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Running head: VOLUNTARY WEIGHT-LIFTING PERFORMANCE

Control and Quantization of Voluntary Weight-Lifting Performance of Rats

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Abstract

The present paper describes an exercise model that produces a voluntary hind limb weight-lifting response. Each rat was operantly conditioned to enter a vertical tube, insert its head into a weighted ring (either 70 g or 700 g), lift the ring until its nose interrupted an infrared detector, and then lower the ring. Load cells measured the external force generated and displacement transducers measured the vertical displacement of the ring during each lifting and lowering movement. The apparatus and training procedures were computer automated. Peak force, velocity, work, and power were calculated for each movement. Rats in both groups easily acquired the task after 12 to 15 training sessions, on average, conducted five days per week. Once trained, the lifting patterns were quite stable during several more weeks of posttraining exercise, however, the lighter 70-g load gave rise to more variable performances across rats. Results demonstrate the utility of quantitating the biomechanics of volitional movements and suggest that the present model can establish and maintain controlled repetitive movements necessary for studies of adaptation and/or injury in muscles, tendon, and bone.

Key Words: resistance exercise, weight lifting; operant conditioning; voluntary performance; rats

Introduction

There have been numerous attempts to model human skeletal-muscle performance with laboratory animals, particularly with rodents. The similarities between the micro architecture of rat and human skeletal muscle and the ability to precisely control the biomechanics of contractile activity in rats through various *in vitro*, *in situ*, or *in vivo* methods are major advantages of using rat preparations. One limitation the use of electrical stimulation to induce involuntary muscle contractions is a common feature of these models. Unlike voluntary contractile activity, which is submaximal and characterized by a selective recruitment of motor units, involuntary contractile activity induced by electrical stimulation is typically supramaximal and involves the activation of all motor units of the target muscle. Thus, efforts to make viable inferences from comparisons between muscle responses to supramaximal electrical stimulation and voluntary submaximal contractions have limited utility.

In contrast to electrical stimulation models, several *exercise* or *strength training* models have produced repetitive voluntary muscle movements that can be maintained over long periods of time (33). Some forms of operant conditioning with food rewards or other kinds of positive or negative consequences, such as reinforcing electrical brain stimulation or foot shock, have been employed with some success to motivate repetitive movements. Because these approaches produce voluntary contractile activity, normal neuromuscular control processes remain intact, and thus are more representative of muscle function in the real world. Despite this advantage, exercise models are less capable of generating the loading conditions necessary to propagate injury (23). Most exercise models, therefore, have been useful, not for the study of injury, inflammation, or repair processes, but for studying muscle adaptation or enlargement due to endurance and strength-training exercise over extended periods of time.

Alternatively, motorized treadmills have become increasingly common for the study of muscle injury in rodents (2, 21, 30). In the typical treadmill preparation, rats are forced to run to avoid the presentation of an aversive stimulus, usually electric shock. This approach often produces wide-ranging amounts and intensities of exercise that allow the study of both adaptive and pathological responses in hind limb muscle. For example, treadmill studies have shown that downhill running can produce either a training effect (hypertrophy and reduced muscle injury) or muscle injury with eccentric-like myofiber lesions (19, 28). Although downhill running models produce voluntary movements noninvasively, they do not control the mechanics of the movement precisely or quantify the biomechanical loads during the activity. This lack of quantification makes it difficult to relate either adaptive or injurious physiological outcomes to specific parameters of performance and loading history, which can differ widely across individual animals.

Overcoming the limitations associated with controlling and quantifying voluntary movement topographies, while also maintaining a significant amount and intensity of biomechanical loading, is a major challenge associated with volitional models. In this regard, operant conditioning, if properly applied, can be a promising tool for arranging the appropriate training and exercise conditions. Operant technology has been used for decades in behavioral research with rats, pigeons, and primates, and has proven to be the technique of choice to maintain significant amounts of repetitive behavior in daily sessions conducted over several months or years (18).

Only a few researchers have employed operant conditioning procedures to produce the kinds of repetitive muscle loadings that are relevant for the study of exercise-induced physiological responses, particularly muscle hypertrophy. In these approaches, volitional responses were motivated by various consequences such as food rewards (16, 20, 36), intracranial stimulation (13) and electric shock to the tail or feet (9, 11, 17, 32). The species, target muscle groups, and training protocols, however, differed widely among these models. For example, Gonyea and colleagues (14, 15, 16) trained cats to grasp and move a weighted bar with the fore limb repeatedly in 30-min sessions conducted 5 days per week for up to 87 weeks. Yarasheski and colleagues (36) trained rats over an 8-week period to climb a wire-mesh ladder with weights secured to their tails, and Klitgaard (20) trained rats over 36-week period to enter a vertical tube and use their hind limbs to lift a weighted ring. In other approaches, rats wore weighted jackets and were trained in sessions conducted 8 to 16 weeks to rear up on their hind limbs to avoid an electric shock or to receive brain stimulation (9, 13, 17, 32).

Despite the ability of various volitional exercise models to induce representative, voluntary perturbations to targeted muscle groups, these models have not been adopted widely. It is likely that the extensive training required to produce an appreciable physiological effect and the lack of control or quantitation of the biomechanics of the movement have hindered their use. We believe that these limitations can be eliminated by a more effective application of operant conditioning techniques and through better apparatus and interface design.

In the present paper, we describe an improved exercise model that produces a hind limb weight-lifting movement with rats. Each rat was trained using operant conditioning techniques with food rewards to enter a vertical tube, insert its head into a ring, lift the ring until its nose interrupted an infrared detector, and then lower the ring. A force plate was used to record the reaction forces generated by the plantar flexors about the ankle axis during each lift, and a displacement transducer was used to measure the vertical displacement of the ring assembly during each lift. Most important, the apparatus and training procedures were computer automated to control and quantify the lifting dynamics in real time. To assess the potential usefulness of this approach for producing well-controlled, repetitive voluntary movements, the reaction forces, velocity, work, and power associated with the lifting and lowering movements were examined. Two groups of rats were tested to provide a comparison of the effects of a light and heavy loading condition on the ease of training and biomechanical performance.

Materials and Methods

Subjects

Thirty-two male Sprague-Dawley (Hilltop, PA, USA) rats were obtained at 12 weeks of age. They were housed individually in ventilated home cages in a temperature, humidity-controlled room with a reversed 12-hr light cycle.

