Published in final edited form as:

Med Sci Sports Exerc. 2010 February ; 42(2): 355–360. doi:10.1249/MSS.0b013e3181a6d88f.

Wheel Access Does Not Attenuate Weight Gain in Mice Fed High-Fat or High-CHO Diets

Alan P. Jung and **David R. Luthin**
Samford University

Abstract

Purpose—To determine the effect of a high-fat or high-carbohydrate diet and running wheel activity on body composition, body mass, and caloric intake in C57Bl/6 mice.

Methods—At four weeks of age, five groups of C57Bl/6 mice were housed individually. Two groups had running wheels, while the other three groups did not. Within the running wheel groups, FAT-W consumed a high-fat diet (60.3% fat) and CHO-W consumed a high-carbohydrate diet (70.4% carbohydrate). Within the non-running groups, FAT consumed the high-fat diet, CHO consumed the high-carbohydrate diet, and CON consumed standard chow. All groups consumed food *ad libitum*, and were exposed to their respective conditions for 12 weeks. Wheel activity, food consumption, body mass (BM), and body fat (%BF) were recorded.

Results—There was no significant difference in %BF or BM at the end of 12 weeks between FAT-W and FAT or between CHO-W and CHO (p>0.05). %BF was significantly higher in both FAT-W (42.9±0.6%) and FAT (45.9±0.8%) compared to CHO-W (30.8±1.4%) or CHO (33.4±1.0%; p<0.001). BM was significantly higher in both FAT-W (42.8±0.7g) and FAT (44.7±1.2g) compared to either CHO-W (32.8±1.6g) or CHO (37.1±0.8; p<0.01). There was no difference in wheel activity between FAT-W and CHO-W (p>0.05). Daily caloric intake was higher in both FAT-W (17.0 ±0.8kcal) and FAT (15.9±0.9kcal) compared to CHO-W (13.9±0.7kcal) and CHO (13.6±0.5kcal; p<0.01).

Conclusion—Access to a running wheel had no protective effect on BM or %BF in C57Bl/6 mice that consumed either a high-fat or high-carbohydrate diet over a 12-week period. Access to a running wheel did not affect caloric intake; however, average daily caloric intake was higher in mice on high-fat diets compared to mice on a high-carbohydrate diet.

Keywords

C57Bl/6 mice; voluntary exercise; body fat; carbohydrate; PIXImus; purified diets

Introduction

Energy intake and energy expenditure are critical factors in determining body mass and percentage of body fat (%BF). The use of purified research diets in animal models has provided the opportunity to manipulate the content of diets while maintaining precise knowledge of

---

Corresponding Author: Alan P. Jung 800 Lakeshore Dr Birmingham, AL 35229 Phone: 205.726.2716 Fax: 205.726.2607 apjung@samford.edu .

ingredients. Variations in the ingredients of these purified diets are known to influence gains in body mass and %BF. Typically, mice fed high-fat diets will gain more body mass and %BF compared to mice fed high-carbohydrate or standard chow diets (2-6,9,17,22). This increased mass and %BF in mice fed high-fat diets is likely due to greater caloric intake and increased feeding efficiency (2,6,17,22,28).

The impact of physical activity on body mass and %BF is less clear. While it is logical to assume that physical activity attenuates, or even prevents, increases in body mass, this assumption is not consistent in human or animal models. Research in humans has shown that increased physical activity alone may not result in substantial changes in body mass or %BF in the absence of dietary modification (7,15). Studies in rodents have also shown that access to a running wheel does not influence body mass (6,10,19). However, other studies in humans and mice did find that increased physical activity decreased, or attenuated increases in, body mass and %BF (3,4,8,14,23,24).

A few studies have considered the collective influence of different diets and voluntary wheel activity on body mass and %BF, and the results are equivocal. Some suggest running wheel activity increases food consumption and decreases %BF (4,25), while others found that wheel access did not affect caloric intake or body mass (10). Additionally, it is not well-known how running wheel activity and type of diet, collectively, influence caloric intake or how type of diet influences running wheel activity. Therefore, the purpose of this study was to determine the effect of a high-fat or high-carbohydrate diet and running wheel activity on body composition, body mass and caloric intake in C57Bl/6 mice during the developmental stage of the lifespan.

