BIOTEMAS, 1(1): 28-32, 1988

EFFECT OF PROPRANOLOL ON BEHAVIORAL THERMOREGULATION IN RATS WITH LATERAL HYPOTHALAMIC LESIONS

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RESUMO

Efeito do propranolol sobre a termorregulação comportamental em ratos com lesões do hipotálamo lateral

Ratos expostos ao frio foram treinados a pressionar uma barra para obter pulsos de calor e então receberam lesões bilaterais da área hipotalâmica lateral. Tanto antes quanto após as lesões, a taxa de resposta aumentou em decorrência da injeção de propranolol. Portanto, ratos com lesões do hipotálamo lateral retêm a habilidade de compensar através do comportamento uma deficiência autonômica de produção de calor.

UNITERMOS: Lesão, Hipotálamo, Propranolol, Rato

ABSTRACT

Cold-exposed rats were trained to press a lever to obtain pulses of heat and then received bilateral lateral hypothalamic lesions. Both

*The data reported in this paper are part of a dissertation submitted in partial satisfaction of the PhD degree at the University of California, Santa Barbara. Author's current address is: Institute of Environmental Stress, University of California, Santa Barbara, CA 93106, U.S.A.

before and after the lesions, response rate increased in response to injection of propranolol. Thus, rats with lateral hypothalamic lesions retain the ability to compensate behaviorally for an autonomic deficit in heat production.

KEY WORDS: Lesion, Hypothalamus, Propranolol, Rat

INTRODUCTION

Early studies on thermal neuroscience suggested that lesions of the lateral hypothalamus (LH) produce a significant deficit in behavioral temperature regulation (Rudiger & Seyer, 1965; Satinoff & Shan, 1971; Van Zoeren & Stricker, 1977). Recent evidence indicates that this deficit is not a specific thermoregulatory dysfunction but only a consequence of a general impairment produced by the lesions (Refinetti & Carlisle, 1986, 1987). According to these recent studies, LH-lesioned rats show a strong reduction in metabolic heat production, but retain the ability to thermoregulate behaviorally. However, the ability of the behavioral response to compensate for a decrease in heat production has not been tested directly. This was done in the present experiment by measuring operant thermoregulatory behavior before and after injections of propranolol, a drug that lowers metabolic heat production. If LH-lesioned rats work for more heat after than before an injection of propranolol, which decreases metabolic activity, then behavioral compensation for low metabolism will have been demonstrated

METHOD

Subjects

Six male albino rats (350-400 g), housed individually at 24°C and fed Purina laboratory chow and water ad libitum, were used as subjects. They were schaved twice a week and tested every other day during the light phase of a 12:12 hr light-dark cycle. Each animal was tested at the same time of the day throughout the experiment.

Apparatus

The experimental chamber was a Plexiglas box (19 x 25 x 18cm) with Plexiglas-rod flooring and ceiling. A Plexiglas lever (4 x 5 cm) was

attached to the wall 3 cm above the floor. A 250 W red-bulb infrared lamp was positioned perpendicularly to and 30 cm above the floor. Lever-pressing responses were rewarded with 1-sec pulses of 160 mW/cm². Ambient temperature was 2°C. Colonic temperature (6 cm deep) was measured with a Sensortek thermocouple meter (Model BAT-12).

Propranolol injections were performed subcutaneouly at the dose of 5 mg/Kg. This drug was used to decrease metabolic heat production because of its know depressive effect on metabolism (e.g., Rothwell & Stock, 1980). Propranolol temporarily reduces or abolishes the action of nerves that innervate the brown adipose tissue via postsynaptic beta-noradrenergic receptor blockade. Brown adipose tissue, on its turn, is considered to be the main site of heat production in cold-adapted animals and a possible contributor to heat production in warn-adapted animals (Rothwell & Stock, 1984).

Procedure

All animals were trained to press the lever to obtain pulses of heat for five 2-hr sessions. Preoperative test sessions were then conducted. For each animal, a 15-min warm-up period was followed by a 15-min control (baseline) period, at the end of which the animal was removed from the chamber, injected with propranolol and rapidly returned to the chamber for additional 45 min (only the last 15 min being used in data analysis). On the day after the preoperative test session, the rat was anesthetized with Nembutal (55 mg/kg, IP) and bilateral lesions were produced in the lateral hypothalamus by 12 sec of 1.5 mA anodal direct current. Three days after the lesions, a postoperative test session identical to the preoperative one was conducted. At the end of the experiment, the animals were sacrificed and their brains treated for histological analysis.

Pilot tests showed no significant effect of saline injections on the number of rewards obtained either before or after LH lesions.

RESULTS AND DISCUSSION

The results are shown in Fig. 1. Preoperatively, the reduction in heat production caused by injections of propranolol was compensated for by an increase in heat intake, as indicated by the increase

in number of rewards obtained. Postoperatively, the animals were still able to compensate for the decrease in heat production. This is shown by the absence of a significant effect due to the interaction of drug and lesion: $F(1,15) = 3.32$, $p > 0.05$.

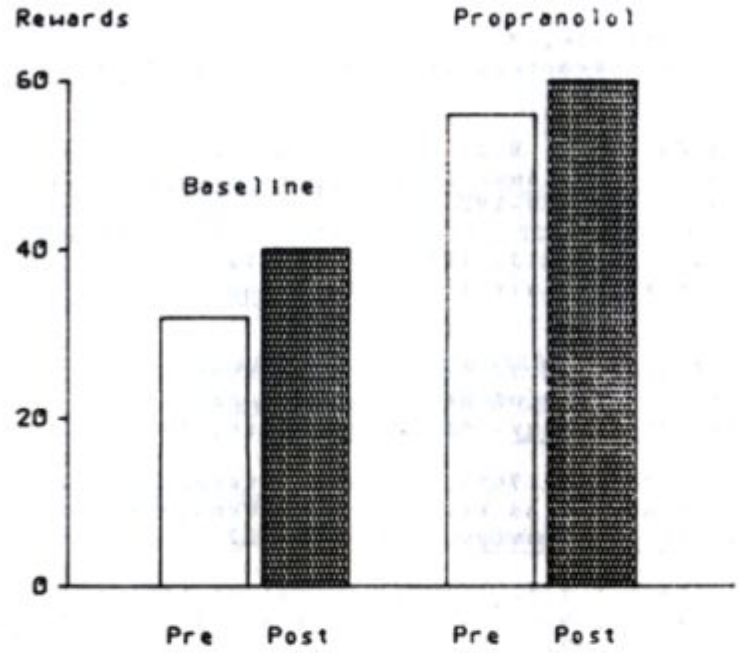

FIG. 1 - Number of rewards obtained during 15-min periods before and after injections of propranolol preand post-lesion. Each bar is the mean of six rats.

Histological examination and records of food intake showed that the lesions were effectively located in the lateral hypothalamic area. Postoperative rectal temperature was lower than preoperative temperature both before and after the sessions, but no animal became seriously hypothermic. Mean post-test rectal temperature was 37.7°C before and 36.3°C after the lesions.

Since LH-lesioned animals can, to a certain extent, compensate behaviorally for reductions in metabolic heat production, it seems that the drop in body temperature results not from behavioral deficiency but from a serious deficit in metabolism that cannot be compensated completely by the operant response. The increase in responding after metabolic impairment by propranolol is further evidence for the contention that animals with lateral hypothalamic lesions can

respond to cold stress by behavioral means (Refinetti & Carlisle, 1986, 1987).

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