Pharmacology Biochemistry & Behavior, Vol. 39, pp. 421–422. © Pergamon Press plc, 1991. Printed in the U.S.A. 0091-3057/91 $3.00 + .00

An Animal Model of Bulimia Nervosa: Opioid Sensitivity to Fasting Episodes[1]

M. M. HAGAN AND D. E. MOSS

Laboratory of Psychobiochemistry, Department of Psychology, University of Texas at El Paso, El Paso, TX 79968-0553

Received 7 December 1990

HAGAN, M. M. AND D. E. MOSS. *An animal model of bulimia nervosa: Opioid sensitivity to fasting episodes.* PHARMACOL BIOCHEM BEHAV **39**(2) 421–422, 1991.—A group of female rats was deprived and maintained at 75–80% of body weight at three different times during development. Following recovery to normal weight, food intake was measured with and without butorphanol tartrate, a kappa-sigma agonist, 8 mg/kg SC. Animals with a history of deprivation (DEP) showed an increase in postrecovery feeding when they were tested at normal body weight and not food deprived. More importantly, butorphanol prolonged food intake in the 3-h eating test only in the rats with a developmental history of food restriction. A developmental history of fasting in eating disorders may trigger changes in opiate systems that result in atypical feeding behavior in the adult.

Bulimia nervosa Opioids Food restriction Animal model Butorphanol tartrate

ENDOGENOUS opiates appear to have a central role in feeding (1,7). Opiates also affect preference for highly palatable foods (6), decrease reproductive functions (5), and induce analgesia (2,4), symptoms expressed in bulimic patients. The "autoaddiction" model of anorexia nervosa specifically attributes atypical eating in this disorder to an addiction to one's own opioids triggered by food deprivation experiences (5). The experiment reported here shows that a developmental history of deprivation experiences (DEP) will produce increased feeding (binging) to butorphanol tartrate (BUTR) in fully satiated, normal-weight adults.

METHOD

History of Deprivation

Thirteen female Sprague-Dawley rats (12 h/day artificial light, 1100–2300 h) were weaned at 21 days of age. At the beginning of the first DEP episode, the animals were 24 to 30 days of age (30–70 g). The experimental group (n = 7) was deprived down to 75% of normal body weight (food-restricted goal weight) by limiting their access to standard Purina rat chow pellets to 4 hours per day. The rats reached 75% body weight (goal weight) in two days. Ad lib water was available. Recovery to normal weight by ad lib feeding on rat chow followed immediately. This procedure was repeated for a second and third DEP episode on the same rats at ages 89 and 95 days (210–250 g), and 138 and 144 days (260–300 g), respectively. For the second and third episodes, the experimental group was limited to 1- to 3-h feeding times per day, adjusted according to rate of weight loss. The second and third DEP episodes required a three-week period to reach 80% of normal body weight. Again, recovery to normal weight followed these episodes. Normal weight was maintained for at least one week before testing. Controls were maintained throughout on ad lib rat chow to establish the "normal" body weight.

Feeding Trials

Feeding tests were started at the beginning of the light phase. At the time of testing, the experimental rats had recovered their normal body weights and were fully satiated, except that food was removed for 40 to 60 minutes before testing while rats acclimated to the test cages. Intake of Purina rat chow was measured 1, 2, and 3 hours after SC injection of 8 mg/kg BUTR (a gift from Bristol-Myers Laboratories, Evansville, IN), a potent kappa-sigma agonist (3), or vehicle. All rats were tested twice with BUTR and twice without BUTR in a counterbalanced design following the second and third DEP episodes. At least 20 days separated each test.

RESULTS

The results obtained after the second and third DEP episodes were the same and were combined. As might be expected, rats ate more the first hour than the second and third hour, $F(2,22) = 47.28$, $p<0.001$. The overall effect of BUTR and the interaction of BUTR with DEP history was not significant, while a history of DEP had a highly significant effect on the amount eaten, $F(1,11) = 16.24$, $p<0.01$. Most importantly, however, the three-way interaction between DEP history, BUTR, and the three one-hour intervals during testing was highly significant, $F(2,22) = 9.31$, $p<0.01$. The interaction between BUTR and the hour of meal test is due to BUTR causing continued eating (i.e., binging) during the second and third hours in rats with a history of DEP (Fig. 1). In the total 3-hour test, DEP rats consumed a cumulative amount of 11.3 and 6.9 g with and without BUTR, respectively, whereas controls consumed approximately 5.7 g under both conditions.

[1]Supported in part by N.I.M.H. (MH47167).

