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# Time-Dependent Changes in Hypothalamic Dopamine Metabolism During Feeding in the Rat

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HEFFNER, T. G., G. VOSMER AND L. S. SEIDEN. *Time-dependent changes in hypothalamic dopamine metabolism during feeding in the rat.* PHARMACOL BIOCHEM BEHAV **20**(6) 947–949, 1984.—The accumulation of the dopamine metabolite dihydroxyphenylacetic acid (DOPAC), but not the serotonin metabolite 5-hydroxyindoleacetic acid, in the hypothalamus is increased in rats during the second, third and fourth hours of a four hour period of access to food following a 20 hour period of food deprivation. This metabolic change does not correlate with duration of access to food or with amount of food consumed. These results suggest that increased hypothalamic dopamine metabolism during feeding is not related in any simple way to either the onset or termination of feeding.

Dopamine Feeding Hypothalamus

THE metabolism of dopamine (DA) in brain is increased during access to food following food deprivation in the rat [3]. This metabolic change is reflected by an increased accumulation in brain of dihydroxyphenylacetic acid (DOPAC), the major metabolic product of DA in brain [8,11], and appears to result from increased turnover of DA in central neurons [3]. Increased DA turnover during feeding is seen in the hypothalamus, the nucleus accumbens, and the amygdala but not in the corpus striatum, septum, olfactory tubercle, or frontal cortex [3]. These results are consistent with many previous studies implicating central DA neurons in the control of ingestive behaviors [6, 9, 10]. However, the role of feeding-related increases in brain DA metabolism in the control of food intake remains uncertain.

The present experiment was designed to further examine the relationship between feeding and increased brain DA metabolism. Specifically, we sought to determine if the increased brain DA turnover during feeding was correlated with the onset or termination of eating, the duration of access to food, or the quantity of food consumed. In addition, we sought to determine if alterations in the metabolism of another central neurotransmitter, serotonin (5-HT) also occurred during feeding. For these studies, DA and 5-HT metabolism during feeding were estimated by measurment of their major metabolic products DOPAC and 5-hydroxyindoleacetic acid (5-HIAA), respectively, in the hypothalamus, a brain region previously implicated in the control of food intake. The results indicate that the apparent turnover of DA, but not of 5-HT is enhanced during feeding. However, feeding-related increases in hypothalamic DA turnover do not correlate with either the duration of access to food or the amount eaten.

## METHOD

### *Animals and Food Intake Measurement*

Male albino rats of the Holtzman/Sprague-Dawley strain (Holtzman Co., Madison, WI), weighing 200–250 g were housed singly in wire mesh cages in a room maintained at 21–22°C with fluorescent lighting on from 0600 to 1800 hr After 1 week of free access to food (Teklad Laboratory Chow, Teklad Co., Rockford, IL) and water, access to food was limited to four hours per day (0100–0400 hr) for a period of two weeks. Food intake was determined by measuring the difference in weight (±0.1 g) between food pellets placed in the cage (plus any spillage in excess of 0.1 g beneath the cage) and food pellets remaining in the cage after access. Water was available continuously in the home cages. On the test day, groups of 8 rats were sacrificed prior to access to food (control group) or after 1, 2, 3 or 4 hr of access to food.

### *Neurochemical Determinations*

Rats were sacrificed by decapitation and the hypothalamus was dissected rapidly from the brain as described previ-

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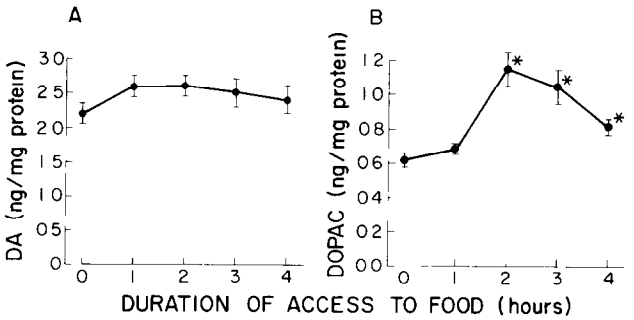


FIG. 1 Effect of access to food following food deprivation on the levels of DA (A) and DOPAC (B) in the hypothalamus Each point represents the mean (±S E.M.), results from 8 rats. *$p<0$ 05

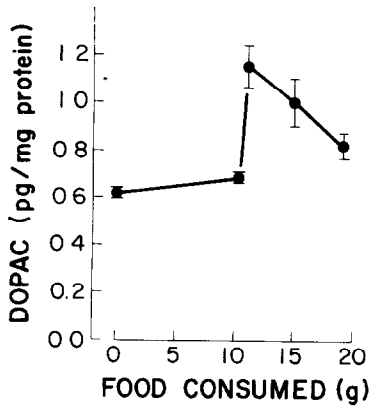


FIG 2. DOPAC accumulation in the hypothalamus as a function of food consumed during the four hour access period Each point represents the mean (±S E M ), results from 8 rats sacrificed after 1, 2, 3, or 4 hours of access to food.

