Effects of genetic selection and voluntary activity on the medial gastrocnemius muscle in house mice

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Departments of 1Anesthesiology and 2Physiology and Biophysics, Mayo Foundation, Rochester, Minnesota 55905; and 3Department of Zoology, University of Wisconsin, Madison, Wisconsin 53706-1381

Zhan, Wen-Zhi, John G. Swallow, Theodore Garland, Jr., David N. Proctor, Patrick A. Carter, and Gary C. Sieck. Effects of genetic selection and voluntary activity on the medial gastrocnemius muscle in house mice. J. Appl. Physiol. 87(6): 2326–2333.—In a previous study (J. G. Swallow, T. Garland, J r., P. A. Carter, W.-Z. Zhan, and G. C. Sieck, J. Appl. Physiol. 84: 69–76, 1998), we found that in house mice both genetic selection (10 generations of artificial selection for high voluntary activity on running wheels) and access to running wheels (7–8 weeks) elicited a modest increase in maximal oxygen consumption. Based on these results, we hypothesized that genetic selection would affect the changes in endurance and oxidative capacity of the medial gastrocnemius (MG) muscle induced by wheel access (training response). Wheel access increased the isotonic endurance of the MG in both genetically selected and random-bred (control) mice. However, this exercise-induced improvement in isotonic endurance of the MG was similar between genetically selected and control mice. Wheel access also increased the succinate dehydrogenase activity of MG muscle fibers in both selected and control lines. However, this exercise-induced increase in succinate dehydrogenase activity was comparable between genetically selected and control animals. Taken together, these results indicate that the modest increase in maximal oxygen consumption associated with genetic selection is not reflected by the training-induced changes in oxidative capacity and endurance of MG muscle fibers.

In a previous study (21), we proposed the use of laboratory house mice as a novel model to examine both genetic (10 generations of artificial selection for high voluntary activity on running wheels) and environmental effects (7–8 wk of access or no access to running wheels) on physiological activities. The genetically selected mice (20) were representatives of four replicate lines selectively bred for increased total wheel running (revolutions/day). Through 10 generations, the increased wheel running was accomplished mainly by an increase in average speed while running on wheels, rather than by an increase in the number of minutes per day during which any wheel activity occurred (20, 21). The base population was Hsd:ICR laboratory house mice, a widely available and commonly studied random-bred strain (4, 9). The Hsd:ICR strain shows genetically heritable individual variation in both voluntary wheel running (20) and measures of forced locomotor performance ability (6).

Consistent with previous studies of both mice and rats, we found (21) that wheel access reduced body mass and increased maximum oxygen consumption (V\textsubscript{O2max}) during forced treadmill exercise. We also found that mice from genetically selected lines had higher V\textsubscript{O2max} than random-bred control lines. The magnitude of effects on V\textsubscript{O2max} was similar for selection and wheel access: each caused a modest increase of ~6% (21).

In the present study, we used a subset of the same individual mice to test for effects of genetic selection and endurance exercise (voluntary wheel running) on oxidative capacity [succinate dehydrogenase (SDH) activity] and endurance properties of the medial gastrocnemius (MG) muscle. The MG muscle was studied because it contains a mixture of fiber types (3, 25) and it is recruited during locomotion in rodents (14). We hypothesized that access to running wheels would increase isotonic endurance and enhance SDH activity of all fiber types in this hindlimb muscle. We also hypothesized that muscles of mice genetically selected for high wheel-running activity would exhibit a greater improvement in isotonic endurance and oxidative capacity compared with random-bred controls. To our knowledge, this is the first study of muscle function in lines of rodents selectively bred for high activity levels.

METHODS

Animal model. The male house mice (Mus domesticus) used in this study were sampled from an artificial selection experiment for increased voluntary activity levels on running wheels, including four replicate selected lines and four randomly bred control lines (20). These mice were the result of 10 generations of within-family selection for total wheel-running activity. Mice in each generation were housed individually with access to running wheels and scored for activity over a 6-day period; selection was based on the total number of revolutions run on days 5 and 6. After 10 generations of selective breeding, during the eighth week of wheel access, mice in the present study averaged 17 m/min running speed. Total wheel-running activity in the selected lines was ~76% higher than in the nonselected lines (20).

