Short-term voluntary exercise in the rat causes bone modeling without initiating a physiological stress response

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Rosa BV, Firth EC, Blair HT, Vickers MH, Morel PCH, Cockrem JF. Short-term voluntary exercise in the rat causes bone modeling without causing stress. Am J Physiol Regul Integr Comp Physiol 299: R1037–R1043, 2010. First published July 28, 2010; doi:10.1152/ajpregu.00112.2010.—Recent research has revealed a neuroendocrine connection between the skeleton and metabolism. Exercise alters both bone modeling and energy balance and may be useful in further developing our understanding of this complex interplay. However, research in this field requires an animal model of exercise that does not cause a physiological stress response in the exercised subjects. In this study, we develop a model of short-term voluntary exercise in the female rat that causes bone modeling without causing stress. Rats were randomly assigned to one of three age-matched groups: control, tower climbing, and squat exercise (rising to an erect bipedal stance). Exercise for 21 days resulted in bone modeling as assessed by peripheral quantitative computed tomography. Fecal corticosterone output was used to assess physiological stress at three time points during the study (preexercise, early exercise, and late in the exercise period). There were no differences in fecal corticosterone levels between groups or time points. This model of voluntary exercise in the rat will be useful for future studies of the influence of exercise on the relationship between skeletal and metabolic health and may be appropriate for investigation of the developmental origins of those effects.

REFERENCES


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content (BMC), bone area, or bone mineral density (BMD) without a concomitant rise in fecal corticosterone.

**MATERIALS AND METHODS**

**Animals.** Twenty-nine female Wistar rats were habituated to their surroundings and to a low phytoestrogen diet (AIN-93G; Research Diets) for 19–22 days before commencing the exercise protocols. All rats were housed in the same room in a climate-controlled dedicated animal research facility with a 12:12-h light-dark cycle. Rats were bedded on kiln-dried wood shavings, and all were housed in pairs during the study period. Feed and water were provided ad libitum, and intake was monitored by weighing initial and residual feed and measuring initial and residual water volume every 1–2 days throughout the exercise trial. Body weight was measured two times weekly. The study protocol and all animal procedures were approved by the Massey University Animal Ethics Committee.

**Exercise.** After the habituation period, when they were 100 ± 8 days of age, the rats were randomly assigned to one of three age-matched exercise groups: control, squat exercise, and tower climbing.

Control rats were housed conventionally for the duration of the trial in a 419 mm × 279 mm × 152-mm high cage (Fig. 1A), with their feed and water at a height of ~90 mm from the cage floor.

Rats in the squat exercise group were housed in a modified cage, the sides of which were gradually raised in height over a 5-day period. At full height, the food and water available to the rats was ~220 mm above the cage floor (Fig. 1B), requiring the rats to stand on fully extended hindlimbs to obtain food and water. This model has been previously shown to induce bone modeling in sexually intact rats and to reduce bone loss in gonadectomized rats (63).

For the tower climbing group, the cage lid was replaced with a 2-m-high tower made of wire mesh (12 × 12 × 220 mm) as shown in Fig. 1C. Over a 5-day period, the water bottle in the cage was incrementally raised from an initial height of 90 mm to a final height of 2 m. Tower climbing has been previously shown to induce bone modeling in rats (43).

During their 5-day gradual introduction to exercise, the rats were observed daily to ensure they were able to reach the food and water and that they were maintaining body weight and feed and water intake. Any rats with reduced water intake were examined by a veterinarian to ensure there were no clinical signs of dehydration. Following this orientation period, the rats remained in their exercise cages for 21 days.

**Imaging.** Peripheral quantitative computed tomography (pQCT) and dual energy X-ray absorptiometry (DXA) were performed two times during the trial, at 6 days before beginning the orientation period (baseline) and on day 26 (5 days of orientation plus 21 days of exercise) after which the rats were killed. Before imaging, the rats were anesthetized with a mixture consisting of 0.5 ml ketamine (100 mg/ml) + 0.2 ml acepromazine (2 mg/ml) + 0.1 ml xylazine (100 mg/ml) + 0.2 ml sterile water injected intraperitoneally at a dose rate of 0.6 ml/100 g via a 25-gauge needle. A level of anesthesia suitable for noninvasive imaging procedures was obtained within 5–10 min and was maintained for ~1 h.

