Genetic influence on daily wheel running activity level


—This project was designed to determine the genetic (between-strain) and environmental (within-strain) variance in daily running wheel activity level in inbred mice. Five male and five female mice, 9.7–15.3 wk old, from each of 13 strains (A/J, AKR/J, BALB/cJ, C3H/HeJ, C57Bl/6J, C57L/J, C3HeB/FeJ, CBA/J, DBA/2J, SWR/J, MRL/Mpj, SPRET/Ei, and CAST/Ei) as well as five female NZB/ BinJ mice were housed individually. A running wheel in each cage was interfaced with a magnetic sensor to measure total daily distance (m/min) for each strain was then calculated. Significant interstrain variability of mice and humans, we have chosen to use a mouse model to determine the genetic and environmental variance in daily running wheel activity level between 14 strains of inbred mice. Another goal of the study was to determine the impact of sex upon daily running wheel activity and whether sex affected the heritability of daily activity. The use of a mouse model allows the control of environmental factors that may affect daily running wheel activity, and, as a result, analysis of the genetic contribution to the variation in daily running wheel activity levels is possible.

METHODS

Animals. All procedures used in this study were reviewed and approved by the UNC Charlotte Institutional Animal Care and Use Committee for appropriate treatment of animal subjects as outlined by the United States Department of Agriculture, the Animal Welfare Act, and the National Research Council (31). All mice were housed in the University Vivarium with 12:12-h light/dark cycles and were provided water and food ad libitum. All mice were fed a standard diet (Teklad 8604 rodent diet, 24.5% protein, 4.4% fat, 3.7% fiber, and 48.6% nitrogen-free extract; Harlan, Madison, WI). All cages were kept in the same room in the University Vivarium, which was maintained at 18–21°C and 20–40% humidity. Each mouse was weighed weekly to determine whether body weight was a covariate. We measured the daily wheel running activity of 5 female and 5 male mice in 13 different inbred strains (A/J, AKR/J, BALB/cJ, C3H/HeJ, C57Bl/6J, C57L/J, C3HeB/FeJ, CBA/J, DBA/2J, SWR/J, MRL/Mpj, SPRET/Ei, CAST/Ei, NZB/BinJ). Male NZB/BinJ mice were unavailable for investigation. Because daily activity reaches a peak and plateaus at 9–10 wk of age in mice (39), we monitored daily wheel running activity for 3 wk (i.e., 21 consecutive days) starting at ~9 wk of age where possible. All mice were purchased from the Jackson Laboratory (Bar Harbor, ME).

Daily wheel running activity level. Although the amount of wheel running exercise can be substantially different between individual outbred mice (5), the amount of wheel running in selected strains appears to be consistent and repeatable within a generation of animals (14, 39). To prevent confounding due to the mice learning to run on the wheels (9, 23) as well as to account for any fluctuations in daily wheel running due to menstrual cycling in the female mice (1), daily activity was monitored for 3 wk (i.e., 21 consecutive days). Mice were housed individually upon receipt (age range from 5–9 wk), and in each cage a solid surface running wheel (127 mm; Ware Manufacturing, Phoenix, AZ) was mounted. The running wheel was interfaced to a magnetic sensor (either BC600 or BC500; Sigma Sport, Olney,
calculated the intraclass correlation, which is a more liberal heritability (7). However, we also tested per strain (8). Since the coefficient of genetic determination inbreeding, was calculated by using the following formula:

\[ r_i = \frac{(MS_B - MS_W)}{[MS_B + (n-1)MS_W]} \]

where \( r_i \) is the intraclass correlation estimate, \( MS_B \) is the mean square of the between strain comparison, \( MS_W \) is the mean square of the within-strain comparison, and \( n \) is number of animals tested per strain with appropriate corrections for differences in animal numbers per strain (7, 8). The coefficient of genetic determination, which takes into account the doubling of the additive genetic variance with inbreeding, was calculated by using the following formula:

\[ g^2 = \frac{(MS_B - MS_W)}{[MS_B + (2n-1)MS_W]} \]

where \( g^2 \) is the coefficient of genetic determination estimate, \( MS_B \) is the mean square of the between strain comparison, \( MS_W \) is the mean square of the within-strain comparison, and \( n \) is number of animals tested per strain (8). Since the coefficient of genetic determination results in more conservative heritability estimates, it has been noted to be a better indicator of broad-sense heritability (7). However, we also calculated the intraclass correlation, which is a more liberal heritability estimate, because it is commonly used as a heritability indicator (11, 17, 18, 23, 24).