The rats were randomly assigned to one of two loading conditions with 16 rats in each group. Rats in one group were required to lift 70 g whereas the other group lifted 700 g (hereafter 70-g and 700-g groups, respectively). We chose 700 g for the higher load because it was approximately 2 times the average body mass of the rats and could be reliably and repeatedly lifted by most rats. The 70-g load was chosen because it was light but still provided some resistance to the lifting movement. Each rat was trained to perform the lifting and lowering movement with operant conditioning procedures and a food reward. Food can function as a reinforcer, however, only when the rat is hungry. Therefore, access to food was restricted so that each rat's mass was maintained at 80% ± 5% of its *ad libitum* mass, the generic standard in behavioral research (3). The rat's daily ration of standard lab chow was adjusted in the home cage as necessary to maintain their target mass. Access to water in the home cage was unlimited at all times.

Each rat was weighed daily to ensure that the proper mass was maintained for a minimum of one week prior to training. Thereafter, normal growth was accounted for by adjusting weekly each rat's target mass by 80% of the weekly change in the mean mass of a group of weight-control rats that were housed previously in our lab and fed *ad libitum* (8). Prior to training, the mean body masses of rats in the 70-g and 700-g groups were 347.3 g (SD = 19.9) and 354.9 g (SD = 10.5), respectively. This difference was not statistically significant, t(30) = -1.367, p = .182. After eight weeks, mean body mass increased to 389.9 g (SD = 11.7) for the 70-

g group and 393.8 g (SD = 8.7) for the 700-g group; this difference also was not statistically significant, t(30) = -1.062, p = .297.

All experimental procedures were approved by the Animal Care and Use Committee at the National Institute for Occupational Safety and Health in Morgantown, West Virginia, USA.

Apparatus

Figure 1 shows the apparatus developed for the present study. It consisted of a standard operant chamber that was modified to accommodate a custom-designed device for training and recording a hind limb weight-lifting response. Each rat was tested in the apparatus in a room that was adjacent to their home quarters.

Operant chambers. A standard operant chamber (ENV-008; Med Associates, VT, USA) was placed inside a fan-ventilated and sound-attenuated cubicle. The chamber was 305 cm long, 24.1 cm wide, and 29.2 cm high. It was illuminated with a low-wattage house light positioned at the rear of the chamber. Throughout each session, constant white noise (approximately 80 dB) was generated through a speaker on the rear panel to mask extraneous noise, and the house light was turned on for general illumination. Food rewards consisted of 45-mg nutritionally complete pellets (Noyes Formula P; Research Diets, NJ, USA) that were dispensed into a food trough located on the left side of the front panel. The food trough was bisected by an infrared detector so that head entries into the trough (i.e., retrieval of the pellet) could be recorded.

During training conditions (described below), a nose-poke response device (ENV-114BM; Med Associates, VT, USA) was mounted on the right side of the front panel 3.3 cm above the grid floor. This device consisted of a 2.54 cm by 2.1 cm access hole, which was bisected by a sensitive infrared detector placed 6.4 mm in from the front edge. A nose poke that broke the infrared beam was recorded as a response. A yellow-colored LED cue light was located behind the access hole. When illuminated, the LED cue light signaled that the nose-poke device was active.

Lifting Apparatus. An opening 10.1 cm high and 9.6 cm wide in the center of the front panel of the operant chamber allowed the rat access to an acrylic tube that was mounted vertically (see Figure 1). The tube measured 48.3 cm high and 14.0 cm wide on the inside. Inside the tube, a neck ring was supported by a yoke that moved along two vertical shafts via linear bearings. The neck ring had an inner diameter of 3.5 cm and an outer diameter of 7.4 cm. It consisted of 1.3-cm thick Teflon sandwiched between two stainless steel rings. The bottom ring was interchangeable with other rings with different inner diameters to accommodate rats of various sizes. The entire ring assembly weighed 388 g; however, a counterweight system was used to reduce the effective mass to 70 g for one group of rats. For the other group, weights were placed on pans attached to the ring assembly to increase the total load to 700 g.

An infrared nose-poke response device, identical to the one described above, was positioned near the top of the tube to record each lifting and lowering response. The height of the nose-poke device could be adjusted to vary the range of motion of plantar flexion. When illuminated, the LED cue light above the nose-poke response device signaled when the device was active. An electromechanical relay, mounted at the top of the tube, was used to correlate a click sound with each nose-poke response.

Force Measurement

To measure the reaction forces exerted by the hind limbs of the rat, a force plate was designed to depress a load cell (13/2443-06; Sensotec, OH, USA) embedded in the base of the tube. The base of the tube was machined from a solid block of aluminum and measured 11.4 cm wide, 3.8 cm high, and 10.4 cm long. The base supported a force plate that was machined to fit over the load cell that was embedded in the base. Four 6.35 mm by 20.32 mm stainless steel shafts were mounted on force plate using a press fit and Lock Tite solution. The shafts slid along four sealed linear bearings (Thompson Super 4; IKO International, NJ, USA) that were embedded in the base. This ensured that all vertical forces generated by the rat (including body mass) were translated normal to the force plate permitting accurate measurement of the reaction forces. The load cell required an excitation voltage of 5.0 V and produced an output of 2.10 mV/V. The signal from the load cell was amplified using a signal conditioning amplifier (2310, Vishay Measurements Group; NC, USA) and sent to an analog-to-digital computer board (PCI-MIO-16XE-10; National Instruments, TX, USA) for processing. The load cell was calibrated using precision weights ranging from 100 g to 1000 g. The voltage output was determined to be linear over the range of weights tested ($R^2 = 0.9999$). The voltage was converted to load in grams with the control software.

Displacement Measurement

Vertical displacement of the ring assembly was measured using a linear variable differential transformer (LVDT; B-Series; Solartron Metrology, NC, USA). The LVDT was attached to the ring assembly to measure the vertical displacement during the lift and permit determinations of velocity of the lifting and lowering movements. A Solartron OD4 conditioning unit powered the LVDT and provided a DC output that was proportional to the vertical displacement to the analog-to-digital computer board. Sensitivity of the LVDT was 16 mV/V/mm. Output voltage was converted to displacement in cm. The voltage output of the LVDT was linear over a 2.5-cm range ($R^2 = 0.9992$).

Training Procedure

Training the rat to perform the lifting and lowering movement occurred in stages across several sessions that were conducted 5 days per week for 1 to 2 weeks. Table 1 shows the number of sessions conducted in each training session.

Magazine training. Initially, the rat was trained to retrieve and consume food pellets quickly and reliably after every delivery. This involved delivering food pellets into the trough at irregular intervals until, eventually, the rat retrieved the pellets reliably and immediately. Access to the vertical tube was blocked off during this stage of training and the nose-poke response device was removed from the chamber. Magazine training usually required 1 session that lasted approximately 1 hr.

