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Behavioural and Pharmacological Investigations of 5-HT Hypophagia and Hyperdipsia

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MONTGOMERY, A. M. J., P. J. FLETCHER AND M. J. BURTON. *Behavioural and pharmacological investigations of 5-HT hypophagia and hyperdipsia.* PHARMACOL BIOCHEM BEHAV **25**(1) 23–28, 1986.—Treatment with 5-hydroxytryptamine (5-HT) reliably induced hypophagia in non-deprived rats and in rats tested following a period of food-deprivation, regardless of the presence or absence of water during testing. The hyperdipsic effect of 5-HT, however, was sensitive to changes in the length of food-deprivation, suggesting a possible interaction between 5-HT hyperdipsia and prandial drinking. Both 5-HT hypophagia and hyperdipsia were attenuated by methysergide pretreatment, thus confirming the involvement of peripheral post-synaptic 5-HT receptors in both effects. Pretreatment with propranolol blocked 5-HT hyperdipsia, but did not alter 5-HT hypophagia, thus suggesting that 5-HT hypophagia and hyperdipsia are mediated by different mechanisms at some point subsequent to the stimulation of peripheral 5-HT receptors. These results are consistent with other evidence that 5-HT hyperdipsia is mediated by stimulation of the renin-angiotensin system. It is tentatively suggested that 5-HT hypophagia could result from 5-HT-induced inhibition of cephalic phase insulin secretion.

Peripheral 5-HT Hypophagia Hyperdipsia Methysergide Propranolol

PREVIOUS investigations of feeding have indicated that food consumption, or the presence of food in the gut, is associated with increased peripheral 5-HT levels. Examples of such evidence include the prandial release of 5-HT and increased peripheral 5-HT levels in response to intraduodenal infusion of hypertonic glucose [2]. Increased pressure on the intestinal mucosa also enhances peripheral 5-HT levels [1]. In rats, subcutaneously administered 5-HT (which does not cross the blood-brain barrier [12]) has been shown [10] to reduce feeding which follows a period of food-deprivation and to enhance drinking, suggesting that peripheral 5-HT might play some physiological role in the control of both feeding and drinking. More recently there has been renewed interest in the effects on consummatory behaviours of increasing the availability of 5-HT at peripheral post-synaptic receptors [4, 8, 11, 13].

Both 5-HT hypophagia and hyperdipsia have been shown to be dose-dependent [4,11] and exhibited at doses which "do not produce appreciable sensorimotor dysfunctions; neither do they support a conditioned taste aversion" [13].

The aim of the present study was to investigate possible explanations of the hypophagic and dipsogenic effects of 5-HT in terms of non-specific actions of 5-HT, before going on to investigate the pharmacological mechanisms involved.

EXPERIMENT 1—EFFECTS OF 5-HT ON FOOD AND WATER CONSUMPTION IN FOOD-DEPRIVED AND NON-DEPRIVED RATS

The first two investigations aimed to confirm the concurrent hypophagic and dipsogenic responses to 5-HT (2 mg/kg) in rats tested after a period of food-deprivation (Part 1) and in non-deprived rats (Part 2). This dose of 5-HT has previously been shown to support an asymptotic increase in drinking [4]. Parts 3 and 4 were included to determine whether 5-HT hypophagia and 5-HT hyperdipsia might be demonstrated independently of each other. Part 3 aimed at investigating the possibility that 5-HT hypophagia might be a result of response competition from 5-HT hyperdipsia, by measuring the effects of 5-HT on feeding in the absence of water. In order to measure 5-HT hyperdipsia uncontaminated by prandial drinking, the final investigation (Part 4) assessed the effects of 5-HT on water consumption in rats tested in the absence of food.