RESULTS

Demographic data. Data from 133 of the 135 mice that began the protocol were presented because one female A/J and one male MRL/MpJ mice died inexplicably during the 3 wk exercise period (Table 1). MRL/MpJ mice were significantly heavier than all of the other strains, and the CAST/Ei and SPRET/Ei mice were lighter than the other strains (Table 1). Male mice tended to be heavier than the female mice in each strain (Table 1). Female mice were slightly older than the strain-matched male mice at the beginning and throughout the 3-wk exercise period (\( P = 0.001 \)).

Indices of daily running wheel activity. Significant strain (\( P < 0.0001 \)) and sex (\( P = 0.01 \); Fig. 1) effects but not a strain \( \times \) sex effect (\( P = 0.11 \)) were found in average daily distance run. Regardless of sex, C57L/J ran the farthest on a daily basis (7.9 \( \pm \) 3.0 km; Table 2), which was 395% more than the strain that ran the shortest distance (NZB/BinJ = 2.0 \( \pm \) 0.91 km). Female mice ran 20% farther on average than the males, although post hoc analysis found no between-sex differences within any of the strains (Fig. 1). Neither age (\( P = 0.49 \)) nor weight (\( P = 0.38 \)) contributed significantly to the distance run by the mice. Additionally, body weight per se was not significantly associated with daily distance run (Table 3).

Strain (\( P < 0.0001 \)), sex (\( P = 0.009 \)), and strain \( \times \) sex interaction (\( P = 0.06 \)) contributed significantly to the statistical model that explained 41% of the variation in exercise duration. Regardless of sex, CBA/J mice had the highest duration of exercise [342.03 \( \pm \) 18.51 min; Table 2], which was 395% more than NZB/BinJ mice, which had the lowest average duration of exercise (99.89 \( \pm \) 16.34 min/day; 1.67 h/day). C57L/J mice, which ran the farthest on a daily basis (7.9 \( \pm \) 3.0 km; Table 1), which was 395% more than the strain that ran the shortest distance (NZB/BinJ = 2.0 \( \pm \) 0.91 km), female mice ran 20% farther on average than the males, although post hoc analysis found no between-sex differences within any of the strains (Fig. 1). Neither age (\( P = 0.49 \)) nor weight (\( P = 0.38 \)) contributed significantly to the distance run by the mice. Additionally, body weight per se was not significantly associated with daily distance run (Table 3).

Strain (\( P < 0.0001 \)), sex (\( P = 0.009 \)), and strain \( \times \) sex interaction (\( P = 0.06 \)) contributed significantly to the statistical model that explained 41% of the variation in exercise duration. Regardless of sex, CBA/J mice had the highest duration of exercise [342.03 \( \pm \) 18.51 min; Table 2], which was 395% more than NZB/BinJ mice, which had the lowest average duration of exercise (99.89 \( \pm \) 16.34 min/day; 1.67 h/day). C57L/J mice, which ran the farthest on a daily basis (7.9 \( \pm \) 3.0 km; Table 2), which was 395% more than the strain that ran the shortest distance (NZB/BinJ = 2.0 \( \pm \) 0.91 km), female mice ran 20% farther on average than the males, although post hoc analysis found no between-sex differences within any of the strains. Additionally, body weight per se was not significantly associated with daily distance run (Table 3).

Strain (\( P < 0.0001 \)), sex (\( P = 0.009 \)), and strain \( \times \) sex interaction (\( P = 0.06 \)) contributed significantly to the statistical model that explained 41% of the variation in exercise duration. Regardless of sex, CBA/J mice had the highest duration of exercise [342.03 \( \pm \) 18.51 min; Table 2], which was 395% more than NZB/BinJ mice, which had the lowest average duration of exercise (99.89 \( \pm \) 16.34 min/day; 1.67 h/day). C57L/J mice, which ran the farthest on a daily basis (7.9 \( \pm \) 3.0 km; Table 2), which was 395% more than the strain that ran the shortest distance (NZB/BinJ = 2.0 \( \pm \) 0.91 km), female mice ran 20% farther on average than the males, although post hoc analysis found no between-sex differences within any of the strains (Fig. 1). Neither age (\( P = 0.49 \)) nor weight (\( P = 0.38 \)) contributed significantly to the distance run by the mice. Additionally, body weight per se was not significantly associated with daily distance run (Table 3).

