

Exercise, Food Intake and Body Weight in Normal Rats and Genetically Obese Adult Mice¹

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IT IS GENERALLY assumed that the relationship of food intake to exercise is one of direct proportionality above the basal level corresponding to inactivity. It is the purpose of the first part of this article to show that such a concept is an oversimplification at variance with the facts. Similarly, it is usually assumed that following exercise an obese animal or person will increase food intake in direct proportion, whatever the intake prior to exercise or the energy expended in exercise. It has been shown (1) that in the hereditary obese hyperglycemic syndrome (2, 3), a decrease in voluntary activity (to less than 2% of the normal in adult animals) is an essential aspect of the etiology of the obesity; this lack of activity was shown to precede the development of the obesity and is not simply a result of the overweight (1). When obese mice also carry the waltzing gene and are in nearly constant rotary movement in their cages, their weight rarely exceeds 40 gm instead of twice that value. In another report (4) it has been demonstrated that mice made obese by goldthiogluucose injection (2) will lose weight if given the opportunity to practice unrestricted exercise. It is the purpose of the second part of this paper to show that the development of hereditary obesity in mice can be considerably slowed down by forcing these animals to exercise.

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METHODS

The treadmill used in this investigation was built by one of us (J. M. C.) in the Harvard Medical School Machine Shop. This treadmill (fig. 1) consists primarily of a 10-in.-wide 'Dresco' 7-ply rubber belt, (It now appears that a 5-ply belt would probably be better) running over two 2-in. diameter aluminum pulleys. One pulley has a horizontal adjustment, so as to make possible a straight run for the belt. The top side of the belt runs over an aluminum platform which is fastened to the 30 x 26-in. plywood base. The motor used is a 1/12 h.p. Emerson, split phase (1725 r.p.m.). There are eight speeds, varying from approximately 0.27 mi. = 0.435 km to 1 mi. = 1.610 km/hr. The frame is made of 1/4-in. lucite, 10 in. wide x 20 in. long x 6 in. high. It has two lengthwise and one crosswise partitions. All of these are removable. This allows for a choice of one to six compartments. A metal screen fits snugly on top. The whole frame has a slight vertical adjustment to bring it close enough to the belt to avoid allowing the tail or paw of an animal being pinched while in the same time preventing the frame from rubbing against the belt. A protective guard (not shown in the picture on fig. 1) is fastened over the V-belts and pulleys. For the experiments reported here, which involved essentially endurance running, these speeds were used: 1.000 mph = 1.610 km/hr. for the rats and 0.27 mph = 0.435 km/hr. for the mice. Rats were usually exercised in two periods, one in the morning and one in the afternoon. They were run 10 minutes, then rested 5 minutes until half of the total duration was obtained. When exercising mice, a timer was used. This is a single cam-operated cycle timer, type CF3-1-5m, obtained from the R. W. Cramer Company, Inc., Centerbrook, Connecticut. It is set for a total cycle of 5 minutes with the switch set to operate for 3 minutes. The timer will therefore turn off the motor for 2 minutes every 5 minutes and will keep repeating the cycle as long as the power is turned on. The mice were exercised 1 hour a day in two equal periods, one in the morning and one in the afternoon.

The rats used were mature, large adult females, homogeneous with respect to age and weight. They were kept in individual cages and fed a diet of the following percentage composition: Casein 25, refined corn oil 3, cod liver oil 2, salt mixture (5) 4, sucrose 65.9, choline 0.1. The following vitamins were added (in mg/kg of diet): thiamine 5, riboflavin 5, nicotinic acid 50, pantothenic acid 50, biotin 0.5, folic acid 0.5. The number of animals used was 12 for durations of exercise of up to 2 hours, 6 for durations of 3-6 hours, and 3 above 6

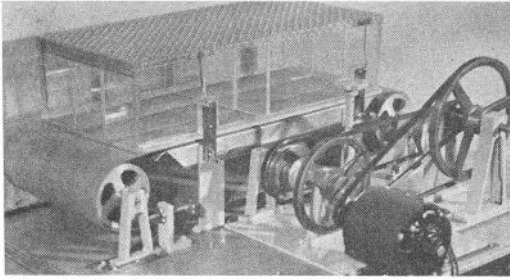


FIG. 1. Treadmill for small animals used in these experiments.

hours. Although a number of animals were exercised for longer periods, they lost weight, became overtired, and the possibility of collecting reliable data was questionable. All animals were given a preliminary period of 15 days with daily, short term (3 min.) running periods to accustom them to the treadmill. They were maintained at each level of activity long enough (at least 14 days) to insure that a steady state had been obtained. Such a steady state could not, however, be obtained above 6 hr/day.

The points in figure 2 represent the values obtained when a steady state had been obtained (usually last 6 or 7 days on each run).

The mice used were young adults almost plateaued in weight, equally drawn from males and females. The non-obese animals weighed on the average 22 gm at the start of the experiment. The obese animals weighed 52 gm. They were kept in individual cages and fed purina laboratory chow, ground to permit accurate determination of food intakes. Twelve obese and non-obese animal were used; half of each group exercised and the other non-exercised. The duration of the experiment was 45 days.

