Effects of Spiperone on Feeding Performance in a Food Preference Test

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Abstract. Spiperone reduced latency to feed and prolonged the total duration of feeding in a food-preference test in which novel and familiar foods were presented simultaneously to food-deprived rats. The increase in feeding duration could be accounted for in terms of an increase in time devoted to eating the novel foods, leaving the time devoted to eating the familiar food relatively unaltered. However, closer analysis of the data revealed that, at the level of mean duration of individual eating episodes, spiperone prolonged the eating-episode duration equally for both novel and familiar foods. This apparent paradox was resolved by noting that whilst spiperone did not alter the number of eating episodes in the test, it did alter the ratio of eating episodes in favour of novel foods. The data was incorporated into a control system model which depicts actions of spiperone in the food-preference situation with total eating duration as the final behavioural output.

Key words: Control system model — Feeding duration — Food-preference test — Novelty — Spiperone

Spiperone is a neuroleptic compound with a marked dopamine receptor blocking action (Andén et al., 1970). Recent work indicates that spiperone displays a specific high affinity for neuroleptic receptors in rat brain where receptor sites appear to be of a mainly, but not exclusively, dopaminergic nature (Laduron et al., 1978a, b; Leysen et al., 1978). There is considerable interest in the role of dopaminergic mechanisms in feeding (Blundell and Latham, 1979; Hoebel, 1978) and spiperone has been employed as a dopamine antagonist in feeding experiments (e.g. Heffner et al., 1977).

This paper is directed not towards neurochemical actions of spiperone in relation to feeding, but to an analysis of the behavioural effects of spiperone as they affect feeding activity. So far two apparently opposite effects of spiperone on food intake have been described. Firstly, at higher doses (above 0.10 mg/kg) spiperone reduces the amount of food intake (Cooper and Sweeney, 1978; Heffner et al., 1977; Rolls et al., 1974). At lower doses, however, it is possible to show that spiperone attenuates the anorexic effects of the dopamine agonists apomorphine, dopa, cocaine, methylphenidate (Heffner et al., 1977) and mazindol (Cooper and Sweeney, 1978, 1979). The first effect, to depress food intake, may be secondary to a relatively non-specific depressant action since locomotor activity (Cooper and Sweeney, 1978), lever pressing for food (Rolls et al., 1974) and the rate of eating (Cooper and Sweeney, 1979) can also be markedly reduced. The second effect, however, is behaviourally more specific (Cooper and Sweeney, 1978) and may point to an action of spiperone which facilitates feeding behaviour.

The main aim of the present experiment was to look for evidence of a facilitatory effect of spiperone on feeding behaviour in a food-preference test. In this test (Cooper and Crummy, 1978; Rolls and Rolls, 1973) the rat is presented simultaneously with novel and familiar foods, and its choice behaviour recorded. The test is sensitive to effects of benzodiazepines which tend to reduce latency to feed and also to prolong the time devoted to feeding (Cooper and Crummy, 1978; Cooper and Skan, unpublished results), effects consistent with other evidence that benzodiazepines facilitate feeding behaviour (Bainbridge, 1968; Soubrié et al., 1975). The effects of spiperone in any form of food-preference situation have not been previously reported; neither have its effects been recorded with time measures rather than amount of food intake. If spiperone does facilitate feeding behaviour we predicted that, like benzodiazepines, it would tend to reduce the latency to feed...
and to prolong the time devoted to feeding. However, we had no basis for predicting the effect spiperone might have on the choice of novel or familiar food.

The results confirmed that spiperone, like the benzodiazepines in the food-preference test, reduced latency to feed and prolonged the duration of feeding. They also revealed an important dissimilarity between spiperone and the benzodiazepines. A further aim of this study was to use data from the experiment to help formulate a control system model which depicts explicitly the detailed behavioural effects of the drug in the experimental test situation.

Materials and Methods

Animals. The subjects were 21 naive, male, blackhooded Lister rats supplied by OLAC Southern Limited. They were allocated into groups of four per cage (Bowman's BRC-type grill cage), and supplied with standard laboratory food pellets (Diet 41B, Robert Morton Limited) and tap water ad libitum. Room temperature was maintained at 21°C - 23°C and humidity > 50%. Room illumination operated on a 12-h light/dark cycle (7 a.m. light on). The rats weighed 250 - 280 g at the time of testing.

Apparatus. The food-preference test was conducted in a Bowman's MRC-type rat cage with a wire grid floor (apertures 0.4 cm square). Six round, plastic trays (diameter 5.5 cm; rim height 1.1 cm) were placed on the floor grid. Before each food-preference test, six types of food were freshly prepared and placed in the containers: the familiar Diet 41B food pellets and the novel foods, apple, carrot, cheddar cheese, currants (Whitworth's) and milk chocolate wholemeal biscuits (McVitie's). All foods were prepared in pieces of comparable size and equivalent volumes were placed in a shallow pile in each dish. There was one type of food per dish.

Procedure. The animals were handled each day for 7 days after arrival in our laboratory as a taming procedure. Each rat was deprived of food from 4 p.m. on the day prior to the test day. On the test day, each animal was tested individually and placed for 10 min in the test cage. The first measure recorded was latency (s) before feeding. Subsequently, the time spent eating was recorded separately for each type of food. The data was recorded in terms of durations of individual eating episodes. Eating durations were recorded only when food was taken into the mouth and chewed; any time spent in contact with food without eating was not scored. After each trial, if necessary, each food container was replaced into position and refilled. Any spillage was removed.

Injections. Injections were given 120 min before the beginning of the session. The rats were randomly assigned to three groups (n = 7): 0.06 mg/kg spiperone, 0.10 mg/kg spiperone, and 0.1 M tartaric acid used as the vehicle for the spiperone solutions. Solutions were injected i.p. in a volume of 1 ml/kg. The spiperone was generously donated by Janssen Pharmaceutica.

Data Analysis. The data were analysed using 1-way ANOVA and t-tests on untransformed data, except in the case of latency scores which were log-transformed before statistical analyses were performed.

Results

Latency to Eat. There was a general trend for spiperone to reduce latency before eating (Fig. 1A). However, an ANOVA on log-transformed latency scores did not yield a significant overall main effect (F(2,18) = 2.61; P = 0.10). Nevertheless, the reduction in latency produced by the higher dose of spiperone (0.10 mg/kg) was reliably different from the control value (t = 2.50; P < 0.025).

Total Eating Duration. The total eating duration is the sum of all eating episodes in the 10-min food-preference test. Spiperone prolonged the total eating duration in a dose-dependent manner (F(2,18) = 6.42; P < 0.008), as shown in Fig. 1B. The higher dose of spiperone very nearly doubled the time devoted to eating.

Type of Food Chosen. The total eating duration can be subdivided into the time devoted to eating familiar food and time devoted to eating novel foods. Under control conditions, rats in this experiment spent approximately as much time eating novel foods as they did eating familiar chow pellets (Fig. 2). Spiperone did not affect eating durations for novel and familiar foods equally.