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BRIEF COMMUNICATION

Effects of Estradiol on Feeding and Locomotion in REM Deprived Rats

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LONGUSKI, P. A., C. A. CUDILLO AND J. J. STERN. *Effects of estradiol on feeding and locomotion in REM deprived rats.* PHYSIOL. BEHAV. 16(1) 97–99, 1976. – Ovariectomized female rats were deprived of REM sleep by being confined to 6.5 cm platforms surrounded by water for 96 hr. Stress controls were emersed in water 1 hr/day. Exogenous estradiol benzoate (5 μg/day) stimulated activity and reduced feeding significantly more in stress and normal controls. On the assumption that REM sleep helps maintain catecholamine functioning in the brain, the data are discussed in terms of estradiol influencing weight regulatory behavior through brain catecholamines.

Estradiol Eating Activity REM Deprivation

THERE is growing evidence that norepinephrine (NE) mediates estradiol's effect on weight regulatory behavior in female rats. Simpson and Dicara [2] report that injections of dopamine (the precursor of NE) in the anterior hypothalamus elicit eating when blood estradiol levels are low; NE administration stimulates feeding irrespective of estradiol titers. These workers conclude that estradiol inhibits the activity of dopamine β hydroxylase (the enzyme that converts dopamine to NE) in the anterior diencephalon thereby reducing NE concentrations and feeding. In contrast, Stern and Zwick [3] suggest that estradiol influences feeding (and activity) by increasing levels of brain NE. They report that intraventricular EB (1 μg) and NE (50–150 μg) stimulate activity and reduce eating when infused in the dark. Pretreatment with phentolamine, an adrenergic receptor antagonist, prevented the activity increase coincident with both agents; imipramine, a catecholamine-potentiating drug, enhanced the effects of EB and NE.

Rapid eye movement sleep (REM or paradoxical sleep) helps maintain catecholamine functioning in the brain [6]. REM deprivation reduces the behavioral consequences of agents known to act through catecholamine pathways e.g. D-amphetamine [4,5]. Also, drugs that increase catecholamine activity (imipramine or pargyline) reverse some of the effects of REM deprivation.

If NE mediates estradiol's effect on weight regulatory behavior, it follows that the effect of EB should be reduced in REM deprived animals. The present study tested and confirmed this prediction.

METHOD

Animals and Maintenance

Female Sprague Dawley rats weighing 180–210 g were used. The animals were housed in standard Wahmann activity wheels with food and water freely available. The laboratory was on a 12 hr on-off light cycle with lights off at 7:00 p.m. Two to 3 weeks prior to REM deprivation (see below) the subjects were ovariectomized under pentobarbital anesthesia.

Procedure

Deprivation. The rats were divided into 3 groups on the basis of body weight. The REM deprivation (RD) group was placed on inverted flower pots 6.5 cm in dia. for 96 hr. The size of the flower pot's platform was such that the animals could not curl up and obtain normal amounts of REM sleep [5]. The flower pots were surrounded by water (22°C) in 50 cm dia. galvanized steel basins. The water level was 0.5–2.0 cm below the platform. Food was freely available from an overhanging wire mesh holder; water was directly available from the tub.

During deprivation, a second group of animals, the stress control (SC) group, was housed in individual metal cages 23 hr/day. For the remaining hour (10:00–11:00 a.m.), the animals were placed in 10 cm water (20°C). This procedure has been shown to reliably produce the adrenal hypertrophy characteristic of the platform animals [5] and was employed to control for the nonspecific stress of the REM

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deprivation technique. The SC rats also had their food intake restricted to 10 g/day. Based upon the literature, it was clear that the RD animals would lose a considerable amount of weight during deprivation; it was hoped that 10 g/day would produce a comparable loss in controls.

Untreated ovariectomized rats served as normal controls (NC). During the deprivation and testing (see below) periods, the animals received either 5 μg EB/day or an equal volume (0.10 ml) of sesame oil.

Testing. Immediately after the deprivation period, animals were returned to the activity wheels. Revolutions, food intake (g) and body weight (g) were recorded daily for the next 14 days.

RESULTS

Activity

Figure 1 shows the activity of the females during testing. On Day 1 (the fifth day of EB administration) the stress and normal estradiol stimulated controls evidenced somewhat more running than the RD-EB rats (N.S.). A comparison of the control groups over the 14 days of testing reveals no difference in running. Each control group, however, ran significantly more than the RD group ($p<0.01$ Mann Whitney U tests).

There was no statistical difference in the activity of the oil treated groups. The groups averaged less than 150 revolutions/day. The estradiol stimulated groups each ran significantly more than its oil control group.

