Sensitivity of the behavioural assay for measuring the action of drugs on feeding: effects of tryptophan and 5-hydroxy-tryptophan

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In anorexic tests animals are usually subjected to food deprivation or cyclic feeding regimes and allowed access to food for limited periods of time during which the weight of food consumed is measured. For agents which easily suppress food intake this technique does not provide information about those adjustments made to the animal's behaviour which result in reduced consumption. For agents which do not appear to suppress intake it may be questioned whether the procedure is sufficiently sensitive to allow the detection of subtle suppressive effects. The compounds 5-hydroxy-tryptophan (5-HTP) and tryptophan (T) provide examples for these two conditions; 5-HTP producing a marked suppression of food intake (Blundell & Leshem, 1975) whereas T appears to exert no suppressive action (Weinberger, Knapp & Mandell, 1978). Recently, techniques for observing the micro-structure of feeding behaviour (Wiepkema, 1971) and for the analysis of meal patterns (e.g. Collier, 1977) have been applied to investigations of the effects of pharmacological agents on food consumption (Blundell, Latham & Leshem, 1976; Blundell & Latham, 1978). These techniques, which improve the sensitivity of the behavioural assay of feeding, have revealed that 5-HTP and T bring about adjustments to feeding behaviour in keeping with other pharmacological agents believed to intervene in serotonin metabolism (Blundell, 1977; Blundell & Latham, 1979).

The observation of micro-structural elements of feeding such as latency to begin eating, number and duration of eating bouts and the local rate of eating has shown that injections of 5-HTP (30 mg/kg) and MK-486 (40 mg/kg) reduce food intake by approximately 30% and slow the rate of eating from 0.28 g/min to 0.20 g/min ($P < 0.01$). When rats were allowed to feed-freely from an automated eatometer and meal patterns were continuously monitored over 24-h periods, 5-HTP (30 mg/kg) and MK-486 (40 mg/kg) reduced the average meal size from 2.4 to 1.6 g ($P < 0.01$) and reduced the intra-meal rate of eating from 0.42 g/min to 0.34 g/min ($P < 0.01$). In addition this treatment significantly altered the satiety ratio (ratio of meal size to following inter-meal interval) from 1.9 to 1.3 ($P < 0.05$).

In free-feeding rats housed singly in sound-proof chambers, injections of (−)-tryptophan (50 mg/kg) significantly reduced daily food intake from 26.9 to 24.3 g ($t = 3.65$, $df = 12$, <0.01, 2-tailed test), and reduced average meal size from 2.3 to 1.9 g ($t = 3.76$, $df = 12$, $P < 0.01$) during the 12-h dark phase of the light cycle. Closer inspection of the data revealed that the action of T on meal size was limited to the first 4 h after injection. Moreover, when T was administered to 24-h food deprived rats kept under carefully controlled conditions, the size of the first large meal taken was reduced from 11.1 to 9.3 g ($t = 2.51$, $df = 6$, $P < 0.05$, 2-tailed test) and the length of the post meal interval was extended from 0.52 h to 1.04 h ($t = 3.78$, $df = 6$, $P < 0.01$). The results of these experiments have provided evidence for an effect of tryptophan on feeding behaviour measured under conditions designed to minimize the effects of novel or stressful experimental procedures, to prevent the contamination of behaviour during periods of data collection, and to maximise the detection of subtle effects on behaviour. The adoption of similar strategies in human studies has revealed some interesting similarities and differences between the effects of pharmacological agents in animals and man (e.g. Blundell, Tombros, Rogers & Latham, 1979).

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