Methods

All procedures were approved by the local Institutional Animal Care and Use Committee, and all procedures adhered to ACSM animal care standards. Thirty-one male C57Bl/6 mice were used in this study (Harlan, Indianapolis, IN) due to their wide use in physiological research, compliance with physical activity tasks, propensity towards obesity, and average daily physical activity patterns compared to other inbred mouse strains (5,6,11-13,17,26). The life span of C57Bl/6 mice is approximately two years, thus the mice were approximately 6-17% of their estimated life span during this study (21)

All mice were housed in separate cages at four weeks of age. Following two weeks of acclimation, each mouse was randomly assigned to one of five experimental groups, at which time the data collection began. Two of the groups were fed a high-carbohydrate purified diet with a caloric composition of 11.8% fat, 70.4% carbohydrate (66% sucrose), and 17.8% protein and caloric density of 4.0kcal/g (TD.98090, Harlan Teklad, Madison,WI), and two groups were fed a high-fat purified diet, with a caloric composition of 60.3% fat, 21.3% carbohydrate, and 18.4% protein with a caloric density of 5.1kcal/g (TD.06414, Harlan Teklad, Madison,WI). Seven mice from each diet condition had running wheels mounted in their cages (CHO-W and FAT-W), while the other groups did not have running wheels (CHO and FAT, n=7 in each group). The fifth group (n=3) was fed standard rodent chow, with a caloric composition of 12.2% fat, 62.3% carbohydrate, and 25.4% protein with a caloric density of 3.3kcal/g (Kaytee Products, Chilton, WI), and did not have running wheels in the cages. All food was in pellet form, and was consumed *ad libitum*.

Voluntary use of cage-mounted running wheels was used to determine daily physical activity. Each solid surface running wheel (114mm; Pets International, Elk Grove Village, IL) was interfaced with a magnetic sensor and bicycle computer (BC800 Sigma Sport, Olney, IL) that counted the total wheel revolutions and time spent exercising by each mouse (11,13,26). Wheel revolutions and time spent exercising were used to measure distance (km) and duration (min). Distance and duration on the running wheels were recorded daily. Average daily running velocity (m/min) was calculated by dividing the distance run by the exercise duration. These methods for determining levels of physical activity were similar to those published previously (11,13,26). Body mass was measured weekly. Food was weighed every 48-72 hours to determine average daily consumption. Uneaten food at the time of weighing was discarded and fresh food was added to the cages. Running wheel activity, food consumption and body mass were recorded for 12 weeks (age 6-17 weeks), at which time the animals were sacrificed. Mice were sacrificed 96 hours after the Week 12 weighing (i.e. -(17.5 weeks of age). Mice were weighed again at the time of sacrifice at which time the mice were analyzed for body fat and lean mass using the Lunar PIXImus densitometer (Lunar Corp, Madison, WI) as previously described (16).

Running duration, distance, and velocity were compared over the 12-week period between FAT-W and CHO-W using a Group × Time repeated measures ANOVA in order to determine a difference between groups across time. Multivariate analyses were then used to determine differences between groups at each time point (i.e. – each week). Body mass between the five groups was compared using a Group × Time repeated measures ANOVA to determine differences across time, with multivariate analysis used to determine differences between groups at each time point. A repeated measures ANOVA was used to determine differences in average daily food consumption between the five groups for the 12-week period. Percentage of body fat at 17.5 weeks of age, lean mass at 17.5 weeks of age, and body mass at 17.5 weeks of age were each compared between the five groups using a oneway ANOVA. Bonferroni tests were used for all post-hoc analyses. Bivariate correlations were used to determine the strength of the relationships between body mass and distance, duration, and velocity, respectively, using all data points throughout the 12-week period for the two groups that had wheel access. The alpha value was set *a priori* at 0.05 for all analyses.