Table 1. Data from 133 of the 135 mice that began the protocol were presented because one female A/J and one male MRL/MpJ mice died inexplicably during the 3 wk exercise period (Table 1). MRL/MpJ mice were significantly heavier than all of the other strains, and the CAST/Ei and SPRET/Ei mice were lighter than the other strains (Table 1). Male mice tended to be heavier than the female mice in each strain (Table 1). Female mice were slightly older than the strain-matched male mice at the beginning and throughout the 3-wk exercise period (\( P = 0.001 \)).

Indices of daily running wheel activity. Significant strain (\( P < 0.0001 \)) and sex (\( P = 0.01 \); Fig. 1) effects but not a strain \( \times \) sex effect (\( P = 0.11 \)) were found in average daily distance run. Regardless of sex, C57L/J ran the farthest on a daily basis (7.9 \( \pm \) 3.0 km; Table 2), which was 395% more than the strain that ran the shortest distance (NZB/BinJ = 2.0 \( \pm \) 0.91 km). Female mice ran 20% farther on average than the males, although post hoc analysis found no between-sex differences within any of the strains (Fig. 1). Neither age (\( P = 0.49 \)) nor weight (\( P = 0.38 \)) contributed significantly to the distance run by the mice. Additionally, body weight per se was not significantly associated with daily distance run (Table 3).

As was the case with the other wheel activity phenotypes, exercise velocity was significantly affected by strain (\( P < 0.0001 \)), sex (\( P < 0.0001 \)), and strain \( \times \) sex interaction (\( P < 0.0001 \)), without significant influence by either age (\( P = 0.82 \)) or weight (\( P = 0.37 \)). Regardless of sex, C57L/J mice ran 176% faster (25.7 \( \pm \) 3.0 m/min) during their activity periods than did the slowest strain (C3H/HeJ; 14.6 \( \pm \) 1.2 m/min; Table 2). Interestingly, C3Heb/Fej mice, which ran the fourth longest on a daily basis, was the second slowest strain (50% slower than C57L/J mice). The strongest effect of sex was found for velocity of daily exercise. Overall, female mice ran 38% faster than male mice, and significant differences in exercise velocity between sexes were found in eight strains (Fig. 3). When considered separately, body weight was significantly associated with velocity of exercise (Table 3) but exhibited a relatively poor predictive fit (\( r^2 = 0.16 \)). When split by sex, only
the body weight of the female was associated with exercise velocity (Table 3). Despite this significant association between weight and velocity in the female mice, the $r^2$ value was still relatively low, with a corresponding low predictive value as exhibited by the $r^2$ value (0.09).

**Wheel running heritability estimates.** Heritability estimates for each daily wheel running index were subdivided by sex (Table 4). Overall, when sex was not considered, all measures of wheel running were low to moderately influenced by heritability (range = 14–30%). However, subdividing by sex increased the heritability estimates, particularly in male mice in regard to distance run (31–48%) and duration of exercise (44–61%), as well as significantly increasing the heritability statistics for exercise velocity in both male (49–66%) and female (44–61%) mice.

**DISCUSSION**

Multiple behavioral or environmental factors influencing daily physical activity have been studied. The significant finding of this study is that genetic background also plays a role in determining daily running wheel activity in inbred mouse strains. Furthermore, it appears that sex influences to some extent the heritability of daily running wheel activity level. These findings can serve as the basis for future studies to identify the genes that control daily running wheel activity, as well as the role sex plays in influencing activity.

