

LETTER TO THE EDITOR

AMPHETAMINE ANOREXIA AND METOCLOPRAMIDE

Sir,

(Received on September 26, 1983)

Metoclopramide, a dopamine antagonist, produces many actions similar to those of typical neuroleptics (4) including antiemetic effect (5, 6, 8) Yet, it lacks clinical antipsychotic effect (7) of typical neuroleptics. The present work shows that it also lacks their known ability to counter amphetamine-induced anorexia (1).

Male Wistar rats (180–300 g, bred in the Institute) were singly housed in a quiet room ($24 \pm 2^\circ\text{C}$, natural illumination) with free access to water.

d-Amphetamine sulphate (Smith, Kline and French, India) and metoclopramide (IPCA Laboratories, Bombay) were dissolved in 0.9% saline and given in 1 ml/kg volume, 30 and 45 min respectively, before feeding. Control rats received only saline.

For measuring food intake, cage bedding was removed and an excess weighed (15–20 g) quantity of food pellets (Hindustan Lever) presented to the rats. After 1 hr, intact pellets and their nibbled pieces were weighed to nearest 50 mg. It was observed in this work, as by others (1), that 1 hr-food intake value is more convenient and equally useful as 4 hr value to assess feeding behaviour. For allowing adequate feeding another stock of pellets was promptly offered and completely removed after 3 hr. On 4 hr feeding schedule 40 out of 50 rats maintained their body weight over 7 days and were used for the study.

The 1 hr-good intake on the day of drug treatment was expressed as a percentage of the mean value of 2 previous days. To prevent weight loss due to drug induced anorexia the pellets were left in the cage, on the day of experiment, for another 20 hr. Rats were reused after 3–7 days drug-free interval during which 4 hr-feeding schedule continued.

The drug effect on food intake was examined for significance by paired 't' test.

4 hr food intake ranged from 7.8 to 15.7 g of which 30 to 85% was consumed in

the first hr. The 1 hr food intake of individual rats on consecutive days varied by less than 25%.

Amphetamine caused a dose-related reduction of food intake which was significant with higher (0.5–2 mg/kg) but not with lower (0.25 mg/kg) doses when compared with saline controls (Table I).

TABLE I: Metoclopramide and amphetamine-anorexia. Each value represents mean % food intake (\pm S.E.M.) of 3–9 rats (calculated in terms of mean intake on 2 previous days) in 1 hr-feeding test.

| Metoclopramide ^a (mg/kg) | Amphetamine (mg/kg) ^a | | | | |
|--|----------------------------------|-----------------------------|-----------------------------|-----------------------------|----------------------------|
| | nil (saline controls) | 0.25 | 0.5 | 1.0 | 2.0 |
| 0.0 (saline controls) | 113 \pm 6.9 | 89 \pm 10.6 | 63 \pm 9.3 ^{**b} | 49 \pm 13.2 ^{**} | 8 \pm 2.7 ^{***} |
| 1.25 | 106 \pm 7.5 | 77 \pm 7.2 | 67 \pm 19.4 | 30 \pm 13.3 | 20 \pm 19.7 |
| 2.5 | 107 \pm 11.1 | 88 \pm 21.3 | 69 \pm 11.0 | 43 \pm 20.7 | 10 \pm 2.6 |
| 5.0 | 86 \pm 10.4 | 82 \pm 9.4 | 42 \pm 6.3 | 52 \pm 30.4 | 32 \pm 26.9 |
| 10.0 | 44 \pm 10.9 ^{***} | 46 \pm 5.9 [*] | 47 \pm 3.5 | 30 \pm 4.7 | 16 \pm 3.4 |
| 20.0 | 18 \pm 5.1 ^{***} | 50 \pm 6.7 [*] | 50 \pm 10.4 | 20 \pm 1.7 | 16 \pm 5.8 |
| 40.0 | 9 \pm 7.2 ^{***} | 17 \pm 5.7 ^{***} | 27 \pm 16.5 [*] | 6 \pm 3 ^{**} | 9 \pm 2.1 |

^a Amphetamine and metoclopramide were given in 30 and 45 min before feeding, respectively.

^b Value differs significantly from saline controls (^{*}P<0.05, ^{**}P<0.01, ^{***}P<0.001).

Metoclopramide alone in doses of 1.25–5 mg/kg had no significant effect on food intake compared with saline controls and failed to significantly reduce anorexia induced by any of the doses of amphetamine (Table I). In higher doses (10–40 mg/kg) metoclopramide itself produced anorexia.

The present work shows that metoclopramide did not antagonize amphetamine anorexia. In this regard, it differs from typical dopamine antagonist-neuroleptics like haloperidol and chlorpromazine.

It is suggested that the three effects of amphetamine namely hyperactivity, stereo-type and anorexia have a common mechanism (1). However, metoclopramide blocks

the first two (2, 3) but not the third effect of amphetamine; these facts do not support the theory of common mechanism.

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