Results

All data are reported as mean±SE. There was no significant difference in initial body mass between groups (p>0.05). Final body mass at the time of sacrifice (i.e. – 17.5 weeks of age) was significantly higher in both FAT-W (42.8±0.7g) and FAT (44.7±1.2g) compared to either CHO-W (32.8±1.6g) or CHO (37.1±0.8g; p<0.01; Table 1). There were no significant differences in body mass at the time of sacrifice between FAT-W and FAT (p>0.05), or between CHO-W and CHO (p>0.05). %BF was significantly higher at the time of sacrifice in both FAT-W (42.9±0.6%) and FAT (45.9±0.8%) compared to either CHO-W (30.8±1.4%) or CHO (33.4 ±1.0%; p<0.001; Table 1). There was no significant difference in %BF at the time of sacrifice between FAT-W and FAT (p>0.05), or between CHO-W and CHO (p>0.05). Body mass and %BF were significantly lower in the standard chow group (27.5+1.1g and 13.4±1.5%, respectively) compared to all other groups at the time of sacrifice (p<0.001), with the exception of body mass for CHO-W, which was not different from the standard chow group. There was no difference in lean body mass at the time of sacrifice between any of the groups (p>0.05; Table 1).

Body mass increased significantly across time for all groups (p<0.001; Figure 1). Beginning at week 9 and each week following, FAT-W had a significantly higher body mass than CHO-W (p=0.001 – 0.02), and FAT had a significantly higher body mass than CHO (p=0.001-0.03). FAT-W was not significantly different from FAT at any time point (p>0.05), nor was CHO-W significantly different from CHO at any time point (p>0.05).

Average daily caloric intake was significantly higher in both FAT-W (17.0±0.8kcal) and FAT (15.9±0.9kcal) compared to either CHO-W (13.9±0.7kcal) or CHO (13.6±0.5kcal; p<0.01;

Figure 2). There were no significant differences in daily caloric intake between FAT-W and FAT ($p>0.05$), or between CHO-W and CHO ($p>0.05$). The average daily caloric intake for the standard chow group (15.3±0.8kcal) was not significantly different than any of the other groups ($p>0.05$).

There was no significant difference in daily distance (Figure 3) or duration (Figure 4) between FAT-W and CHO-W ($p>0.05$). Average daily velocity was significantly higher in CHO-W compared to FAT-W during weeks 9, 11, and 12 ($p<0.05$; Figure 5). The difference in velocity between groups approached significance during weeks 8 and 10 ($p=0.051$ and 0.07, respectively). Additionally, body mass was significantly inversely correlated with distance ($r=-0.74$, $p<0.001$), duration ($r=-0.71$, $p<0.001$), and velocity ($r=-0.59$, $p<0.001$) when combining all data.

A technical issue in this study was that the CHO and CHO-W groups inadvertently were without food in their cages for one to two days prior to the body mass measurement at the end of week 12. This resulted in an average loss in body mass of 1.8 grams (5.2% of body mass). However, after 24 hours of *ad libitum* feeding the average gain in body mass was 2.2g. The body mass measurements taken after the 24-hour feeding period are reflected in Figure 1. The mice were sacrificed 72 hours later, following *ad libitum* feeding. The mice were weighed again prior to sacrifice (i.e. − 17.5 weeks of age), and these values are reflected in Table 1 and in the text. While this technical issue was neither intentional nor desirable, it did not change the results or conclusions of this study. When considering body mass comparisons, all groups that were significantly different from one another in week 12 were also significantly different from one another in week 11, with the exception of the FAT-W group which was significantly different from the CHO group in week 12 but not in week 11. Thus, even when considering this potential source of error, the running wheel did not result in attenuated weight gain compared to the mice without a running wheel.

Discussion

The purpose of this study was to determine the effect of a high-fat or high-carbohydrate diet and running wheel activity on body composition, body mass, and caloric intake in C57Bl/6 mice. At the end of the 12-week intervention, mice on the high-fat diet had significantly higher body mass and %BF compared to mice on the high-carbohydrate diet, independent of running wheel activity. Furthermore, access to a running wheel apparently provided no protection against weight gain and fat gain during the 12-week period, as there was no difference in body mass or %BF between mice with a running wheel and those without a running wheel, within each diet group.

