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Feeding and Satiation Observed in the Runway: The Effects of d-Amphetamine and d-Fenfluramine Compared

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THURLBY, P. L., V. E. GRIMM AND R. SAMANIN. *Feeding and satiation observed in the runway: The effects of d-amphetamine and d-fenfluramine compared.* PHARMACOL BIOCHEM BEHAV **18**(6) 841–846, 1983.—A paradigm involving feeding to satiety over the course of repeated trials in the runway was used to examine the effects of d-amphetamine (1.0, 1.5 mg/kg) and d-fenfluramine (2.0, 3.0 mg/kg). 1.0 mg/kg d-amphetamine was found to have no significant effect on running performance or feeding in the runway. 1.5 mg/kg d-amphetamine significantly reduced the total food intake during the test but had little impact during the first three trials. In contrast, d-fenfluramine, even at the lower dose and during the initial trials, significantly reduced running performance and feeding to levels normally associated with satiation in the non-drugged animals. The results are discussed in relation to the contrasting modes of action of amphetamine and fenfluramine on food intake.

Feeding Runway behaviour Motivation Satiety Anorexia Amphetamine Fenfluramine

AMPHETAMINE and fenfluramine, although structurally related, interact with different neurochemical systems within the central nervous system. Amphetamine preferentially affects catecholamine mechanisms [11]. Fenfluramine, on the other hand, exerts its influence mainly through the release of serotonin and the blocking of the reuptake of this neurotransmitter [12,13]. The general behavioural effects of the two drugs also differ. Amphetamine is a stimulant drug with effects ranging, with increasing dosage, from hyperactivity and the disruption of normal behavioural sequencies [17,20] to stereotypy [21] while fenfluramine generally lends to the inhibition of behavioural output [16,26] and has sedative effects at high doses [15]. Despite these differences the two drugs retain one feature in common: they induce anorexia. However, in view of their dissimilarity with respect to both neurochemical and general behavioural effects, it is not surprising that closer experimental investigation has pointed to substantial differences in the modes of action of these two compounds on feeding. While both reduce food intake, the two drugs differ in their effects on the pattern of meal taking [6], on the rate of eating [4] on the self-selection of protein and carbohydrates [27] and on eating in response to tail pinch [1].

In the present study the effects of these two drugs were compared in a situation where eating is part of a well established and highly overlearned response pattern. Rats were trained under 23 hr food deprivation and considerable reduction in body weight to feed in the goal area of a runway. The tests were conducted using rats that were performing, after lengthy training, at stable asymptotic levels in the runway. Starting and running speeds were measured as well as the amount of food consumed at the end of the alley during two minute time periods allotted for feeding. The effects of amphetamine and fenfluramine on these selected aspects of behaviour were tested in sessions of fifteen consecutive trials. This experimental paradigm was selected on the basis of pilot studies showing that non drug treated animals take 10–15 trials (20–30 minutes feeding) before they become satiated and stop eating.

A previous study [25] indicated that amphetamine and fenfluramine, at doses normally found to give an equivalent suppression of food intake in a hour feeding test, may differ with respect to their ability to influence food-rewarded runway behaviour. However, the paradigm used did not permit the detailed observation of anorectic effects since the test involved only three short (30 sec) feeding periods. In contrast, the present study permitted the observation of both runway performance and feeding itself thus allowing an examination of the relationship between runway behaviour and the development of satiety in the control rats and the exhibition of anorexia in the drug treated animals.

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METHOD

Animals

Male CD-COBS (Charles River, Italy) rats, initially weighing 175–200 g, were used for these experiments. They were housed under conditions of constant temperature (21 ± 1°C) and relative humidity (50%) with a 12 hour light-12 hour dark cycle (dark period commencing at 19.30). The rats were caged in groups of three and every day 50 g food, (Altromin MT for rats, Rieper, Italy), was placed in each cage at 18.30. Using this procedure the animals maintained approximately 70–80% of their free-feeding weight during runway training and weighed about 300 g at the time of the test.