Nose-poke training. In the next session, the nose-poke device was introduced to the chamber, and the LED lamp behind the nose-poke device was lit. Invariably, the rat, while exploring the chamber, would poke its nose into the device breaking the infrared beam. A nose-poke response initiated a distinctive, audible 0.5-s click of the electro-mechanical relay and the reinforcement cycle. In each reinforcement cycle, the following events occurred: two food pellets were delivered 1 s apart, white noise was turned off for 0.5 s, and the LED cue light behind the nose-poke device was turned off. To minimize the likelihood of the rat continuing to respond through the reinforcement cycle, additional nose pokes that occurred during the reinforcement cycle had no programmed consequences. These responses were rare. When a head entry into the food trough was detected (i.e., food pellets were retrieved), the LED cue light behind the nose-poke device was turned on to signal that the device was again active. Nose-poke training sessions ended either after 50 reinforced nose pokes occurred in a session or one hour had elapsed, whichever occurred first.

Standing inside the tube. When nose pokes occurred frequently and consistently (usually after one or two sessions), the nose-poke device was removed from the chamber and access was provided to the vertical tube. At this stage, control over food-pellet delivery was transferred to the nose-poke device inside the tube. The ring assembly was fixed at the top of the tube just under the nose-poke device at a position that required the rat to rear up on its hind limbs. To earn food pellets, the rat was required to enter the tube, stand up, and break the infrared beam of the nose-poke device. A nose poke initiated the reinforcement cycle, and the rat was required to exit the tube to retrieve the food pellets. Most rats' behavior adjusted quickly to this arrangement of the apparatus. Occasionally, however, some rats were reluctant to enter the tube or stand up initially. In these cases, baiting the tube with a few food pellets or selectively reinforcing successive approaches toward or movement inside the tube encouraged the appropriate standing response, usually within a few minutes. Once the standing response was established, the final height of the nose-poke response device was adjusted as necessary to ensure full plantar flexion (i.e., heel raises) through its range of motion.

Lifting the ring assembly. To transition from a mere "nose-poke" task to a weight-lifting task, it was necessary to place the ring at successively lower positions. Across the next several sessions, the entire ring assembly (either weighted or counter-weighted depending on the group) was lowered gradually by 0.5 cm increments. The gradual lowering of the ring assembly allowed the rat to become accustomed to the load and increases in the required vertical displacement. This procedure was continued until the ring assembly was displaced approximately 2.5 cm.

Posttraining sessions. After training, additional sessions were conducted until the number of responses, or lifts, stabilized for most rats across a minimum of 20 sessions. Each session ended after 100 responses were performed (i.e., lifts that terminated in a nose-poke) or after a predetermined amount of time had elapsed, whichever came first. Sessions lasted up to 30 min for the 70-g group and 60 min for the 700-g group to account for expected differences in the rates of responding caused by the different loading conditions. Because we were interested in characterizing the voluntary performances of rats, however, no further constraints, such as the rate of responses, were placed on the rats' behavior. This enabled us to determine the extent and nature of any intersubject variability obtained on various performance measures. Sessions were conducted Monday through Friday at the same time each day. In each session, the rat's behavior and all experimental events, such as the presentation of food pellets and visual or auditory stimuli, were monitored and controlled by computer throughout the test session. Vertical displacement, time, and force during each lifting and lowering movement were sampled at 100 Hz.

Statistical Analyses

We relied on descriptive statistics, including measures of sample variation and distribution, to quantify the performances of the rats across each session and during each lifting and lowering movement. In most cases, medians and interquartile ranges (25th to 75th percentiles) were calculated for various performance measures described below to assess and compare performance across groups. Measures of performance by individual rats also were detailed to better assess the utility of the present volitional exercise model for producing controlled movements reliably. In addition, t-tests were used to assess differences between the 70-g and 700-g groups, and between concentric and eccentric movement parameters within each group.

Number of lifts and movements. To compare the effects of the different loading conditions across the posttraining sessions, the total number of responses, or lifts, that were performed by each rat in a session was recorded for each posttraining session. Because not all lifts resulted in full displacement of the ring assembly, lifts that terminated in a nose-poke (hereafter "full lifts") were recorded separately from those that did not (hereafter "partial lifts") (see Figure 2 for examples). A full or partial lift was triggered by ring assembly displacement $\geq$ 0.1 cm from the starting position. Termination of a full or partial lift was triggered when the ring position was < 0.1 cm. The median number of full and partial lifts were plotted for each group across the sessions.

Second, each full and partial lift was decomposed further into any instance of a positive or negative change in displacement of the ring assembly (see Figure 2). It therefore was possible to record more than one such movement during the ascending and descending portions of each full or partial lift. Because positive ring displacements involve concentric (shortening) contractions of the plantar flexor muscle group and negative displacements involve eccentric (lengthening) contractions, these lifting and lowering movements hereafter are termed *concentric* and *eccentric* movements, respectively, to characterize the dynamics of hind limb lifting. The number of concentric and eccentric movements in each full or partial lift and across all lifts per session were summed to obtain the total number of concentric or eccentric movements performed by each rat in each session. Group medians and interquartile ranges were generated and plotted across the sessions.

Analysis of individual subject performances by movement. For each rat in the 70-g and 700-g groups, peak force, average velocity, total work, and average power were calculated for each concentric and eccentric movement across the last six sessions to obtain an adequate sampling of the terminal performances. Median and interquartile ranges of the measures were calculated. Peak force, which included the rat’s body mass, was expressed in Newtons (N). Average velocity (positive for concentric movements and negative for eccentric movements) was calculated by dividing the change in displacement of the ring assembly (in cm) by the time of the displacement (in ms). Concentric work (i.e., work performed) and eccentric work (i.e., work absorbed) were calculated by numerical integration of force and displacement data and expressed in Joules (J). Average power for each concentric (i.e., power performed) and eccentric movement (i.e., power absorbed) were calculated by dividing the work by the time of the displacement and expressed in Watts (W).

Results

Training

One rat in the 700-g group failed to maintain responding in the final training phases and subsequently was dropped from further analyses. Table 1 shows the mean number of sessions conducted across the stages of training with the remaining rats. In general, approximately 13 to 15 training sessions were conducted before each rat was able to lift the ring assembly reliably through its maximum displacement of approximately 2.5 cm. Most training sessions occurred in the “standing stage” suggesting that this stage was the most difficult. Thereafter, most rats progressed rapidly through the next training stage wherein the ring assembly was lowered gradually across sessions. The number of sessions in each training phase was not different between the 70-g and 700-g groups.