14 Previous data have shown that mice fed a high-fat diet, *ad libitum*, will gain substantial amounts of body mass and fat mass (2-6,9,17,22). Typical increases in body mass in C57Bl/6 mice fed a high-fat diet *ad libitum* have ranged from 1.3-1.7 grams per week, depending on the amount and type of fat in the diet (2,3,5,6,9,17,27). Independent of running wheel access, mice on the high-fat diet in our study gained an average of approximately 1.9g/wk, compared to approximately 1.1g/wk for the high-carbohydrate groups. This difference in body mass may be explained by the 18% higher daily caloric intake in the high-fat groups compared to the high-carbohydrate groups. C57Bl/6 mice fed high-fat diets have been shown to have a higher caloric intake than mice fed high-carbohydrate diets (17,22,28). Additionally, it has been shown that feeding efficiency (i.e. – weight gained per kilocalorie consumed) is higher when mice consume high-fat diets compared to low-fat diets, which could lead to greater weight gain even without greater caloric intake (2,6,17,22). Finally, C57Bl/6 mice fed high-fat diets have been shown to have lower levels of activity compared to mice fed low-fat diets, which could further explain the difference in body mass and %fat between the two diets (9).

The high-carbohydrate groups in our study increased body mass an average of 1.3 g/wk, compared to previous studies that have shown gains in body mass of 0.5-1.0 g/wk in mice on high-carbohydrate diets when fed *ad libitum* (3,5,6,17,28). In our study, mice fed the high-carbohydrate (low-fat) diet gained approximately 70-80% of the fat mass and body mass gained by the mice fed the high-fat diet. Most studies in which mice were fed low-fat diets gained approximately 50-60% of the fat mass and body mass gained by mice on high-fat diets (3,5, 17,28). However, Surwit et al. (22) found gains in body mass and fat mass similar to our findings in C57Bl/6 mice fed a high-carbohydrate diet. From ages 4-16 weeks, C57Bl/6 mice will typically increase body mass approximately 500mg per week when fed standard chow *ad libitum* (11,26). This is consistent with mice in our study that were fed standard chow and gained six grams of body mass in 12 weeks. It should be noted that this study was conducted during the developmental stage in mice in which body mass typically increases at its fastest rate, and thus, the results cannot be generalized through the entire life span of the animals.

It might be expected that the running wheel group would gain less weight and have lower %BF compared to the non-running wheel group in each diet condition, assuming caloric intake was similar. Some studies have found access to running wheels attenuated increases in, or decreased diet-induced, body mass and/or %BF (3,4,23,24). Other studies have reported access to a running wheel had little impact on body mass (6,10). Our study found no significant difference in body mass or %BF between the wheel group and the non-wheel group for each diet conditions, suggesting the wheel provided no protection against gains in body mass and %BF.

Previous studies have also shown that mice with running wheels tended to consume more calories compared to mice without running wheels, and have suggested that the mice compensate for their increased activity by increasing food intake (4,25). However, our data agree with Harri et al. (10), who showed no difference in indirect measures of caloric intake between the wheel group and the non-wheel group for each diet condition. With no difference in caloric intake between FAT-W and FAT, and between CHO-W and CHO, groups, it would be logical to assume that the wheel groups would gain less weight than the non-wheel groups; however, this was not the case in our study. One possible explanation for similar gains in body mass and %BF between the wheel and non-wheel groups is that C57Bl/6 mice have relatively low levels of wheel activity compared to other more active strains (13,26); thus, the mice without wheels were able to achieve the same level of activity by climbing on the cage lid, among other activities (10). Perhaps the running wheel provides no increase in activity level above what could be achieved without a wheel for C57Bl/6 mice. This would be logical since the mice within each diet group had similar caloric intakes and had similar body mass and %BF, independent of wheel access. Additionally, when estimating the oxygen cost of running wheel activity using a prediction equation (18), there was no difference between FAT-W and CHO-W through the duration of the study or at any week. While these equations only address oxygen cost of wheel activity and not free cage activity, this finding is not surprising since average daily wheel distance and duration were similar between groups. It is also interesting to note that there was no difference in lean mass between any of the five groups, suggesting that the differences in body mass were due exclusively to differences in fat mass, a finding that has been previously reported (4,25).