pQCT of the right tibia of each rat was performed ( XCT2000 pQCT scanner; Stratec, Pforzheim, Germany). Tibial length was measured from the palpable lateral aspect of the tibial plateau to the distal end of the lateral malleolus, using callipers. The rat was then placed in right lateral recumbency and affixed to a cardboard platform with adhesive tape. Scans were made 5 mm distal to the tibial plateau (proximal metaphysis) and at 50% of the tibial length (mid-diaphysis) (23) with a voxel size of 0.1 mm and scan speed of 10 mm/s. Scans were analyzed using the manufacturer’s software. Metaphyseal bone was analyzed by contour mode 3, peel mode 2, with an outer threshold of 214 g/cm³ and an inner threshold of 606 g/cm³ as described elsewhere (2), and diaphyseal bone was analyzed using contour mode 1 with a threshold of 710 g/cm³. The coefficient of variation (CV) for total density ranged from 0.48 to 1.47% at the midtibial diaphysis and from 1.32 to 2.23% at the proximal tibial metaphysis, and the CV for total area ranged from 1.47 to 1.72% at the midtibial diaphysis and from 3.73 to 7.11% at the proximal tibial metaphysis without and with repositioning between scans.

BMc, areal bone mineral density (BMDa), and whole body composition data were determined with a fan beam densitometer (Hologic Discovery A, Bedford, MA) using the small animal application. Anesthetized rats were placed in dorsal recumbency on an acrylic platform with their hindlimbs in a frog-legged position with the femurs fully abducted and a femorobital joint angle of 90 degrees, and held in position with adhesive tape. Regional high-resolution scans of both hindlimbs (femur and tibia) and the lumbar spine were performed, as well as whole body scans. Quality control scans were performed daily to ensure that the precision met the required DXA manufacturer’s CV, which was 0.98–1.01%. High-resolution scans of the femur and tibia were analyzed using cortmode 1 elsewhere (2), and diaphyseal bone was analyzed using cortmode 1 with a threshold of 710 g/cm³. The coefficient of variation (CV) for total density ranged from 0.48 to 1.47% at the midtibial diaphysis and from 1.32 to 2.23% at the proximal tibial metaphysis, and the CV for total area ranged from 1.47 to 1.72% at the midtibial diaphysis and from 3.73 to 7.11% at the proximal tibial metaphysis without and with repositioning between scans.

**Fecal sample collection and corticosterone measurement.** To measure the stress response to voluntary exercise, fecal samples were collected from all groups during three periods: preexercise, during early exercise (day 6–9), and toward the end of the exercise period (day 18–21). Feces were collected by a protocol similar to that described by Boggiano et al. (5). Briefly, the cage bedding was changed 1 h before the start of the dark period. All feces were collected from the bedding 4 h after the start of the dark period. Urine-soaked feces were discarded (this occurred only one time, since the high-quality bedding instantly absorbed any voided urine). The first 4 h of the dark period are approximately the time of the fecal corticosterone nadir (5, 9), at which time between-group differences in corticosterone would be most apparent (60). Female rats produce varying levels of fecal corticoids during the different phases of their estrous cycle (9). To minimize the effects of the estrous cycle on corticosterone levels, samples were collected for four consecutive days during each sampling period.

Fecal samples were stored at −20°C until the completion of the study period. Samples were then freeze-dried and ground, and ethanol extraction was performed by the nonboiling method described by Fraisse and Cockrem (22) with the following slight modifications. The dried ethanol extracts were reconstituted in 1 ml of 0.1 M phosphate-buffered saline with 0.1% gelatin, pH 7.0 (PBSG), and the final supernatant was diluted in PBSG by a factor of two before freezing. The recovery of corticosterone following extraction was measured as previously described (22). The mean recovery of corticosterone from spiked control samples was 70.7 ± 0.8% (n = 15). The CV for the

![Fig. 1. A: control cage. B: squat exercise cage. C: tower exercise cage.](image-url)
mean percentage recovery was low (5.2%), and the mean percentage recovery was used to calculate results for all the samples. All samples were assayed in duplicate by a commercially available radioimmunoassay kit (Double Antibody Corticosterone 125I RIA kit for rats and mice; MP Biomedicals), and radiation counts were determined in a LKB Wallac 1261 Multigamma gamma counter for 3 min each. The sample and reagent volumes that were used in the assay were all 1/10 those of the kit protocol. Following addition of the precipitant and vortexing, 20 μl starch [25 g/l starch (Sigma) + 0.05 g/l neutral red (BDH) in PBSG] were added to increase adhesion of the pellet to the tube. The intra-assay CV for corticosterone were 8.4, 6.0, and 7.2%, and interassay CV for corticosterone were 7.8, 8.4, and 11.5% for low-, medium-, and high-concentration solutions, respectively. Fecal samples were weighed after drying and before extraction. Corticosterone is expressed as total nanograms excreted over the collection period, calculated as the fecal corticosterone concentration (ng/g) multiplied by the weight of the fecal sample.

