

Effect of Age on Hyperphagia in the Genetically Obese Zucker Rat^{1,2} (39589)

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Obese animals, such as the genetically obese Zucker rat (1-3), consume excessive amounts of food as compared to lean littermates. Obese rats also weigh more than lean rats (3), so it is reasonable that obese rats consume more total food per day. Extrapolation from several studies utilizing mature rats (2-4), however, revealed that when food intake was expressed per unit of body weight (FI/BW), obese rats were not hyperphagic. Because several reports indicated that metabolic activity was elevated in the young, rapidly growing obese rat (5, 6), we speculated that hyperphagia in terms of increased FI/BW would most likely occur in young rats. The objective of the present study was to determine the effect of age on FI/BW in lean and obese Zucker rats. Our results demonstrated that hyperphagia was present in the young obese rat but disappeared in the older animal.

Materials and methods. Experiment 1. Ten lean rats and 12 obese rats of the Zucker strain were individually caged and maintained at $22 \pm 1^\circ$. A commercial diet³ was ground and supplemented with 1% oil to yield the following nutrient composition: 23.0% protein, 5.5% fat, 56.5% carbohydrate, 6.0% fiber, and 9.0% ash. Food and water were offered *ad libitum*. Food intake (FI) was measured daily and body weight (BW) was recorded on alternate days from 7 to 19 weeks of age. Weekly averages for FI and BW were calculated. At 7 weeks of age, it was not difficult to determine which rats were obese on the basis of FI, BW, and conformation.

Experiment 2. Thirty-three Zucker rats

from four complete litters were weaned and placed in individual cages maintained at $22 \pm 1^\circ$. A semipurified diet (Table I) and water were offered *ad libitum*. This powdered diet consisted of 22.9% protein, 4.0% fat, 65.0% carbohydrate, 1.9% fiber, 4.0% ash, and 2.2% vitamin mixture. FI was measured daily and BW was recorded every 2 days from 3 to 11 weeks of age. BW and FI differences at 3.5 weeks of age confirmed our tentative visual identification of 26 lean and 7 obese rats when the trial was initiated. Weekly averages for FI, BW, and FI/BW for both experiments were compared by the unpaired Student's *t* test.

Results. Obese rats were observed to have a higher FI per day and BW than lean rats ($P < 0.01$) throughout Experiment 1 (Fig. 1). A faster rate of gain was apparent in the obese rats. Hyperphagia, defined as a higher FI/BW, was evident only up to 10 weeks of age ($P < 0.01$). From 13 to 18 weeks of age, there were no differences in FI/BW. At 19 weeks of age, obese rats were hypophagic compared to lean rats ($P < 0.01$).

TABLE I. COMPOSITION OF DIET USED IN EXPERIMENT 2 WITH WEANLING RATS.

Ingredient	%
Casein	22.5
DL-Methionine	0.4
Peanut oil	4.0
Corn starch	39.0
Glucose	19.5
Sucrose	6.5
Cellulose (Alphacel)	1.9
Vitamin mixture ^a	2.2
Mineral mixture ^b	4.0
	100.0

^a Vitamin Diet Fortification Mixture; Nutritional Biochemicals Corporation, Cleveland, Ohio 44128.

^b Jones and Foster Salt Mixture; Nutritional Biochemicals Corporation, Cleveland, Ohio 44128.

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² Authorized for publication on November 20, 1975 as Paper No. 4975 in the journal series of the Pennsylvania Agricultural Experiment Station.

³ Purina Laboratory Chow, Ralston Purina Company, St. Louis, Missouri 63199.