While statistically there was no difference in body mass or %BF as a result of running wheel activity, Figure 1 suggests a trend toward higher body mass in the non-wheel groups for both the high-fat and high-carbohydrate diets. The trend lines might suggest that if the study was extended for several more weeks, the difference in weights between the wheel and non-wheel groups may be significant. However, it is well-established that most inbred mouse strains decrease running wheel activity after approximately eight to ten weeks of age (11,23,26). This decrease in wheel activity was also found in our study; thus, as body mass continues to increase with age for all mice, it is possible that any potential differences in body mass between the wheel and non-wheel groups would be less noticeable as the running wheel activity decreased with increasing age.

According to the results, it appears the standard chow group ate a similar number of calories as the other groups, yet the gains in body mass and body fat were significantly lower. There are two possible explanations for this. First, the fiber content was 1.0% and 6.5% by weight in the high-carbohydrate and high-fat diets, respectively. In these purified diets, a known amount of fiber was added to the diets. However, because standard chow uses more complex ingredients that include fiber (e.g. corn), it is more difficult to accurately measure the amount of fiber. Standard chow tends to have a fiber content closer to 12-15%, and fiber intake is known to be inversely related to body weight and body fat (20). This higher fiber content in the standard chow was evidenced by casual observance of greater fecal output in the standard chow group compared to the other groups. Perhaps, the additional dietary fiber and subsequent increase in fecal output in the standard chow group reduced the ability of the animals to absorb the same amount of energy from their diets and prevented as much weight gain compared to the other groups (20). This remains to be determined. Second, the standard chow tended to turn to powder, and thus the caloric consumption could have been over-estimated.

20 While previous studies have shown a relationship between body mass and running wheel duration, distance, or velocity, the relationships have been weak and have not been consistent for all activity measures (13,24). For example, Lightfoot et al. (13) found a weak correlation between body weight and velocity in female inbred mice, but no other significant relationships were found between activity and body weight in male or female mice. In our study, body mass was significantly inversely correlated with distance, duration, and velocity. The strong correlational finding in our study may be due to the mice being ~40-50% heavier than those reported in the in the Lightfoot et al. (13) study. While average daily duration and distance did not differ between groups, velocity was significantly higher in the CHO-W group compared to the FAT-W group during Weeks 9-12. This coincided with body mass being significantly higher in the FAT-W group compared to the CHO-W group in Weeks 9-12, suggesting that heavier mice ran slower. One could speculate as to whether the increased body mass caused a decrease in the activity, or vice versa. However, the previous analysis of differences in body mass included all five groups. When a multivariate analysis was run to include only the CHO-W and FAT-W groups, the results showed a significant difference in body mass between groups beginning at week 8, as opposed to week 9 as previously found. Thus, because the difference in running velocity between groups was not significant until week 9, we suggest that the increase in body mass preceded the decrease in running velocity. Finally, it appears that the composition of the food itself (high-fat vs-high-CHO) did not have an impact on the running wheel activity since there was no difference in wheel activity until a difference in body mass existed (2).

Previous research has shown a strong genetic influence on running wheel activity in inbred mouse strains (13,23,26). Additionally, body mass and body composition in inbred mouse strains are genetically influenced (27). The genetic influence on body composition and body mass as a result of dietary and wheel activity intervention has not been well studied and warrants further investigation, though there is some evidence to suggest a genetic influence (25). C57Bl/6 mice are known to be obesity-prone, which made this strain useful in our study (1,27). However, mouse strains of differing activity levels may respond differently than the C57Bl/6 mice; thus, future studies would need to include mouse strains over a variety of activity levels in order to make general statements regarding the genetic influence of diet and activity on body mass and %BF changes. It is possible that the highly active inbred strains with access to running wheels would show attenuated gains in body mass and %BF compared to the non-wheels groups if the non-wheel groups could not match the activity levels of the wheels groups.

Additionally, a study of longer duration (beyond 12 weeks) may provide insight as to whether or not wheel access could have a beneficial impact on body mass and %BF. A study of longer duration would also indicate the effects of varied diet and wheel activity after the primary developmental stage of the mice in which weight increases at the greatest rate relative to the entire lifespan.