Despite their limitations, human studies have begun to suggest that physical activity may have a genetic component. One of the earliest estimations of the heritability of physical activity level came from the large Finnish Twin Registry study (16), which surveyed 1,537 monozygous male twins and 3,057 dizygous male twins regarding their daily physical activity levels. After adjusting for age and using inter-pair correlations, Kaprio et al. (16) estimated that heritability of physical activity was 62% and that the common environmental effects were zero (0%). Perusse and coworkers (33) collected 3-day activity records from 1,610 subjects from 375 different families from Quebec city and concluded that heritability of physical activity level was between 20% and 29% (depending on the statistical model used) while the environmental effect was $\sim$12%. More recently, Lauderdale et al. (22) surveyed 3,344 twin pairs in the Vietnam Era Twin Registry by using sets of questions that dealt with moderate (e.g., climbing stairs, walking) and intense (e.g., running, racquet sports, cycling) physical activities. They found 38% heritability for their overall index of moderate activity, with intense activity resulting in higher heritability estimates (39–58%). Although these studies all indicated a significant genetic effect on daily physical activity, Simonen et al. (37) noted that maximal heritability values of activity levels were only 16–25% after measuring physical activity using a 3-day activity diary and a questionnaire in 696 subjects enrolled in the Quebec Family study.

Limited estimates of the inheritance of daily physical activity levels exist in animal models. Festing (9) noted that the broad-sense heritability of daily distance run in 26 inbred strains (intraclass correlations, sex not reported) ranged from 0.26 (7-day running) to 0.29 (48-h running), similar to our estimates of 0.30 (intraclass correlation) for distance run in all of the mice, regardless of sex. Similar to our heritability estimates (Table 4), Lerman et al. (23), reported significant heritability estimates for distance run (39–56%), duration of exercise (42–59%), and exercise velocity (24–38%) in male mice in seven inbred strains. Interestingly, exercise duration,
distance, and velocity differ between the Lerman study and the current study for the three common strains (C3H/HeJ, DBA/2J, and C57BL/6J). Because the method of measurement of daily physical activity in both studies was identical, it appears that either laboratory environment or age of the mice (20–24 wk vs. 10–13 wk) possibly played a role in the differing results. We have preliminary evidence that daily activity decreases at differing rates for these three strains over the first 9 mo of their life, indicating that age must be considered in any cross-study comparisons (M. Turner, unpublished observation, 2004). Furthermore, Crabbe and coworkers (3) observed differences in locomotive activity in nine different mouse strains not only by strain, but also by location of laboratory. For example, mice tested in Edmonton, Alberta, were more active than mice tested in Albany, New York or Portland, Oregon. The investigators suggested that differences in personnel at each laboratory could have influenced behavior of the mice, given that the methods were rigorously standardized among the three laboratories. Therefore, although interstrain differences in daily physical activity appear to be fairly robust and estimations of the magnitude of heritability of daily activity are similar among studies, unique differences in laboratory environment (see below) may complicate direct comparisons between studies, especially where strain differences are minimal (3).

Differences in activity by sex have been suggested by previous studies. Animal studies that control the majority of environmental influences indicate that female mice tend to be more active than males. While Swallow et al. (39) tested only male mice because “females tend to run more on the wheels”, similar to our study, Koteja and coworkers (19) observed that females in a strain of mice bred for high activity tended to run 58% farther, have 29% more periods of activity daily, and run 21% faster on a daily basis than did male high-activity mice. They noted that this trend was also present in the control mice, with the control female mice running 50% farther and having 43% more periods of activity daily but being only 3% faster than the control male mice. Koteja et al. (19) suggested that female mice may be more economical runners than males or that females differed in behavioral patterns that would affect the measurement of physical activity. Since it has been noted that female rats are more active during proestrus (early follicular phase) and less active during metestrus (luteal phase) (1), it is also possible that the hormonal differences between the sexes are responsible for differences in daily activity.

The role of body weight in determining daily wheel running activity remains unclear, with weight being shown to have no association with daily activity (4, 10), a positive association with duration and distance (23), or a negative association with wheel performance (40). Although we found that body weight did not contribute significantly to any of the overall statistical models used (i.e., that included strain, sex, and interactions), when body weight alone was correlated with exercise velocity, we did observe a significant negative correlation in the female mice strains (Table 3). Although Lerman et al. (23) found no relationship between weight and exercise velocity in male mice, which was similar to our study, no other study with the exception of Friedman et al. (10) has considered the association between weight and daily activity in female mice. Given the multiple strains tested by Lerman et al. (23) and the 14 strains in the current study (only 3 of which are common with the Lerman study), it appears that using multiple strains to determine whether a relationship exists between body weight and daily wheel running activity is difficult, due to interstrain differences. It has been observed in at least two studies (6, 41) that ICR mice selectively bred over several generations for high activity are lighter than control ICR mice, thereby indicating that selective breeding for activity may result in smaller body size. Interestingly, we observed that the SPRET/Ei and CAST/Ei strains, which were ranked first and third on a scale for difficulty in capturing and holding (i.e., “wildness scale”; Ref. 43), exhibited the second and third highest daily exercise velocities while also being the lightest two strains we tested. These findings support data from the laboratory of Garland and colleagues (6, 41) suggesting that mice bred for activity were lighter. Although those investigations (6, 41) have not shown an association between weight and activity, they have shown that active mice have more lean tissue than sedentary mice. Therefore, the role of weight in determining daily wheel running activity is still unclear, with our data and the literature suggesting that this association depends significantly upon the strain tested with an unknown contribution of sex.