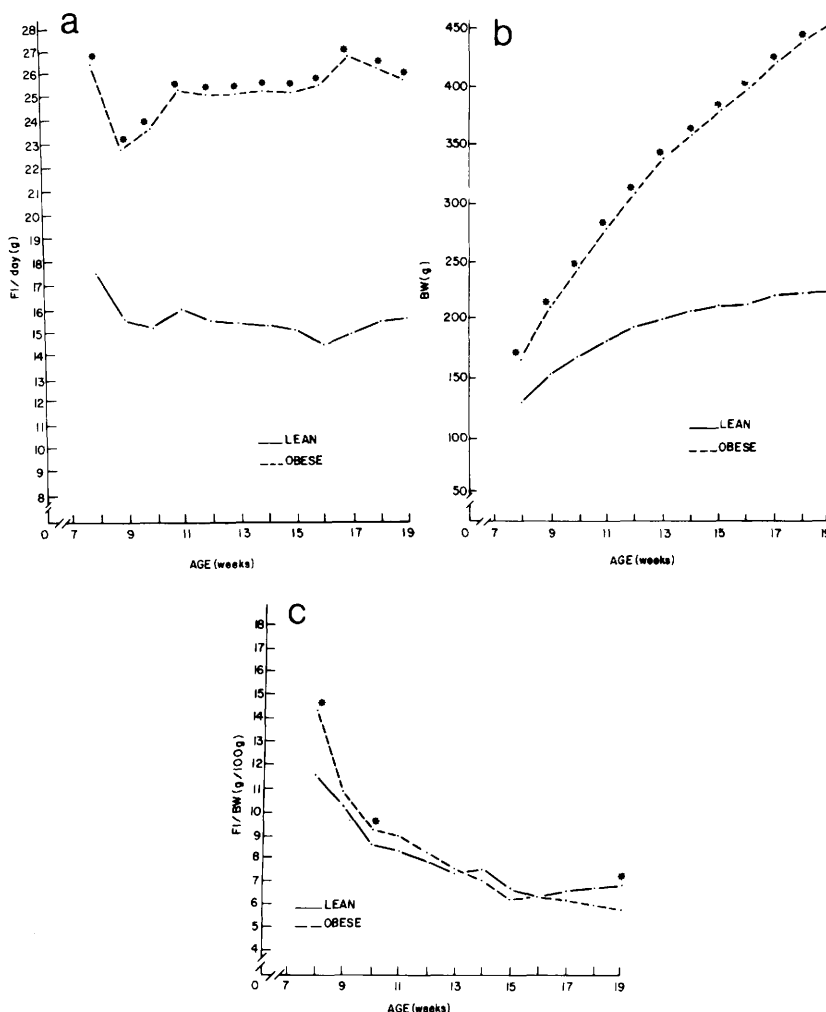


FIG. 1. (a) Food intake of lean and obese Zucker rats, 7 to 19 weeks of age. (b) Body weight of lean and obese Zucker rats, 7 to 19 weeks of age. (c) Food intake per 100 g of body weight of lean and obese Zucker rats, 7 to 19 weeks of age. * Significantly different from lean value ($P < 0.01$).

In Experiment 2 (Fig. 2), both total daily FI and BW were elevated in obese rats ($P < 0.01$) as was observed in Experiment 1. However, at this younger age, total food intake was increasing during the first 3 weeks of the experiment in both lean and obese groups, as compared to the relatively constant food intake in Experiment 1 with older rats. Daily FI leveled off in lean and obese rats at about 7 weeks of age to approximately the same FI observed at the initiation of Experiment 1 at 7 weeks of age. Rate of weight gain also appeared to be more rapid in the young lean and obese rats. FI/BW was higher in obese rats from 3 to 7

weeks of age ($P < 0.01$). There was no difference in FI/BW at 8 and 9 weeks of age and, thereafter, obese rats had lower FI/BW ($P < 0.01$).

When food intake was expressed on the basis of metabolic size ($BW^{0.75}$), similar relationships as those shown in Figs. 1 and 2 were observed. However, when $BW^{0.75}$ was used, the degree of hyperphagia of obese rats was even greater than when $BW^{1.0}$ was used.

Discussion. These experiments demonstrate that designating obese animals as hyperphagic, solely on the basis of excessive daily FI, is inappropriate. It has been shown