Method

Each of the investigations in Experiment 1 employed male Lister hooded rats (220–360 g) maintained on a 12-hour light/dark cycle. Groups were matched for body weight except where stated to the contrary. Water was available at all

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TABLE 1

EXPERIMENTAL CONDITIONS EMPLOYED IN EXPERIMENT 1 PARTS 1–4

Part No.	Test Conditions: Food Deprivation*	Food Present	Water Present
1	Yes	Yes	Yes
2	No	Yes	Yes
3	Yes	Yes	No
4	No	No	Yes

*Refers to the 18 hr period immediately prior to testing.

times except during the 15-minute interval between treatment (5-HT or vehicle) and the start of testing, and during the food consumption test in Part 3. Food was available during all tests except Part 4 and in Parts 1 and 3 testing followed a period of food-deprivation. In each investigation half of the subjects (Parts 1, 2 and 4, n=6; Part 3, n=9) received 5-HT (2 mg/kg SC) [serotonin creatinine sulphate (Sigma)]; the remaining subjects (n=6 or 9) received an injection of vehicle (distilled water). With the exception of Part 2 all testing commenced three hours into the light phase of the light/dark cycle.

In Parts 1 and 2 food and water consumption were measured concurrently. In Part 1, subjects were food-deprived 18-hours before the start of testing, in which food and water consumption were recorded concurrently. In Part 2, food and water consumption were recorded in non-deprived subjects tested at the start of the dark phase, when free-feeding rats normally consume a large proportion of their total daily intake [14]. In Parts 3 and 4, subjects were given access to either food (Part 3) or water (Part 4). In Part 3, subjects were food-deprived 18-hours before the start of testing and food consumption was tested in the absence of water. Finally, in Part 4 water consumption was tested in the absence of food in non-deprived subjects.

Details of food and water availability are summarised in Table 1.

At the start of testing all subjects were presented with a pre-weighed amount of food and/or a pre-weighed water bottle, as appropriate. Food and water bottles were re-weighed after intervals of 1- and 2-hours. Care was taken to collect food spillage (which was minimal) and bottle spouts contained a small ball-bearing to minimise water spillage. Cumulative food and water consumptions were subjected to independent analyses of variance, subsequent tests of simple main effects were employed where appropriate.

Results

5-HT hypophagia and 5-HT hyperdipsia were both apparent during concurrent testing (Parts 1 and 2). Food consumption was suppressed by 5-HT in subjects tested following a period of food-deprivation (Fig. 1.1), $F(1,10)=25.50$, $p<0.001$, and in free-feeding subjects tested at the start of the dark phase (Fig. 1.2), $F(1,10)=15.42$, $p<0.005$. The water consumption of the previously food-deprived subjects (Fig. 1.1) was enhanced, but only during the second hour of testing (drug × interval interaction, $F(1,10)=10.84$, $p<0.01$),

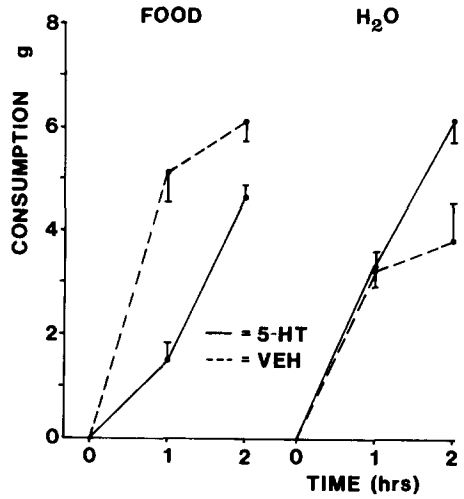

FIG. 1.1. Mean (±S.E.M.) cumulative food (lab chow) and water consumption 1 and 2 hours after treatment with 5-HT (2 mg/kg) or vehicle (distilled water). All subjects were 18-hour food-deprived at the start of testing.

