with other behavioral effects of these injections. Intra-accumbens amphetamine has previously been shown to produce increases in activity levels [34]. These injections also produce conditioned place preferences [9] and rats self-administer the drug directly into the accumbens [25]. The anorexia, adipsia, increased activity, conditioned place preference and self-administration that are produced by intra-accumbens amphetamine can be interpreted as suggesting that the injections increase the tendency for an animal to approach all environmental stimuli as if they were "rewarding." On this hypothesis, the increased activity caused by the accumbens injections reflects the animal's attempt to approach many environmental stimuli as if they were rewarding. The conditioned place preference and self-administration reflect the secondary rewarding properties acquired by environmental stimuli that are associated with the injections. Since all stimuli are reacted to as if they were rewarding, the prepotent capacity of natural rewards (such as food and water) to direct behavior is diminished, and as a result, the animal's eating and drinking are decreased. This explanation for the observed anorexia and adipsia may account for the failure of Leibowitz [29] to demonstrate anorexia from intra-accumbens injections. The higher deprivation level used in that study would have resulted in food being a more potent reward than it was in the present study. It would therefore be more likely to retain its capacity to direct behavior, even when the rewarding value of other stimuli are enhanced by the injections.

It might be argued that the anorexia and adipsia observed following intra-accumbens amphetamine were due simply to the stimulation of locomotor activity [34]. If amphetamine stimulated a motor output system then the animal would be incapable of eating or drinking, and this would account for the present data. However, this explanation would not account for the conditioned place preference and self-administration that are produced by these injections and it is inconsistent with the pattern of results observed in the present study. Although the average intake of the accumbens-injected rats was lower than that of saline-injected controls, several of the amphetamine-injected rats ate amounts that were in the upper range of the saline control values and it was clear by informal observation of these rats that they were very active during the test. The stimulation of activity in these rats was confirmed later in the open field. The ability of some amphetamine-injected rats to eat normal amounts of food suggests that they were not simply exhibiting locomotor stimulation. This observation is more compatable with the hypothesis that the increased activity reflected an increased tendency of the animals to approach environmental stimuli, one of which was still food.

It can be concluded from the present data that amphetamine acts on the nucleus accumbens and to a lesser extent on the amygdala to produce anorexia and adipsia.

REFERENCES

1. Ahlskog, J. E. Food intake and amphetamine anorexia after selective forebrain norepinephrine loss. *Brain Res* **82:** 211–240, 1974.
2. Ahlskog, J. E. and B. G. Hoebel. Overeating and obesity from damage to a noradrenergic system in the brain. *Science* **182:** 166–169, 1973.
3. Andersson, B. and S. Larsson. Water and food intake and the inhibitory effect of amphetamine on drinking and eating before and after "prefrontal lobotomy" in dogs. *Acta Physiol Scand* **38:** 22–30, 1957.
4. Berger, B. D., R. Backner and E. Grauer. Environmental influences on the anorectic action of amphetamine. *Int Congr Physiol Sci Abstr* **26:** 42, 1974.
5. Blundell, J. E. and C. J. Latham. Pharmacological manipulation of feeding behavior: possible influences of serotonin and dopamine on food intake. In: *Central Mechanisms of Anorectic Drugs*, edited by S. Garattini and R. Samanin. New York: Raven Press, 1978, pp. 83–109.
6. Burridge, S. L. and J. E. Blundell. Amphetamine anorexia: antagonism by typical but not atypical neuroleptics. *Neuropharmacology* **18:** 453–457, 1978.
7. Carey, R. J. Effects of selective forebrain depletions of norepinephrine and serotonin on the activity and food intake effects of amphetamine and fenfluramine. *Pharmacol Biochem Behav* **5:** 519–523, 1976.
8. Carlisle, H. J. Differential effects of amphetamine on food and water intake in rats with lateral hypothalamic lesions. *J Comp Physiol Psychol* **58:** 47–54, 1964.
9. Carr, G. D. and N. M. White. Conditioned place preference from intra-accumbens but not intra-caudate amphetamine injections. *Life Sci* **33:** 2551–2557, 1983.
10. Carr, G. D. and N. M. White. Anatomical disassociation of amphetamine's rewarding and aversive properties: an intracranial microinjection study. *Psychopharmacology (Berlin)*, in press.
11. Cole, S. O. Brain mechanisms of amphetamine-induced anorexia, locomotion, and stereotypy: A review. *Neurosci Biobehav Rev* **2:** 89–100, 1978.
12. Dourish, C. T. Dopaminergic involvement in the control of drinking behavior: a brief review. *Prog Neuropsychopharmacol Biol Psychiatry* **7:** 487–493, 1983.
13. Dourish, C. T. and S. J. Cooper. Effects of ET 495 (Piribedil) on water intake in the rat: evidence for a dopaminergic involvement in thirst. *Ir J Med Sci* **147:** Suppl 1, 19–23, 1978.
14. Dourish, C. T. and S. T. Cooper. Effects of acute or chronic administration of low doses of a dopamine agonist on drinking and locomotor activity in the rat. *Psychopharmacology (Berlin)* **72:** 197–202, 1981.
15. Fallon, J. H., D. A. Koziell and R. Y. Moore. Catecholamine innervation of the basal forebrain: II. Amygdala, suprarhinal cortex and entorhinal cortex. *J Comp Neurol* **180:** 509–532, 1978.
16. Fallon, J. H. and R. Y. Moore. Catecholamine innervation of the basal forebrain: III. Olfactory bulb, anterior olfactory nuclei, olfactory tubercle and piriform cortex. *J Comp Neurol* **180:** 533–544, 1978.
17. Fallon, J. H. and R. Y. Moore. Catecholamine innervation of the basal forebrain: IV. Topography of the dopamine projection to the basal forebrain and neostriatum. *J Comp Neurol* **180:** 545–580, 1978.