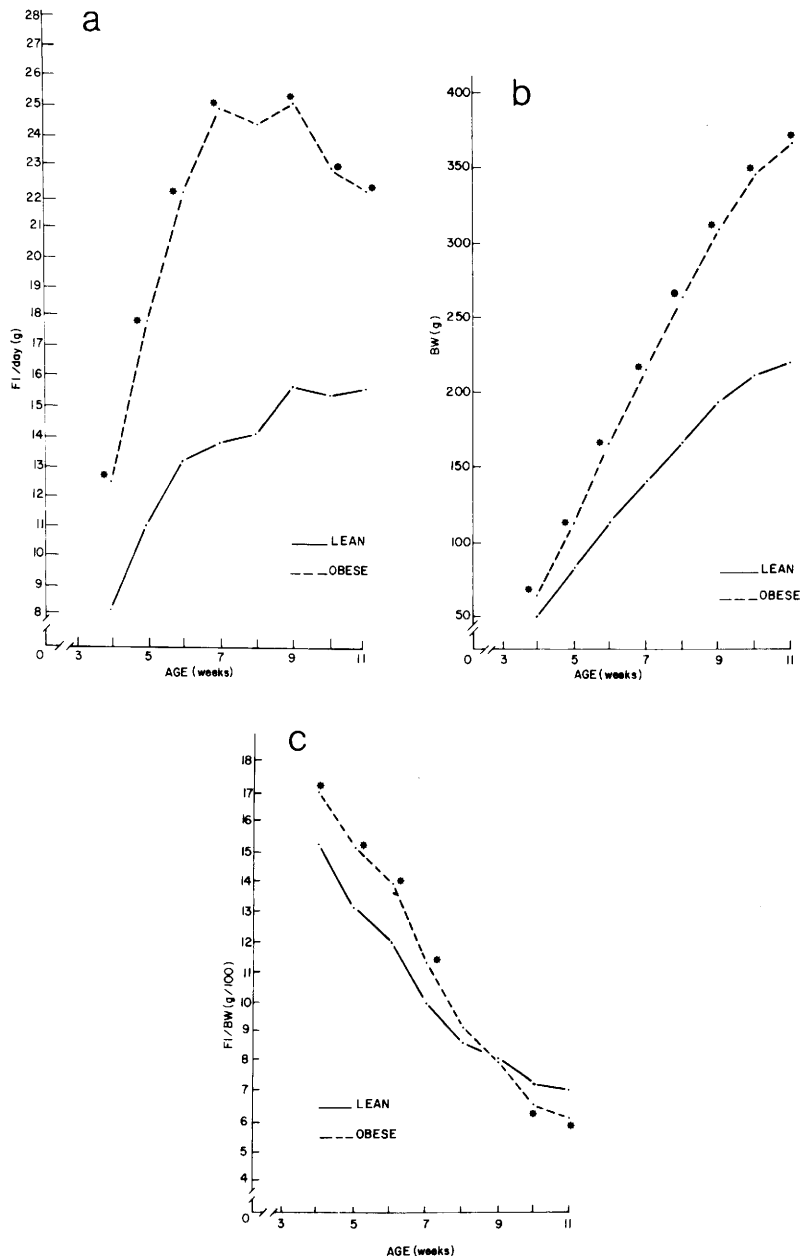


FIG. 2. (a) Food intake of lean and obese Zucker rats, 3 to 11 weeks of age. (b) Body weight of lean and obese Zucker rats, 3 to 11 weeks of age. (c) Food intake per 100 g of body weight of lean and obese Zucker rats, 3 to 11 weeks of age. * Significantly different from lean value ($P < 0.01$).

that FI per day is greater in the Zucker obese rat as compared to the lean littermates (1, 2). When FI is expressed per unit of BW to compensate for large differences in BW, it is clear from our studies that obese rats were hyperphagic only from 3 to 7 weeks of age. Recalculation of data from several reports involving rats 6 to 12 weeks of age indicated no difference in FI/BW between lean or obese rats (2-4); 10- to 12-week-old obese rats had a lower FI/BW than leans (2). These results are in agreement with the present study since no difference in FI/BW was seen in rats from 7 to 10 weeks of age, and beyond 10 weeks of age, as the rate of body weight gain started to plateau, the obese rats were hypophagic compared to the lean rats.

The increased gain in body fat relative to protein with increasing age is a well-known phenomenon. In addition, rate of body gain generally decreases with age. Collectively, these observations could account for the general decrease in FI/BW observed in both the lean and obese animals with age in our studies. However, the differences in these age-related changes between lean and obese animals are not yet well defined. Inactivity in the older obese rat may also account for part of the difference in the FI/BW changes between lean and obese rats observed in our studies. Young obese Zucker rats have been shown to be less active and to have a lower basal metabolism than lean littermates (7). Also, older obese rats have been reported to be more sluggish and to have a lower maintenance requirement (2) than lean rats.

The age at which hyperphagia disappeared in the two experiments reported was not the same. In Experiment 1, hyperphagia ceased at about 10 weeks of age whereas it ended at about 7 weeks of age in Experiment 2 with the weanling rats. Rats in Experiment 2 grew faster and were approximately 25% heavier than those of Experiment 1 at 8 weeks of age. The semipurified diet used in Experiment 2 was lower in fiber and probably more palatable and more digestible than the chow diet used in Experiment 1. This probably enhanced maximal FI and enabled the weanling rats in Experiment 2 to grow faster, and thus allowed the obese rats to reach a set point of body en-

ergy balance (8) with a shorter period of hyperphagia.

The hyperphagia observed in early life would be consistent with the elevated lipid deposition, glucose metabolism, lipogenesis, and lipolysis observed in weanling obese rats (5, 6, 9). An overall increase in energetic efficiency during this early stage of development in the obese rat may be related to the observed hyperphagia. Obese rats, however, still retained significantly more energy as fat compared to lean rats (3, 10, 11) when food intake was restricted. These studies suggest that it would be advantageous to study metabolism as related to the control of food intake in the obese animal at an early age when hyperphagia is most evident.

Summary. Two experiments were conducted to determine if and when hyperphagia occurs in the genetically obese Zucker rat. In Experiment 1, lean and obese rats were offered food *ad libitum* from 7 to 19 weeks of age. Obese rats consumed significantly more total food than lean rats throughout the experiment. However, when food intake (FI) was expressed per unit of body weight (FI/BW) to compensate for the large differences in body weight between lean and obese rats, hyperphagia in the obese rats was only evident from 7 to 10 weeks of age. Thereafter, FI/BW became similar and at 19 weeks of age, FI/BW was significantly lower for obese rats compared to leans. Experiment 2 studied younger rats (3 to 11 weeks of age) and produced similar results. However, the increased FI/BW in obese rats was more pronounced at the early age and was evident from 3 to 7 weeks of age. It is concluded that obese rats were hyperphagic compared to lean rats, but only at an early age.

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