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STUDIES OF THE SATIETY RESPONSE IN MICE[1]

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The increase in general activity which follows food deprivation in animals is well known (1). Less well known is the marked decrease in spontaneous running activity which occurs after a period of refeeding. Working with rats, Finger (2) demonstrated that after a period of food deprivation, feeding produced a marked decrease in spontaneous running activity as measured by the revolving cage technique. He called this response a "satiation syndrome." Studies in this laboratory (3) have confirmed this satiety response in mice. The present study was designed to determine some of the factors involved in this response.

METHODS AND MATERIALS

Female mice of the DBA strain obtained from the Jackson Memorial Laboratories, Bar Harbor, Maine, were used in this study. These mice were housed at constant temperature (72 F.), relative humidity (48 per cent), and with 12 hours of light each day. Mice under active study were placed in revolving activity cages modified from those described by Richter and Wang (4). After their daily activity, weights and food intakes had become relatively stable, they were subjected to the various manipulations described in the section Procedures and Results. Water was allowed *ad libitum* at all times. Ground Purina Chow pellets were fed unless otherwise indicated.

PROCEDURES AND RESULTS

Since the spontaneous activity covers a wide range among individual mice, the average activity for each mouse during the six day control periods has been taken as 100 per cent activity for charting purposes. The percentage of this base line for the mice in each study has been averaged for each day. Thus, the activity data are charted in terms of changes in activity during each study.

Figure 1 illustrates the changes in spontaneous running activity which occurred when six mice were deprived of food for 48 hours. On the first and second day of refeeding, there was a marked decrease in spontaneous running activity associated with a food intake above the control period average.

Figure 2 represents a study in which nine mice were allowed to have only 0.6 gram of food in the 24 hour period following a one day period of food deprivation. This limited amount of food produced a significant decrease in spontaneous running activity.

A mouse with electrolytic lesions (5) in the ventromedial centers of the hypothalamus which produced hyperphagia and obesity was subjected to a similar study. It is apparent in Figure 3 that this animal exhibited no significant activity changes on food deprivation or refeeding.

Figure 4 illustrates the results of a study of 12 mice given 0.1 mg. of chlorpromazine and 12 mice given 5 γ of reserpine subcutaneously twice daily. While both of these drugs produced marked decreases in spontaneous running activity, they did not affect the type of response to food deprivation and refeeding. The effect of oophorectomy on the

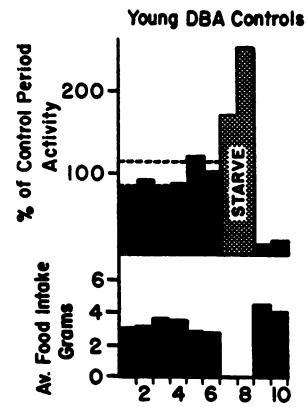

FIG. 1. DAILY PERCENTAGE OF CONTROL PERIOD ACTIVITY AND AVERAGE FOOD INTAKE FOR SIX NORMAL MICE DURING *Ad Libitum* FEEDING, STARVATION, AND REFEEDING

Broken lines indicate one standard deviation on either side of the control period average.

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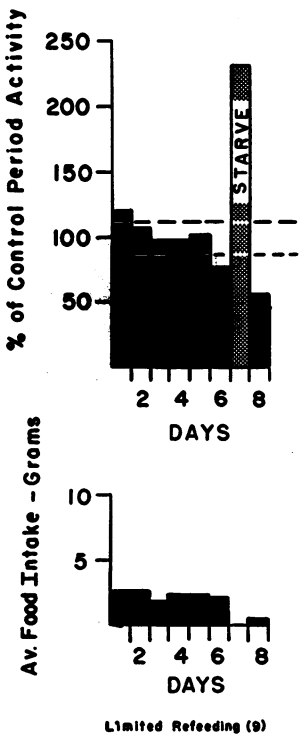

FIG. 2. DAILY PERCENTAGE OF CONTROL PERIOD ACTIVITY AND AVERAGE FOOD INTAKE FOR NINE MICE ALLOWED ACCESS TO ONLY 0.6 GM. OF FOOD THE DAY FOLLOWING A 24 HOUR PERIOD OF FOOD DEPRIVATION

Broken lines represent one standard deviation on either side of the control period average.

response to food deprivation and refeeding is given in Figure 5. Here oophorectomy produced the well known decrease in activity but it did not change the character of the response to starvation and refeeding.