Statistical analysis. All statistical analysis was performed with SAS 9.1 and an α level of 0.05. Significance of final imaging bone parameters was determined by covariate analysis using Proc GLM. Fixed effects initially tested were exercise group and age, and covariates were baseline parameter value and initial body weight at the start of the exercise training period. The final model included exercise group, baseline bone parameter value, and their interaction. Baseline differences between groups were assessed by simple ANOVA. Fecal corticosterone was assessed by repeat measures ANOVA. The final model included exercise group, cage, collection period, and the interaction of exercise group and collection period. A covariance analysis was conducted to analyze the relationship between cumulative feed intake and body weight gain during the experiment. A linear model (Proc GLM; SAS), with exercise as a fixed effect, cage within exercise as a random effect, the covariates body weight gain and body weight gain squared, and the interactions between the covariates and the fixed effect (to test for homogeneity of the linear and quadratic regression coefficients), was fitted to the cumulative feed intake data. Where appropriate, 95% confidence intervals for the linear and quadratic regression coefficients were calculated to show differences between exercise groups. All data are expressed as least square means ± SE unless otherwise indicated.

RESULTS

Animals. All rats successfully performed the exercise required by their group without injury or compromised health. Rats in all groups gained weight over the study period as shown in Fig. 2, with control rats gaining the most weight and tower-climbing rats gaining the least. Feed intake was very similar between groups (Fig. 3) although the relationship between feed intake and weight gain differed between exercise groups. This relationship was most variable in the tower-climbing group, with an initial decrease in weight gain per gram of feed intake followed by a marked increase in feed efficiency [the ratio of weight gain to feed intake (47)]. Figure 4 shows the relationship between weight gain and cumulative feed intake. The regression coefficients of the line demonstrating the relationship between intake and weight gain in the tower-climbing rats were significantly different from that of the controls. Feed efficiency over time is shown in Fig. 5. Although the feed efficiency of rats in the control group remained unchanged over the exercise period, rats in the squat exercise and tower-climbing groups demonstrated an improvement in feed efficiency over the course of the trial.

Imaging. The results of pQCT imaging of the proximal tibial metaphysis are presented in Table 1. Postexercise (day 26), the

![Fig. 2. Bar graph of mean change in body weight over the experiment for each group. *Significant difference from control value (P < 0.05). Below each bar, the baseline (weight at preexercise scan) and postexercise (day 26) mean body weight are shown for each exercise group. There was no significant difference in baseline body weight between groups.](http://ajpregu.physiology.org/)

![Fig. 3. Mean cumulative feed intake over the exercise period for each group.](http://ajpregu.physiology.org/)

![Fig. 4. Mean change in body weight per gram of cumulative feed intake on a per cage basis (2 rats/cage) throughout the exercise period.](http://ajpregu.physiology.org/)
tower-climbing group had a significantly larger total BMC, total bone area, and trabecular and cortical/subcortical (c/sc) BMC than did the control group. Squat exercise rats gained total BMC and c/sc BMC without gaining significant total bone area, leading to a significantly greater volumetric bone mineral density than that of day 26 controls.

The results of pQCT imaging of the midtibial diaphysis are presented in Table 2. After the exercise period, both exercise groups had significantly greater cortical BMC and cortical bone area than did the control group. The periosteal circumference also increased over the exercise period in both exercised groups, whereas it decreased in control animals. Volumetric BMD was significantly greater at the end than at the beginning of the experiment in all three groups.

DXA imaging revealed no significant differences in BMDa values between groups. Because of a malfunction of the densitometer, the baseline soft tissue values were unusable, so only day 26 values were available for analysis. The control group mean body fat percentage on day 26 was 30.8 ± 1.8%, which was numerically (but not significantly) higher than that of either the squat exercise group (24.8 ± 1.6%, P = 0.05) or the tower exercise group (25.7 ± 1.6%).

Fecal corticosterone. Mean daily fecal corticosterone excretion during the first 4 h of the dark cycle over each 4-day collection period is shown in Fig. 6. There were no significant differences between groups during any collection period, and there were no significant differences across collection periods in any group.