Details of husbandry conditions for mice studied herein are described in our previous paper (21). Briefly, experiments were performed on four groups of individuals: 1) sedentary control (i.e., nonselected), 2) wheel-access control (i.e., nonselected), 3) sedentary selected, and 4) wheel-access selected. In both wheel-access groups, mice were placed individually, at 22 days of age, in normal housing cages attached to activity wheels of 35.7-cm diameter (1.12-m circumference), so that they had continuous access to wheels. The wheel-exposure period continued for ~8 wk before measurement of V\textsubscript{O2max} (21). Mice were then transported from Madison, WI, to Rochester, MN, where housing conditions remained the same until termination, which occurred during the next 2 wk (wheel access continued, but running was not recorded during
Muscle contractile and endurance properties. Animals were anesthetized with ketamine (60 mg/kg im) and xylazine (2.5 mg/kg im), and the right and left MG muscles were excised: one was used for contractile measurements and the other for immunohistochemistry. To determine MG contractile properties, muscle segments were vertically mounted in a glass tissue chamber that was constantly perfused with Rees-Simpson solution [(in mM) 135 NaCl, 5 KCl, 2 CaCl₂, MgCl₂, 120 Cl⁻, 25 HCO₃⁻ and 0.012 d-tubocurarine] aerated with 95% O₂-5% CO₂ and maintained at 26°C (pH 7.4). The Achilles tendon of the MG muscle was glued onto a thin plastic strip, which was attached to a force transducer and a dual-mode length-force servo controller (Cambridge Technologies, model 300B). The other end of the MG muscle was fixed by using a surgical clamp mounted in series to a micropositioner near the base of the tissue chamber.

Force and length signals were acquired, and stimulation protocols were controlled by a personal computer running a custom-made program based on LabView (National Instruments) via a data-acquisition card (AT-MIO16 L9, National Instruments). Muscle segments were stimulated directly by using 0.5-ms-duration current pulses delivered via platinum-plate electrodes placed on both sides of the muscle. Stimulus intensity was increased until maximum twitch force (Pₛ) was obtained. The stimulus intensity was then set to 125% of this value (200–250 mA) to ensure supramaximal stimulation. During single-pulse stimulations, muscle length was adjusted until maximum force responses were obtained. This optimal length (Lₒ) was then measured by using a digital caliper. Maximum tetanic force (Pₜ) was determined by stimulation at 100 Hz in a 1-s-duration train. Both Pₛ and Pₜ were normalized for the cross-sectional area (CSA) of the muscle, which was estimated by using the following formula: CSA = muscle weight (g)/muscle specific density (1.056 g/cm³). Lₒ and Lₜ were multiplied by 10.220.32.246 on July 10, 2017 http://jap.physiology.org/ Downloaded from

Isotonic shortening velocities were measured at different loads ranging from 3 to 100% of Pₜ. At each load clamp level, muscle segments were stimulated at 100 Hz for 600 ms. The duration of stimulation was limited by the range of movement for the lever arm of the Cambridge system (~5 mm), especially at low-load clamp levels. To determine velocity, muscle displacement was measured over a 30-ms period beginning 10 ms after the initiation of muscle shortening. The force-velocity measurements were least squares fitted to a hyperbolic curve by using the Hill equation, and maximum shortening velocity (Vₜₚₑₓ, expressed as Lₒ/s) was determined by extrapolation (11). Power output (expressed as W·m⁻²) of the MG muscle at each load was calculated as the product of isotonic load and shortening velocity, and the load corresponding to maximum power output (Pₜₚₑₓ) was determined.

Isotonic endurance of the MG muscle was assessed at a load corresponding to Pₜₚₑₓ (30% Pₜ). Repetitive shortening contractions at a constant load of 30% Pₜ were induced by stimulation at 100 Hz in trains of 350-ms duration repeated each second. Changes in shortening velocity and power output were determined. Isotonic endurance was defined as the time required for Pₜₚₑₓ to decline to zero (i.e., the time when the muscle lost its ability to shorten).