Runway Apparatus

The runway, a 2.4 m straight alley, was constructed of chipboard and the internal height and width were both 10 cm. The top was a metal grill allowing the animals to be observed in all parts of the apparatus. The startbox region was 30 cm long and separated from the remainder of the runway by a hand-operated plastic guillotine gate. A Petri dish containing Noyes 45 mg pellets (P. J. Noyes Co. Inc., Lancaster, NH) was placed in the goal area. Two time intervals were measured using hand-held stopwatches: the time from the opening of the startbox gate until the front paws of the rat reached a black line painted on the floor of the alley 12 cm from the gate (latency to run) and the time taken to run from this point to another painted 20 cm before the food dish (running time). The distance between these two lines was 150 cm. From these two measurements starting speeds (1/latency, sec^{-1}) and running speeds (m/sec) were calculated.

Runway Training

Training was based on an established procedure [14]. After one week of restricted feeding the rats, in groups of four, were placed into the runway for a period of 10 min and allowed free access to food pellets in the goal area. After four such habituation sessions conducted on separate days, the rats were given 30 individual trials over 10 days (3 trials per day with an intertrial interval of 5 min). Each trial involved placing the rat in the start box for 10 s before opening the gate. Thirty sec was then allowed for feeding after the animal had reached the food. After completion of this training the rats were found to have stable starting and running speeds. On the last three days of training the rats were injected intraperitoneally with 0.5 ml saline, 30 min before the training session, in order to habituate them to the stress associated with subsequent drug administration.

Runway Test Procedure

Each rat was allowed 15 consecutive trails in the runway. These trials were separated by a 30 sec period during which the animals were kept in the startbox with the gate closed (the intertrial interval). After opening the gate the rats were allowed to run to the goal, a dish initially containing about 25 g Noyes pellets. They were then left to eat for two minutes, after which time they were placed once more in the startbox. Starting speed, running speed and the weight of the food eaten were recorded for each trial. Two observers were employed, one measured starting speed and also handled the animals and the other measured the running time and the amount of food eaten. This second observer was unaware of the treatment received by each rat. On every trail the rats were allowed the same two minute period for feeding regardless of the starting or running speeds. On those trials where the latency to run was greater than 30 sec the rats were gently removed from the startbox and placed at the food dish. A starting speed of 0.01 sec^{-1} and a running speed of 0.01 m/sec was recorded for such trials.

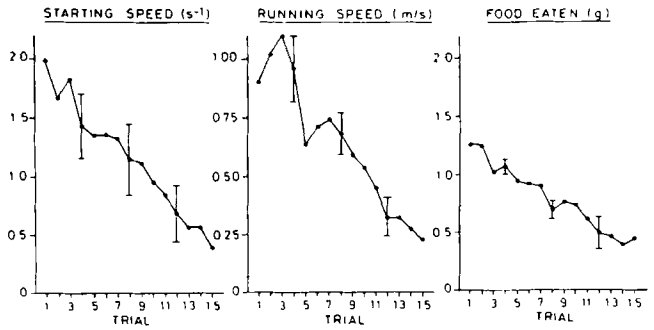

FIG. 1. The normal responses of saline treated rats in the runway feeding paradigm. Each point represents the mean value for 12 rats and the vertical bars indicate ±SEM.

Experimental Design

A within-subjects design was employed using two separate groups of six animals. In the first group each rat received saline, d-amphetamine (1.0 mg/kg) and d-fenfluramine (2.0 mg/kg) on three different occasions separated by four intervening days on which normal training was continued. These training trials served to maintain the running and eating responses at a high level and to check for any possible residual effects of the drugs. On any one day three animals were tested, one in each treatment condition. A balanced design was employed using a selected pair of 3×3 Latin Squares such that each treatment followed each of the other two treatments an equal number of times. The experiments were conducted between 10.00 and 13.00 hr with each individual rat being tested at the same time of day. The second group of six animals were used in the same way but to compare saline, d-amphetamine (1.5 mg/kg) and d-fenfluramine (3.0 mg/kg). This design ensured that each animal had only one exposure to each type of drug, thus minimizing the possibility of interference from the development of either pharmacological or behavioural tolerance.

Drug Administration

d-Amphetamine sulphate (Recordati, Milan, Italy) and d-fenfluramine hydrochloride (Servier Laboratories, France) were dissolved in bi-distilled water and injected intraperitoneally in a volume of 0.2 ml per 100 g body weight. Saline (0.0% w/v sodium chloride) was injected as the control treatment. All injections were made 30 min before the first trial in the runway, or in the case of the home cage feeding 30 min before the presentation of the food.