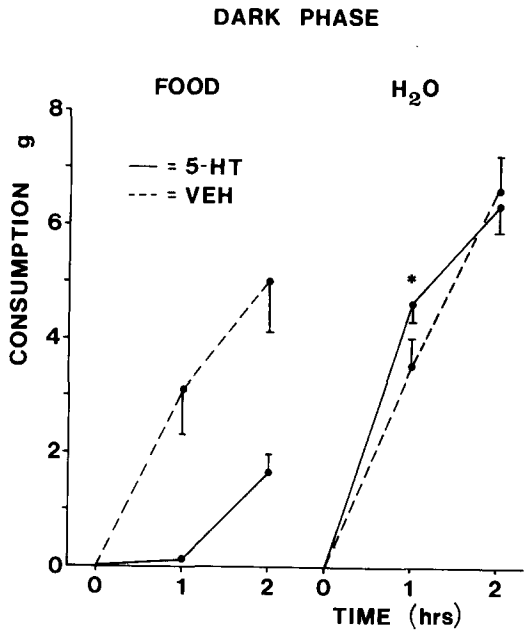

FIG. 1.2. Mean (±S.E.M.) cumulative food (lab chow) and water consumption 1 and 2 hours after treatment with 5-HT (2 mg/kg) or vehicle (distilled water). Subjects were non-deprived and testing commenced at the start of the dark phase of the light/dark cycle. Star indicates a significant difference ($p<0.05$) from the control condition as revealed by a test of simple main effects.

whereas the water consumption of the free-feeding subjects (Fig. 1.2) was enhanced, but only during the first hour of testing (drug × interval interaction, $F(1,10)=13.88$, $p<0.005$).

Food consumption in the absence of water (Part 3, see Fig. 1.3) was suppressed by 5-HT, $F(1,16)=38.10$, $p<0.001$, and water consumption in the absence of food (Part 4, see

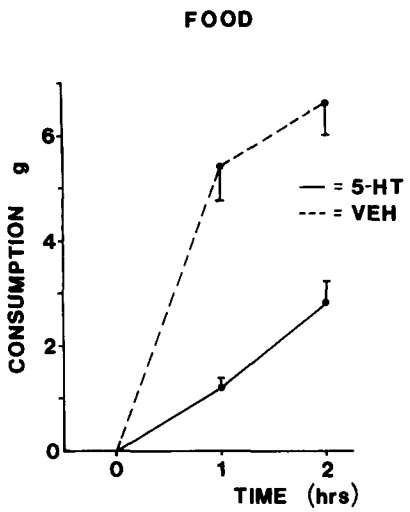

FIG. 1.3. Mean (±S.E.M.) cumulative food (lab chow) consumption 1 and 2 hours after treatment with 5-HT (2 mg/kg) or vehicle (distilled water). Subjects were 18-hour food-deprived at the start of testing and no water was available during the test period.

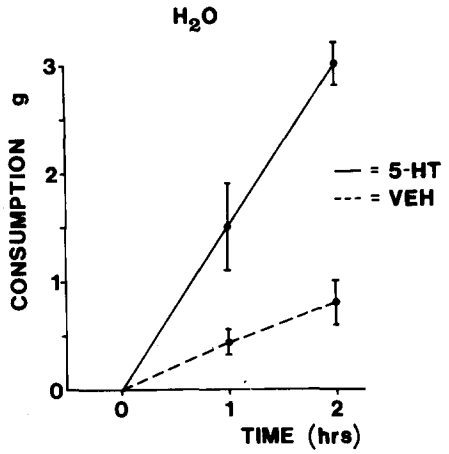

FIG. 1.4. Mean (±S.E.M.) cumulative water consumption 1 and 2 hours after treatment with 5-HT (2 mg/kg) or vehicle (distilled water). Subjects were non-deprived except for the absence of food during the drinking test.

Fig. 1.4) was reliably enhanced by 5-HT, $F(1,10)=26.25$, $p<0.001$.

Discussion

Treatment with 5-HT reduced feeding regardless of the level of food-deprivation and regardless of the presence or absence of water during testing. These results confirm that 5-HT reliably induces hypophagia and rule out the possibility that 5-HT hypophagia can be explained solely in terms of response competition from drinking.