Muscle histochemistry. The MG muscle was stretched to 1.5 times resting excised muscle length (approximating Lₒ) and rapidly frozen in isopentane cooled to its melting point by liquid nitrogen. In each muscle, serial sections were cut at 10 µm by using a cryostat kept at ~20°C (model 2800E Frigocut, Reichert-Jung) and reacted with mouse primary antibodies against different myosin heavy chain (MHC) isoforms. Fibers were classified as MHCslow, MHC2α, MHC2x, and MHC2b. In some cases, only a single antibody was used, e.g., anti-MHCslow (Novocastra, IgG), anti-MHC2α (Blau A4.74, IgG or Blau N1.551, IgM), anti-MHC2x (Schiaffino BFF3, IgM), and anti-MHC2b (Novocastra). Primary antibodies were diluted in PBS containing 0.5% bovine serum albumin (5 mg/ml) and applied to the muscle section for ~2 h at room temperature. Slides were then washed in PBS and reacted with Cy3- or Cy5-conjugated secondary antibodies (goat anti-mouse IgG or goat anti-mouse IgM) for 45 min at room temperature. The use of antibody pairs allowed for double labeling of MHC isoform expression in the same section with minimal cross-reactivity. This was confirmed by adding the opposite secondary antibody to a section incubated with only IgG or IgM primary antibody. Sections incubated with only the secondary antibodies served as controls for nonspecific reactivity of all primary antibodies. The slides were then washed in PBS and imaged with a Bio-Rad (MRC500/600) confocal system mounted on an Olympus (BH2) microscope and equipped with an Ar-Kr laser.

MG muscle fiber CSA was determined from microscopic (Olympus BH2) images of muscle sections digitized into an array of 1,024 × 1,024 pixels (picture elements) with a computer-based image-processing system (Megavision 1024 XM) calibrated for densitometry and morphometry as previously described (19). Use of a 20-power microscope objective produced pixel areas of 0.15 µm². The CSA of individual fibers was determined from the number of pixels within outlined fiber boundaries.

MUSCLE FUNCTION

Table 1. Body weight and mass of the medial gastrocnemius muscle

<table>
<thead>
<tr>
<th></th>
<th>Sedentary Control</th>
<th>Wheel-Access Control</th>
<th>Sedentary Selected</th>
<th>Wheel-Access Selected</th>
<th>Main Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>8</td>
<td>8</td>
<td>11</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Body weight, g</td>
<td>38.9 ± 1.3</td>
<td>32.2 ± 1.1</td>
<td>36.7 ± 1.3</td>
<td>33.4 ± 1.1</td>
<td>P &lt; 0.05; ω² = 0.30</td>
</tr>
<tr>
<td>Muscle mass, mg</td>
<td>73.8 ± 5.4</td>
<td>68.8 ± 5.0</td>
<td>74.4 ± 4.5</td>
<td>71.1 ± 6.1</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of mice.

This period). In sedentary control and sedentary-selected groups, four mice were group housed in normal cages for the same period. All experimental procedures were approved by the Institutional Animal Care and Use Committees at the University of Wisconsin and at the Mayo Clinic and were in strict accordance with the American Physiological Society Guiding Principles in the Care and Use of Animals.
**Table 2. Contractile and endurance properties of the mouse medial gastrocnemius muscle**

<table>
<thead>
<tr>
<th></th>
<th>Sedentary Control</th>
<th>Wheel-Access Control</th>
<th>Sedentary Selected</th>
<th>Wheel-Access Selected</th>
<th>Main Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_t$, N·cm⁻²</td>
<td>7.1 ± 0.6</td>
<td>6.0 ± 0.6</td>
<td>6.7 ± 0.3</td>
<td>6.5 ± 0.5</td>
<td></td>
</tr>
<tr>
<td>$P_o$, N·cm⁻²</td>
<td>20.2 ± 1.6</td>
<td>16.7 ± 1.4</td>
<td>19.5 ± 0.9</td>
<td>17.8 ± 1.3</td>
<td></td>
</tr>
<tr>
<td>$V_{max}$, Lₗ·s⁻¹</td>
<td>5.0 ± 0.5</td>
<td>3.9 ± 0.4</td>
<td>4.7 ± 0.5</td>
<td>3.9 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>$P_{max}$, W·m⁻²</td>
<td>995 ± 155</td>
<td>880 ± 152</td>
<td>922 ± 106</td>
<td>926 ± 130</td>
<td>$P &lt; 0.05$; $\omega^2 = 0.21$</td>
</tr>
<tr>
<td>Endurance time, s</td>
<td>10.9 ± 2.1</td>
<td>21.1 ± 4.3</td>
<td>7.7 ± 0.8</td>
<td>16.8 ± 3.5</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SE. $P_t$, maximum twitch force; $P_o$, maximum tetanic force; $V_{max}$, maximum shortening velocity; $P_{max}$, maximum power output. Interactive effects between selection and wheel-access factors were not significant.