Posttraining Performance

As shown in Table 1, approximately 26 to 28 additional posttraining sessions were conducted in which full displacement of the ring was required. The top panel of Figure 3 shows the median number of responses that terminated in a nose-poke (i.e., full lifts) in addition to the number of partial lifts displacements of the ring ≥ 0.1 cm that did not terminate in a nose poke. In the 70-g group, the median number of full lifts per session was fairly stable across posttraining sessions, and varied little around 100 full lifts per session, the maximum possible. In the 700-g group, the median number of full lifts per session gradually increased before stabilizing at approximately 80 full lifts per session. For both groups, the number of partial lifts exceeded the number of full lifts by approximately 25% to 50% in most sessions. The number of partial lifts also was more variable than full lifts across the rats as indicated by the greater interquartile ranges. Furthermore, it was determined that partial lifts accounted for approximately one-half of the total work performed in the last six sessions (mean = 48% for the

70-g group and 51% for the 700-g group). Because an appreciable proportion of session responses were partial lifts, both full and partial lifts in each session were combined for further analyses and calculations of all other performance measures reported hereafter.

The second panel of Figure 3 shows the total number of concentric movements. Because the number of concentric movements was equal to the number of eccentric movements, only the number of concentric movements was plotted in the figure. The median number of concentric (or eccentric) movements per session was slightly greater than the total number of full and partial lifts per session (top panel), suggesting that each lifting and lowering response contained one or more oscillations between lifting and lowering. In addition, the 70-g group exhibited greater variability in the number of concentric (or eccentric) movements per session than the 700-g group.

Response Profiles during the Last Six Sessions

To better characterize the typical biomechanical profile of the lifting and lowering movements performed by each group, Figures 4 and 5 show the median number of concentric and eccentric movements, peak force, velocity, work, and power calculated from among all full and partial lifts recorded during the last six sessions. Group performances were based on the median performances calculated from data recorded with each rat (detailed individual subject performances are available from the authors upon request). Median were used as a measure of central tendency because they are less susceptible to outliers and skewed data. Boxplots were then used to depict the variability of the medians for each measure. Each box depicts the median and lower and upper quartile, and error bars depict the range, excluding the outliers that are outside the interquartile range by at least 1.5 times. Shaded portions of the boxes depict the 95% confidence intervals. A heteroscedastic t-test (this form assumes unequal sample variances) was used to test differences in the means between 70-g and 700-g groups. Paired t-tests were used to test differences between concentric and eccentric movement parameters within each group.

As Figure 4 shows, significantly more concentric movements were recorded across the last six sessions for the 70-g group than for the 700-g group. A similar significant difference in the number of eccentric movements was found between the 70-g group and the 700-g group. The total number of concentric and eccentric movements also varied considerably across the rats, especially in the 70-g group. As stated previously, this difference in variability suggests that the lighter 70-g load may have given rise to more variation in the topography of the lifting response. For example, some rats may have lifted the ring assembly with a rather fluid motion whereas others tended to move the ring with more bounce or jerk. In contrast, the heavier 700-g load appeared to restrict the range of movement strategies as evidenced by the narrower range of variability within the group.

Despite the intersubject variability in the amount of responding across the terminal sessions, the groups were clearly differentiated on several performance measures. As Figure 5 shows, peak forces (N), work (J) and power (W) were dependent on the loading condition as well as type of movement. In general, the median peak force, work, and average power per lift for both concentric and eccentric movements were significantly greater for the 700-g group than the 70-group. Median velocities for the 70-g and 700-g groups also were significantly different for eccentric movements, but not for concentric movements, indicating that rats in the 700-g group lowered the ring more quickly than the 70-g group.

In addition, some differences were found within each group between concentric and eccentric movements. For example, peak forces of concentric movements were significantly greater than the peak forces of eccentric movements for both 70-g and 700-g groups. Furthermore, the average velocities for eccentric movements were significantly greater than for concentric movements for the 700-g group, but not for the 70-g group. No other within-group differences between work and power of concentric and eccentric movements were evident.

Because the number of movements performed may have affected peak force, velocity, work, or power, a correlation analysis using individual subject data was conducted to determine the degree of association between the number of movements recorded during the last six sessions and measures of peak force, velocity, work, and power. As shown in Table 2, significant negative relations were found between the number of concentric movements performed and measures of velocity, work, and average power, but only for the 70-g group. Specifically, velocity, work, and power decreased as the number of concentric movements increased. Similarly, velocity and work were related significantly and positively to the number of eccentric movements performed in the 70-g group (i.e., velocity and work increased as the number of movements increased); the correlation with average power was not significant. In both groups, peak force was not related to the number of movements. No significant relations were found with the 700-g group.

Discussion

Biomechanics of the Movement

A common limitation of existing volitional exercise models is the inability to quantify biomechanical and performance parameters other than the external load applied or the number of repetitions. In the present preparation, computerized data acquisition and real-time monitoring of ring displacement and the external forces generated by the lifting and lowering movements provided the raw data necessary to calculate or derive a wealth of information about the lifting and lowering performance of the rat hind limbs. It also was possible to record the many partial lifts that significantly impacted the overall amount of biomechanical exposure for each animal. Biomechanical risk factors such as forceful exertions, lift frequency, and velocity of lift have been shown to be correlated with increased incidences of workplace injury (24). Indeed, investigating the association between biomechanical exposure and physiological outcomes would be beneficial in elucidating which factors result in skeletal muscle injury or adaptation. In addition, because muscle damage has been associated with eccentric muscle actions (31), but not concentric muscle actions at the same force level (26), the ability to measure the biomechanical loads during concentric and eccentric movements separately is important for the investigation of either long-term adaptation or injury processes.

In the present study, the different loading conditions resulted in clearly differentiated performances by the two groups of rats. For instance, peak concentric and eccentric forces in the 700-g group were approximately two times higher than in the 70-g group. This result is not surprising because higher forces must be generated in the concentric mode to overcome the inertia of the heavier 700-g weight. In addition, higher eccentric forces must be generated to absorb more potential energy from the heavier weight. It is interesting to note that the average eccentric velocities were higher in the 700-g group than the 70-g group, whereas average concentric velocities were similar. This lifting strategy may have been selected to minimize energy expenditure. Although higher concentric velocities, in theory, require more power to be generated by the plantar flexors, particularly with a 700-g weight, the higher eccentric velocity in the 700-g group would reduce the time that the muscle is generating tension and thus energy expenditure of the plantar flexors during lowering of the weight. Indeed, a slower eccentric velocity with a higher weight requires more energy expenditure of the plantar flexors. This lifting strategy also is found in human studies where lowering tasks typically require about 40% less work than lifting tasks using the same external load because subjects tend to capitalize on the potential energy of the external load during lowering (12).

In addition, the 700-g load resulted in somewhat more work per concentric or eccentric movement. This result was not surprising because more force was needed over the prescribed range of motion to complete the lifting and lowering task. However, it is of interest to note that concentric work was higher than eccentric work in the 700-g group. Although it has been established in other studies that concentric work is more metabolically demanding than eccentric work (5, 35), this result should be considered in the context of minimizing total cycle work (i.e., the sum of lifting and lowering work). Higher concentric forces, and thus higher concentric work, were needed to complete the lifting task; however, lower forces, and thus lower eccentric work, were expended for the lowering task which would minimize cycle work.

