brain 5-HT and 5-HIAA and preventing 5-HT accumulation after pargyline. Thus D-PCPA, like its L-isomer, inhibits 5-HT synthesis. As previously shown for the racemic compound (Koe & Weissman, 1966), the depletion of brain 5-HT and 5-HIAA induced by D- or L-PCPA was maximal after a long latency and persisted for several days. These results suggest that the inhibition of 5-HT synthesis by either isomer is an irreversible process and depends on the slow formation of an active metabolite.

Since D-amino acids are not incorporated into proteins (Berg, 1959), the incorporation of D-PCPA into tryptophan hydroxylase is unlikely. A conversion of D-PCPA *in vivo* to L-PCPA is theoretically possible via its deamination by D-amino acid oxidase (Blaschko & Stiven, 1950) to *p*-chlorophenylpyruvic acid followed by transamination of the latter to L-PCPA (Spencer & Brock, 1962).

However, this is difficult to reconcile with the fact D-PCPA decreases the level of 5-HT and 5-HIAA at the same rate, to the same extent, and for the same time as the L-isomer.

These considerations lead to the conclusion that stereoisomerism is not essential for PCPA-induced inhibition of 5-HT synthesis.

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Reduction of food intake by apomorphine: a pimozide-sensitive effect

Some of the central effects of amphetamine are the result of an enhancement of dopaminergic nerve activity (Carlsson, 1970). Apomorphine, a selective stimulant of dopamine receptors (Ernst, 1967; Andén, Rubenson & others, 1967), like amphetamine, is capable of causing stereotyped (Ernst, 1965, 1969) or aggressive (McKenzie & Karpowicz, 1970) behaviour in rodents, hypo- or hyperthermia according to species (Kruk, 1972; Hill & Horita, 1972), and increased motor activity (Randrup & Munkvad, 1968).

We have investigated the reported similarities between dopamine and amphetamine, including the feeding behaviour. While the anorexic effect of amphetamine is well known (Ulrich, 1937; Nathanson, 1937), less is known about the involvement of dopamine in the eating response, although there is evidence of a stimulatory role for brain catecholamines (Booth, 1968; Slangen & Miller, 1969). The effect of direct stimulation of central dopamine receptors by apomorphine was examined on the

feeding behaviour of food-deprived rats and compared with that evoked by amphetamine administration.

Charles River C.D. rats (240–250 g) were placed in single cages and were trained for ten days to take food during 4 out of 24 h (from 1 p.m. to 5 p.m.) while free access to water was allowed. On the day of the experiment a weighed meal was given 10 min after drug treatments and the amount of food ingested was recorded each hour for 2 h.

Each of 4 doses of apomorphine HCl (Sandoz, Basel) drastically reduced food consumption during the first hour of access to food. This effect was directly proportional to the dose of apomorphine: a dose of 2·0 mg kg^{-1} (i.p.) induced the maximal effect, but a dose as low as 0·25 mg kg^{-1} caused a significant reduction of food intake. The action of apomorphine was short-lasting since it did not last into the second hour.

There was a clearcut reduction in food intake following (+)-amphetamine sulphate (Recordati, Milano) administration, which was maximal with a dose of 5·0 mg kg^{-1} (i.p.) and present after 2·5, 1·25 and 0·62 mg kg^{-1}. The effect of amphetamine was much reduced during the second hour (Table 1). Both apomorphine and amphetamine induced a specific stereotypic pattern throughout but this was not evident with the lower dose of apomorphine.

In another experiment rats received a solution of pimozide (Janssen Pharm., Beerse) (500 μg kg^{-1} in dilute tartaric acid) 3 h before the apomorphine or amphetamine. This pretreatment almost completely abolished the effect of apomorphine (1·0, 0·5, 0·25 mg kg^{-1}) on food consumption and markedly reduced the action of the higher dose of the drug (2·0 mg) and only at this dose was there a significant difference from the control value. Similarly, pimozide was effective in counteracting anorexia induced by amphetamine (2·5, 1·25 and 0·62 mg kg^{-1}); its effect was only partial when amphetamine was given at the 5·0 mg dose which again was the only dose effecting a significant decrease. Pimozide did not affect food intake.

Thus apomorphine is even more effective than amphetamine in reducing food consumption; a dose as low as 0·25 mg of apomorphine had the same efficacy as a dose of amphetamine almost three times higher (0·62 mg). The effect on food intake induced by either drug could be inhibited by pimozide, which at the dose used selectively affects dopamine receptors (Janssen, Niemegeers & others, 1968;

Table 1. *Effect of apomorphine and (+)-amphetamine on food intake in the rat.* Rats received an intraperitoneal injection of either saline or apomorphine or (+)-amphetamine 10 min before access to food. Drug doses are expressed as free base. 10 animals per group were used. * = $P < 0{\cdot}05$, ** = $< 0{\cdot}01$, *** = $< 0{\cdot}001$ relative to controls. The significance of the differences between groups was calculated according to Student's *t* test.

Treatment	Dose mg kg^{-1} i.p.	Food intake (g per 100 g) mean ± s.e. 1st hour	% Control = 100	2nd hour	% Control = 100
Saline	—	1·39 ± 0·25	100	0·83 ± 0·29	100
Apomorphine	2·0	0·07 ± 0·01***	5·4	0·40 ± 0·11	48·2
,,	1·0	0·11 ± 0·01***	7·9	0·81 ± 0·19	97·6
,,	0·5	0·42 ± 0·18**	30·2	0·80 ± 0·19	96·4
,,	0·25	0·69 ± 0·09*	49·6	1·45 ± 0·22	175·0
Amphetamine	5	0·016 ± 0·01***	1·2	0·10 ± 0·02**	12·0
,,	2·5	0·10 ± 0·07***	7·2	0·29 ± 0·10	34·9
,,	1·25	0·27 ± 0·09***	19·4	0·50 ± 0·13	60·2
,,	0·62	0·70 ± 0·07*	50·4	0·73 ± 0·09	88·0

Andén, Butcher & others, 1970). The findings support the possibility that dopaminergic neurons in the cns mediate the effect of apomorphine on food intake in the rat. There is a fairly consistent body of evidence for the participation of neuronal adrenergic receptors in the control of food intake in rats (Booth, 1968; Slangen & Miller, 1969), although the role of individual catecholamines in the control of feeding remains unclear.

Electrolytic hypothalamic lesions are known to induce aphagia in rats (Morgane, 1961). Zigmond & Stricker (1972) have suggested that the cause of the eating behaviour might be the chemical (Ungerstedt, 1971) or mechanical (Gold, 1967) interruption of a nigrostriatal pathway transversing the hypothalamus, that includes a large dopamine fibre system (Ungerstedt, 1971). Therefore, a stimulatory role in the feeding mechanisms was envisaged for brain dopaminergic neurons (Zigmond & Stricker, 1972). The present results do not favour this view and suggest instead an inhibitory role for brain dopamine in feeding behaviour. It has been recently proposed (Ungerstedt, 1971) that the aphagia induced by amphetamine-like drugs might be due to the release of dopamine from the dopaminergic nerve terminals in the striatum (Fuxe & Ungerstedt, 1968). The observed counteraction of amphetamine-anorexia by pimozide is consistent with the existence of a dopaminergic mechanism in the effect of amphetamine on food intake.

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