Statistical Analysis

All data were subjected to an appropriate ANOVA for a within subjects design. F tests for significant treatment effects were followed by Dunnett's test to compare treatments with the saline control or by Duncan's multiple range test to compare the effects of fenfluramine and amphetamine treatments.

TABLE 1

RUNWAY PERFORMANCE AND FEEDING OF RATS TREATED WITH AMPHETAMINE AND FENFLURAMINE

	Starting Speed (sec^{-1})	Running (Speed (m/sec)	Food Intake (g)
Saline control (Mean ± SEM, n=12)	1.15 ± 0.16	0.62 ± 0.06	11.9 ± 0.3
		% Control (Mean Values ± SEM; 6 Rats per Group)	
d-Amphetamine			
1.0 mg/kg	88.8 ± 14.4	91.9 ± 10.8	82.1 ± 10.3
1.5 mg/kg	66.4 ± 9.7	58.7 ± 8.7*	50.0 ± 7.4*
d-Fenfluramine			
2.0 mg/kg	20.7 ± 3.4*	37.8 ± 8.1*	64.1 ± 11.9*
3.0 mg/kg	15.9 ± 7.1*	21.7 ± 8.7*	39.3 ± 11.5*

The starting and running speeds are average values for fifteen trials; food intake is the cumulative values. The statistical significance of the differences from the appropriate saline control group: *$p<0.05$; *$p<0.01$. See text for details of the analysis used.

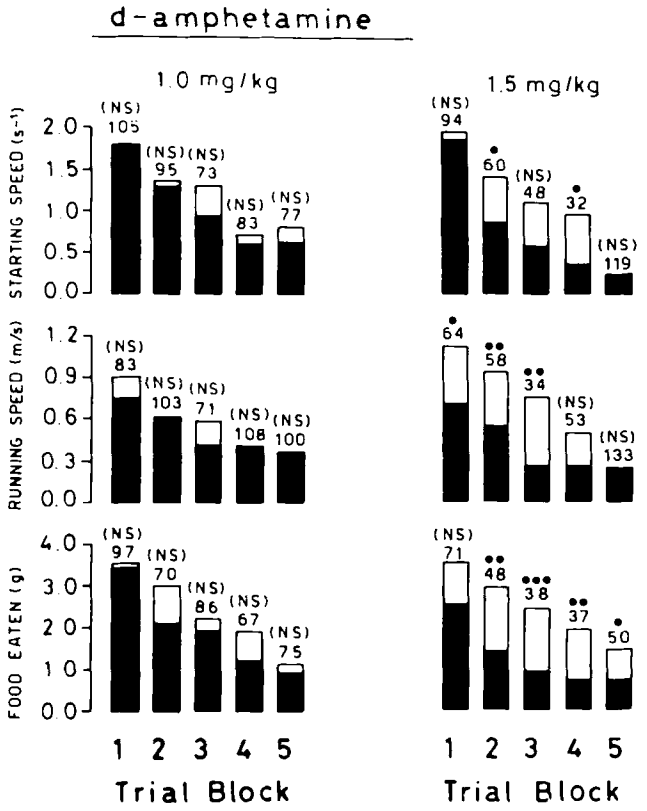

FIG. 2. The effect of amphetamine on runway behaviour. The data for 6 rats per treatment has been consolidated into five blocks of three trials. The shaded portion of each bar represents the treatment mean and the outline the control mean. The number above each bar indicates the treatment mean as a % of the control and the statistical significance of these differences are shown as follows: ●—$p<0.05$; ●●—$p<0.01$; ●●●—$p<0.001$. See text for details of statistical analysis. NS=not significant.

RESULTS

The Normal Response

The behaviour of the saline treated animals is shown in Fig. 1. The starting speed showed a linear decline from a mean value of a about 2.0 sec^{-1} (i.e., a latency of 0.5 sec) on the first trial to a value of less than 0.4 sec^{-1} on the last trial. Running speed was found to be stable for the first four trials at a level of about 1.0 m/sec, but then also showed a steady decline over the subsequent trials to a value of approximately 0.25 m/sec on the last trial. The mean food intake was also found to decline in a linear fashion from 1.25 g on the first trial to 0.45 g on the last.