The effects of 5-HT on water consumption were found to be more variable than its effects on feeding. In Part 4 (where drinking was assessed in non-deprived rats tested in the absence of food) water consumption was reliably enhanced by 5-HT. However, when drinking was tested in free-feeding rats, 5-HT hyperdipsia was only evident during the first hour of testing. Subjects tested following food-deprivation, on the other hand, only exhibited hyperdipsia during the second hour of food access. These results indicate that 5-HT hyperdipsia is sensitive to changes in the level of food-deprivation. This is not surprising given that food-deprived rats exhibit reduced water consumption during thier period of deprivation and both food-deprived and non-deprived rats exhibit prandial drinking when given food [14]. The presence of food in the stomach is also known to influence the level of peripheral 5-HT [2].

It seems reasonable to assume, therefore, that the variability in the time-course of 5-HT hyperdipsia reflects an interaction of drinking induced by 5-HT with prandial drinking and changes in water consumption resulting from food-deprivation. What these results show is that 5-HT hyperdipsia is most reliably demonstrated in non-deprived rats that are not feeding.

EXPERIMENT 2—EFFECTS OF METHYSERGIDE PRETREATMENT ON 5-HT HYPOPHAGIA AND HYPERDIPSIA

The previous experiment indicated that 5-HT hypophagia cannot be explained solely in terms of response competition from 5-HT hyperdipsia. A recent study [4] which included dose-response studies of 5-HT hypophagia and hyperdipsia revealed that low-dose 5-HT hypophagia had an early onset and relatively short duration, whilst 5-HT hyperdipsia had a later time of onset and a longer duration. These observations might indicate that 5-HT hypophagia and hyperdipsia are mediated by different physiological mechanisms.

The present experiment attempted to assess the importance of peripheral post-synaptic 5-HT receptor stimulation in 5-HT hypophagia and hyperdipsia by investigating the effects of pretreatment with the 5-HT antagonist methysergide. Previous studies of the effects of methysergide on 5-HT hyperdipsia have produced conflicting results; one reporting that 5-HT hyperdipsia was blocked by methysergide [8], another reporting that it was not [4]. The present study aimed to resolve this conflict by investigating the ability of methysergide to block 5-HT hyperdipsia, under circumstances which most reliably reveal the hyperdipsic action of 5-HT. In view of the results presented in Experiment 1 this study investigated the effects of methysergide on 5-HT hyperdipsia in non-deprived rats. The investigation of 5-HT hypophagia however, used rats which had been habituated to a food-deprivation schedule, in order to stabilise baseline food consumption prior to repeated feeding tests.

Method

Twenty-eight male Lister hooded rats (235–340 g) served as subjects. In order to stabilise baseline food intakes prior to repeated food consumption tests, twelve of these subjects were habituated to an 18-hour food-deprivation schedule for 7 days prior to the start of testing. These subjects were divided into 2 groups (n=6) matched for 6-hour food consumption. Both groups were tested for 2-hour food consumption twice; once starting 15-minutes after administration of 5-HT (2 mg/kg, SC) and once 15-minutes after vehicle (distilled water) injection. Water was available during testing, but consumption was not recorded. Treatment order was counterbalanced within groups and 48-hours were

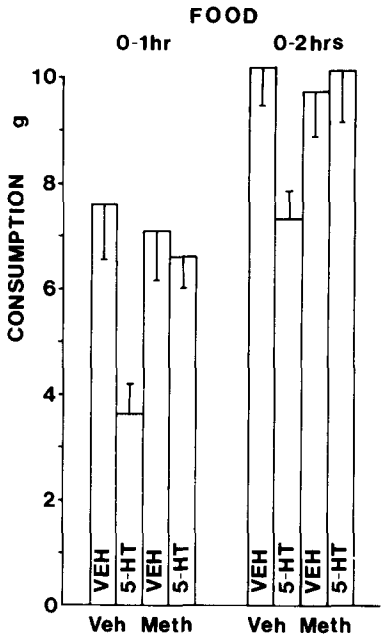

FIG. 2.1. Mean (±S.E.M.) cumulative food (lab chow) consumption following pretreatment with methysergide (3 mg/kg) (Meth) or its vehicle (distilled water) and treatment with 5-HT (2 mg/kg) or its vehicle (distilled water). Subjects were habituated to an 18-hour food-deprivation schedule prior to the start of testing. Intake was recorded after intervals of 1 and 2 hours.

