Pharmacology Biochemistry and Behavior, Vol. 1, pp. 591–592. ANKHO International Inc., 1973. Printed in the U.S.A.

BRIEF COMMUNICATION

Ventromedial Hypothalamic Lesions and Brain Catecholamines[1]

S. D. GLICK, S. GREENSTEIN AND D. H. WATERS

Department of Pharmacology, Mount Sinai School of Medicine, Fifth Avenue and 100th Street, New York, N. Y. 10029

and

H. M. Singer Laboratory of Neurosciences and Addictive Diseases, Beth Israel Medical Center, 307 Second Avenue, New York, N. Y. 10003

(Received 12 July 1972)

GLICK, S. D., S. GREENSTEIN AND D. H. WATERS. *Ventromedial hypothalamic lesions and brain catecholamines.* PHARMAC. BIOCHEM. BEHAV. 1(5) 591–592, 1973.–Hyperphagic rats with bilateral ventromedial hypothalamic lesions were killed on either the fifth or tenth day after surgery and their brains were assayed for tel-diencephalic norepinephrine and striatal dopamine. Lesion-induced weight gain was highly correlated with depletion of tel-diencephalic norepinephrine; the lesion produced no change in striatal dopamine levels and there was no significant correlation between dopamine levels and weight gain. These results support the conclusion that damage to a noradrenergic bundle is responsible for hypothalamic hyperphagia.

Ventromedial hypothalamic lesions Norepinephrine Dopamine

INCREASING experimental efforts have been directed towards ascertaining neurochemical correlates of behavioral phenomena associated with lesions of particular brain structures. Most commonly, attention has been focused on the aphagic and adipsia syndrome [6] following bilateral lateral hypothalamic lesions in rats. Such lesions deplete the brain of both norepinephrine and dopamine; however, the severity of the syndrome appears to be best correlated with depletion of dopamine [6]. Surprisingly, there has been relatively little neurochemical information on the converse hyperphagic syndrome which is well-known to follow bilateral ventromedial hypothalamic lesions [1] in rats. Recently, Kapatos and Gold [3], using asymmetrical lesions, attempted to relate the neural substrate of hypothalamic hyperphagia to damage of an ascending ventral noradrenergic bundle described in independent histochemical studies [5]. The present experiment was an attempt to provide a more direct neurochemical correlate of the hyperphagic syndrome.

METHOD

Twenty-two female Sprague-Dawley rats (250–270 g) were anesthetized with methohexital and were given bilateral lesions in the ventromedial hypothalamus by a direct anodal current of 2 mA for 10 sec. Coordinates were 0.4 mm posterior to bregma, 0.7 mm lateral to midline and 1.5 mm from the base of the skull. Sham-operated controls (N = 10) had the electrodes lowered but did not receive lesions. Rats were weighed preoperatively and on each postoperative day until being killed. Eleven rats with lesions and 5 control rats were killed on the fifth postoperative day; the remaining rats (11 ventromedial, 5 control) were killed on the tenth postoperative day. Immediately after rats were killed, the brains were removed and the corpus striati were dissected. The combined (left–right) striati of each rat were then assayed for dopamine and the rest of the teldiencephalon (excluding striati) was assayed for norepinephrine. Fluorometric methods [4] were used for both assays.

[1] This research was supported by NIMH grant MH21156 and NIMH Research Scientist Development Award (Type 2) DA 70082 to S. D. Glick.

RESULTS

Ventromedial hypothalamic rats gained an average of 45.6 g by the fifth postoperative day (47.5 g for rats killed on the fifth postoperative day and 43.7 g for rats killed on the tenth postoperative day) and 65.2 g by the tenth postoperative day; control rats gained 19.1 g (significantly less than lesion at $p<0.001$, t-test) by the fifth postoperative day and 34.7 g (significantly less than lesion at $p<0.001$, t-test) by the tenth postoperative day. Ventromedial hypothalamic lesions depleted tel-diencephalic norepinephrine by 12.9% (control = 0.372 μg/g) on the fifth postoperative day and 11.0% (control = 0.350 μg/g) on the tenth postoperative day (both effects significant at $p<0.02$, t-tests). Ventromedial hypothalamic lesions had no significant effect (increase of 1.1% and 2.7% at 5 and 10 days, respectively; $p>0.2$) on striatal dopamine levels at either postoperative interval (control = 8.06 μg/g and 8.33 μg/g at 5 and 10 days, respectively). Regression correlation coefficients between weight gain at 5 and 10 days after surgery and catecholamine levels in ventromedial hypothalamic rats were subsequently determined. There was no significant ($p>0.2$) correlation ($r=-0.21$ and -0.07 at 5 and 10 days after surgery, respectively) with striatal dopamine. However, an inverse correlation with tel-diencephalic norepinephrine was significant at both postoperative intervals ($r=-0.74$, $p<0.01$ at 5 days after surgery; $r=-0.61$, $p<0.05$ at 10 days after surgery). Rats gaining more weight had lower norepinephrine levels.

DISCUSSION

The present results demonstrate a selective and persistent depletion of tel-diencephalic norepinephrine by ventromedial hypothalamic lesions. The correlation of this depletion with weight gain strongly supports the conclusion that damage to a noradrenergic bundle is responsible for hypothalamic hyperphagia [3]. This finding may be relevant to studies reporting no correlation of tel-diencephalic norepinephrine levels with the aphagic and adipsic syndrome following lateral hypothalamic lesions. That is, to the extent that lateral hypothalamic lesions include some ventromedial hypothalamic tissue, the depletion of tel-diencephalic norepinephrine would be enhanced whereas the severity of aphagia and adipsia would be diminished [2]. It is possible that the presence of two noradrenergic feeding systems, one inhibitory and one facilitatory, may be responsible for failure to demonstrate a noradrenergic correlate of the lateral hypothalamic syndrome.

REFERENCES

1. Anand, B. K. and J. R. Brobeck. Hypothalamic control of food intake in rats and cats. *Yale J. biol. Med.* **24:** 123–140, 1951.
2. Ellison, G. D., C. A. Sorenson and B. L. Jacobs. Two feeding syndromes following surgical isolation of the hypothalamus in rats. *J. comp. physiol. Psychol.* **70:** 173–188, 1970.
3. Kapatos, G. and R. M. Gold. Evidence for ascending noradrenergic mediation of hypothalamic hyperphagia. *Pharmac. Biochem. Behav.* **1:** 81–87, 1973.
4. Laverty, R. and K. M. Taylor. The fluorometric assay of catecholamines and related compounds: Improvements and extensions to the hydroxyindole technique. *Anal. Biochem.* **22:** 269–279, 1968.
5. Ungerstedt, U. Stereotaxic mapping of the monoamine pathways in the rat. *Acta physiol. scand.* Suppl. **367:** 1–48, 1971.
6. Zigmond, M. J. and E. M Stricker. Deficits in feeding behavior after intraventricular injection of 6-hydroxydopamine in rats. *Science* **177:** 1211–1214, 1972.