NBT-dfz deposited within a fiber during the SDH reaction was determined from optical density (OD) measurements by using the Beer-Lambert equation

$$ [\text{NBT - dfz}] = \frac{\text{OD}}{k} $$

where fiber OD was measured at 570 nm (the peak absorbance wavelength for NBT-dfz, 26,478 mol⁻¹·cm⁻¹), and $l$ is the path length for light absorbance (6 µm). From these measurements, the maximum velocity of the SDH reaction was determined, and the mean SDH activity of each fiber was expressed as millimoles fumarate per liter tissue per minute. The SDH activities of ~125 fibers were analyzed in each muscle sample, representing at least 20 fibers of each MHC phenotype. The total SDH activity of all MG fiber types combined was estimated by using the following calculation

$$ \Sigma (\text{for all fiber types} \times \text{mean SDH activity } \times \text{relative contribution to total muscle CSA}) $$

Statistical analysis. Based on an a priori power analysis of data obtained in previous studies (22, 23, 24), it was determined that seven animals (muscles) per group were sufficient to detect a 20% change in isotonic endurance (at $P < 0.05$) between experimental and control groups at a $\beta$ level of 0.80. Similarly, based on an a priori power analysis of previously obtained data on muscle fiber SDH activities (1, 18, 19, 24), it was determined that a minimum sample of 20 fibers of each MHC phenotype was required in at least six animals to detect a 10% change (at $P < 0.05$) between experimental and control groups at a $\beta$ level of 0.80. A nested two-way analysis of covariance (ANCOVA) was performed with type III sums of squares in the SAS general linear models (GLM) procedure. Exercise group (sedentary vs. wheel access) and linetype (selected vs. control) were the grouping factors; replicate line was nested within linetype. The foregoing are mixed models (selected vs. control) were the grouping factors; replicate line was nested within linetype. Omega squared ($\omega^2$) was also calculated as an index of the degree of relationship between the control and treatment groups. For all variables where the $P$ value was < 0.05, the values of $\omega^2$ are listed. In all cases, statistical significance was established at the 0.05 level. All data are presented as means ± SE.

**RESULTS**

Average body mass was reduced in mice with wheel access compared with sedentary animals, but genetically selected mice were not significantly different from controls (Table 1). This result is the same as reported previously for these mice when weighed ~2 wk earlier (21). MG muscle mass was not significantly different across groups (Table 1).

Muscle contractile and endurance properties. A summary of the isometric and isotonic contractile properties of the MG muscle in the varying groups of mice is provided in Table 2. Neither genetic selection nor wheel access significantly affected $P_t$, $P_o$, $V_{max}$, or $P_{max}$ of the MG muscle. In each group, the force-velocity relationship of the MG muscle was hyperbolic, and there was no significant difference in shortening velocity at the varying load clamp levels among the four groups (Fig. 1A). Accordingly, in all groups, $P_{max}$ of the MG muscle was generated at ~30% of $P_o$ (Fig. 1B).

During repetitive isotonic activation at peak power output (~30% of $P_o$), the ability of the MG muscle to

\[ A \]

\[ B \]

Fig. 1. Force-velocity relationships (A) and force-power relationships (B) of medial gastrocnemius (MG) muscle in the 4 experimental groups of mice. Neither genetic selection nor wheel access affected maximum shortening velocity ($V_{max}$) or maximum power output ($P_{max}$). $L_o$, optimal length; $P_o$, maximum tetanic force.
shorten declined progressively in each group (Fig. 2). However, in both control and selected groups, the decline of muscle shortening was more rapid in sedentary animals (Fig. 2, A and B) compared with wheel-access animals (Fig. 2, C and D). After a period of repetitive isotonic contractions, the MG muscle ultimately failed to shorten and reached a point where it no longer was able to generate 30% of \( P_0 \). The end point was defined as the endurance time of the muscle under these conditions. Endurance time of the MG muscle was significantly improved in mice with access to activity wheels (increase by 94 and 118% in the control and selected groups, respectively; Table 2 and Fig. 3). However, endurance time did not differ significantly between selected and nonselected mice (Fig. 3).