The Effects of Amphetamine and Fenfluramine

The drug doses used in this study were selected, on the basis of many experiments in this laboratory, as those which normally lead to an approximately equivalent suppression of food intake in one hour feeding tests using cyclically food-deprived rats, i.e., d-amphetamine, 1.0 mg/kg is found to be equianoreactic with d-fenfluramine, 2.0 mg/kg and d-amphetamine, 1.5 mg/kg with d-fenfluramine, 3.0 mg/kg.

The overall picture of the effects of the two drugs on runway performance and feeding is presented in Table 1. The data collected for each animal over the 15 trials has been pooled to provide mean values for starting and running speeds and a cumulative measure of food intake. 1.0 mg/kg d-amphetamine was found to have no significant effect on food intake in the present paradigm. Neither did it have any significant effects on the starting or running speeds. The higher dose of amphetamine (1.5 mg/kg) caused a significant reduction in food intake ($p<0.05$) but the starting speed was not significantly affected. Running speed was significantly reduced ($p<0.05$) by a degree that was similar to the reduction in food intake. The administration of fenfluramine led to a pattern of behaviour that was different to that seen in the animals treated with amphetamine. The reduction in food intake was statistically significant at both doses of fenfluramine. Starting speed and running speed were both greatly reduced, even at the lower dose.

The contrast between the effects of the two drugs is easily seen by comparing 1.5 mg/kg d-amphetamine with 2.0 mg/kg d-fenfluramine. Looking at the entire 15 trial session this dose of amphetamine produced the greater reduction in food intake of the two treatments, yet the decrement in mean starting and running speeds was found to be far more marked after fenfluramine (20.7 and 37.8% the control values respectively) than after amphetamine (66.4 and 58.7% of the control values).

A more detailed analysis of the data is given in Figs. 2 and 3 which show the effects of the drug treatments over the course of the test period. The trials have been grouped together into five blocks (of three trials each) in order to provide a more consolidated picture of the responses. At 1.0 mg/kg d-amphetamine was found to have no significant effect on the starting speed, running speed or the amount of food eaten in any of the trial blocks (Fig. 2). At the higher dose of amphetamine (1.5 mg/kg) the behaviour of the rats was only slightly altered during the first trial block: starting speed was not significantly different from the control value and the running speed was only reduced by 36%, although this effect was statistically significant ($p<0.05$). Feeding was not significantly altered (29% reduction). Amphetamine appeared to

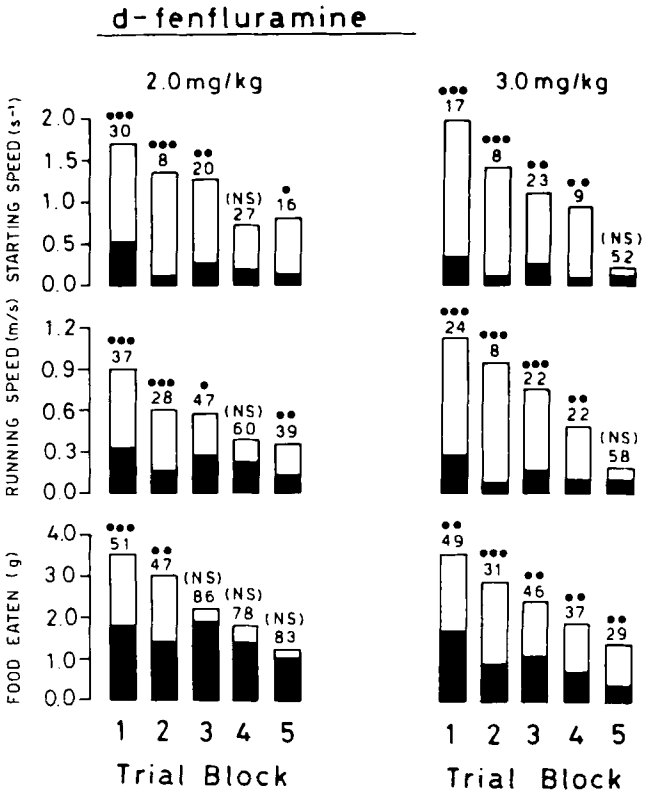

FIG. 3. The effect of fenfluramine on runway behaviour. The data, from 6 rats per treatment, has been consolidated into five blocks of three trials. The shaded portion of each bar represents the treatment mean and the outline the control mean. The number above each bar indicates the treatment mean as a % of the control and the statistical significance of these differences are shown as follows: ●—$p<0.05$; ●●—$p<0.01$; ●●●—$p<0.001$. See text for details of statistical analysis. NS=not significant.

