Locomotor Activity of Various Types of Genetically Obese Mice (36522)

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Mice become obese due to single gene mutations at various loci such as obese (1), diabetes (2) or agouti (3, 4) or due to polygenic inheritance such as in the New Zealand obese mice (5). A comprehensive review on genetically obese rodents recently appeared in *Physiological Reviews* (6). In order to gain some insight into the relationship between activity and obesity, the locomotor activity of these mice before and after they became obese was compared with that of normal mice of the same strains.

Materials and Methods. Only male mice were used in this study. C57BL/6J—*ob/ob* (obese), *ob/ob*$^+$ (heterozygous) and *ob*$^+$/*ob*$^+$ (normal) and C57BL/KsJ—*db/db* (diabetic), *db/db*$^+$ (heterozygous) and *db*$^+$/*db*$^+$ (normal) mice were supplied by the Jackson Laboratory, Bar Harbor, Maine; VY/Wf—A^{vy}/a (viable yellow) and *a/a* (normal) and YS/ChWf—A^y/a (lethal yellow) and *a/a* (normal) mice were supplied by Dr. George L. Wolff of the Institute for Cancer Research, Fox Chase, Philadelphia. New Zealand obese mice (NZO) of NZO/BlWfL strain were bred in our laboratory. The ambient temperature was maintained at about 24°. Lights were on from 6 a.m. to 6 p.m. Purina Laboratory Chow and water were available *ad libitum* to all the tested mice.

Three activity cages (Woodard Research Corp.) were used to test the locomotor activity of the mice. Each cylindrical activity cage measured 14.5 in. in diameter and 9.5 in. in height. In the center of the cylinder was a second small cylinder which housed the infrared generator that emitted beams toward the photocells placed in the wall of the outside cylinder. A top view of the cage looked like a donut with mice moving in a raceway between the walls of the inside and the outside cylinders. Six infrared beams were symmetrically located at 60° intervals around the circular raceway, 0.5 in. above the wire mesh floor. The interruption of each beam due to the movement of a mouse was registered as one count by the impulse counter. The total number of interruptions were automatically summed by the counter.

Preliminary tests showed that:

1. Testing a group of mice (two mice or more) in a cage at the same time reduces the locomotor activity per mouse, presumably due to mouse to mouse interaction;

2. Mice seem to be less active in the afternoon than in the morning;

3. The activity of VY and YS strains of mice does not change significantly upon repeated testings, whereas, the activity of C57BL strains of mice decreases significantly at the second testing, but changes very little from the second testing to the third and fourth testings.

Our measurements of locomotor activity were thus performed in the following fashion:

1. Measurements were only made in the morning, mostly between 7:30 and 11 a.m. in a room with no other activity at the time of testing. The three cages we used were exposed to about the same intensity of light.

2. Only one mouse was tested in a cage at one time.

3. For each measurement, a mouse was left in the cage for 5 min for acclimation. Then the counter was activated to count for 10 min.

4. Each mouse was tested twice in the same morning with an interval of at least 15 min between the two tests. The counts of the second measurement were taken as an activity index.

Results and Discussion. Mice of the

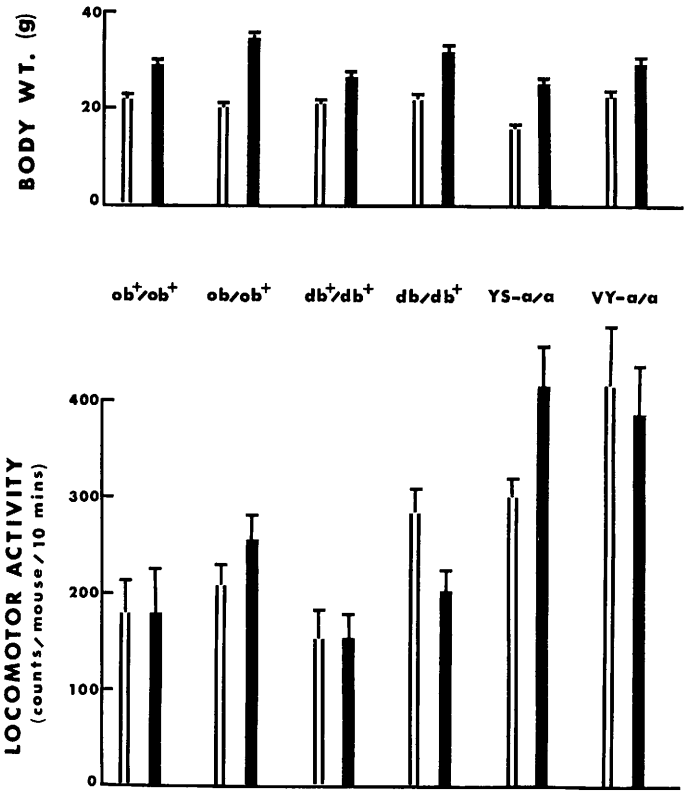

FIG. 1. Locomotor activity of young (hollow bar) and old (solid bar) normal (C57BL/6J-ob^+/ob^+, C57BL/KsJ-db^+/db^+, VY-a/a and YS-a/a) and heterozygous (C57BL/6J-ob/ob^+ and C57BL/KsJ-db/db^+) mice with reference to body weight. Each bar represents the mean ± SE of six mice. The age of these mice was: ob^+/ob^+, 10 and 35 weeks old; ob/ob^+, 6 and 45 weeks old; db^+/db^+, 8 and 34 weeks old; db/db^+, 6 and 25 weeks old; YS-a/a, 5 and 14 weeks old; and VY-a/a, 11 and 22 weeks old.