Fatigue during repetitive isotonic activation was also evidenced by a progressive decline in \( P_{\text{max}} \) (Fig. 4). In both control and selected groups, the rate of decline in \( P_{\text{max}} \) was significantly less profound in wheel-access mice compared with sedentary mice.

Muscle fiber histochemistry and morphometry. Four different fiber types were found in the deep portion of the mouse MG muscle, as determined by immunoreac-
Muscle fiber-type composition, CSA, and SDH activity of the medial gastrocnemius muscle

Table 3. Muscle fiber-type composition, CSA, and SDH activity of the medial gastrocnemius muscle

<table>
<thead>
<tr>
<th>MHC</th>
<th>Sedentary Control</th>
<th>Wheel-Access Selected</th>
<th>Main Effects Wheel Access</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 8</td>
<td>n = 6</td>
<td>n = 7</td>
</tr>
<tr>
<td>MHC&lt;sub&gt;Slow&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>14.2 ± 1.9</td>
<td>16.9 ± 3.5</td>
<td>17.0 ± 2.0</td>
</tr>
<tr>
<td>CSA, µm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>793 ± 54</td>
<td>873 ± 195</td>
<td>874 ± 69</td>
</tr>
<tr>
<td>SDH activity</td>
<td>5.6 ± 0.2</td>
<td>7.1 ± 0.4</td>
<td>5.3 ± 0.5</td>
</tr>
<tr>
<td>MHC&lt;sub&gt;2α&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>41.5 ± 3.0</td>
<td>47.1 ± 4.3</td>
<td>41.9 ± 2.2</td>
</tr>
<tr>
<td>CSA, µm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>828 ± 72</td>
<td>838 ± 153</td>
<td>870 ± 83</td>
</tr>
<tr>
<td>SDH activity</td>
<td>8.8 ± 0.2</td>
<td>10.4 ± 0.4</td>
<td>8.6 ± 0.6</td>
</tr>
<tr>
<td>MHC&lt;sub&gt;2x&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>26.6 ± 2.1</td>
<td>20.1 ± 1.7</td>
<td>26.0 ± 1.7</td>
</tr>
<tr>
<td>CSA, µm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1,334 ± 83</td>
<td>1,230 ± 155</td>
<td>1,339 ± 98</td>
</tr>
<tr>
<td>SDH activity</td>
<td>7.0 ± 0.3</td>
<td>10.1 ± 0.6</td>
<td>7.6 ± 0.7</td>
</tr>
<tr>
<td>MHC&lt;sub&gt;2b&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>17.7 ± 5.0</td>
<td>15.9 ± 5.6</td>
<td>15.1 ± 2.5</td>
</tr>
<tr>
<td>CSA, µm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1,828 ± 132</td>
<td>1,560 ± 158</td>
<td>1,936 ± 131</td>
</tr>
<tr>
<td>SDH activity</td>
<td>4.3 ± 0.2</td>
<td>6.0 ± 0.8</td>
<td>4.1 ± 0.4</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of mice. CSA, cross-sectional area; SDH, succinate dehydrogenase; MHC, myosin heavy chain. Interactive effects between selection and wheel-access factors were not significant.
Evidence of training effect in wheel-access mice. We found that 7–8 wk of access to running wheels significantly increased whole body \( V\hat{O}_2\text{max} \) (21) and muscle fiber SDH activity of both selected and random-bred mice. The significant increases in \( V\hat{O}_2\text{max} \) (6%) and SDH activity (30%) confirm that an aerobic training effect was induced as a result of access to running wheels. The relative differences in SDH activities across fiber types in the mouse MG muscle (deep region) are also in general agreement with our previous observations in the rat diaphragm (17, 24) and rat MG (1) muscles. SDH activities are highest in fibers expressing MHC2A and lowest in those expressing MHC2B.