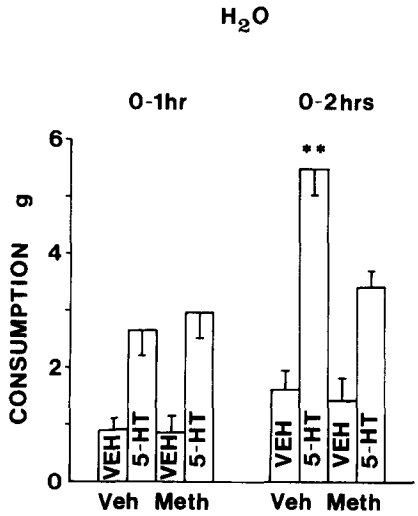

FIG. 2.2. Mean (±S.E.M.) cumulative water consumption following pretreatment with methysergide (3 mg/kg) (Meth) or its vehicle (distilled water) and treatment with 5-HT (2 mg/kg) or its vehicle (distilled water). Subjects were non-deprived except that food was withheld during drinking tests. Water consumption was recorded after intervals of 1 and 2 hours. Stars indicate a significant difference ($p<0.001$) from the group receiving the methysergide + 5-HT combination, as revealed by a test of simple main effects.

allowed between tests. On test days one group received a pretreatment of methysergide bimaleate (Sandoz) at a dose of 3 mg/kg (IP) calculated as the salt, 45-minutes before the start of food access [4]; the other group received vehicle pretreatment. Food consumption was recorded at hourly intervals for two hours.

The remaining sixteen (free-feeding) subjects received two 2-hour drinking tests; one test commenced 15-minutes after administration of 5-HT (2 mg/kg, SC) the other followed a vehicle injection. Treatment order was counterbalanced within groups and 48-hours were allowed between tests. Prior to the start of testing subjects were randomly allocated to two groups (n=8); one group received methysergide (3 mg/kg, IP) pretreatment 45-minutes prior to the start of testing, the other received vehicle pretreatment. Food and water were removed immediately before pretreatment and 15-minutes after the second injection subjects were given access to water. Consumption was recorded at hourly intervals for two hours.

Cumulative food and water consumptions were subjected to independent analyses of variance.

Results

5-HT hypophagia. As in Experiment 1, food consumption (Fig. 2.1) was reduced by 5-HT, $F(1,10)=10.42, p<0.01$. The overall difference between vehicle and methysergide pretreated groups was not significant, $F(1,10)=2.61, p>0.10$, but methysergide pretreatment did attenuate the hypophagic effect of 5-HT (drug × pretreatment interaction, $F(1,10)=10.02, p<0.05$).

5-HT hyperdipsia. As in Experiment 1, water consumption (Fig. 2.2) was increased by 5-HT, $F(1,14)=83.98$, $p<0.001$, and methysergide pretreatment attenuated 5-HT hyperdipsia during the second hour of testing (drug × pretreatment × interval interaction, $F(1,14)=13.38, p<0.001$), as confirmed by tests of simple main effects (see Fig. 2.2).

Discussion

The complete failure of methysergide to block 5-HT hyperdipsia during the first hour of the drinking test was unexpected. This result may indicate that the onsets of 5-HT hypophagia and hyperdipsia require different levels of receptor occupancy, or alternatively could result from an early action of 5-HT at sites other than classical 5-HT receptors.

Nevertheless, the fact that pretreatment with methysergide blocked 5-HT hypophagia and during the second hour of testing attenuated 5-HT hyperdipsia supports the suggestion that both the hypophagic and hyperdipsic effects of 5-HT are dependent upon post-synaptic peripheral 5-HT receptor stimulation (particularly as the ability of methysergide to cross the blood-brain barrier has been questioned [6]).

