PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE 147, 698-700 (1974)

Effects of Warm and Cold Temperatures on Release of TSH, GH, and Prolactin in Rats (38420)

G. P. MUELLER, H. T. CHEN, J. A. DIBBET, H. J. CHEN, AND J. MEITES[1,2]

Department of Physiology, Michigan State University, East Lansing, Michigan 48824

Pronounced alterations in temperature have been reported to produce rapid changes in release of thyroid-stimulating hormone (TSH) and growth hormone (GH) in the rat. Reichlin *et al.* (1, 2) noted an inverse relationship between environmental temperature and plasma TSH levels, with cold producing an increase and heat a decrease in TSH release. Cold was reported to decrease plasma GH levels (3, 4). The effects of warm temperatures on GH release and of warm or cold temperature on prolactin (PRL) release have not been reported previously, to our knowledge. The present investigation was undertaken to determine the effects of warm and cold temperatures on blood levels of TSH, PRL, and GH in male rats.

Materials and Methods. Mature Sprague–Dawley male rats (Spartan Research Animals, Haslett, MI) weighing 250–275 g, were housed in an air-conditioned (24 ± 1°) and light-controlled (lights on from 6 AM to 8 PM) room. They were fed a diet of Purina Rat Chow (Ralston Purina Co., St. Louis, MO) and water *ad libitum*. All blood samples were collected by decapitation, and serum and plasma were separated and stored at −20° until assayed by radioimmunoassays. Serum PRL was measured by the method of Niswender *et al.* (5), plasma GH by the method of Dickerman *et al.* (6), and TSH by the method described in the NIAMD kit. Values were expressed in terms of NIAMD-rat prolactin-RP-1, NIAMD-rat TSH-RP-1, and NIAMD-rat GH-RP-1, respectively.

The control animals, maintained at a room temperature of 24°, were decapitated immediately upon removal from their cages. For high temperature, the animals were placed in a ventilated drying oven at 40 ± 2°, and decapitated 30 or 60 min later. For cold temperature, the rats were placed in individual cages in a room at 4 ± 1°, and decapitated 1 or 2 hr later. Two experiments were performed at different times by different individuals. Student's *t* test was used to test significance of difference between control and experimental blood hormone levels.

Results. In Expt. 1 (Table I), a temperature of 40° for 30 min decreased serum TSH to 27% of control values and plasma GH to 45% of control levels, and produced about a fivefold elevation in serum PRL. The GH differences in this experiment were not significant due to large animal variations in the control group. A temperature of 4° for 2 hr evoked almost a twofold increase in serum TSH, and a significant fall in serum PRL from 25 to 6 ng/ml. Plasma GH levels were not significantly altered by cold exposure.

In Expt 2, a temperature of 40° for 1 hr again produced decreases in serum TSH and plasma GH, and a rise in serum PRL. All of these differences were significant. Heat caused serum TSH to fall to 25% and GH to 30% of control values, whereas serum PRL rose about tenfold over control levels. Cold exposure for 1 or 2 hr produced a 3.4- and 4.6-fold increase in serum TSH, respectively, and a small but significant reduction in serum PRL. Plasma GH was unchanged by 1 hr and was lower by 2 hr after cold exposure but the latter difference was not significant as compared with control values. Although the hormonal responses in Expts 1 and 2 differed somewhat in magnitude to the temperature changes, the direction of the responses was the same in both experiments.

Discussion. A warm temperature of 40° produced a rapid decrease in circulating TSH and

[1] This work was supported in part by NIH Grant No. AM 04784 from the National Institute for Arthritis and Metabolic Diseases, and Grant No. CA 10771 from the National Cancer Institute.

[2] Approved for publication by the Michigan Agricultural Experiment Station as Journal Article No. 6891.

TABLE I. Effects of Heat and Cold on Blood Levels of TSH, GH, and Prolactin in Male Rats.