The increase in muscle oxidative capacity was modest in relation to the increase reported in prior treadmill-training studies in rats (5, 7, 12). However, the average running speed (during week 8) in the wheel-access groups was ~17 m/min, which is only 50% of the speed at which the mice reached \( V\hat{O}_2\text{max} \) during forced treadmill running (21). In addition, although we have not measured bout lengths, other studies in both mice (15) and rats (16) reported that wheel activity typically involves multiple but brief (i.e., <3 min) bouts of running rather than the continuous running (up a grade) that characterizes most treadmill training studies. Therefore, the relatively low intensity and short duration of individual wheel-running bouts probably explains the modest improvements observed in muscle oxidative capacity.

The low intensity of wheel-running activity in house mice may also explain why muscle mass and fiber size, as well as force-generating capacity (i.e., maximum isometric force), did not increase in wheel-access mice. These results are consistent with previous studies in...
Endurance, which we did find (Table 2). Third, average muscle fatigue may result from an imbalance between energy supply and energy demand. The higher SDH activity in MG fibers of the wheel-access mice suggests an enhancement in the overall energy supply potential during contractile activity (17, 19). Therefore, it is likely that in the wheel-access mice the elevated oxidative capacity of muscle fibers contributed to the enhanced endurance of the MG muscle during repetitive activation.

Muscle fiber-type composition. We studied the MG muscle because of its mixed fiber-type composition and its extensive involvement in locomotor activity. Fiber-type proportions in the deep region of the MG muscle in these mice, determined by MHC isoform expression (Table 3), are generally consistent with those reported previously for house mice of the same strain (unpublished observations), as determined by using standard histochemical procedures. We used antibodies specific to MHC isoforms to permit detection of MHC isoform coexpression (19, 26). However, there was minimal evidence of MHC isoform coexpression in MG fibers in wheel-access mice. In sedentary mice, a few fibers coexpressed MHC2x and MHC2b (~3%). It is important to note that, in the present study, there was no evidence suggesting that wheel-running-induced improvement in endurance of MG muscle was associated with alterations in muscle fiber-type composition.

Characterizing voluntary wheel activity in mice. Rats given access to running wheels reportedly run at speeds close to or exceeding that at which aerobic capacity is reached (16). It has therefore been suggested that voluntary wheel running may involve a preponderance of sprint-type activity rather than endurance activity. Our results suggest that this idea may not apply to mice tested on relatively large wheels. First, wheel access had no effect on peak isometric force or maximum power, factors that theoretically should influence locomotor speed (13). Second, wheel running elicited an increase in muscle fiber oxidative capacity. Such adaptations typically accompany increased muscle endurance, which we did find (Table 2). Third, average running speed (during week 8) in the wheel-access groups was ~17 m/min, which is only 50% of the speed at which the mice reached VO2max during forced treadmill running (21). Finally, siblings of the mice studied here did not differ in forced maximal sprint running speed (unpublished observations). Consequently, we have no evidence to suggest that wheel running by mice in the present study could be characterized as sprinting. This points to the need for further studies of exercise and muscle physiology in mice.

Effects of genetic selection. The physiological factors that influence voluntary wheel-running behavior are multifactorial. "Motivation" will determine how much an animal runs but within the limits set by its physical abilities to exercise. Our previous study (21) showed that both genetic selection and wheel access increased VO2max by similar amounts (6%). In the present study, we found that genetic selection history had no detectable effect on fiber-type composition, oxidative capacity, or the contractile and endurance properties of the MG muscle. This suggests that enhanced hindlimb muscle performance is not the basis for the augmented total wheel-running activity observed in house mice resulting from 10 generations of artificial selection. Taken together, these results suggest that the modest increase in VO2max associated with genetic selection is not reflected by enhanced oxidative capacity or improved endurance of the MG muscle.

As in our previous study of whole animal traits (21), we found no statistically significant interactions between line type (selected vs. control) and activity group (wheel access vs. sedentary). This suggests that trainability of the MG muscle was not affected by artificial selection. However, we view the possibility of genotype-sensitive training effects as worthy of further study in later (i.e., >10) generations.

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7. Received 29 July 1998; accepted in final form 16 August 1999.

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