In summary, C57Bl/6 mice fed a high-fat diet increased body mass and %BF to a greater extent than mice fed a high-carbohydrate diet. This difference is likely due to a higher caloric intake in the high-fat groups. Additionally, access to a running wheel seemed to provide no protection against gains in body mass or %fat as seen in the similar gains between mice that had access to running wheels and those that had no access. It is also important to note that increases in activity do not necessitate increases in caloric intake. Finally, it appears that increased weight gain is negatively correlated with volume and speed of activity.

Acknowledgments

This research study was partially supported by the Samford University Faculty Development Program and the UAB Small Animal Phenotyping Core (NIH P30DK56336 and NIH P60DK079626).

Results of the present study do not constitute endorsement by ACSM.

References

1. Alexander J, Chang GQ, Dourmashkin JT, Leibowitz SF. Distinct phenotypes of obesity-prone AKR/J, DBA2J, and C57BL/6J mice compared to control strains. International Journal of Obesity 2006;30(1):50–9. [PubMed: 16231032]
2. Almind K, Kahn CR. Genetic determinants of energy expenditure and insulin resistance in diet-induced obesity in mice. Diabetes 2004;53(12):3274–85. [PubMed: 15561960]
3. Bell RR, Spencer MJ, Sheriff JL. Diet-induced obesity in mice can be treated without energy restriction using exercise and/or a low fat diet. The Journal of Nutrition 1995;125(9):2356–63. [PubMed: 7666253]
4. Bell RR, Spencer MJ, Sheriff JL. Voluntary exercise and monounsaturated canola oil reduce fat gain in mice fed diets high in fat. The Journal of Nutrition 1997;127(10):2006–10. [PubMed: 9311958]
5. Black BL, Croom J, Eisen EJ, Petro AE, Edwards CL, Surwit RS. Differential effects of fat and sucrose on body composition in A/J and C57BL/6 mice. Metabolism 1998;47(11):1354–9. [PubMed: 9826212]
6. Brownlow BS, Petro AE, Feinglos MN, Surwit RS. The role of motor activity in diet-induced obesity in C57BL/6J mice. Physiology and Behavior 1996;60(1):37–41. [PubMed: 8804640]
7. Donnelly J, Smith B. Is exercise effective for weight loss with ad libitum diet? Energy balance, compensation, and gender differences. Exercise and Sport Science Reviews 2005;33(4):169–74.
8. Fontana L, Villareal DT, Weiss EP, Racette SB, Steger-May K, Klein S, Holloszy JO, the Washington University School of Medicine CALERIE Group. Calorie restriction or exercise: effects on coronary heart disease risk factors. A randomized, controlled trial. American Journal of Physiology. Endocrinology and Metabolism 2007;293(1):197–202.
9. Funkat A, Massa CM, Jovanovska V, Protietto J, Andrikopoulos S. Metabolic adaptations of three inbred strains of mice (C57BL/6, DBA/2, and 129T2) in response to a high-fat diet. The Journal of Nutrition 2004;134(12):3264–9. [PubMed: 15570023]
10. Harri M, Lindblom J, Malinen H, Hyttinen M, Lapvetelainen T, Eskola S, Helminen HJ. Effect of access to a running wheel on behavior of C57BL/6J mice. Laboratory Animal Science 1999;49(4):401–5. [PubMed: 10480645]
11. Jung AP, Curtis TS, Turner MJ, Lightfoot JT. Influence of age of exposure to a running wheel on activity in inbred mice. Medicine and Science in Sports and Exercise 2006;38(1):51–6. [PubMed: 16394953]