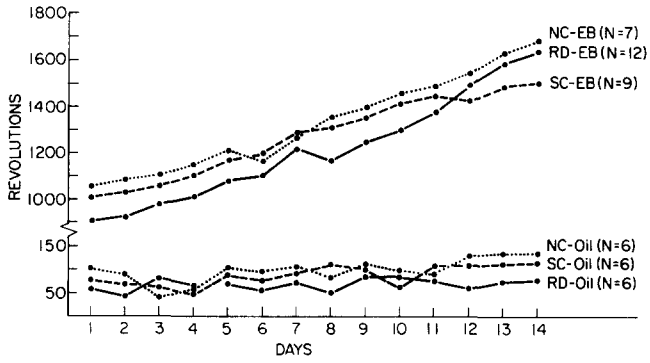

FIG. 1. Mean wheel running (revolutions/day) of the females with estradiol benzoate (5 μg/day) or sesame oil administration.

Food Intake

The food intake of the females is shown in Fig. 2. Kruskall Wallis analyses of variance were performed for the first 5 and last 5 days of testing. With respect to the oil treated animals, there was no overall difference in eating for either 5 day period. In contrast, the estradiol stimulated rats showed a significant difference during the first 5 day period ($p<0.01$). Individual comparisons, using Mann-Whitney U tests, show that the RD-EB group ate significantly more than the NC-EB ($p<0.01$) and the SC-EB ($p<0.05$) groups. During the last 5 days of testing, the estradiol stimulated rats showed no overall difference in eating.

Body Weight

Prior to deprivation, the groups were equated for body weight. During deprivation, the RD animals (EB and oil) lost 14%, the SC animals lost 11%, and the NC animals gained 1.6% of their initial weight.

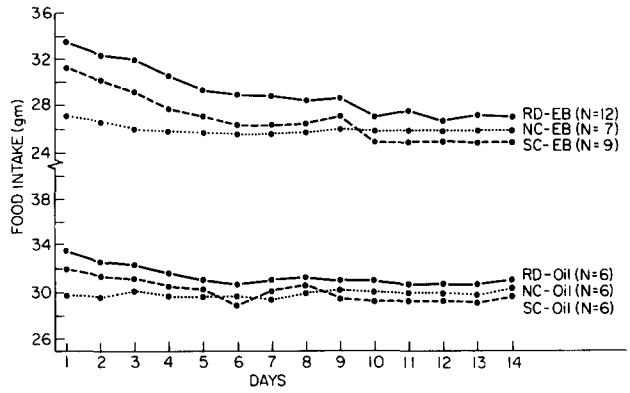

FIG. 2. Mean food intake (g/day) of the females with estradiol benzoate (5 μg/day) or sesame oil administration.

Adrenal Weight

Immediately following deprivation, 5 animals from each of the 6 groups were adrenalectomized and the wet weights of the glands determined. The RD glands (EB and oil) weighed 34.6 ± 5.9 g, the SC glands weighed 31.0 ± 4.6 g, and the NC glands weighed 28.2 ± 2.7 g.

DISCUSSION

The present findings clearly show that the effects of exogenous EB on activity and food intake are reduced in REM deprived rats. Following deprivation, the REM deprived animals ran significantly less (Fig. 1) and ate significantly more (Fig. 2) than controls. If, as discussed by both Simpson and Dicara and Stern and Zwick, EB influences weight regulatory behavior through NE pathways and REM sleep helps maintain catecholamine functioning in the brain, the data are readily explained. Estradiol did not fully express itself in REM deprived subjects because of a disturbance in their brain catecholamine tracts.

In addition, the present results demonstrate that while estradiol had a reduced effect in REM deprived rats, it did have an effect. The food intake of the RD-EB rats was lower than the RD-oil group, and the activity of the RD-EB rats was greater than the RD-oil group. Moreover, the elevated eating of the RD-EB animals relative to the SC and NC estradiol rats was not due to some unsuspected stimulating effect of REM deprivation on feeding: the RD-oil rats ate at a level comparable to SC-oil rats. Finally, the finding that RD-oil animals ran as much (even though at a minimal level) as SC and NC-oil rats shows that the reduced activity of RD-EB rats was not due to something peculiar to REM deprivation.

The present data also suggest similar rates of catecholamine recovery in the brain regions managing activity and feeding. The activity of the RD animals reached control levels at about Day 10; their food intake reached control levels by about Day 12. Other studies report differences between the neurochemical systems controlling activity and feeding. Estradiol produces a temporary drop in feeding but prolonged heightened activity in ovariectomized rats [1,7].

The SC animals were employed to control for the weight loss and nonspecific stress characteristic of the flower pot technique. Given the 11% drop in body weight and the adrenal hypertrophy, these objectives appear satisfied.

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