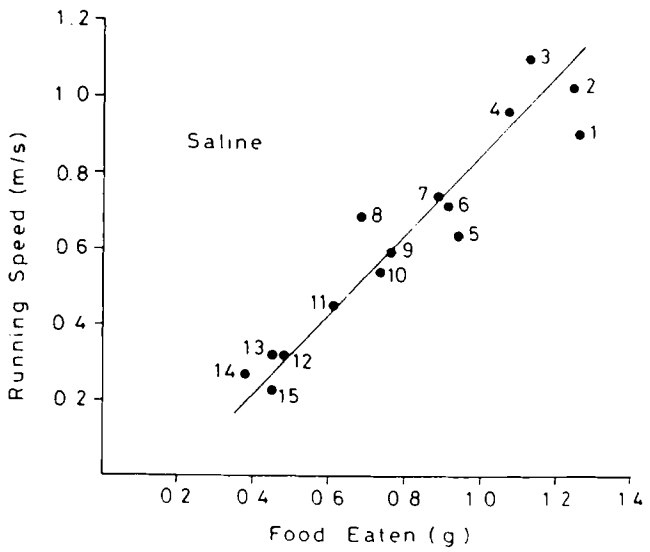

FIG. 4. The relationship for saline treated rats between running speed and food eaten on each trial. Each point represents the mean value for 12 rats and the number of the trial is indicated. The line of best fit is drawn.

have more impact during the subsequent trial blocks with significant reductions in starting speed, running speed and feeding occurring on most but not all of the last four blocks (see Fig. 2).

The effects of fenfluramine are shown in Fig. 3. The lower dose (2.0 mg/kg) led to a significant reduction in the starting and running speeds on all but one of the trial blocks (the fourth). The depression of runway performance was most marked on the second trial block with the starting speed only 8% of the control and running speed only 28% of the control level. Feeding was also significantly depresssd on the first block (51% of the control value; $p<0.001$) and second block (47% of the control; $p<0.01$) but was not signficiantly lower on the last three blocks. The higher dose of fenfluramine (3.0 mg/kg) gave rise to a very marked depression of the starting speed and running speed, again with the greatest effects being seen during the second trial block. Feeding was also depressed, but in contrast to the lower dose of this drug, this effect was statistically significant for all five blocks.

Figures 4 and 5 illustrate the relationship between runway performance (instrumental response) and feeding itself, both in the control animals as they progress from hunger to satiety during the course of the test period and also in the animals exhibiting drug-induced anorexia. In saline treated rats a close relationship appears between running speed and feeding (Fig. 4). The relationship between these two variables is altered by drug treatment (Fig. 5). Amphetamine treated rats run at normal speeds when feeding at high levels during the first few trials but there is a tendency for them to continue to run at higher than normal speeds in association with lower levels of feeding as occur during those trials towards the end of the test period. Fenfluramine treatment leads to yet another relationship. High levels of feeding are never found but those levels that are seen during the test are associated with more or less normal running speeds.

DISCUSSION

In the field of behavioural pharmacology the straight runway has often been used to investigate the influence of drugs on a simple rewarded behaviour. Most of these studies have concentrated on such areas as learning and reward, determining the effects of drugs on the acquisition or extinction of the running response [18,22] or on such phenomena as the partial reinforcement extinction effect [14] or patterned responding [10]. Although food is the most commonly used reward, the system is seldom used for the primary purpose of investigating a behaviour related to feeding. In those few studies where feeding has been a central consideration the runway performance has been regarded as a measurement of the drive or motivation of the animal for food, with the running speed being quantitatively related to the motivational level [2, 8, 9].

The present study has made use of the straight runway to evaluate possible differences between the altered feeding behaviour seen after treatment with two anorectic drugs, amphetamine and fenfluramine. In the experimental paradigm used the feeding observed in the goal area of the runway is a strongly established habit which may be presumed to be stimulated not only by internal hunger cues but also to be under strong external stimulus control.