Calculations of power generally were consistent with obtained measures of force and velocity. More power was generated (concentric) and absorbed (eccentric) in the 700-g group than the 70-g group. This was the result of higher concentric and eccentric forces generated in the 700-g group and a higher eccentric velocity. In the 700-g group, concentric and eccentric power were similar due to higher peak forces in the concentric mode and a higher velocity in the eccentric mode.

Despite the appreciable intragroup variability in the amount of responding obtained in each session, the heavier load resulted in a more uniform lifting topography than the lighter load. For example, the number of concentric and eccentric movements and various performance parameters were more variable across rats in the 70-g group. This also suggests that the easier, lighter load allowed for greater variety in movement strategies, whereas the variety of movements in the more difficult, heavier load tasks tended to be restricted. Further research is necessary to test the reliability of this finding as it may be an important consideration when planning parametric manipulations and comparisons of different work loads across individual rats or groups of rats.

The ability to quantify measures of peak concentric and eccentric forces and velocities, total concentric and eccentric work, and average concentric and eccentric power during lifting tasks is a unique aspect of the present approach. In previous volitional weight-lifting models, quantitation of performance was limited to specifying the number of lifts and the load lifted within and across sessions. An exception was Klitgaard's model (20) which could also derive measures of work. The ability to precisely quantify the biomechanics of a lifting and lowering movement can greatly expand the scope of musculoskeletal research. For example, studies of volitional weight-lifting exercise, in which various biomechanical factors are systematically manipulated or controlled, could reveal how specific biomechanical factors play a role in the genesis or maintenance of various adaptive or pathological processes in muscle, tendon, and bone. Such studies thus could lead to greater understanding of the links between biomechanics and various physiological outcomes.

Computer-Controlled Reinforcement Contingencies

Other unique aspects of the present preparation include the training protocol and the use of operant conditioning techniques to establish the controlled voluntary exertions of the hind limbs. All rats except one were able to learn and maintain the task in sessions conducted across several weeks. Soon after initial training, these rats, including those in the 700-g group, were able to lift the terminal load through its full displacement and maintain a steady rate of responding across several successive sessions. The ability to acquire and maintain the target exertions rapidly (within approximately 12 to 15 sessions on average) differs from most other volitional weight lifting models where loads were incremented gradually over several weeks or months (9, 13, 17, 20, 32). Although a thorough analysis of physiological responses were not a focus of the present study, the number of repetitions performed by most rats and the forces generated with each movement are consistent with the kinds of loading conditions that have been shown previously to produce adaptive or hypertrophic responses in muscle (9, 13, 20).

Preliminary data from a separate study, presented in Figure 6, show that as little as 8 weeks of exposure to the repetitive weight-lifting task with a 700-g load resulted in significantly increased muscle wet mass of the plantar flexor muscle group (i.e., gastrocnemius and soleus only) compared with that of age-matched cage-control rats. Muscles of the dorsi flexors of the exercised rats did not exhibit an increase in wet mass; however, this was not surprising because the dorsi flexors would not be expected to undergo contractions during resistive plantar flexion activity due to reciprocal inhibition. Although the increase in muscle wet mass alone does not definitively indicate a hypertrophic response, alternative explanations, such as edema caused by acute-phase events (e.g., inflammation and fluid shifts), are not likely because the 8-week exercise period was well beyond the time course of these acute events (1). Nevertheless, the results are promising and suggest that our model is capable of producing a physiological response.

Perhaps the most noteworthy, but expected, finding associated with the use of operant conditioning is the degree of intersubject variability obtained in the various performance measures. Because the target responses were voluntary, it was not possible to obtain the degree of precision and uniformity of exertions across all subjects as in involuntary stimulation models. The extent to which individual performances were measured and recorded, however, allowed for a thorough assessment of common and idiosyncratic lifting topographies that could, for example, serve as a basis for identifying over or under performers. The ability to differentiate individual differences in performances during future studies also may provide clues about the relative effects of various biomechanical factors and other subject factors such as age, sex, and genetics on performance and physiological measures.

The present approach also allows some control over the pattern of responding depending on the schedule of reinforcement selected. In the present study, a fairly simple schedule of reinforcement was used two pellets for each full lift. However, other reinforcement schedules in which pellets are delivered intermittently after the occurrence of either a fixed or variable number of lifts, or after the passage of a fixed or variable amount of time, can result in different patterns of behavior (22). Depending on the schedule used, characteristic patterns of responding that are slow, fast, steady, or punctuated by brief pauses may be obtained reliably from session to session. The ability to control the pattern of responding may be useful for studies of various work-organization factors on performance and risk of injury.

Automating the reinforcement contingencies via computer allows greater flexibility and control over the movement topography compared to nonautomated food delivery devices in other models (20). For instance, it is possible to gain better control over intersubject variability in responding by altering parameters of the reinforcement contingencies (29), such as increasing the magnitude or frequency of rewards. In addition, reinforcement can be made contingent on the occurrence of specific features of various response topographies, such specifying a minimum or maximum pace of responding, movement duration, or displacement of the ring assembly. It also is possible to control the velocity of lifting and lowering movements by making food-pellet deliveries contingent on obtaining a specific rate of positive or negative change in displacement of the ring assembly. Because the apparatus is computer controlled and performance monitored in real time, these adjustments in the reinforcement contingencies pose no special problem.

Decades of research on reinforcement schedules have documented the reliability of reinforcement contingencies in establishing and maintaining a variety of simple and complex behavioral patterns (10, 18). In theory, there is no reason to preclude a similar degree of precision with behaviors that are relevant for the study of muscle biomechanics as demonstrated in the present study.

The use of positive-reinforcement schedules to establish and maintain repetitive responding has several advantages over the other procedures that have been used to motivate volitional behavior. For example, studies have shown that the restricted feeding regimens that produce stable masses below *ad libitum* levels do not cause stress to the animals but rather have been shown to enhance health and extend life (6, 25). Furthermore, there is no evidence that this type of food restriction provides physiological or psychological stress (34). It is important to note that the method of food restriction used in the present study differs from schedules of intermittent fasting (20) which may risk imbalances or frequent fluctuations of nutritional requirements. In addition, the method of food-restriction used in the present study is arguably more representative than behavior evoked by shock avoidance procedures (9, 11, 17, 32) and less invasive (and less demanding of resources) than reinforcement with electrical brain stimulation (13). The potential for habituation to develop in response to repeated exposures to electric shock and concerns over health or ethical considerations associated with aversive stimulation are eliminated or minimized by using food rewards. The present procedures thus allow for long-term and minimally invasive longitudinal studies with no adverse effects on the health of the animal.