18. Fibiger, H. C., A. P. Zis and E. G. McGeer. Feeding and drinking deficits after 6-hydroxydopamine administration in the rat: Similarities to the lateral hypothalamic syndrome. *Brain Res* **55:** 135–148, 1973.
19. Glick, S. D. and R. U. Muller. Paradoxical effects of low doses of d-amphetamine in rats. *Psychopharmacologia* **22:** 396–402, 1971.
20. Grossman, S. P. Eating or drinking elicited by direct adrenergic or cholinergic stimulation of the hypothalamus. *Science* **132:** 872–882, 1960.
21. Grossman, S. P. Direct adrenergic and cholinergic stimulation of hypothalamic mechanisms. *Am J Physiol* **202:** 872–882, 1962.
22. Heffner, T. G., M. J. Zigmond and E. M. Stricker. Effects of dopamine agonists and antagonists on feeding in intact and 6-hydroxydopamine-treated rats. *J Pharmacol Exp Ther* **201:** 386–399, 1977.
23. Heffner, T. G., J. A. Hartman and L. S. Seiden. Feeding increases dopamine metabolism in the rat brain. *Science* **208:** 1168–1170, 1980.
24. Hoebel, B. G. The psychopharmacology of feeding. In: *Handbook of Psychopharmacology*, vol 8, edited by L. L. Iversen, S. D. Iversen and S. H. Snyder. New York: Plenum Press, 1977.
25. Hoebel, B. G., A. P. Monaco, L. Hernandez, E. F. Aulisi, B. G. Stanley and L. Lenard. Self-injection of amphetamine directly into the brain. *Psychopharmacology (Berlin)* **81:** 158–163, 1983.
26. Kalai, M., K. Fuxe, M. Goldstein, A. Harfstrand, L. F. Agnati and J. T. Coyle. Evidence for the existence of putative dopamine-, adrenalin- and noradrenalin-containing vagal motor neurons in the brainstem of the rat. *Neurosci Lett* **50:** 57–62, 1984.
27. Koob, G. F., S. J. Riley, S. C. Smith and T. W. Robbins. Effects of 6-hydroxydopamine lesions of the nucleus accumbens septi and olfactory tubercle on feeding, locomotor activity and amphetamine anorexia in the rat. *J Comp Physiol Psychol* **92:** 917–927, 1978.
28. Leibowitz, S. F. Alpha-adrenergic receptors mediate suppression of drinking induced by hypothalamic amphetamine injection. *Fed Proc* **32:** 754, 1973.
29. Leibowitz, S. F. Amphetamine: possible site and mode of action for producing anorexia in the rat. *Brain Res* **84:** 160–167, 1975.
30. Levitt, P. and R. Y. Moore. Origin and organization of brainstem catecholamine innervation in the rat. *J Comp Neurol* **186:** 505–528, 1979.
31. Neilson, E. B. and M. Lyon. Drinking behavior and brain dopamine: antagonistic effect of two neuroleptic drugs (Pimozide and Spiramide) upon amphetamine- or apomorphine-induced hypodipsia. *Psychopharmacologia* **33:** 299–308, 1973.
32. Pellegrino, L. J., A. S. Pellegrino and A. J. Cushman. *Atlas of the Rat Brain*. New York: Plenum Press, 1979.
33. Pharmaceutical Society of Britain. *Martindale: The Extra Pharmacopoeia*. London: The Pharmaceutical Press, 1977.
34. Pijnenburg, A. J. J., W. M. M. Honig, J. A. M. van der Heyden and J. M. van Rossum. Effects of chemical stimulation of the mesolimbic dopamine system upon locomotor activity. *Eur J Pharmacol* **35:** 45–58, 1976.
35. Rogers, P. J. and J. E. Blundell. Effect of anorexic drugs on food intake and the micro-structure of eating in human subjects. *Psychopharmacology (Berlin)* **66:** 159–165, 1978.
36. Silverstone, T., B. Wells and E. Trenchard. Differential dose-response effects of dexamphetamine sulphate on hunger, arousal and mood in human volunteers. *Psychopharmacology (Berlin)* **79:** 242–245, 1983.
37. Tombaugh, T. N., J. Tombaugh and H. Anisman. Effects of dopamine receptor blockade on alimentary behaviors: home cage food consumption, magazine training, operant acquisition, and performance. *Psychopharmacology (Berlin)* **66:** 219–225, 1979.
38. Unrich, H. Narcolepsy and its treatment with benzedrine sulphate. *N Engl J Med* **217:** 696–701, 1937.
39. Winn, P., S. F. Williams and L. J. Herberg. Feeding stimulated by very low doses of d-amphetamine administered systemically or by microinjection into the striatum. *Psychopharmacology (Berlin)* **78:** 336–341, 1982.