YS/ChWf and VY/Wf strains were more active than mice of both C57BL substrains (Fig. 1). For normal mice (ob^+/ob^+, db^+/db^+, YS-a/a and VY-a/a) and heterozygous ob/ob^+ mice, no significant decrease in locomotor activity was observed as a function of age in spite of a slight increase in body weight (Fig. 1). The only exception was the heterozygous db/db^+ mice whose activity decreased 30% ($p < .025$) (Fig. 1).

After the *ob/ob* and *db/db* mice became obese, their locomotor activity decreased significantly (Fig. 2, for *ob/ob*, $p < .005$; for *db/db*, $p < .0005$). Such is not the case for A^{vy}/a ($p > .20$), A^{y}/a ($p > .05$) and NZO ($p > .05$) mice (Fig. 2).

Comparing *ob/ob*, *db/db*, A^{vy}/a, A^{y}/a and NZO mice before they became corpulent to normal mice of similar body weights, we found that all the mutant mice were as active as the normal mice (Fig. 3). Hypoactivity thus does not play a major role in the development of obesity in these mutant mice. It has been documented that starvation leads to an increase in general activity (7, 8). Although these mutant mice have higher food intake than normal mice (6), their basal locomotor activity is not particularly higher than that of normal mice (Fig. 3). Their hyperphagia is, therefore, not motivated by lack of satiety, which would have caused them to be more active.

Our observations are in contrast to those of Mayer on the *ob/ob* mice (9). Using squirrel-type cages, Mayer tested mice for 21 days continuously. The body weights of the

young *ob/ob* mice were comparable to those of normal mice at the beginning of his experiments. At the end of 21 days, however, each *ob/ob* mouse gained about 10 g, whereas each normal mouse lost some weight. The decrease of the mean activity of *ob/ob* mice in Mayer's study can thus be accounted for by the decrease of activity of *ob/ob* mice after they became corpulent as we have demonstrated in our test.

In conclusion, our data suggest that all these genetically obese mice are corpulent because of factors other than differences in locomotor activity. No genetic predisposition for inactivity was observed. In the case of *ob/ob* and *db/db* mice, inactivity is secondary to obesity. In the case of A^{vy}/a, A^{y}/a and NZO mice, even obesity does not reduce locomotor activity.

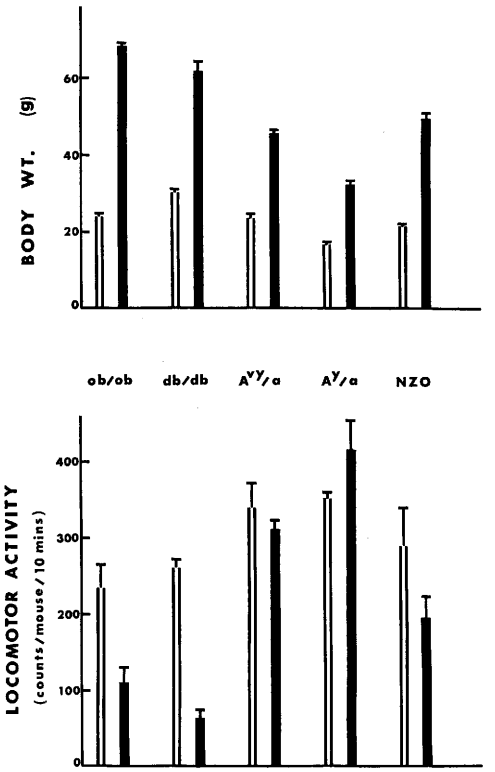

FIG. 2. Locomotor activity of mutant mice before (hollow bar) and after (solid bar) they became corpulent. Each bar represents the mean ± SE of a group of mice. For obese *db/db*, lean A^{vy}/a and lean NZO mice, $N = 5$; for obese NZO, $N = 4$; and for others, $N = 6$.

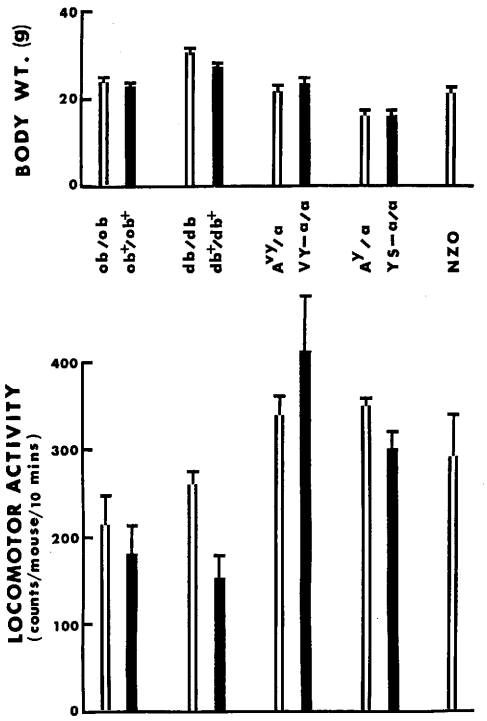

FIG. 3. Locomotor activity of mutant mice before they became corpulent (hollow bar) compared with that of normal mice of the same strain and similar body weight (solid bar). In the case of NZO mice, comparison has to be made with normal mice of other strains. Each bar represents the mean ± SE of a group of mice. For A^{vy}/a and NZO mice, $N = 5$ and for others, $N = 6$.

Summary. Locomotor activity of mice was not affected by age up to 10 months. Mice of the VY/Wf and YS/ChWf strains were more active than mice of the C57BL/6J and C57BL/KsJ strains. Locomotor activity of *ob/ob* and *db/db* mice decreased significantly after these mice became corpulent. This is not the case for A^{vy}/a, A^{y}/a and NZO mice. Before they became corpulent, none of the mice genetically destined to become obese were less active than normal mice.

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