The main purpose of the experiment was to compare the effects of the two drugs on the instrumental response for food (starting and running speeds) and on feeding itself. Moreover, a trial by trial analysis has allowed a description of the normal process of satiation in terms of the relationship

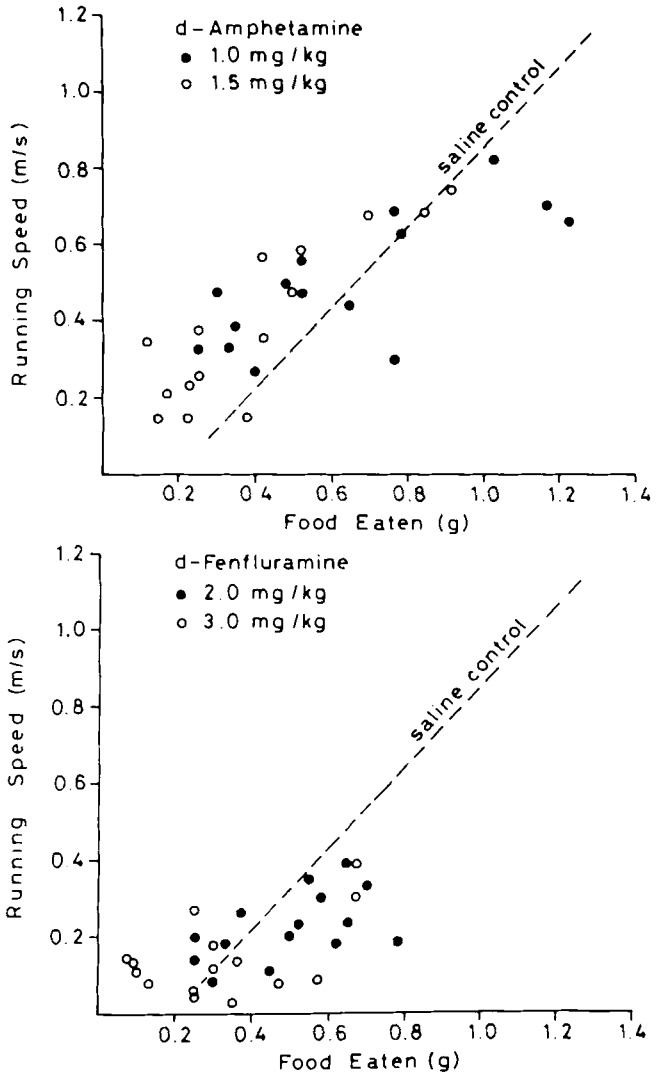

FIG. 5. The relationship between running speed and food eaten on each trial in rats treated with amphetamine and fenfluramine. Each point represents the mean value for 6 rats on each of 15 trials. The line of best fit for the saline control is drawn.

between declining instrumental and feeding responses (see [19]) and a comparison of this normal behaviour with that induced by the anorectic drugs. The protocol used whereby even non-running animals were placed at the food dish permits the consummatory response to be observed even in the absence of the instrumental response.

Satiation in the Control Animals

The process of satiation, the progression from hunger to satiety [3], is characterized in this experiment by a decline in starting and running speed and a reduction in the eating rate, measured as the food consumed in descrete two minute periods on each trial (Fig. 1). Figure 4 demonstrates the close relationship between the running speed and the food eaten. The instrumental response (running) and the consumatory response (feeding) decline together, which is to be expected if running speed is indeed a reflection of the motivation for food.

Amphetamine-Fenfluramine Differences

The drugs were found to differ in two major respects. First, it is clear that for the same degree of anorexia amphetamine reduces starting and running speeds far less than fenfluramine (Table 1). Secondly, the two drugs were found to differ with respect to the time-course of their effects on running and feeding. d-Amphetamine was found to have little impact initially but to exert its effects more strongly in later trials. Even with the higher dose (1.5 mg/kg) the effects on starting speed and on feeding were not statistically significant over the first three trials (Fig. 2). Fenfluramine had quite a different effect. Levels of running and feeding were reduced even during the first three trials and remained at low levels throughout the test period.