EXPERIMENT 3—EFFECTS OF PROPRANOLOL PRETREATMENT ON 5-HT HYPOPHAGIA AND 5-HT HYPERDIPSIA

Drinking induced by beta-adrenergic stimulation (isoproterenol) is mediated by the renin-angiotensin system and can be blocked by pretreatment with the beta-adrenergic antagonist propranolol [7]. An elegant series of experiments [9] has shown that 5-HT hyperdipsia is mediated by stimulation of the renin-angiotensin system and can also be blocked

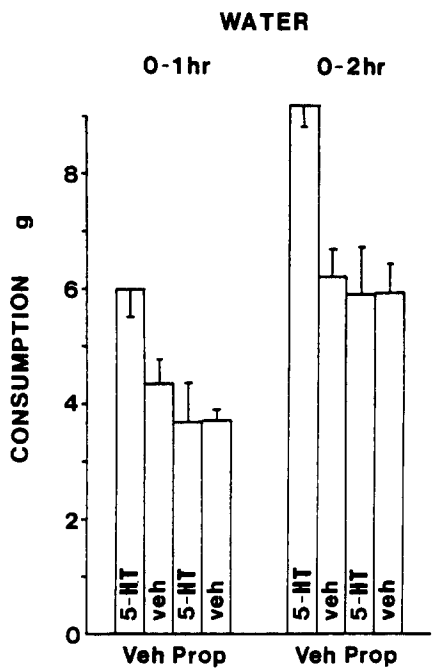

FIG. 3.1. Mean (±S.E.M.) cumulative water consumption following pretreatment with propranolol (5 mg/kg) (Prop) or its vehicle (distilled water) and treatment with 5-HT (2 mg/kg) or its vehicle (distilled water). Consumption was recorded at intervals of 1 and 2 hours and subjects were habituated to an 18-hour food-deprivation schedule.

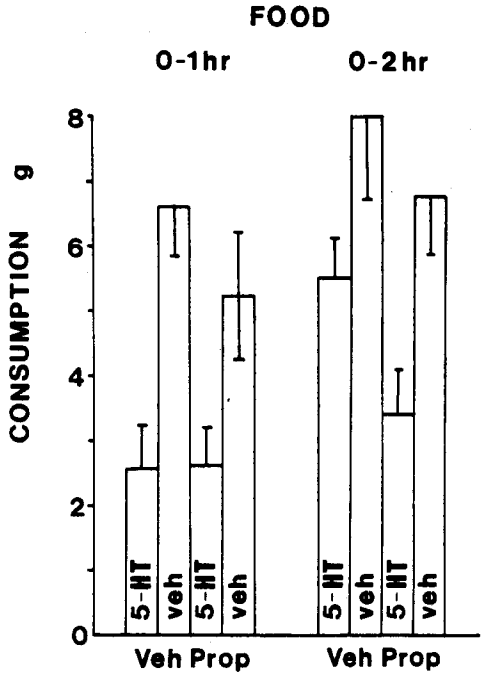

FIG. 3.2. Mean (±S.E.M.) cumulative food (lab chow) consumption following pretreatment with propranolol (5 mg/kg) (Prop) or its vehicle (distilled water) and treatment with 5-HT (2 mg/kg) or its vehicle. Consumption was recorded at intervals of 1 and 2 hours and subjects were habituated to an 18-hour food-deprivation schedule.

by propranolol pretreatment. This indicates that 5-HT acts at some point prior to beta-adrenergic receptor stimulation. Very little is known about the physiological mechanism involved in 5-HT hypophagia, but if 5-HT hyperdipsia and hypophagia are mediated by different mechanisms, then 5-HT hypophagia might not be blocked by propranolol pretreatment. The present experiment investigates this possibility.