**DISCUSSION**

Weight gain and feed efficiency. Over the exercise period, tower-climbing rats gained less weight than either control or squat exercise rats, which is expected given the increased opportunity for exercise available to the tower-climbing rats. The rats were observed to climb the towers frequently, often without drinking, and at times spent extended periods (up to 45 min observed) at the top of the tower clinging to the wire mesh. It is thus likely that the metabolic effects of exercise were greatest in the tower-climbing rats. This is also suggested by the rapid improvement in feed efficiency seen in tower-climbing rats over the exercise period. At the start of the exercise period, the tower-climbing rats’ very low feed efficiency is reflective of a sudden increase in activity level when they were first put in the tower cages. As they adjusted to exercise, their feed efficiency improved rapidly, until by day 15 it was equal to that of the control rats. After day 15, the weight gain per gram of feed intake of the tower-climbing rats exceeded that of the control animals. The less rapidly, but still greatly, improving feed efficiency of the squat exercise rats suggests a more moderate but still present metabolic effect of exercise in this group. Control rats experienced no change in feed efficiency over the study period.

Studies of exercise and feed efficiency in the rat have yielded varying results ranging from decreases in feed efficiency with exercise (35) to significant improvements in feed efficiency (50). Interpretation of these studies is complicated by the use of varying types and amounts of exercise, strains and ages of rats, diets, and experimental conditions. It is possible that more strenuous exercise may decrease efficiency, whereas moderate exercise such as performed in our trial may increase it. A similar response has been seen in broiler chickens that were encouraged to exercise moderately through provision of ramps and toys; the improvement in feed efficiency was sufficient for the authors to suggest that such interventions might be commercially worthwhile (4). Certainly very moderate amounts of exercise have been shown to have profound effects on metabolism in the rat; intrauterine growth...

**Table 1. In vivo pQCT values at the proximal tibial metaphysis**

<table>
<thead>
<tr>
<th></th>
<th>Control Baseline</th>
<th>Squat Baseline</th>
<th>Tower Baseline</th>
<th>Control Postexercise (day 26)</th>
<th>Squat Postexercise (day 26)</th>
<th>Tower Postexercise (day 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total BMC, mg</td>
<td>11.1 ± 0.3</td>
<td>11.0 ± 0.3</td>
<td>10.6 ± 0.3</td>
<td>11.5 ± 0.2</td>
<td>12.5 ± 0.2*</td>
<td>12.6 ± 0.2*</td>
</tr>
<tr>
<td>Total area, mm²</td>
<td>16.2 ± 0.5</td>
<td>16.4 ± 0.5</td>
<td>16.0 ± 0.5</td>
<td>15.6 ± 0.3</td>
<td>16.5 ± 0.3</td>
<td>17.0 ± 0.3*</td>
</tr>
<tr>
<td>Total BMDa, mg/cm³</td>
<td>688.2 ± 12.5</td>
<td>668.3 ± 11.2</td>
<td>662.4 ± 11.2</td>
<td>727.8 ± 5.5</td>
<td>745.9 ± 4.4*</td>
<td>730.3 ± 4.6</td>
</tr>
<tr>
<td>Trabecular BMC, mg</td>
<td>2.21 ± 0.15</td>
<td>2.29 ± 0.14</td>
<td>2.31 ± 0.14</td>
<td>1.74 ± 0.07</td>
<td>1.96 ± 0.06</td>
<td>2.01 ± 0.06*</td>
</tr>
<tr>
<td>Trabecular area, mm²</td>
<td>6.1 ± 0.4</td>
<td>6.4 ± 0.3</td>
<td>6.6 ± 0.3</td>
<td>5.3 ± 0.1</td>
<td>5.4 ± 0.1</td>
<td>5.6 ± 0.1</td>
</tr>
<tr>
<td>Trabecular BMDa, mg/cm³</td>
<td>361.9 ± 12.4</td>
<td>360.3 ± 11.1</td>
<td>346.0 ± 11.1</td>
<td>336.3 ± 9.6</td>
<td>365.1 ± 8.5</td>
<td>361.2 ± 8.7</td>
</tr>
<tr>
<td>Cort/subcort BMC, mg</td>
<td>8.9 ± 0.2</td>
<td>8.7 ± 0.2</td>
<td>8.3 ± 0.2</td>
<td>9.7 ± 0.2</td>
<td>10.5 ± 0.2*</td>
<td>10.6 ± 0.2*</td>
</tr>
<tr>
<td>Cort/subcort area, mm²</td>
<td>10.1 ± 0.3</td>
<td>10.0 ± 0.2</td>
<td>9.4 ± 0.2</td>
<td>10.5 ± 0.3</td>
<td>11.2 ± 0.2</td>
<td>11.4 ± 0.3</td>
</tr>
<tr>
<td>Cort/subcort BMDa, mg/cm³</td>
<td>883.7 ± 11.9</td>
<td>865.5 ± 10.7</td>
<td>880.5 ± 10.7</td>
<td>938.3 ± 8.7</td>
<td>942.6 ± 7.9</td>
<td>914.0 ± 7.4</td>
</tr>
<tr>
<td>Periosteal circumference, mm</td>
<td>14.2 ± 0.2</td>
<td>14.4 ± 0.2</td>
<td>14.2 ± 0.2</td>
<td>14.0 ± 0.1</td>
<td>14.4 ± 0.1</td>
<td>14.6 ± 0.1*</td>
</tr>
</tbody>
</table>

