drome of destructive self-grooming emerged.

When haloperidol was administered (phase II) destructive self-grooming ceased abruptly; checking and social contact were unaltered while inactivity was increased further ($P<.001$). Locomotion was initially further decreased ($P<.01$) but returned to normal levels by the end of phase II.

When haloperidol was withdrawn (phase III) checking was initially increased ($P<.001$) but then returned to normal (cf phase I). Destructive self-grooming did not reappear. Locomotion and social contact remained unchanged while inactivity was comparable to that during phase I.

During phase IV when no drugs were administered, all behaviours including social contact were within the normal range except inactivity which was elevated initially ($P<.05$).

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Effects of spiperone on feeding parameters in the rat and interactions with (+)-amphetamine, mazindol or (±)-fenfluramine

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Spiperone is a neuroleptic with a marked dopamine receptor blocking action (Andén, Butcher, Corrodi, Fuxe & Ungerstedt, 1970), and it has been employed as a dopamine antagonist in feeding experiments (Cooper & Sweeney, 1978; Heffner, Zigmond & Stricker, 1977; Rolls, Rolls, Kelly, Shaw, Wood & Dale, 1974). Previously, we have described a feeding test in which effects of drug treatments are described not only in terms of the amount of food intake, but also in terms of the duration of feeding and the rate at which food is consumed (Cooper & Francis, 1978). This report describes the behavioural effects of spiperone in this test, administered either alone or in combination with the anorectic compounds, (+)-amphetamine, mazindol or (±)-fenfluramine.

The subjects were 144 naive, male, adult black-hooded rats, weighing 220–260 g. On the day before testing, food was removed at 17.00 h, and feeding tests were run the following morning. Each rat was tested for 10 min in a test-cage with familiar food pellets available. The rats were first divided into 3 groups which determined the first injection given i.p. 120 min before the feeding test: (i) tartaric acid (0.1 M, control injection), (ii) spiperone (0.06 mg/kg), (iii) spiperone (0.10 mg/kg). Each group was then subdivided into 6 groups (n = 8/group): (i) mazindol (0.065 mg/kg), (ii) mazindol (1.25 mg/kg), (iii) (+)-amphetamine (0.5 mg/kg), (iv) (+)-amphetamine (1.0 mg/kg), (v) fenfluramine (4.0 mg/kg), (vi) control vehicle injection. These groups determined the second injection given 30 min before the test (mazindrol, s.c.; (+)-amphetamine, (±)-fenfluramine, i.p.).

Spiperone shortened the latency to begin feeding ($F = 10.63$, d.f. 2,63, $P<0.001$), alone and in combination with (+)-amphetamine and mazindol; in contrast, it prolonged the latency in combination with (±)-fenfluramine. Spiperone prolonged the duration of feeding ($F = 11.15$, d.f. 2,63, $P<0.001$), alone and in combination with (+)-amphetamine and mazindol, but at the higher dose (0.10 mg/kg) it significantly reduced the feeding duration in combination with (±)-fenfluramine. As expected, (+)-amphetamine and mazindol markedly prolonged the latency to feed ($F + 10.30$, d.f. 2,63, $P<0.001$; $F = 37.49$, d.f. 2.63, $P<0.001$, respectively), and shortened the duration of feeding ($F = 29.62$, d.f. 2,63, $P<0.001$; $F = 50.50$, d.f. 2,63, $P<0.001$). However, (±)-fenfluramine (4.0 mg/kg) exerted only minor effects on latency and feeding duration. Spiperone markedly reduced the rate of eating ($t = 3.05$, 14 d.f., $P<0.005$), an action it shared with (±)-fenfluramine ($t = 3.23$, 14 d.f., $P<0.005$). Their joint effect on eating rate was additive. In contrast, (+)-amphetamine and mazindol significantly increased eating rate, an effect that was antagonized in the presence of spiperone. All 3 anorectic drugs reduced the amount of food-intake significantly; mazindol and (+)-amphetamine by reducing eating duration but not rate, (±)-fenfluramine by reducing rate but not eating duration. Spiperone also significantly reduced food-intake ($F = 3.46$, d.f. 2,63, $P<0.04$), by reducing eating rate and not by reducing eating duration. Spiperone counteracted the anorectic

effects of mazindol and (+)-amphetamine by prolonging the feeding duration, whilst strongly enhancing that of (±)-fenfluramine, particularly by an additional reduction in eating rate.

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Effect of cooling on efflux of [^{3}H]-noradrenaline in canine cutaneous veins

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In the dog saphenous vein, moderate cooling augments the constrictor response to exogenous noradrenaline (Vanhoutte & Shepherd, 1970). This augmented response is due to the increased affinity of the alpha-adrenoceptors of the venous smooth muscle cells for the catecholamine (Janssens & Vanhoutte, 1978). In the same preparation, the contractile response to sympathetic nerve stimulation is also augmented by moderate cooling (Vanhoutte & Shepherd, 1970), although in veins previously incubated with [^{3}H]-noradrenaline the overflow of labelled transmitter is depressed (Vanhoutte & Verbeuren, 1976). The present experiments were performed to try to explain this discrepancy.

Isolated strips of dogs' saphenous veins were incubated with [^{3}H]-noradrenaline, mounted for isometric tension recording, and superfused with Krebs-Ringer solution (Vanhoutte, Lorenz & Tyce, 1973). The amounts of intact labelled transmitter and its metabolites present in the superfusing fluid were determined by column chromatography (Verbeuren, Coen & Vanhoutte, 1977). Since the neuronal uptake of noradrenaline is depressed by moderate cooling (Janssens & Vanhoutte, 1978), all experiments were performed in the presence of cocaine (3×10^{-5}M).

In basal conditions, cooling from 37 to 24°C caused a decrease in tension and in the efflux of [^{3}H]-noradrenaline and its metabolites; this was seen both in the control solution and in the presence of phentolamine (3×10^{-6}M) and yohimbine (3×10^{-7}M). Electrical stimulation (2 Hz) caused an increase in tension and in efflux of tritiated compounds; cooling (from 37 to 24°C) augmented the contractile response, but depressed the efflux of tritiated transmitter and its metabolites. In the presence of phentolamine or yohimbine, cooling still decreased the efflux of tritiated compounds. Increasing the K^+ concentration from 5.9 to 50 and 120 mEq/l caused release of [^{3}H]-noradrenaline; in these conditions cooling from 37 to 24°C decreased the efflux of [^{3}H]-noradrenaline and its metabolites significantly more than during electrical stimulation.

The present experiments indicate that: (1) unlike the augmented response to exogenous noradrenaline, the decrease in neurotransmitter overflow caused by cooling cannot be explained by an increased affinity of the prejunctional alpha-adrenoceptor, since it persisted in the presence of both a specific (yohimbine) and a non-specific (phentolamine) presynaptic alpha-adrenergic antagonist; and (2) since the contractile response to nerve stimulation is augmented to the same extent by cooling as that to exogenous noradrenaline, the decrease in tritiated overflow noted in the present experiments with cooling may not reflect the effect of the latter on the synaptic cleft concentration of the adrenergic transmitter.

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