RESULTS

Results of the experiment in normal rats are given in figure 2. It is seen that durations of exercises of 20, 40, and 60 minutes are not followed by an increase in food intake over the amount corresponding to absolute inactivity. In fact, a small decrease is the result. While this decrease is of a relatively low order of significance ($P < 0.05$), it was consistent, and it is felt that it represents a reproducible physiologic finding. The weight of the animals decreased correspondingly. Above 1 hour of exercise, the food intake increased in direct proportion until a total duration of 6 hours was reached. Because of the slight drop in food consumption with an hour's duration of exercise, it was not until with 2 hours of exercise that food intake was increased above the initial amount. Body weight was maintained at a level slightly lower than that reached after

1 hour exercise durations. Above the 6 hours, the animals became generally too tired to exercise any further. Extreme prodding was required, accidents tended to occur (digits pinched) and the animals rapidly lost weight. For this reason, the points at or above 6 hours are not fully representative.

Results of the experiment on obese and non-obese mice are given in table 1 and figure 3. From the former it is seen that the 1-hour period of exercise forced on the animals increased the food intake of the non-obese animals only slightly while it increased that of the obese animals considerably. Nevertheless, from figure 3 it is seen that the weight of the exercised non-obese animals did not differ significantly from that of their non-exercised controls, while the rate of weight gain of obese animals was considerably decreased by the 1-hour exercise period.

DISCUSSION

Laboratory animals under the usual conditions of care might be considered to be sedentary. Their only activity is moving themselves in a relatively small cage. The first experiment seems to show clearly that a certain amount of physical activity in such sedentary rats is possible without a corresponding increase in caloric intake. The existence of such a 'sedentary range' in which activity may be increased without a corresponding increase in energy intake had previously been observed in this laboratory by a number of experiments on young rats, involving climbing or swimming (6). It was observed that there existed a point below which a decrease in activity was not accompanied by a corresponding decrease in food intake. It had been shown previously, by Gasnier and A. Mayer (7, 8) that rabbits, when restricted in their activity by confinement in a small cage, will consume a fixed percentage in excess of requirements and accumulate fat. The excess food intake consumed is characteristic of the species. Within the species there are strain differences. Finally within each strain there are characteristic individual idiosyncrasies. In the rat, Ingle (9) found that he could make animals obese by immobilization. It is of course a well known practice in agriculture to restrict the activity of animals which are being fattened. This practice is applied in particular to hogs and geese. Greene (10)

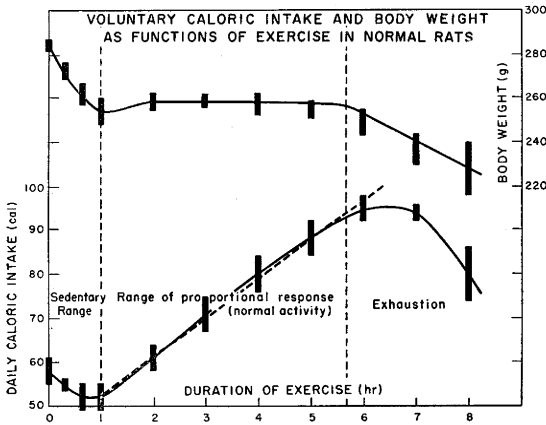


FIG. 2. Food intake and body weight as functions of duration of exercise in normal adult rats.

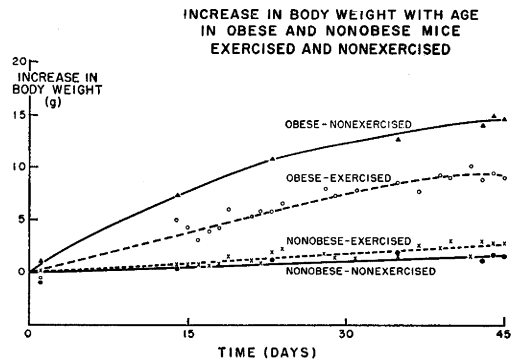


FIG. 3. Body weight variations with time of exercised and non-exercised obese and non-obese mice.

studied more than 200 overweight patients in whom the beginning of obesity could be traced directly to a sudden decrease in activity. All these facts indicate that when activity is progressively decreased, a certain level (characteristic of the species, strain and individual) is reached under which no further decrease in food intake is observable.

Preliminary findings on young animals, exercised and unexercised (6) suggest that the nature of the diet influences the position of this critical level. If diets low in carbohydrates are used, the 'non-responsive range' is shortened; preferential oxidation of glucose causing a greater relative depletion of carbohydrate reserves in diets low in glucogenic (protein or carbohydrate) material, and hence, as could be predicted in the light of the glucostatic scheme of the regulation of food intake (11), an earlier increase in food intake because of a more rapid decline of blood sugar and thus a shorter 'non-responsive range.'