12. Lerman I, Harrison BC, Freeman K, Hewett TE, Allen DL, Robbins J, Leinwand LA. Genetic variability in forced and voluntary endurance exercise performance in seven inbred mouse strains. Journal of Applied Physiology 2002;92:2245–55. [PubMed: 12015333]
13. Lightfoot JT, Turner MJ, Daves M, Vordermark A, Kleeberger SR. Genetic influence on daily running wheel activity level. Physiological Genomics 2004;19:270–6. [PubMed: 15383638]
14. McTiernan A, Sorensen B, Irwin ML, Morgan A, Yasui Y, Rudolph RE, Surawicz C, Lampe JW, Lampe PD, Ayub K, Potter JD. Exercise effect on weight and body fat in men and women. Obesity 2007;15(6):1496–512. [PubMed: 17557987]
15. Miller WC, Koceja DM, Hamilton EJ. A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. International Journal of Obesity and Related Metabolic Disorders 1997;21(10):941–7. [PubMed: 9347414]
16. Nagy TR, Clair A-L. Precision and accuracy of dual-energy X-ray absorptiometry for determining in vivo body composition of mice. Obesity Research 2000;8(5):392–8. [PubMed: 10968731]
17. Petro AE, Cotter J, Cooper DA, Peters JC, Surwit SJ, Surwit RS. Fat, carbohydrate, and calories in the development of diabetes and obesity in the C57BL/6J mouse. Metabolism 2004;53(4):454–7. [PubMed: 15045691]
18. Rezende EL, Kelly SA, Gomes FR, Chappell MA, Garland T. Effects of size, sex, and voluntary running speeds on costs of locomotion in lines of laboratory mice selectively bred for high wheel-running activity. Physiological and Biochemical Zoology 2006;79(1):83–99. [PubMed: 16380930]
19. Schemmel RA, Hannum SH, Rosekrans JA, Heusner WW. Moderate exercise in young female S5B/P1 rats does not reduce body fat. Physiology and Behavior 1992;52(3):577–81. [PubMed: 1409923]
20. Slavin JL. Dietary fiber and body weight. Nutrition 2005;21(3):411–8. [PubMed: 15797686]
21. Storer JB. Longevity and gross pathology at death in 22 inbred strains of mice. J Gerontol 1966;21:404–9. [PubMed: 5944803]
22. Surwit RS, Feinglos MN, Rodin J, Sutherland AE, Petro AE, Opara EC, Kuhn CM, Rebuffe-Scrive M. Differential effects of fat and sucrose on the development of obesity and diabetes in C57BL/6J and A/J mice. Metabolism 1995;44(5):645–51. [PubMed: 7752914]
23. Swallow JG, Garland T, Carter PA, Zhan W-Z, Sieck GC. Effects of voluntary activity and genetic selection on aerobic capacity in house mice (Mus domesticus). Journal of Applied Physiology 1998;84(1):69–76. [PubMed: 9451619]
24. Swallow JG, Koteja P, Carter PA, Garland T. Artificial selection for increased wheel-running activity in house mice results in decreased body mass at maturity. Journal of Experimental Biology 1999;202:2513–20. [PubMed: 10460738]
25. Swallow JG, Koteja P, Carter PA, Garland T. Food consumption and body composition in mice selected for high wheel-running activity. J Comp Physiol [B] 2001;171(8):651–9.
26. Turner MJ, Kleeberger SR, Lightfoot JT. Influence of genetic background on daily running-wheel activity differs with aging. Physiological Genomics 2005;22:76–85. [PubMed: 15855385]
27. West DB, Boozer CN, Moody DL, Atkinson RL. Dietary obesity in nine inbred mouse strains. The American Journal of Physiology 1992;262:R1025–R32. [PubMed: 1621856]
28. Williams EA, Perkins SN, Smith NCP, Hursting SD, Lane MA. Carbohydrate versus energy restriction: effects on weight loss, body composition, and metabolism. Annals of Nutrition and Metabolism 2007;51(3):232–43. [PubMed: 17587795]

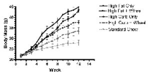

FIGURE 1.

Average body mass over the 12-week period (mean±SE).

Weeks 5-12, significant difference between High Fat Only and High Carb+Wheel and between High Fat Only Standard Chow ($p<0.05$). Weeks 8-12, significant difference between High Fat +Wheel and Standard Chow ($p<0.05$). Weeks 9-12, significant difference between High Fat +Wheel and High Carb+Wheel and between High Fat Only and High Carb Only and between High Carb Only and Standard Chow ($p<0.05$). Week 12, significant difference between High Fat+Wheel and High Carb Only ($p<0.05$).