Although animal studies to this point have shown that genetic background can have a significant role in the determination of daily physical activity level, suggestions as to the specific genes or other factors involved in this regulation are limited. Tsao et al. (42) found that relative to controls, mice overexpressing GLUT4, a type of glucose transporter, ran fourfold farther (≈3.7 km/day total) on an average daily basis.

### Table 3. Association of physical activity and body weight

<table>
<thead>
<tr>
<th>Physical Activity Measure</th>
<th>Model</th>
<th>P Value</th>
<th>Pearson’s r</th>
<th>( r^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg. distance</td>
<td>Overall</td>
<td>0.26</td>
<td>-0.10</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Female only</td>
<td>0.96</td>
<td>0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Male only</td>
<td>0.37</td>
<td>-0.11</td>
<td>0.01</td>
</tr>
<tr>
<td>Avg. duration</td>
<td>Overall</td>
<td>0.09</td>
<td>0.15</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Female only</td>
<td>0.12</td>
<td>0.19</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Male only</td>
<td>0.92</td>
<td>-0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Avg. velocity</td>
<td>Overall</td>
<td>&lt;0.01</td>
<td>-0.40</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>Female only</td>
<td>0.02</td>
<td>-0.29</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>Male only</td>
<td>0.07</td>
<td>-0.23</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Fig. 2. Average daily exercise duration (min) parsed by sex within strain. Open bars = females; solid bars = males. There were no significant differences between sexes within each strain upon post hoc testing.
Although these distances would rank fourth lowest among the strains if compared with the present study, the study of Tsao et al. (42) did support the hypothesis that a particular physiological factor controlled by genetic influences could significantly affect daily activity.

A variety of environmental factors could influence activity of mice. Food composition, temperature, and housing conditions can affect behavioral responses of mice. It has been suggested that both food composition (44) and volume (35) may affect physiological parameters that could directly impact daily activity in mice. However, we controlled for this possible extraneous variable by providing the same diet to all mice ad libitum.

Gordon et al. (12) showed that female CD-1 mice preferred ambient temperatures of 26.2–29.5°C and were more active when their preferred ambient temperatures were cooler. These preferred ambient temperatures were actually higher than the 18–26°C recommended for rodent housing vivarium operations (31) and higher than the housing temperature used in the current study (18–21°C). However, although the mice of the current study may have been more active because of the cooler housing temperatures, all mice were exposed to the same housing temperature, and thus temperature should have affected all mice equally.

Since it is generally agreed that mice are highly social, the type of housing (i.e., single housed or group housed) can alter baseline physiology of mice and pheromone effects of close housing may exist. Gordon et al. (12) noted that individually housed mice (i.e., single-housed mice) preferred warmer ambient temperatures and appeared to have less activity when in a group housing situation. Single-housed male mice have been noted to have increased heart rate but not an increased activity level after “several weeks” of acclimation to isolated housing (38), whereas male mice isolated for 4 mo had higher locomotor activity than isolated female or group-housed mice (13). Therefore, it is possible that group housing of the strains would result in different strain distribution patterns of daily activity. However, it would be technically difficult to separate individual mouse activity with group housing, a difficulty clearly delineated by Gordon et al. (12), and thus repeating this study with group housing would probably not yield further information than the single-housing model we used in this study.