Treatment and No. of rats	Serum TSH (μg/ml)	Plasma GH (ng/ml)	Serum PRL (ng/ml)
	Expt. 1		
Controls, 24° (8)	0.46 ± 0.08	152 ± 55	25 ± 3
Heat, 40° for 30 min (8)	0.12 ± 0.02[c]	69 ± 4	123 ± 8[c]
Cold, 4° for 2 hr (7)	0.84 ± 0.16[a]	196 ± 55	6 ± 1[c]
	Expt. 2		
Controls, 24° (8)	0.68 ± 0.10	264 ± 62	11 ± > 1
Heat, 40° for 1 hr (8)	0.17 ± 0.03[c]	77 ± 3[a]	112 ± 16[c]
Cold, 4° for 1 hr (8)	2.3 ± 0.41[c]	272 ± 78	9 ± > 1[a]
Cold, 4° for 2 hr (8)	3.11 ± 0.50[c]	174 ± 37	9 ± > 1[a]

[a] $P > 0.05$.
[b] $P > 0.01$.
[c] $P > 0.001$.

GH levels and a marked increase in PRL, whereas cold produced an increase in blood TSH, no significant change in GH, and a reduction in PRL. Whether these results were due solely to changes in temperature or also to the possible stress experienced by these animals is unknown at present. The rats appeared to be in some discomfort while in the warm or cold temperatures, and perhaps were stressed temporarily. At 40° the rats perspired heavily, and at 4° there was noticeable piloerection. Stresses have been reported to inhibit TSH–thyroid function (1, 2, 7, 8). However, there is ample evidence that cold temperatures *per se* can increase whereas warm temperatures can decrease TSH and thyroid secretion (1, 2). The present results are in agreement with the earlier work, suggesting that temperature was the major factor responsible for altering TSH release.

The effect of 40° in reducing plasma GH levels may be due in part to stress since stresses have been found to inhibit GH release in rats (9, 10). The decrease in GH levels also may be due in part to the reduction in TSH release, since a fall in thyroid function results in a decrease in GH release (6). Cold had no significant effect on plasma GH in the present study, although it was reported previously to reduce plasma GH in rats (3, 4). The conditions of our study were different, and may not have been as stressful to the rats as in the earlier work. There also is the possibility that enhanced TSH-induced thyroid hormone release during cold prevented any possible fall in GH release, since thyroid hormones stimulate GH secretion in the rat (6; also, unpublished observations).

The pronounced rise in serum PRL as a result of heat, and the fall in serum PRL produced by cold, are just opposite to the response of TSH to these temperature changes. This suggests that different mechanisms in the hypothalamus are activated by temperature changes to alter secretion of these two hormones. Many stresses can increase PRL release in rats (11), but it appears doubtful that stress was mainly responsible for the changes noted in serum PRL levels in the present study. The decrease in serum PRL in response to cold cannot be explained on the basis of stress.

Little is known at present about the effects of temperature on the hypothalamic releasing and release-inhibiting factors which control the secretion of anterior pituitary hormones. TRH induces PRL as well as TSH release in rats (12, 13) and other species, and cold was observed to increase TRH synthesis by the rat hypothalamus (14). However, the observation that cold increased serum TSH but decreased serum PRL, whereas heat produced the opposite effects on release of these two hormones, indicates that TRH is not responsible for the changes observed on PRL release. The changes in PRL release probably were mediated via PIF and/or PRF, although this remains to be established. Somatostatin administration to the rat has been reported to depress GH release (15), to inhibit TRH-induced release of TSH but not of PRL (16), and not to affect basal levels of PRL secretion (16). Whether Somatostatin or GRF were involved in the heat-induced fall in plasma GH is

unknown, but as already indicated a decrease in thyroid function during heat could account for this fall in GH release.

The effects of temperature on hypothalamic biogenic amines also remain to be evaluated, since there is ample evidence that they can alter release of hypothalamic factors (17). However, there is practically no information at present on the effects of temperature on hypothalamic biogenic amines. It is apparent that marked changes in temperature may alter release of the three hormones via changes in hypothalamic hypophysiotropic factors and biogenic amines, through general stress effects and perhaps by other mechanisms.