Method

Twelve male Lister hooded rats (185–350 g) served as subjects. One week prior to the start of testing all subjects were habituated to an 18-hour food-deprivation schedule. Water was available constantly. Subjects were allocated into two groups (n=6), both of which received two tests of food and water consumption. One test followed 15-minutes after 5-HT (2 mg/kg, SC) treatment, the other followed vehicle treatment. Treatment order was counterbalanced within groups and 72-hours were allowed between tests. One group received propranolol (5 mg/kg, IP) pretreatment 45-minutes prior to the start of testing, the other received a vehicle (distilled water) injection. The dose of propranolol was selected following a dose-response study to determine the maximum dose of propranolol which, in its own right, would not alter food or water consumption. Food and water consumption were recorded at hourly intervals during the 2-hour test periods. Cumulative feeding and drinking data were subjected to independent analyses of variance.

Results

Water consumption (Fig. 3.1) was enhanced by 5-HT, $F(1,10)=5.51$, $p<0.05$, and reduced by propranolol pretreatment, $F(1,10)=14.89$, $p<0.001$, but the drug × pretreatment interaction was also significant, $F(1,10)=5.83$, $p<0.05$. Subsequent analysis of simple main effects revealed that propranolol reduced 5-HT hyperdipsia at both intervals ($ps<0.025$) without changing the drinking of vehicle-treated subjects.

A similar analysis of cumulative feeding data (Fig. 3.2) revealed a 5-HT-induced suppression of food consumption, $F(1,10)=22.18$, $p<0.001$. There were no other significant effects involving factors of drug or pretreatment ($ps>0.05$).

Discussion

Propranolol pretreatment blocked 5-HT hyperdipsia, but did not block 5-HT hypophagia. These results support the suggestion [9] that 5-HT hyperdipsia is mediated by stimulation of the renin-angiotensin system, but indicate that some other mechanism must be involved in 5-HT hypophagia.

A previous study [10] reported that propranolol pretreatment (6.2 mg/kg) did reverse the hypophagic action of a low dose (1 mg/kg) of 5-HT. However, propranolol is known to have a weak antagonist action at 5-HT receptors [15]. It is possible, therefore, that the block of 5-HT hypophagia by propranolol [10] was a result of 5-HT antagonism rather than beta-adrenergic blockade. The results of the present study indicate that the 5-HT blocking properties of propranolol (5 mg/kg) were not great enough to reverse the hypophagic action of a larger dose (2 mg/kg) of 5-HT. It is unlikely, therefore, that the propranolol-induced reversal of 5-HT hyperdipsia can be explained in terms of 5-HT antagonism rather than beta-adrenergic receptor blockade.

GENERAL DISCUSSION

The results of Experiment 1 revealed that 5-HT

hypophagia is a robust phenomenon which can be demonstrated in free-feeding rats and in rats tested following food-deprivation, both with and without access to water. The hyperdipsic response to 5-HT was less reliable, being sensitive to alterations in the length of the preceding period of food-deprivation, when tested in feeding rats. Nonetheless 5-HT hyperdipsia was reliably demonstrated in non-deprived rats, when tested in the absence of food.

Pretreatment with methysergide blocked 5-HT hypophagia and attenuated 5-HT hyperdipsia, thus confirming that both effects are mediated via stimulation of post-synaptic 5-HT receptors. The involvement of neuronal 5-HT in these effects is also supported by a series of experiments [3] which revealed alterations in the consummatory effects of 5-HT following pretreatment with xylamidine (a peripheral 5-HT antagonist), clorgyline (a specific type A monoamine oxidase inhibitor) and LM 5008 (a 5-HT reuptake inhibitor). The hyperdipsic action of 5-HT was also blocked by propranolol pretreatment, a result which supports the suggestion [9] that 5-HT hyperdipsia is mediated via stimulation of the renin-angiotensin system.

Propranolol pretreatment did not block 5-HT hypophagia in the same experiment in which a propranolol block of 5-HT hyperdipsia was demonstrated. This result provides support for the suggestion that the hyperdipsic and hypophagic responses to 5-HT are mediated by different physiological mechanisms. Further evidence for a dissociation between 5-HT hypophagia and hyperdipsia derives from studies of vagotomised rats and studies using MK 421 (which prevents conversation of angiotensin I to angiotensin II). Vagotomy has been shown to reduce 5-HT hyperdipsia [16] and enhance [5], or fail to alter 5-HT hypophagia [16]. MK 421 has been shown to block 5-HT hyperdipsia, but not 5-HT hypophagia (Montgomery and Burton, in press).