Applications of the Model

The present model is volitional, noninvasive, and well suited for the study of a broad range of topics surrounding the effects of repetitive resistance exercise on performance and physiology. The ability to control and quantitate various biomechanical parameters of the lifting and lowering movement is perhaps the most significant advantage over other *in vivo* weight-lifting models. Although existing injury and exercise models have been useful in elucidating the muscle response to repetitive contractile activity, most have not controlled biomechanical exposures adequately to allow for dose-response characterizations of the biomechanical perturbations and subsequent muscle response. Further studies with the present preparation, or the like, can be conducted to determine how manipulations of various work and biomechanical factors (e.g., load, number or rate of repetitions, and work-rest cycles) affect the response dynamics. Even if intersubject variability is found among the performances of individual animals, several parameters of the movement dynamics are quantifiable allowing comprehensive dose-response assessments of exercise intensity or volume.

In addition, because of the volitional nature of the performance, the reinforcement contingencies themselves can be the subject of study. For example, the effects of appetitive versus aversive stimuli, stress, work organization factors (e.g., load, work-rest cycles, number or rate of repetitions), magnitude of rewards, and type of response consequence (positive, negative, reinforcing, or punitive) may be studied with minor alterations of the apparatus or computer-controlled reinforcement contingencies. Evidence for a role of physical and nonphysical factors in the incidence of musculoskeletal disorders in workplace (4, 27) and other settings further supports the use of noninvasive, volitional animal models.

The present model also allows the study of a variety of outcomes related to the impact of repetitive loading of muscle, tendon, or bone. Biomechanical performance and physiological response in soft tissue can be assessed with biochemical and histological techniques or with *in vivo* functional tests using rodent dynamometry (7). This model also can be adapted for studying mitigating factors of exercise on bone loss or remodeling and tissue atrophy due to disuse, aging, or disease. If combined with biochemical and histological techniques, this preparation can provide a comprehensive and externally valid model for studying adaptive and/or pathophysiological processes in muscle, tendon, or bone that can broaden the scope of musculoskeletal research.

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Figure Legends

Figure 1. Key components of the front panel of the operant test chamber as seen by the rat (A) and the weight-lifting apparatus as seen behind the front panel (B): 1) food-pellet trough, 2) nose-poke response device with LED lamp, 3) opening to vertical tube, 4) vertical tube, 5) ring assembly, 6) linear bearings supported by vertical shafts, 7) weight and counterweight, 8) weight pans, 9) nose-poke response device, LED lamp, and clicker, 10) force plate, 11) displacement transducer, and 12) food-pellet dispenser.

Figure 2. Examples of a full and partial lift as defined by the minimum displacement above 0.1 cm from the lowest resting position of the ring assembly and whether a nose-poke response occurred near the maximum displacement possible at 5 cm. The response on the left represents a full lift composed of two concentric movements (A and C) and two eccentric movements (B and D). The response on the right represents a partial lift with one concentric movement (E) and one eccentric movement (F) and no nose-poke response. Both full and partial lifts often were comprised of more than one pair of concentric and eccentric movements. Parameters of peak force, velocity, work, and power were calculated for each concentric and eccentric movement performed irrespective of their participation in a full or partial lift (see text for details).

Figure 3. Number of full and partial lifts and number of concentric movements recorded for the 70-g and 700-g groups across successive posttraining sessions. Group medians and interquartile ranges are shown.

Figure 4. Boxplots showing the variability of the median of the number of concentric and eccentric movements recorded across the last 6 sessions for the 70-g and 700-g groups. Each box depicts the median and lower and upper quartile. Error bars depict the range, excluding the outliers that are depicted by solid circles. Shaded portions of the boxes depict the 95% confidence intervals. a = significantly different from 700-g group, $p < .05$.

Figure 5. Boxplots showing the variability of the median of the peak force, velocity, work, and power of concentric and eccentric movements recorded across the last 6 sessions for the 70-g and 700-g groups. All other details as in Figure 4. *a* = significantly different from eccentric movements; *b* = significantly different from the 70-g group; *c* = significantly different from concentric movements.

Figure 6. Mean muscle wet mass, normalized for each rat as mg/g body mass for the plantar flexors (sum of soleus, plantaris, and gastrocnemius) and dorsi flexors (sum of tibialis anterior and extensor digitorum longus) for a group of exercised rats and age-matched cage controls. Muscles for the exercised group were weighed after an 8-week-period during which each rat performed 80 full lifting and lowering movements with a 700-g load in sessions conducted 5 days per week. Error bars depict standard errors. Asterisks depict significant differences between exercised and cage controls, $p < .05$.

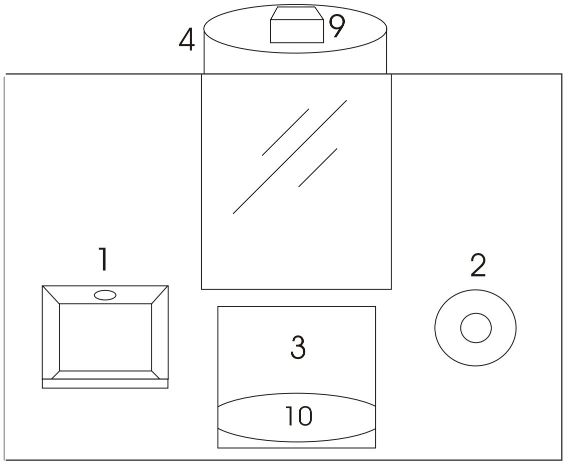
Table 1. Stages of training and testing and the mean number of sessions (and range) in each stage of training and posttraining for the 70-g and 700-g groups.