A similar pattern of behaviour has been observed previously for fenfluramine in experiments where the microstructure of feeding has been investigated. Latency to eat is not much affected but eating rate is low even during the initial stages of feeding [5]. However, the effect of amphetamine in the present study is in contrast to some previous findings relating to the feeding behaviour in the home cage. After amphetamine treatment there is normally a very long latency before feeding begins although once it starts the local eating rate is high [5]. In the present study even the highest dose of amphetamine did not evoke a period of latency before feeding began; the animals ate immediately after reaching the food dish on the first trial and the feeding in the first two minutes was not significantly different from that of the control animals. This is a clear demonstration of how a behavioural modification of feeding i.e. the training to eat in the runway may influence a normally found characteristic of drug-induced anorexia. The level of external stimulus control may be the crucial factor in explaining the difference between these two situations, or alternatively the pattern of feeding in relation to other behaviours may be relevant. In the home cage the initiation of feeding may be observed to involve and "compete" with other behaviours such as locomotion and drinking. However, in the runway the training leads to a suppression of these other behaviours and feeding begins immediately after arrival at the food. If, as has been suggested [17,20] the effects brought about by amphetamine derive mainly from a disruption of the normal sequencing of different types of behaviour then the initiation of feeding in the runway may be little affected since it has been reduced to a single continuous behaviour—eating at the dish—rather than a sequence involving drinking, selection of a feeding position, etc.

The effect of drug treatments on the relationship between running speed and feeding may be seen in Fig. 5. Amphetamine treated animals tend to run faster than saline treated controls at low levels of feeding whereas after fenfluramine treatment the running response is essentially equivalent to that of the saline controls at low levels of feeding. In fact, the data presented are consistent with the hypothesis that fenfluramine induces a behavioural state that is comparable with that of the control rats at the end of the test period i.e., similar to the satiety that results from feeding in the runway. In addition, some recent findings in our laboratory using a similar protocol to that of the present study indicate that the behaviour of rats that had received 1.25 mg/kg d-fenfluramine is indistinguishable in terms of starting speed, running speed and feeding from that of rats that had been allowed to eat about 10 g of laboratory chow before being tested in the runway. In the present study it appears

that although starting and running speeds are low (after fenfluramine treatment) they are consistent with the level of observed feeding: the animals behave as if they had previously received food. Also there is little to suggest that sedation could be responsible for the observed anorectic effects of fenfluramine since the spontaneous activity of the fenfluramine treated rats was observed to be no less than that the control rats towards the end of the test period i.e., the behaviour is yet again similar to that of satiate rats.

In conclusion, the results presented in this paper demonstrate that amphetamine and fenfluramine differ with respect to their influence on the behaviour that may be observed in a runway feeding paradigm. Amphetamine, even at a dose of 1.5 mg/kg had little effect on runway performance and feeding during the initial part of the test when the control performance was at a higher level. Treatment with fenfluramine led to another pattern of behaviour in which runway performance and feeding were both depressed, even during the early part of the test. This behaviour resembled that of non-drugged rats that had become satiated in the runway. In view of the considerable evidence that the actions of fenfluramine are mediated by serotonin [7, 13, 23, 24] the data lend support to the idea of an involvement of serotoninergic mechanisms in the physiological suppression of feeding.