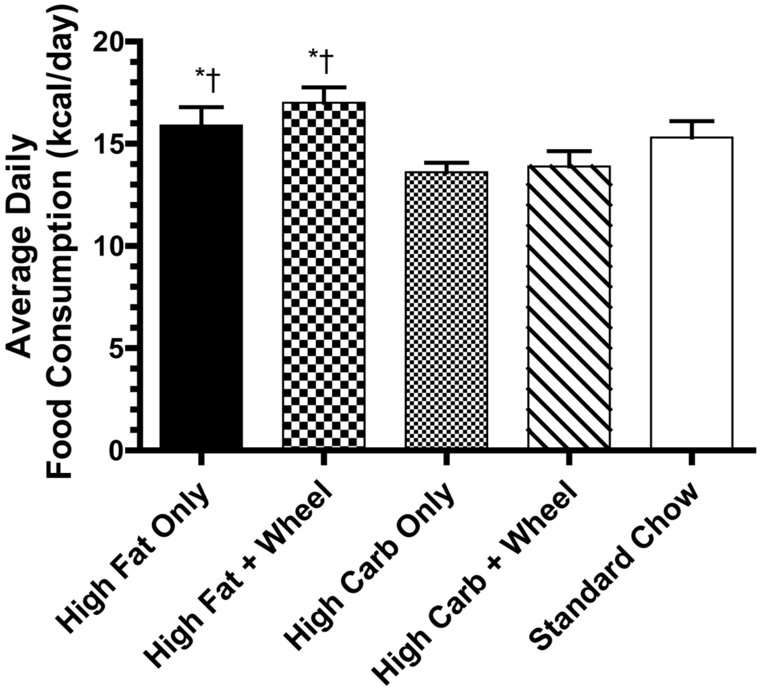

FIGURE 2.

Average daily food consumption over the 12 week period (mean±SE).
*significantly different from High Carb Only ($p<0.05$); †significantly different from High Carb +Wheel ($p<0.05$).

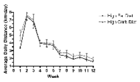

FIGURE 3.

Average daily distance (mean±SE) on a running wheel for each group. No significant difference between groups (p>0.05).

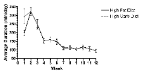

FIGURE 4.
Average daily duration (mean±SE) on a running wheel for each group. No significant difference between groups (p>0.05).

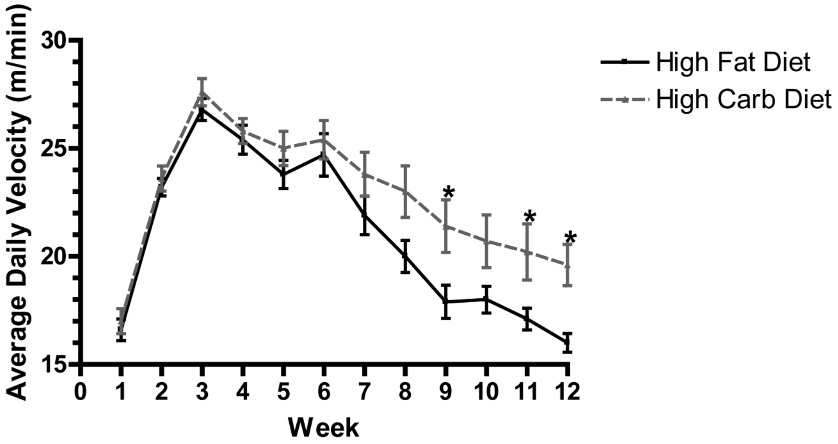

FIGURE 5.

Average daily velocity (mean±SE) on a running wheel for each group.
*Significant differences between groups. ($p<0.05$).

TABLE 1

Final body mass, body fat, and lean mass at the time of sacrifice (i.e. − 17.5 weeks of age) (mean±SE).

Group	Body Mass (g)	Body Fat (%)	Lean Mass (g)
FAT	44.7±1.2[*†‡]	45.9±0.8[*†‡]	24.1±0.7
FAT-W	42.8±0.7[*†‡]	42.9±0.6[*†‡]	24.4±0.5
CHO	37.1±0.8[‡]	33.4±1.0[‡]	24.6±0.4
CHO-W	32.8±1.6	30.8±1.4[‡]	22.6±0.7
Standard Chow	27.5+1.1	13.4±1.5	23.8±0.8

[*] significantly greater than CHO (p<0.05);

[†] significantly greater than CHO-W (p<0.05);

[‡] significantly greater than Standard Chow (p<0.05).