case the capacity of the serum to neutralize exogenous relaxin was markedly greater in the nonpregnant than in the pregnant state (Table II). Also, the relaxin content of the serum from the immunized pregnant female was low or not detectable in contrast to the high relaxin titers of non-immune pregnant animals.

These data lend credence to the hypothesis that circulating relaxin in pregnant rabbit serum is complexed with a serum component which hinders combination of the hormone with exogenous antibody, inasmuch as treatment designed to disrupt protein-protein combination tends to render the hormone susceptible to the action of antibody. An alternative possibility is that glacial acetic acid or urea treatment causes a change in the structure of the hormone such as an unfolding of or actual reduction in size of the molecule. In the pregnant rabbit immunized to porcine relaxin prior to mating, the circulating antibody appears to react with the native hormone, since both a decrease in relaxin activity and in antibody titer as measured by ability of the serum to inactivate exogenous relaxin are observed. This observation indicates successful competition for the hormone by the circulating antibody and is evidence that favors our first hypothesis.

Summary. Antibody to porcine relaxin fails to inactivate the biological activity of circulating pregnant rabbit serum relaxin. However, treatment of the serum with protein dissociating agents such as glacial acetic acid or 8 M urea makes the circulating hormone amenable to neutralization by the exogenous antibody. A possible explanation for this phenomenon is discussed.

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Received January 31, 1966. P.S.E.B.M., 1966, v122.

Food Intake and Activity of Rats with Rostral Hypothalamic Lesions.* (31108)

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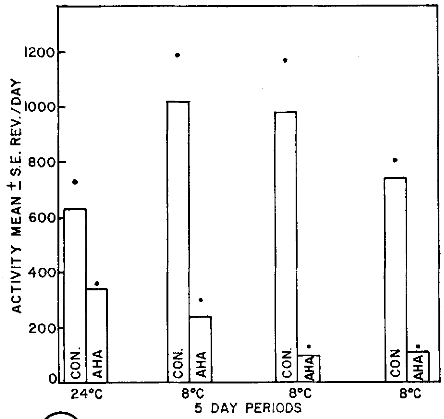
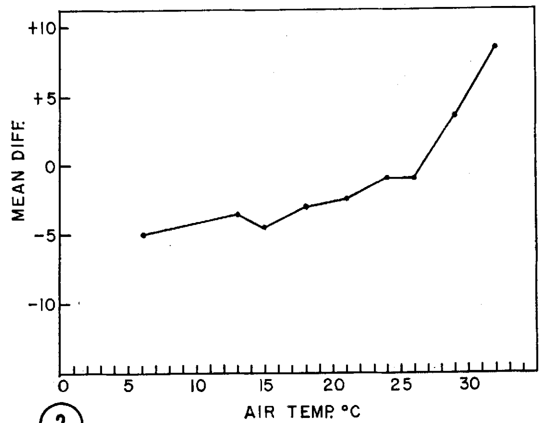
When they are transferred to a warm environment, rats eat less food. Thus, a rise in air temperature from 24° to 32°C reduces food intake by 75% in the first 24-hour period. Rats with bilateral lesions of the anterior hypothalamic area (AHA) when similarly heat stressed do not reduce their food intake so much, and may not reduce it at all if the lesions are of proper size and position(1). We have now extended our study of animals with these lesions by confirming their responses to acute exposure to heat or cold, and then performing experiments to investigate the following: (a) their spontaneous activity levels during chronic exposure to heat or cold, and (b) their food intake during 24-hour exposure to 9 different environmental temperatures ranging from 6° to 32°C.

Methods. The *S*s were 11 male Sprague-Dawley rats, 60 days old at the time of operation, and maintained on powdered Purina chow and water *ad libitum.* In 5 rats selected randomly, bilateral electrolytic lesions were placed stereotaxcially in the Horsley-Clark plane at 8½ mm anterior to the ear bars, ¾ mm from the base of the skull, and ¾ mm lateral to the midline. Later histology showed the lesions to be placed dorsal to the optic chiasma and ventral to the anterior commissure with some asymmetry. After operation, the animals were kept in individual cages at

* Supported in part by USPHS Grant 10179. The authors are grateful to W. Spanakos and P. Ciaccia for technical assistance.



(1)



(2)

FIG. 1. Running scores of lesioned and control rats before (24°C) and during cold stress (8°C). Data are plotted for successive 5-day periods.