		Loading Condition	
Stages	Displacement Required?	70-g (n=16)	700-g (n=15)
Training sessions			
Magazine	No	1.1 (1-2)	1.0 (1-1)
Nose poke	No	1.8 (1-4)	2.1 (1-4)
Standing	No	8.6 (2-22)	7.1 (1-17)
Lifting	Yes (Partial)	4.0 (2-15)	3.6 (1-9)
Total training		15.4 (7-30)	11.9 (6-21)
Posttraining sessions	Yes (Full)	26.6 (14-36)	28.3 (22-37)

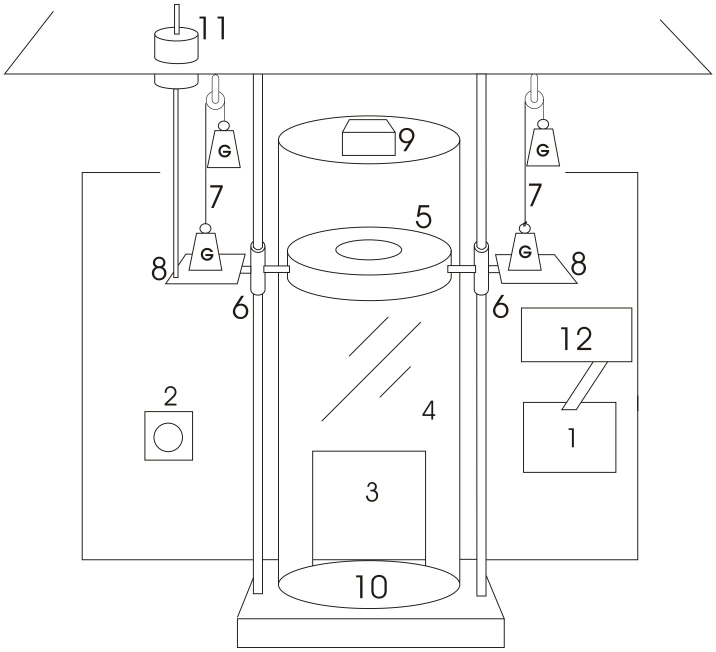
Table 2. Correlations between the biomechanics of the lifting and lowering movements and the number of movements recorded during the last six sessions for the 70-g and 700-g groups.

		Concentric Movements		Eccentric Movements	
Load	Parameter	Pearson's R	Significance	Pearson's R	Significance
70 g					
	Peak Force	-0.218	.418	0.333	.208
	Velocity	-0.541	.031*	0.536	.032*
	Work	-0.543	.030*	0.505	.046*
	Power	-0.521	.039*	0.472	.065
700 g					
	Peak Force	0.278	.316	0.134	.633
	Velocity	0.061	.828	0.040	.888
	Work	-0.025	.930	-0.028	.650
	Power	0.161	.566	-0.014	.962

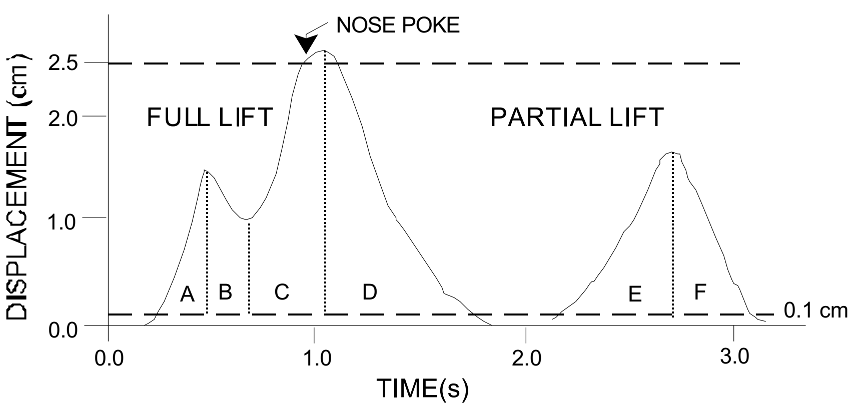
* Denotes $p < .05$.