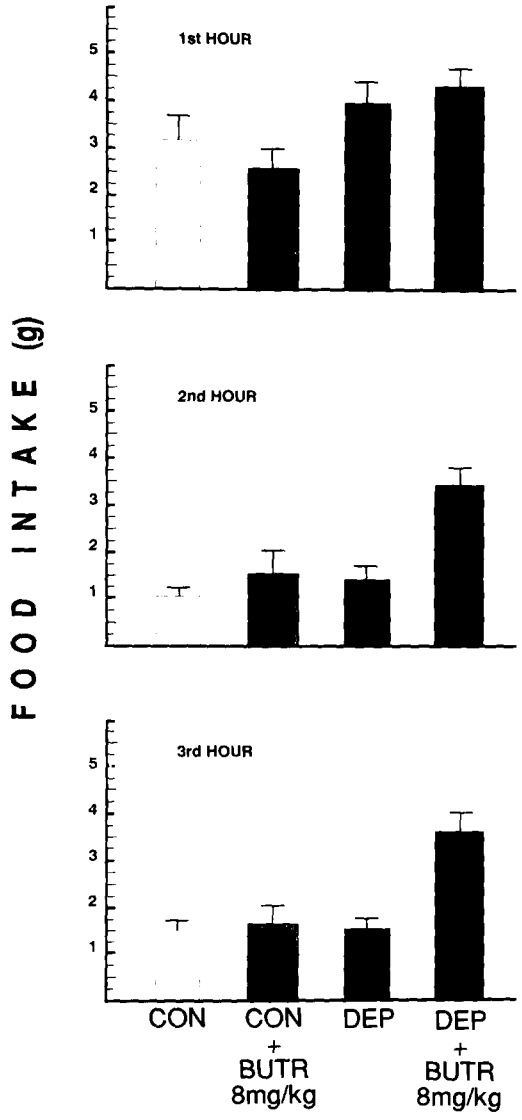

FIG. 1. The effect of butorphanol tartrate (BUTR) and a history of deprivation (DEP), with normal body weight restored at time of eating trials, on food intake. There was no difference between groups at the end of the first hour of eating. There was a highly significant interaction between DEP history, BUTR, and the three one-hour test periods.

DISCUSSION

Our results support the growing body of evidence showing that food DEP may produce changes in behavioral sensitivity to opioids (8). Although 8 mg/kg BUTR did not produce potent effects on food intake by itself (3), BUTR caused an exaggerated (binge-like) food intake response in rats with a history of food DEP episodes. These rats continued feeding, very likely beyond satiety, during the second and third hours of the eating tests (Fig. 1). The results of our experiment indicate that early food restriction may produce an animal model of bulimia nervosa. As an explanation of binge-eating in bulimia, we speculate that sustained patterns of fasting affect opiate receptors controlling food intake.

REFERENCES

1. Cooper, S. J.; Jackson, A.; Kirkham, T. C.; Turkish, S. Endorphins, opiates and food intake. In: Rodgers, R. A.; Cooper, S. J., eds. Endorphins, opiates, and behavioural processes. New York: John Wiley; 1988:143–186.
2. Faris, P. L.; Raymond, N. C.; Howard, L. A.; McCollister, R.; Mitchell, J. E.; Eckert, E. D. Elevation in pain thresholds in bulimia nervosa. Soc. Neurosci. Abstr. 16:141; 1990.
3. Levine, A. S.; Morley; J. E. Butorphanol tartrate induces feeding in rats. Life Sci. 37:781–785; 1983.
4. McGivern, R.; Bernston, G. G. Mediation of diurnal fluxuations in pain sensitivity in the rat by food intake patterns: Reversal by naloxone. Science 210:210–211; 1980.
5. Marrazi, M. A.; Luby, E. D. An auto-addiction opioid-model of chronic anorexia nervosa. Int. J. Eat. Disord. 5:1175–1178; 1986.
6. Smith, G. P. Animal models of human eating disorders. In: Schneider, L. H.; Cooper, S. J.; Halmi, K. A., eds. The psychobiology of human eating disorders: Preclinical and clinical perspectives. New York: The New York Academy of Sciences; 1989:63–74. (Ann. NY Acad. Sci., vol. 575.)
7. Thornhill, J. A.; Saunders, W. Ventromedial and lateral hypothalamic injections of naloxone or naltrexone suppresses the acute food intake of food-deprived rats. Appetite 5:25–30; 1984.
8. Vaswani, K. K.; Tejwani, G. A. Food deprivation-induced changes in the level of opioid peptides in the pituitary and brain of rat. Life Sci. 38:197–201; 1986.