FIG. 2. Differences in food intake between lesioned rats and controls as a function of 24-hour measurements at various air temperatures. The data show that the lesioned rats eat less than the controls at and below 26°C and more at the high temperatures. Food intake at 6°C was taken from data collected before the activity studies.

ambient temperature of 24°C. Under all of the following conditions daily records were made of food intake, body weight and temperature. During the period in the activity cages daily records were made of the number of revolutions of the wheels. To test the efficacy of the lesions, two 24-hour temperature stresses were employed, one at 31°C followed 7 days later by one at 6°C. In the heat, the lesioned rats ate 50% more than the controls and in the cold they ate 16% less than the controls. After this test, the animals were placed in Wahmann wheel type activity cages and maintained in a controlled temperature room at 24°C unless otherwise noted. After 21 days at 24°C, the temperature of the room was elevated to 32°C and maintained at that level for 7 days, at which time it was returned to 24°C. Fifteen days later the room temperature was reduced to 8°C and the rats maintained at that level for 15 days; they were then returned to 24°C and placed in individual cages without wheels. After 12 days, food intake was observed for a 24-hour period, in 6 of the controls and the 5 lesioned rats over a wide range of test temperatures in the following order, with 7 days at the control temperature of 24°C between each test: 32°, 15°, 29°, 18°, 26°, 21°, 13°C. The experiment was terminated 2 weeks later (9 months postoperation) by exposing both groups of rats to (1) a 4-hour cold stress (0°C) followed 5 days later by (2) a 4-hour heat stress (35°C).

Results and discussion. Activity measures had not been recorded before the operations but postoperative data showed the controls to be more active than the experimentals ($p < .02$ with t test). When the ambient temperature was elevated to 32°C for 7 days, both groups showed a drop in running activity. Thus, the lesioned animals responded to heat stress in a manner similar to controls. On exposure to cold stress for 15 days, the lesioned animals showed a drop in activity level and the difference between the two groups on this measure increased. Fig. 1 portrays the behavior of the animals, analyzed in terms of successive 5-day periods. During the last 10 days of cold stress the lesioned rats' activity levels were significantly lower than their prestress levels ($p < .01$). Daily mean body temperature of the lesioned rats averaged .8°C below the controls during the cold stress and .5°C above the controls during the heat stress. To test if the lesioned rats could in some manner be forced to run more, the 2 groups were fasted for one day in the cold after the main experiment had been completed. The data showed a rise of 1633% in running activity for the lesioned animals and 452% for the controls.

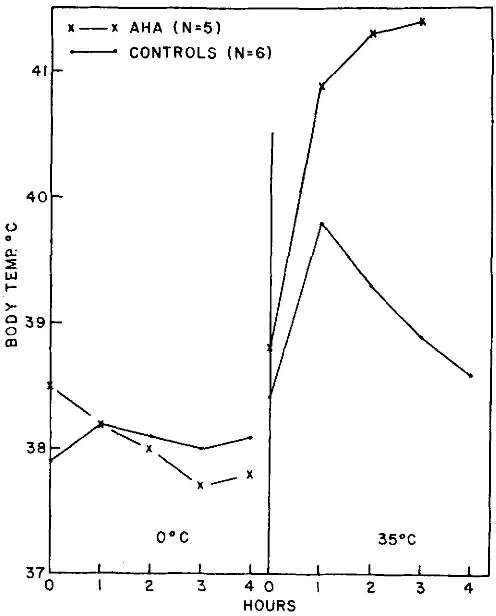


FIG. 3. Response of lesioned and control rats to 4-hour cold (0°C) and heat (35°C) stress. Air temperature changes were effected after recording colonic temperature at point 0.

The results of the study on food intake at 9 test temperatures are shown in Fig. 2. These data show that below at least 26°C the lesioned rats eat less than the controls. The difference in food intake reached statistical significance only at the two extremes: 32° and 6°C ($p<.01$ with the t test). But the trend is obvious, *i.e.*, only at the warmer temperatures do rats with AHA lesions eat as much or more than normal animals.

Fig. 3 shows data for the final test. In the cold (0°C), the lesioned rats showed a drop in body temperature while the controls showed no change. In the heat (35°C), 2 of the lesioned rats were dead at the end of 3 hours' exposure. Up until that time, the data from the lesioned rats differ radically from that of the controls. Thus, 9 months after the operations, rats with AHA lesions still show a deficit in temperature regulation.

It appears that the AHA is involved in a complex manner with mechanisms of temperature regulation which include not only the physiological adjustments made during heat and cold stress but also behavioral adjustments such as eating and running. At present it is not clear why the lesioned rats show abnormal feeding responses, but normal activity responses, to heat stress. It appears from the data on food intake (Fig. 2) that the rat with AHA lesions maintains near normal control of food intake over the range 18° to 27°C. Thus, the animal does not become truly poikilothermic although the food and body temperature data indicate a trend in that direction. Most of our lesions that have been followed by changes in behavioral phenomena invade only a small portion of the preoptic area of the brain. With large preoptic lesions, the survival rate of the animals is so poor as to obviate definitive testing. Perhaps with combination lesions of the preoptic and AHA, a rat would become truly poikilothermic. It now seems a certainty that during any such experiment the animal would have to be carefully maintained at an environmental temperature somewhat below 28°C. For a discussion of similar phenomena in goats see Andersson *et al*(2).

Summary. Rats with lesions placed bilaterally in the region of the anterior hypothalamus, when compared with control rats, eat more food in the heat, eat less food at cool and cold temperatures, and run less in response to cold stress. In addition, it was demonstrated that abnormalities in temperature regulation following the lesions are not transitory, but are clearly evident 9 months after the operations.

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Received February 3, 1966. P.S.E.B.M., 1966, v122.