

## PEPTIDERGIC MECHANISMS IN FEEDING BEHAVIOUR\*

P. R. DUA\*\* AND V. L. SHARMA

Central Drug Research Institute,  
Lucknow - 226 001

( Received on April 30, 1994 )

**Abstract:** Hyperphagia was induced in mice by p.o. administration of different types of CNS depressant drugs, like chlordiazepoxide 25 mg/kg diazepam 2.5 mg/kg, cyproheptadine 2 mg/kg and phemobarbitone 25 mg/kg. Such hyperphagia was abolished by pretreatment with naloxone 0.1 mg/kg sc. Naloxone *per se* at this dose produced no significant effect on the food intake. This is suggestive of the role of peptidergic mechanisms in the feeding behaviour in mice.

**Key words:** peptidergic                      feeding behaviour                      hyperphagia  
naloxone                      hypothalamus                      mesolimbic system

### INTRODUCTION

Feeding behaviour is regulated by the centers located in the hypothalamus. Ventrolaterally situated feeding center is regulated by the catecholaminergic (1, 2) mechanisms and ventromedially located satiety center, by tryptaminergic (3) mechanisms. Further, reciprocal hunger regulating circuits involving alpha and beta adrenoceptors, located respectively in the ventromedial and ventrolateral hypothalamus have also been reported (4). Amphetamine and fenfluramine produce anorectic action by acting on the ventrolateral hypothalamus involving catecholaminergic (2) and tryptaminergic (5) mechanisms respectively. The anorectic drugs available produce similar effects and there is little to choose between them, so far as their efficacy is concerned (6).

Beta endorphins have been associated with overeating in obese mice and rats (7). Administered icv Beta endorphins induced overeating in non-deprived rats. CNS depressants have been known to produce increase in body weight. High levels of opiate receptor binding are located in structures regulating feeding behaviour or in structures associated with limbic system (7) which includes hypothalamus, having centers regulating feeding and also mesolimbic system, where psychoactive drugs produce their action. Limbic area has been suggested as a possible region of opiate actions on the basis of ablation and electrical stimulation studies (3, 8).

Most areas of highest concentration of endogenous opioid peptides are located in the limbic system (9, 10). Further, serotonergic mechanisms have been reported to be involved in the release of beta endorphins (11). In view of the above reports, we have studied the effect of naloxone pretreatment on the hyperphagic responses to different types of drugs producing CNS depression, to find out if beta endorphins have a role to play in the overeating induced by different types of CNS depressants used in the study.

### METHODS

Swiss albino mice of either sex weighing between 16-20 g each were used in the study and fasted for 18 hrs. Water was allowed *ad libitum*. Separate groups of 5 mice each were pretreated with different drugs orally. Saline treated control were run concurrently. After one hour the mice were offered one gm of pellet food and were exposed to it for 4 hrs. The food left unconsumed at the end of 4 hrs was weighed again and quantity of food consumed was calculated in each group. The effect of these drugs on food intake was also studied after pretreatment of mice with nonconvulsant dose of naloxone (0.1 mg/kg, sc). Changes in food intake in response to these drugs as a result of naloxone treatment were considered to be receptor (Beta-endorphin) mediated. The nonconvulsant dose of naloxone was also studied for its effect on food intake. Normal saline treated control were run concurrently.

\*CDRI Publication No. 5270

\*\*Corresponding Author

The quantity of food consumed after each drug treatment in different groups was noted. The data were analysed statistically.

## RESULTS

Table I gives the results of the study. All the CNS depressant agents used in the study significantly ( $P < 0.001$ ) increased the consumption of food in mice. Maximum effect was observed with diazepam, and least with phenobarbitone and cyproheptadine. Naloxone *per se* at the dose level used in the study (0.1 mg/kg, sc) did not produce any significant ( $P > 0.05$ ) change in the food consumption. This dose of naloxone was therefore, used to study its effect on hyperphagic responses to drugs used in this study. At higher dose of 0.25 mg/kg, sc, however, naloxone produced a reduction in the food consumption. Pretreatment with naloxone abolished the hyperphagic response to these CNS depressant drugs. Responses to chlordiazepoxide and diazepam returned to control levels, while cyproheptadine and phenobarbitone responses were reduced further, below the control values. The reduction in the food consumption in naloxone (0.1 mg/kg, sc) treated group in mice, was not statistically different from normal saline treated control group ( $P > 0.05$ ).

TABLE I: Effect of some psychoactive agents on food intake in mice and reversal of effects on naloxone pretreatment.

Drug/dose (mg/kg, po)	Food consumption in g		
	Drug	Drug + Naloxone	Control
Chlordiazepoxide 25	0.61 ± 0.03**	0.43 ± 0.0**	0.43 ± 0.0
Diazepam 2.5	0.78 ± 0.045**	0.44 ± 0.03**	0.46 ± 0.022
Cyproheptadine 2	0.525 ± 0.037**	0.28 ± 0.023**	0.41 ± 0.025
Phenobarbitone 25	0.58 ± 0.04**	0.30 ± 0.03**	0.40 ± 0.033
Naloxone 0.1, sc	0.34 ± 0.02*	--	0.40 ± 0.033

\* $P > 0.05$ ;

\*\* $P < 0.001$

## DISCUSSION

The psychoactive drugs, specially the anxiolytic agents are perhaps used very widely now a days to

ward off the stress and strain of modern life. Alcohol is used almost like a recipe of food in the western society. So are the barbiturates used to induce sleep. Cyproheptadine is used to treat anorexia as a result of various types of etiologies. These drugs are used very widely and commonly. Their use is therefore likely to influence the food intake. In the present study types of CNS depressants i.e. anxiolytics, hypnotics, antihistamine anitserotonergic agents used in allergy have been studied for their effect on food consumption on acute p.o. administration in mice. All the three types of drugs were found to significantly increase the food intake in mice. Anxiolytic agent diazepam produced maximum appetite stimulant activity compared to chlordiazepoxide. In their clinical profile as anxiolytic agents, diazepam is more potent than chlordiazepoxide. It is hypothesized that anxiolytics increase the food intake by allaying anxiety. Further they produce anxiolytic action through their action on GABA receptors and chloride channels. Satiety centre is regulated by serotonergic mechanisms. 5-HT agonists induce satiety. Cyproheptadine, a 5-HT and histamine antagonist therefore inhibits satiety and stimulates food intake. Phenobarbitone also stimulated food intake through its GABA agonistic action and its anxiolytic action.

Beta-endorphins have been reported to stimulate food intake (9). We therefore studied the effect of naloxone, an antagonist of opioid peptides on the stimulant responses of the above mentioned psychoactive agents on food intake in mice. A nonconvulsant dose of naloxone 0.1 mg/kg, sc produced blockade of appetite stimulant activity of all the agents studied. This indicates, that, opioid peptides perhaps have a role to play in the effect of these psychoactive agents on food intake in mice. This is substantiated by various experimental studies carried out by other investigators. These studies have also provided evidence regarding the role of opioid peptides in feeding behaviour (9, 10, 12). Our study, however, relates to the role of peptides in enhanced food intake after the administration of some CNS depressant agents. The stimulant action of these agents on the food intake was effectively blocked by naloxone. Naloxone alone produced no significant effect on the food intake in mice compared to the saline treated controls at a dose of 0.1 mg/kg, sc at which it antagonized the effect of these psychoactive agents on food intake in mice.

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