These results suggest that a 'non-responsive range' with regard to change in food intake exists on both sides of the usual zone of activity. This apparent failure or lack of flexibility of a basic regulation in this low range can be interpreted on teleologic grounds; in a natural habitat, the work involved in the quest for food is such that activity is seldom depressed to that level. Exceptional and 'unnatural' situations are encountered in mechanized, urbanized human life and the restricted activity of domestic animals.

The fact that in the rats exercised for an hour

or less there was not only no increase, but even a slight (but significant) decrease in food intake following exercise may appear surprising. It can indicate greater availability of reserves, perhaps because of changes of circulatory conditions. In this connection, it is worth noting that a common cause of insulin coma is a sudden increase in exercise by the patient (12). Apparently the utilization of metabolites and reserves is sufficiently improved by such a practice to reduce drastically the amount of insulin required. It is, of course, possible that a continued decrease in the fat content of the animals takes place when the duration of exercise is increased, but that this is masked by increased muscle mass.

As far as the genetically obese mice are concerned, it had been shown previously (1) that this reduced activity due to physical inertia played an essential role in the development of the obesity: the weight differences between obese and non-obese animals have been found to be accounted for almost exclusively by fat (13). Weight increases of 15-20 gm/mo. in adult mice are frequently observed. It is readily seen, therefore, that differences of food intake between obese and non-obese animals of less than 5 cal/day (14) (confirmed in this study, see table 1) are not sufficient to account for the development of the obesity. The explanation lies in the fact that the resting metabolism does not increase with weight in this form of obesity (15) and that the approximately 8 cal/day expended by non-obese animals on activity (1) are available, in the

TABLE I. EFFECT OF EXERCISE (TREADMILL) ON FOOD INTAKE AND WEIGHT GAIN OF NON-OBESE AND GENETICALLY OBESE MICE

duration of exercise 45 days

	Non- Exercised	Exercised	Non- Exercised	Exercised
	<i>Nonobese Mice</i>		<i>Obese Mice</i>	
Food intake,	3.9	4.2	4.5	7.0
gm.	±.387	±.648	±.533	±1.631
Wt. gain, gm.	1.5	2.8	14.7	9.2
	±.74	±1.54	±2.63	±2.31

extremely inactive obese animals, for fat formation. In the experiment presented here, a considerable slowing down of the rate of development of obesity was obtained when the animals were exercised, even though their food intake was quite significantly increased. It would appear that, if reference is made to the diagram obtained for the rats (fig. 2), a duration of exercise of 1 hour at 0.435 km/hr. for the mice is the equivalent of a 2-hour exercise period at 1.610 km/hr. for the rats, as far as food intake is concerned. The fact that there was no response of body weight may be due to replacement of fat by muscle mass. This difference between reactions of rats and mice may be representative of species' differences in reactions to exercise generally. On the other hand, it is the equivalent of much more than that for the obese mice, the normal weight gain of which is already affected at that level. It would appear, therefore, that genetic factors determine the extent of the 'sedentary' range and the 'normal' activity range and probably also the length of the non-responsive range with respect to food intake.

It has already been mentioned, as reported elsewhere (4), that mice made obese by goldthioglucose injection show a high order of spontaneous activity. This is one of the characteristics differentiating goldthioglucose obesity from genetic obesity. If goldthioglucose animals are given an opportunity to exercise voluntarily by placing them in activity cages, they run vigorously, decrease their food intake, and lose a considerable amount of weight (of the order of 15 gm in the first week). When non-obese mice were placed in similar cages no decrease in food intake and no weight loss were observed. It is manifest that the effect of that form of obesity is to exaggerate considerably

the phenomena observed in the rats. The multiplicity of etiologies of obesity thus leads to differences in rates of voluntary exercise, in extent of effect of exercise on food intake, as well as to differences in nutritional, metabolic and endocrine consequences.

SUMMARY

When mature rats accustomed to a sedentary existence were exercised in a treadmill for increasing daily periods, it was observed that for low durations of exercise (20 minutes to 1 hour) there was no corresponding increase in food intake. Actually food intake decreased slightly but significantly. Body weight also decreased. For longer durations of exercise (1-5 or 6 hours) food intake increased linearly and weight was maintained. For very long durations of exercise, the animals lost weight, their food intake decreased and their appearance deteriorated. These three ranges of activity might be termed sedentary, normal, and exhaustion. Both the sedentary and the exhaustion ranges can be considered 'non-responsive ranges' with respect to food intake as, in these ranges, an increase in activity is not accompanied by a corresponding increase in food intake. When non-obese and genetically obese mice all accustomed to a sedentary exercise were exercised on a treadmill for 1 hour a day, and changes in weight compared to those of non-obese and obese mice not exercised, it was found that exercise did not affect the weight of the normal mice but considerably decreased the weight gain of obese mice even though these obese mice responded to exercise by an increase in food intake. Comparison of reactions to exercise of rats and mice show that there are some species differences in degree of reaction of exercise of normal animals; similarly, comparison of reactions to exercise of genetically obese and goldthioglucose mice show that there are differences in degree of reaction to exercise in different types of obese animals. The importance of considering exercise as well as food intake in problems of obesity is again illustrated by these results.

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