The physiological mechanisms involved in 5-HT hypophagia remain to be identified, but there is evidence which suggests that 5-HT hypophagia is accompanied by a reduction in the incentive value of food-related stimuli [11]. Le Magnen (in press) has suggested that palatability is determined by the level of cephalic phase insulin secretion and 5-HT has been shown [17] to inhibit insulin secretion. Consequently, it is possible that 5-HT hypophagia is a result of inhibition of cephalic phase insulin secretion.

ACKNOWLEDGEMENTS

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REFERENCES

1. Bulbring, E. and A. Crema. The release of 5-hydroxytryptamine in relation to pressure exerted on the intestinal mucosa. *J Physiol (Lond)* **192:** 823–846, 1959.
2. Drapanas, T., J. C. McDonald and J. D. Stewart. Serotonin release following instillation of hypertonic glucose into the proximal intestine. *Ann Surg* **156:** 528–536, 1962.
3. Fletcher, P. J. Unpublished D. Phil thesis, Sussex University, 1984.
4. Fletcher, P. J. and M. J. Burton. Effects of manipulations of peripheral serotonin on feeding and drinking. *Pharmacol Biochem Behav* **20:** 835–840, 1984.
5. Fletcher, P. J. and M. J. Burton. The anorectic effect of peripherally administered serotonin is enhanced by vagotomy. *Physiol Behav* **34:** 861–866, 1985.
6. Haigler, H. J. and G. K. Aghajanian. Peripheral serotonin antagonists: Failure to antagonise serotonin in brain areas receiving a prominent serotonergic input. *J Neural Transm* **35:** 257–273, 1974.
7. Houpt, K. A. and A. N. Epstein. The complete dependence of beta-adrenergic drinking on the renal dipsogen. *Physiol Behav* **7:** 897–902, 1971.
8. Kikta, D. C., R. M. Threatte, C. C. Barney, M. J. Fregly and J. E. Greenleaf. Peripheral conversion of L-5-hydroxytryptophan to 5-HT induces drinking in rats. *Pharmacol Biochem Behav* **14:** 889–893, 1981.
9. Kikta, D. C., C. C. Barney, R. M. Threatte, M. J. Fregly, N. E. Rowland and J. E. Greenleaf. On the mechanism of serotonin-induced dipsogenesis in the rat. *Pharmacol Biochem Behav* **19:** 519–525, 1983.
10. Lehr, D. and W. Goldman. Continued pharmacologic analysis of consummatory behaviour in the albino rat. *Eur J Pharmacol* **23:** 197–210, 1973.
11. Montgomery, A. M. J. and M. J. Burton. Effects of peripheral 5-HT on consumption of flavoured solutions. *Psychopharmacology* **88:** 262–266, 1986.
12. Oldendorf, W. F. Brain uptake of radiolabelled amino acids, amines and hexoses after arterial injection. *Am J Physiol* **221:** 1629–1639, 1971.
13. Pollock, J. D. and N. E. Rowland. Peripherally administered serotonin decreases food intake in rats. *Pharmacol Biochem Behav* **15:** 179–183, 1981.
14. Richter, C. P. Animal behaviour and internal drives. *Q Rev Biol* **2:** 307–343, 1927.
15. Schecter, Y. and M. Weinstock. Beta-adrenoceptor blocking agents and responses to adrenaline and 5-hydroxytryptamine in isolated rat stomach and uterus. *Br J Pharmacol* **19:** 283–287, 1974.
16. Simansky, K. J., K. A. Bourbonais and G. P. Smith. Abdominal vagotomy reduces the dipsogenic but not the anorexic action of systemic serotonin in rats. *Soc Neurosci Abstr* **8:** 605, 1982.
17. Telib, M., S. Raptis, K. E. Schroder and E. F. Pfeiffer. Serotonin and insulin release in vitro. *Diabetologia* **4:** 253–256, 1968.