Values are least square means ± SE. All data are from the proximal tibial metaphysis 5 mm distal to the proximal tibial plateau. pQCT, peripheral quantitative computed tomography; BMC, bone mineral content; BMDa, volumetric bone mineral density (BMD); cort/subcort, cortical/subcortical. There were no significant between-group differences in baseline values. *Significant difference from control values at day 26 (P < 0.05).
Table 2. In vivo pQCT values at the midtibial diaphysis

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Postexercise (day 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Squat</td>
</tr>
<tr>
<td>Cortical BMC, mg</td>
<td>5.7 ± 0.1</td>
<td>5.6 ± 0.1</td>
</tr>
<tr>
<td>Cortical area, mm²</td>
<td>4.5 ± 0.1</td>
<td>4.4 ± 0.1</td>
</tr>
<tr>
<td>Cortical BMDv, mg/cm³</td>
<td>1,280.1 ± 7.4</td>
<td>1,287.5 ± 6.6</td>
</tr>
<tr>
<td>Endosteal circumference, mm</td>
<td>5.0 ± 0.1</td>
<td>5.1 ± 0.1</td>
</tr>
<tr>
<td>Periosteal circumference, mm</td>
<td>9.0 ± 0.1</td>
<td>9.0 ± 0.1</td>
</tr>
</tbody>
</table>

Values are least square means ± SE. All data are from the midtibial diaphysis. There were no significant between-group differences in baseline values.

*Significant difference from postexercise control value (P < 0.05).

At the level of the midtibial diaphysis, the two exercised groups responded to exercise similarly with an increase in bone area, peristeal circumference, and BMC. There was no difference between the day 26 values for cortical BMD between exercised rats and controls; however, exercise resulted in rats with larger cortexes of the same density as control rats and thus effectively stronger bones.

Several studies have demonstrated that exercise causes bone formation in the rat (27, 43, 58, 59) and prevents bone loss in gonadectomized animals (36, 57, 63). However, in most of these studies, the animals exercised for longer periods of time than in our current study. Through the use of pQCT, we have been able to demonstrate a significant bone response to a relatively short exercise exposure. This brief exercise period was selected because it approximates the length of pregnancy in the rat. A nonstressful exercise model that rapidly induces metabolic and bone responses will be essential for studying intergenerational effects of exercise during gestation.

Stress. One possible criticism of any animal exercise model is that exercise may cause stress to the animal, which may affect the outcome measures. Thus we chose voluntary exercises for our rats and measured fecal corticosterone levels at three time points to determine if either exercise protocol induced stress in the rats. Fecal corticosterone levels have been shown to reflect response to a stressor in rats, with fecal levels peaking 7–9 h after a plasma corticosterone peak (54). By collecting feces over the first 4 h of the dark period, we obtained samples at the approximate fecal corticosterone nadir, which is the time most likely to reveal a stress response (5, 45, 60). Although plasma corticosterone levels may be more indicative of acute stress, measurement of fecal corticoids is well-suited to analysis of longer-term stressors (hours to days), since it quantifies a summated index of systemic corticoids proven to reflect stress responses (8, 48). Reporting total fecal corticoids over time, instead of fecal corticoid concentrations, provides a more accurate representation of systemic corticoid production by taking into account the amount of feces produced during the sampling time period, which varies over the light-dark cycle (9). Corticosterone and its metabolites enter the small intestine via the biliary system. The total amount of corticoids excreted in the feces reflects the plasma corticoid concentration and is independent of fecal mass; thus, the measured concentration of corticoids in feces will vary with fecal output (9, 51). Because even some forms of voluntary exercise may induce a stress response in rodents (7), it was important to determine whether the moderate-intensity voluntary exercises we selected caused a stress response in the exercised rats. The lack of significant differences suggests that