The activity levels of nine mice allowed access to the protein lactalbumin, after 24 hours of fasting, are given in Figure 6. Although these mice ate an average of only 0.6 gram of this substance, a significant decrease in running activity occurred. Similar studies allowing only sucrose or lard after a 24 hour fast were done. An average intake of 3.0 grams of sucrose resulted in a decrease in running activity to 50 per cent of the control period activity while an intake of 1.6 grams of lard resulted in a decrease to 60 per cent.

Ten mice were offered kaolin sweetened with saccharin after a 24 hour fast. From Figure 7 it is evident that, though they ate an average of 0.8 gram of this substance, their running activity did not fall below the control period average.

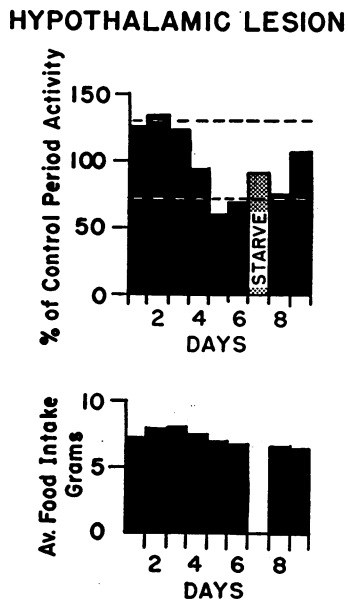

FIG. 3. DAILY PERCENTAGE OF CONTROL PERIOD ACTIVITY AND AVERAGE FOOD INTAKE IN A MOUSE WITH BILATERAL HYPOTHALAMIC LESIONS RESULTING IN HYPERPHAGIA AND OBESITY DURING *Ad Libitum* FEEDING, FOOD DEPRIVATION, AND REFEEDING

DISCUSSION

In planning these experiments, the question arose as to whether the satiety response was due to inanition or fatigue. From the study (Figure 1) in which mice were starved for 48 hours, it is apparent that the decrease in spontaneous running activity on refeeding after a 24 hour fast is

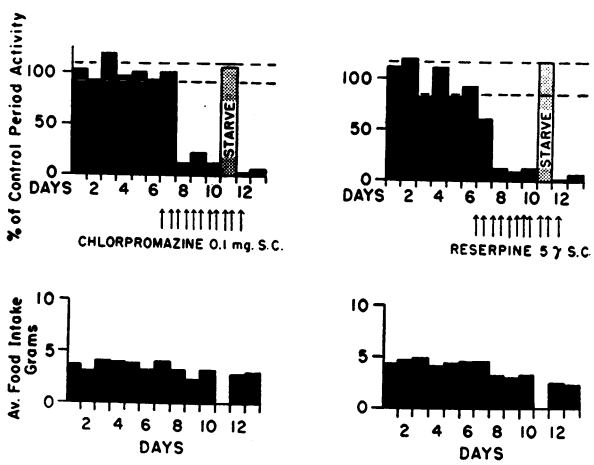

FIG. 4. DAILY PERCENTAGE OF CONTROL PERIOD ACTIVITY AND AVERAGE FOOD INTAKE OF 12 MICE GIVEN CHLORPROMAZINE AND RESERPINE DURING *Ad Libitum* FEEDING, STARVATION, AND REFEEDING

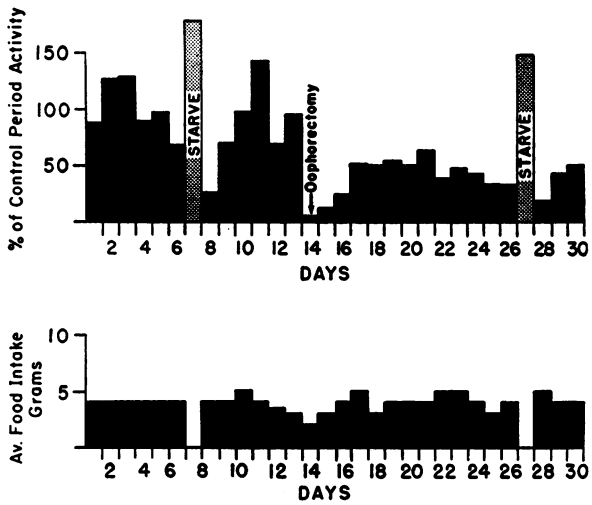

FIG. 5. PERCENTAGE OF CONTROL PERIOD ACTIVITY AND AVERAGE FOOD FOR NINE MICE DURING *Ad Libitum* FEEDING, STARVATION, REFEEDING BEFORE AND AFTER OOPHORECTOMY

not due to these factors. The observation that the mice consume more food than usual on refeeding after food deprivation (Figure 1) prompted the second study (Figure 2) in which mice were allowed access to a very limited amount of food in the refeeding period. This small amount was sufficient to produce a significant satiety response. Thus, the satiety response is not due to overeating.