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REFERENCES

1. Antelman, S. M., A. R. Caggiula, C. A. Black and D. J. Edwards. Stress reverses the anorexia induced by amphetamine and methylphenidate but not fenfluramine. *Brain Res* **143:** 580–585, 1978.
2. Barry, H. Effects of strength of drive on learning and extinction. *J Exp Psychol* **55:** 473–481, 1958.
3. Blundell, J. E. Hunger, appetite and satiety. Constructs in search of identities. In: *Nutrition and Lifestyles*, edited by M. Turner. London: Applied Science, 1979, pp. 21–42.
4. 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.
5. Blundell, J. E. and C. J. Latham. Characterization of the adjustments to the structure of feeding behaviour following pharmacological treatment: Effects of amphetamine and fenfluramine and the antagonism produced by pimozide and methergoline. *Pharmacol Biochem Behav* **12:** 717–722, 1980.
6. Blundell, J. E., C. J. Latham and M. B. Leshem. Differences between the anorexic actions of amphetamine and fenfluramine-possible effects on hunger and satiety. *J Pharm Pharmacol* **28:** 471–477, 1976.
7. Borsini, F., C. Bendotti, A. Aleotti, R. Samanin and S. Garattini. D-Fenfluramine and d-norfenfluramine reduce food intake by acting on different serotonin mechanisms in the rat brain. *Pharmacol Res Commun* **14:** 671–678, 1982.
8. Campbell, B. A. and D. Kraeling. Response strength as a function of drive level during training and extinction. *J Comp Physiol Psychol* **47:** 101–103, 1954.
9. Egan, J., C. J. Earley and B. E. Leonard. The effect of amitriptyline and mianserine (ORG GB94) on food motivated behaviour of rats trained in a runway: Possible correlation with biogenic amine concentration in the limbic system. *Psychopharmacology (Berlin)* **61:** 143–147, 1979.
10. Engelhardt, F. and O. Steward. Entorhinal cortical lesions in rats and runway alternation performance: Changes in patterns of response initiation. *Behav Neural Biol* **29:** 91–104, 1980.
11. Garattini, S., E. Borroni, T. Mennini and R. Samanin. Differences and similarities among anorectic agents. In: *Central Mechanisms of Anorectic Drugs*, edited by S. Garattini and R. Samanin. New York: Raven Press, 1978, pp. 127–143.
12. Garattini, S., S. Caccia, T. Mennini, R. Samanin, S. Consolo and H. Ladinsky. Biochemical pharmacology of the anorectic drug fenfluramine: A review. *Curr Med Res Opin* **6:** Suppl. 1, 15–27, 1979.
13. Garattini, S. and R. Samanin. Anorectic drugs and brain neurotransmitters. In: *Appetite and Food Intake*, edited by T. Silverstone. Berlin: Abakon Verlags Gesellschaft, 1976, pp. 83–108.
14. Gray, J. A., A. R. Mayes and M. Wilson. A barbiturate-like effect of adrenocorticotrophic hormone on the partial reinforcement acquisition and extinction effects. *Neuropharmacology* **10:** 223–230, 1971.
15. Le Douarec, J. C. and C. Neveu. Pharmacology and biochemistry of fenfluramine. In: *Amphetamines and Related Compounds*, edited by E. Costa and S. Garattini. New York: Raven Press, 1970, pp. 75–105.
16. Lindquist, M. P. and K. G. Götestam. Open-field behavior after intravenous amphetamine analogues in rats. *Psychopharmacology (Berlin)* **55:** 129–133, 1977.
17. Lyon, M. and T. Robbins. The action of central nervous system stimulant drugs: A general theory concerning amphetamine effects. In: *Current Developments in Psychopharmacology*, edited by W. B. Essman and L. Valzelli. New York: Spectrum, 1975, pp. 79–163.
18. Mason, S. T., R. J. Beninger, H. C. Fibiger and A. G. Phillips. Pimozide induced suppression of responding: Evidence against a block of food reward. *Pharmacol Biochem Behav* **12:** 917–923, 1980.
19. Morgan, M. J. Resistance to satiation. *Anim Behav* **22:** 449–466, 1974.
20. Norton, S. Amphetamine as a model for hyperactivity in the rat. *Physiol Behav* **11:** 181–186, 1973.
21. Randrup, A. and I. Munkvad. Biochemical, anatomical and psychological investigations of stereotyped behavior induced by amphetamines. In: *Amphetamines and Related Compounds*, edited by E. Costa and S. Garattini. New York: Raven Press, 1970, pp. 695–713.
22. Rosen, A. J. and M. E. Cohen. The effects of cinanserin, a potent serotonin antagonist, on the acquisition of a running response in the rat. *Neuropharmacology* **12:** 501–508, 1973.
23. Samanin, R. and S. Garattini. Neuropharmacology of feeding. In: *Drugs and Appetite*, edited by T. Silverstone. London: Academic Press, 1982, pp. 23–39.
24. Samanin, R., D. Ghezzi, L. Valzelli and S. Garattini. The effects of selective lesioning of brain serotonin or catecholamine containing neurones on the anorectic activity of fenfluramine and amphetamine. *Eur J Pharmacol* **19:** 318–322, 1972.
25. Thurlby, P. L. and R. Samanin. Effects of anorectic drugs and prior feeding on food-rewarded runway behavior. *Pharmacol Biochem Behav* **14:** 799–804, 1981.
26. Weischer, M. L. and K. Opitz. Effect of fenfluramine, chlorphentermine and related compounds on the behaviour of aggressive mice. *Arch Int Pharmacodyn Ther* **195:** 252–259, 1972.
27. Wurtman, J. J. and R. J. Wurtman. Fenfluramine and fluoxetine spare protein consumption while suppressing caloric intake by rats. *Science* **198:** 1178–1180, 1977.