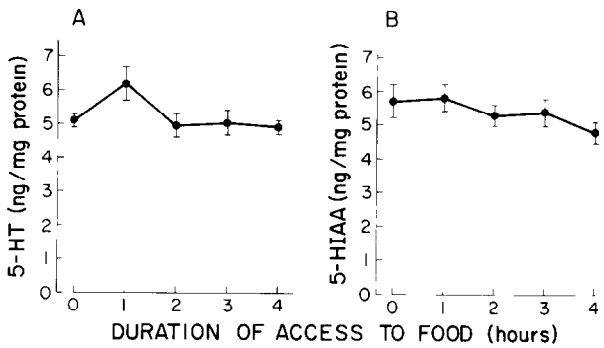


FIG 3 Effect of access to food following food deprivation on the levels of 5-HT (A) and 5-HIAA (B) in the hypothalamus Each point represents the mean (±S.E.M ), results from 8 rats

ously [2]. The concentrations of DA, DOPAC, 5-HT, and 5-HIAA were determined by high performance liquid chromatography, as described elsewhere [4]. The amount of protein in hypothalamic tissue was determined by the Biuret procedure [5]. The concentrations of DA, DOPAC, 5-HT and 5-HIAA in the hypothalamus were expressed as ng/mg of protein.

*Statistical Analysis*

Data from control and experimental groups were compared with an analysis of variance; individual comparisons were made with a two-tailed Student's $t$-test The significance of correlation between variables was assessed with a $t$-test for linear regression.

## RESULTS

Total food intake increased gradually during the four hour period of access to food. Groups of rats (N=8) given access to food for 1, 2, 3 or 4 hours consumed 10.3±0.7 grams (mean±S.E.M.), 11.3±1.3 grams, 15.7±1.6 grams, and 18.8±1.6 grams of food, respectively. The accumulation of DOPAC in the hypothalamus in rats given access to food for 2, 3, or 4 hours was elevated significantly compared to the control group ($t=4.42$; 3.59; 2.97, respectively, all $p<0.05$) (Fig. 1B). The accumulation of hypothalamic DOPAC was not significantly different from that seen in controls in rats given only 1 hour of access to food ($t=1.34$, $p>0.05$ (Fig. 1B). The endogenous level of DA in the hypothalamus was not altered significantly during access to food in any of the groups examined (Fig. 1A). No significant correlation was discovered between the level of DOPAC in the hypothalamus and either the duration of access to food (Fig. 1B; $t=0.44$, $p>0.05$) or the amount of food consumed (Fig. 2; $t=0.14$, $p>0.05$). In fact, the mean level of hypothalamic DOPAC in rats given access to food for 4 hours was significantly lower than in rats given access to food for 2 hours ($t=2.73$, $p<0.05$)

Access to food for 1, 2, 3 or 4 hours following food deprivation did not alter significantly the concentration of either 5-HT (Fig. 3A) or 5-HIAA (Fig. 3B) in the hypothalamus.

## DISCUSSION

The present results confirm earlier reports that feeding induced by food deprivation is associated with an increased accumulation of DOPAC, the major metabolic product of DA, in brain [3]. These findings support previous suggestions that brain DA turnover is increased during food deprivation-induced feeding [1, 3, 7]. Our results further suggest that unlike DA, the turnover rate of 5-HT within hypothalamic neurons remains unaltered during feeding.

The role of the apparent increase in hypothalamic DA turnover during feeding remains uncertain. Our previous study indicated that intragastric intubation of food was not associated with increased DA turnover in the hypothalamus [3], suggesting that this neurochemical change is not the result of postingestional factors The present studies failed to discover a significant correlation between DOPAC accumulation and either duration of access to food or amount of food eaten. In addition, the increased DOPAC accumulation did not coincide with the onset of feeding or with its termination during the four hour access period. As such, the present results do not support the hypothesis that increased hypothalamic DA neuronal activity serves to mediate hunger or satiety

The failure to observe a relationship between DOPAC accumulation and feeding may stem from the insensitivity of our behavioral or neurochemical measurements. Rats consume numerous small meals during each of the hour-long measurement periods used in the present studies In addi-

tion, inter-meal intervals or rate of food consumption were not measured in these studies. It is also possible that critical neurochemical changes occurring within the DA neurons which innervate a discrete hypothalamic nucleus were obscured by analysis of the entire hypothalamus. A finer analysis of feeding and neurochemical changes occurring in discrete brain areas over shorter time courses may reveal important relationships that cannot be detected with the use of the present methodology.

These results support the concept of central DA neuron involvement in the control of ingestive behavior in the rat [6, 9,10]. However, the present results do not reveal the nature of the influence of central DA neurons on feeding.

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