The physiological impact of pheromones from adjoining mouse cages, whether in single- or group-housed conditions, is still largely undocumented. To our knowledge, no data exist regarding the level of mouse activity with the near presence of other male or female mice. It has been shown that male pheromones will induce the estrous cycle in female mice (effect attenuated in single-housed mice; Ref. 15) as well as inducing aggressive behavior in other male mice (20), and these pheromone effects may be mediated through a c-fos immunoreactivity in the accessory olfactory bulb (20, 28). Interestingly, Rhodes et al. (34) have shown that an increased fos immunoreactivity in the caudate-putamen complex, the medial frontal cortex, and the lateral hypothalamus may “play a role in the motivation to run” of mice that were selectively bred for high daily wheel running activity. Thus it is possible that pheromones from either male or female mice in adjoining cages could influence daily wheel running in single-housed mice of either sex, a possibility that has implications for proximity of housing of mice in future studies. However, critical questions regarding range of airborne distribution of pheromones as well as appropriate blockage of pheromones to control their influence are unanswered at this time and thus cannot be knowledgably controlled in the interpretation of these data or any other activity data where mice are housed in the same facility.

It should be noted that daily physical activity level is not analogous to maximal exercise endurance, but appears to be a distinct phenotype. Our earlier strain screen for maximal exercise endurance in female mice in 10 of the 14 strains tested in this study (25) showed the following strain distribution pattern from highest to lowest exercise endurance: BALB/cJ > SWR/J > C57BL/6J > C3Heb/FeJ > C57L/J > C3H/HeJ > C57BL/6J > A/J > AKR/J > DBA/2J > DBA/2J > A/J.

Compared with the results from the female mice in the current study, the two strain distribution patterns are not concordant and thus implicate different genetic contributions to these two phenotypes. Our observation that daily physical activity level and maximal exercise endurance are two distinct phenotypes is supported by other studies. Lerman et al. (23) showed no significant correlation between voluntary wheel activity and treadmill performance (r values range from 0.27–0.68), and Friedman et al. (10) noted that two different measurements of wheel running activity did not significantly correlate (r = 0.15 and r = 0.38) with maximal oxygen consump-

Table 4. Broad-sense heritability estimates

<table>
<thead>
<tr>
<th>Physical Activity Measure</th>
<th>Model</th>
<th>Coefficient of Genetic Determination (g²)</th>
<th>Intraclass Correlation (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg. distance</td>
<td>Overall</td>
<td>0.18</td>
<td>0.30</td>
</tr>
<tr>
<td></td>
<td>Female only</td>
<td>0.12</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td>Male only</td>
<td>0.31</td>
<td>0.48</td>
</tr>
<tr>
<td>Avg. duration</td>
<td>Overall</td>
<td>0.25</td>
<td>0.39</td>
</tr>
<tr>
<td></td>
<td>Female only</td>
<td>0.12</td>
<td>0.21</td>
</tr>
<tr>
<td></td>
<td>Male only</td>
<td>0.44</td>
<td>0.61</td>
</tr>
<tr>
<td>Avg. velocity</td>
<td>Overall</td>
<td>0.14</td>
<td>0.24</td>
</tr>
<tr>
<td></td>
<td>Female only</td>
<td>0.44</td>
<td>0.61</td>
</tr>
<tr>
<td></td>
<td>Male only</td>
<td>0.49</td>
<td>0.66</td>
</tr>
</tbody>
</table>
tion in 35 male ICR mice. Furthermore, Lambert et al. (21) showed that treadmill exercise performance was not correlated with subsequent voluntary wheel running performance in rats ($r = -0.15, P = 0.53$). Given these data, it appears that physical activity level and maximal exercise endurance/aerobic capacity are two distinct phenotypes with differing genetic control.

In summary, both between-strain (i.e., genetic) and sex variation was found on 3 different measures of daily running wheel activity in 14 inbred strains of mice. The influence of heritability on the various indices of physical activity rose substantially when the mice were partitioned by both sex and strain, indicating a significant role for sex in the determination of daily wheel running activity. These results lay the foundation for future investigations to identify the genes responsible for the control of daily running wheel activity in both male and female mice.

ACKNOWLEDGMENTS

We acknowledge the technical skills of Sherin Salama, Mark Lindley, Amber Lowe, and Sarah Carter in the development and collection of the physical activity data, as well as the willingness of Dr. B. Harrison to share his design for the measurement method of daily physical activity.

REFERENCES


Physiol Genomics • VOL 19 • www.physiolgenomics.org