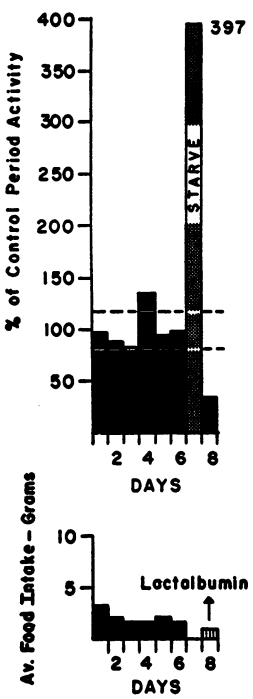

FIG. 6. PERCENTAGE OF CONTROL PERIOD ACTIVITY AND AVERAGE FOOD INTAKE FOR NINE MICE ALLOWED ACCESS TO *Ad Libitum* LACTALBUMIN AFTER 24 HOURS OF FOOD DEPRIVATION

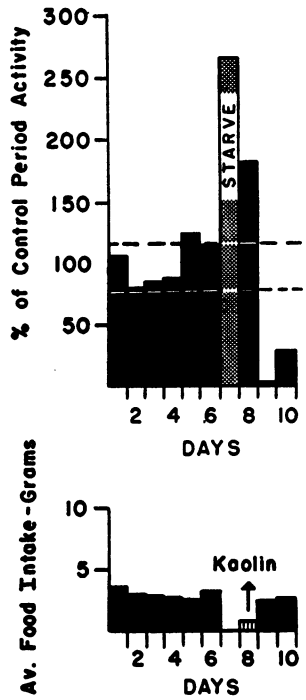

FIG. 7. PERCENTAGE OF CONTROL PERIOD ACTIVITY AND AVERAGE FOOD INTAKE FOR 10 MICE ALLOWED *Ad Libitum* KAOLIN SWEETENED WITH SACCHARIN AFTER A 24 HOUR FAST

The well established observations that rats (6, 7) and mice (5) with injuries in or around the ventromedian nuclei of the hypothalamus overeat and become obese were responsible for the study in Figure 3. Here a mouse with bilateral electrolytic lesions in the hypothalamus which resulted in hyperphagia and obesity was studied. In this study the satiety response did not occur nor did the usual increase in running activity on food deprivation. This, coupled with observations that mice with injury to the hypothalamic feeding centers produced by gold thioglucose (8) do not show changes in running activity on food deprivation or refeeding (3), indicates that intact hypothalamic feeding centers must be present for the satiety response to occur.

The mice given chlorpromazine and reserpine in Figure 4 showed a marked decrease in running activity on refeeding. Oophorectomy also produced a decrease in running activity (Figure 5);

however, this did not change the pattern of the response to food deprivation and refeeding. From these studies it is apparent that changes in the level of activity do not block the satiety response. The sites of action of chlorpromazine (9) and reserpine (10) are not clearly defined, but there is evidence that they do influence some hypothalamic centers.

The evidence that protein will produce a satiety response is given in Figure 6. This and similar studies with sucrose and lard indicate that simple nutrients produce a satiety response. This suggests that there may be a simple chemical substance which is responsible for triggering the satiety response.

The possibility that the satiety response might be due to the presence of material in the gut or the act of eating was explored by giving kaolin sweetened with saccharin in the refeeding period (Figure 7). Even with an average intake of 0.8 gram, running activity did not fall below the control period average.

From these studies it appears that the marked decrease in spontaneous running activity mice exhibit on refeeding after a period of starvation may be termed a satiety response. This response is dependent on intact hypothalamic feeding centers and the ingestion of at least a small amount of a simple nutrient. It is not affected by factors which change the general level of activity. This satiety response is not directly dependent on the volume ingested nor is it due to the act of eating or the presence of material in the gut. The role of the satiety response in the regulation of food intake is not clear. Studies of Brobeck (11) and Stevenson and Rixon (12) offer the idea that activity and food intake are related to the maintenance of body temperature.

SUMMARY

The marked decrease in spontaneous running activity mice exhibit on refeeding after a period of starvation has been studied. This change in running activity appears to be a satiety response. This response is dependent on intact hypothalamic feeding centers and the ingestion of a small amount of a simple nutrient.

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