Summary. When mature male rats were placed in a chamber at 40° for 30 or 60 min, there were significant decreases in serum TSH and plasma GH, and a five- to tenfold elevation of serum PRL. A temperature of 4° for 1 or 2 hr increased serum TSH, did not significantly alter plasma GH levels, and resulted in a significant fall in serum PRL. The observation that TSH and PRL responded oppositely to the same temperature changes suggests that different mechanisms regulate release of these two hormones under these conditions. The possible role of stress, and the interactions of the hypothalamic hypophysiotropic hormones and biogenic amines in the temperature-induced changes remain to be evaluated.

Note in proof: Wettemann and Tucker (Proc. Soc. Exp. Biol. Med. **146,** 908 (1974)) recently reported that cattle exposed to increased ambient temperature showed a significant rise in blood prolactin levels, whereas exposure to cold ambient temperature resulted in a significant fall in blood prolactin. Thus cattle and rats show similar prolactin patterns in response to changes in ambient temperature.

1. Reichlin, S., *in* "Neuroendocrinology" (L. Martini and W. F. Ganong, eds.), Vol. 1 p. 445. Academic Press, New York (1966).

2. Reichlin, S., Martin, J. B., Mitnick, M., Boshans, R. L., Grimm, Y., Bollinger, J., Gordon, J., and Malacara, J., Recent Progr. Horm. Res. **28,** 229 (1972).

3. Collu, R., Leboeuf, G., Letarte, J., and Ducharme, J. R., Endocrinology **94,** A227 (1974).

4. Schalch, D. S., and Reichlin, S., *in* "Growth and Growth Hormone" (A. Pecile and E. E. Mueller, eds.), p. 211. Excerpta Medica Foundation, Amsterdam (1968).

5. Niswender, G. D., Chen, C. L., Midgley, A. R., Jr., Meites, J., and Ellis, S., Proc. Soc. Exp. Biol. Med. **130,** 793 (1969).

6. Dickerman, E., Dickerman, S., and Meites, J., *in* "Growth and Growth Hormone" (A. Pecile and E. E. Mueller, eds.), p. 252. Excerpta Medica Foundation, Amsterdam (1972).

7. Ducommun, P., Sakiz, E., and Guillemin, R., Proc. Soc. Exp. Biol. Med. **121,** 921 (1966).

8. Kraicer, J., Ducommun, P., Jobin, M., Rerup, C., VanRees, G. P., and Fortier, C., Fed. Proc., Fed. Amer. Soc. Exp. Biol. **22,** 507 (1963).

9. Krulich, L., and Illner, P., Fed. Proc., Fed. Amer. Soc. Exp. Biol. **32,** 281 (1973).

10. Collu, R., Jequier, J. C., Letarte, J., Leboeuf, G., and Ducharme, J. R., Neuroendocrinology **11,** 183 (1973).

11. Meites, J., and Clemens, J. A., Vitamins Hormones **30,** 166 (1972).

12. Mueller, G. P., Chen, H. J., and Meites, J., Proc. Soc. Exp. Biol. Med. **144,** 613 (1973).

13. Mueller, G. P., Chen, H. J., and Meites, J., Fed. Proc., Fed. Amer. Soc. Exp. Biol. **33,** 197 (1974).

14. Reichlin, S., and Mitnick, M., *in* "Frontiers in Neuroendocrinology 1973," p. 61. Oxford University Press, New York (1973).

15. Brazeau, P., Vale, W., Burgus, R., Ling, N., Butcher, M., Rivier, J., and Guillemin, R., Science **179,** 77 (1973).

16. Vale, W., Brazeau, P., Rivier, C., Rivier, J., Grant, G., Burgus, R., and Guillemin, R., Endocrinology **92,** A-118 (1973).

17. McCann, S. M., *in* "Frontiers in Neuroendocrinology 1971" (L. Martini and W. F. Ganong, eds.), p. 209. Oxford University Press, London (1971).

Received July 8, 1974. P.S.E.B.M., 1974, Vol. 147.