**Imaging parameters.** The change in pQCT parameters at the proximal tibial metaphysis from baseline in exercised groups compared with controls reveals a significant effect of the exercise on bone modeling in both squat and tower rats. Both exercised groups had significantly greater day 26 total BMC than controls, but the distribution of the increased bone mineral varied with the exercise type. The tower group responded to exercise with a greater gain in bone area than the control group, resulting in bones of comparable density but greater cross-sectional area than those of control rats. S rats did not increase their proximal tibial metaphyseal bone cross-sectional area in response to exercise but did gain total BMC and thus increased their total bone density. These differences in bone response to exercise may reflect the differing forces acting on the tibia caused by the two exercise forms, one of which involves only the hindlimbs (squat exercise) while the other requires the rat to use all four limbs (tower climbing). All groups had a lower mean trabecular area (marrow area) at the day 26 scan (reflecting endocortical bone formation and thus a decrease in the marrow area).

**Restriction (IUGR) in the rat results in obesity as the animals mature; however, when IUGR rats were allowed only 56 meters of treadmill running/day, they did not become obese (40). Such findings indicate that the metabolic effects of exercise are not limited to an increase in the number of calories expended.**

**Imaging parameters.** The change in pQCT parameters at the proximal tibial metaphysis from baseline in exercised groups compared with controls reveals a significant effect of the exercise on bone modeling in both squat and tower rats. Both exercised groups had significantly greater day 26 total BMC than controls, but the distribution of the increased bone mineral varied with the exercise type. The tower group responded to exercise with a greater gain in bone area than the control group, resulting in bones of comparable density but greater cross-sectional area than those of control rats. S rats did not increase their proximal tibial metaphyseal bone cross-sectional area in response to exercise but did gain total BMC and thus increased their total bone density. These differences in bone response to exercise may reflect the differing forces acting on the tibia caused by the two exercise forms, one of which involves only the hindlimbs (squat exercise) while the other requires the rat to use all four limbs (tower climbing). All groups had a lower mean trabecular area (marrow area) at the day 26 scan (reflecting endocortical bone formation and thus a decrease in the marrow area).
the exercised animals experienced no greater stress than the unexercised controls.

Research into the interplay between the HPA axis and metabolism suggests that the relationship between these systems is established during the prenatal and early postnatal period (3, 10, 39, 53), and maternal stress experienced by the fetus during gestation has proven developmental and metabolic effects (26, 34, 37, 38). Persistent stress also influences bone function, with chronic elevations of cortisol leading to low bone mineral in humans (12). Although little work has been done to elucidate the early life factors affecting long-term skeletal health, it has recently been proposed that osteoporosis risk may also be linked to interactions between the genotype and the environment during development (16). The bone mass of an individual in later life is directly related to the peak bone mass attained by that individual during skeletal growth (42a); in humans, birth weight influences future adult bone mass (16). Pregnant rats fed a protein-restricted diet produce offspring with altered osteoblast activity (30), changes in bone structure and mineral density (31), and delayed skeletal maturity (44). As the connections between the skeleton and metabolism become further clarified, it seems likely that the foundations of this chemical and mechanical interplay may also be established during early life.

Perspectives and Significance

A model of moderate exercise that does not cause stress is critical for investigations into exercise effects on the interrelationship between bone and metabolism. Recent research suggests that the basis of this relationship may be established in early life, even before birth. The results of this study demonstrate that both tower climbing and rising to an erect bipedal stance are suitable exercise models for examining the connection between skeletal and metabolic health, since both forms of exercise resulted in bone modeling without causing a physiological stress response. The differences in metabolic effect of the two exercises, as demonstrated by their varying effects on feed efficiency, may prove useful for future examination of the bone-metabolism relationship. Further study in pregnant animals is needed to confirm that these exercises do not cause stress under the different physiological conditions of gestation. If this proves to be the case, these exercise models will be suitable for examining the effects of exercise during gestation on the relationship between bone and energy balance in both mother and offspring and the effects of gestational exercise on the future metabolic and skeletal health of the next generation.

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DISCLOSURES

No conflicts of interest are declared by the authors.

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