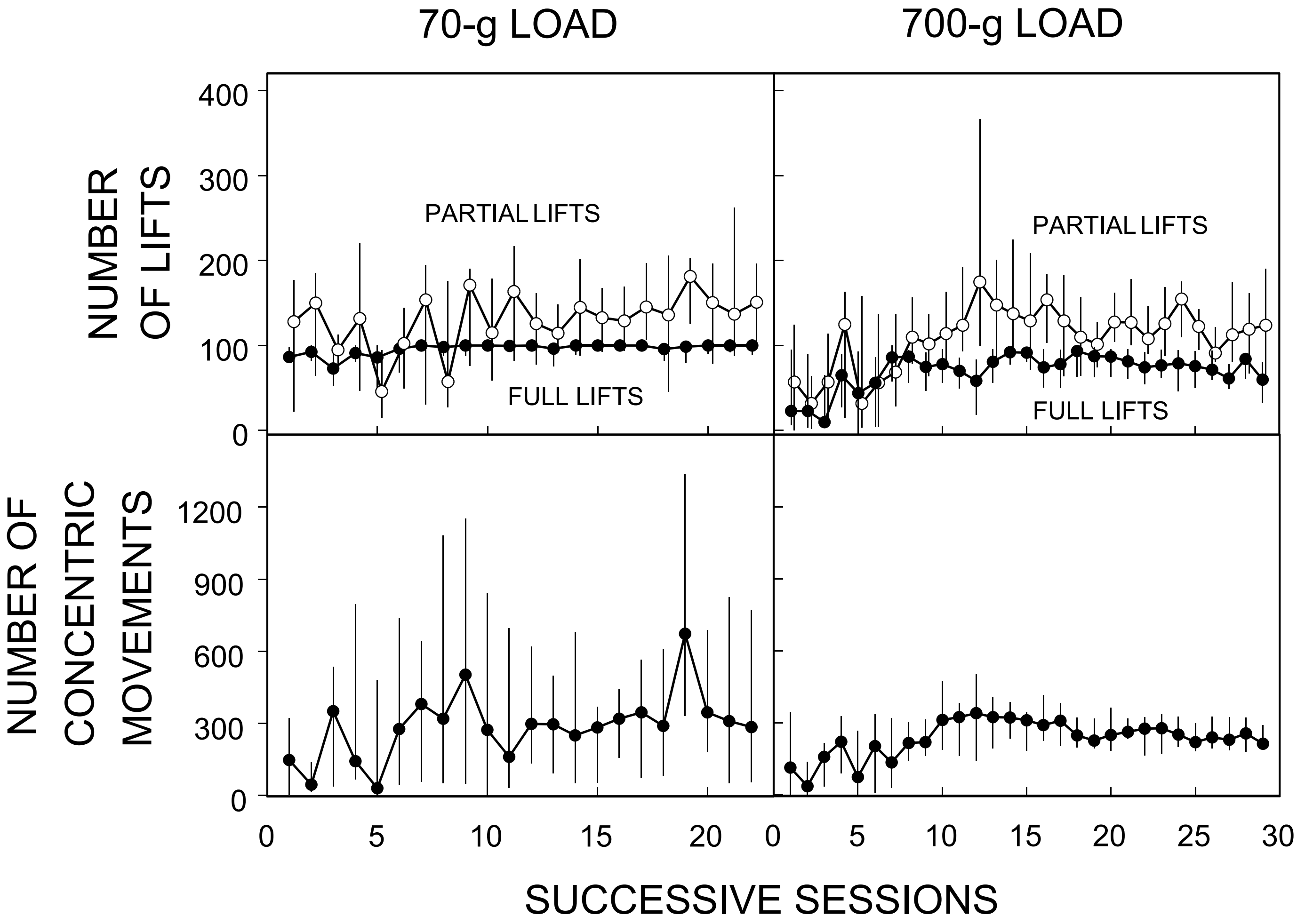
A

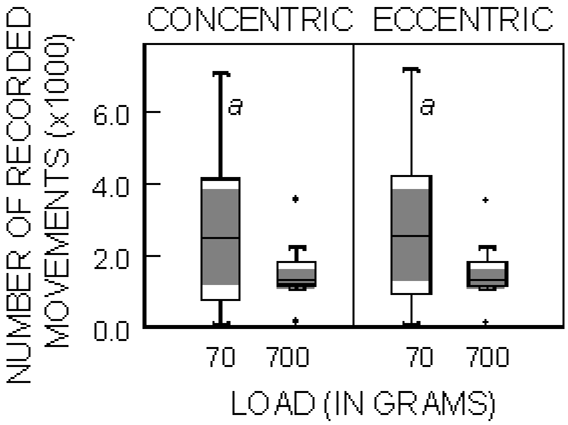


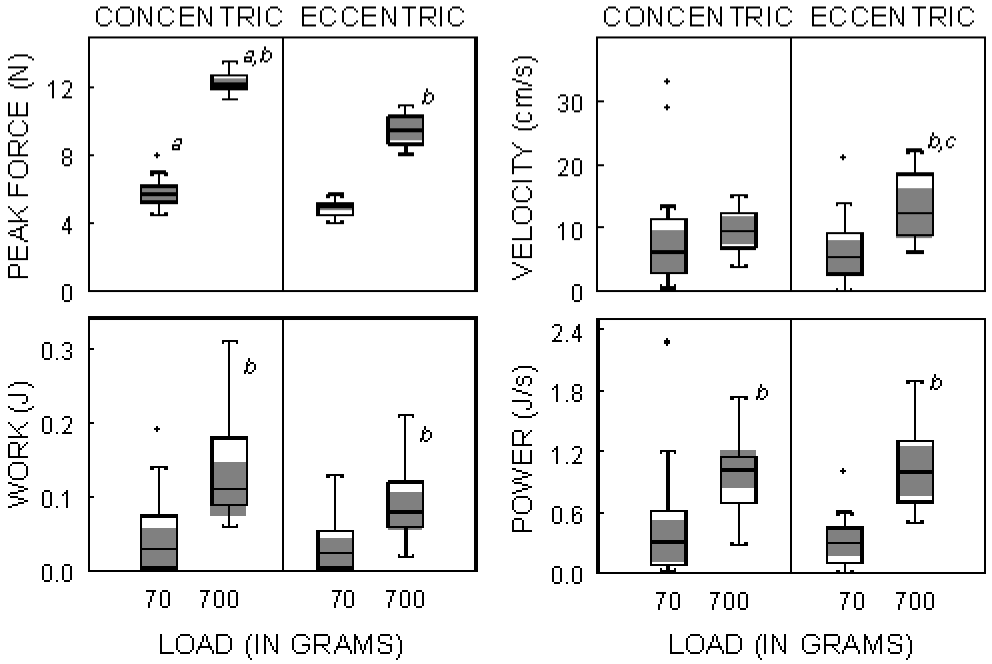
B

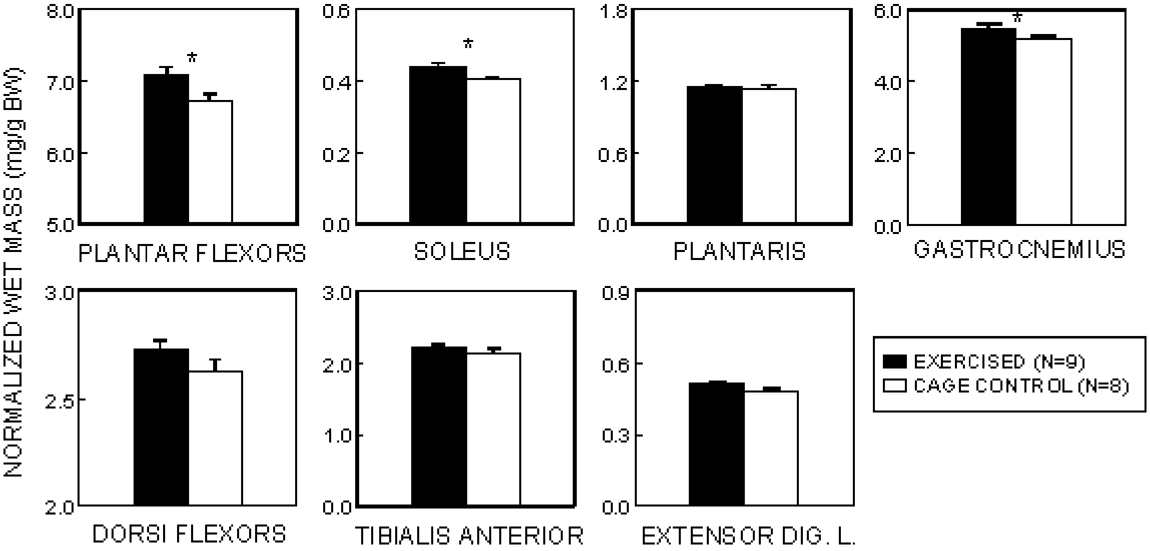


NOSE POKE
2.5
2.0
1.0
0.0
DISPLACEMENT (cm)
FULL LIFT
PARTIAL LIFT
A
B
C
D
E
F
0.1 cm
0.0
1.0
2.0
3.0
TIME(s)


70-g LOAD
700-g LOAD
NUMBER OF LIFTS
400
300
200
100
0
PARTIAL LIFTS
FULL LIFTS
PARTIAL LIFTS
FULL LIFTS
NUMBER OF CONCENTRIC MOVEMENTS
1200
900
600
300
0
0
5
10
15
20
0
5
10
15
20
25
30
SUCCESSIVE SESSIONS


CONCENTRIC
ECCENTRIC
NUMBER OF RECORDED MOVEMENTS (x1000)
6.0
4.0
2.0
0.0
a
a
70
700
70
700
LOAD (IN GRAMS)


CONCENTRIC
ECCENTRIC
PEAK FORCE (N)
0
4
8
12
a
a,b
b
CONCENTRIC
ECCENTRIC
VELOCITY (cm/s)
0
10
20
30
b,c
WORK (J)
0.0
0.1
0.2
0.3
b
b
POWER (J/s)
0.0
0.6
1.2
1.8
2.4
b
b
70
700
70
700
LOAD (IN GRAMS)
70
700
70
700
LOAD (IN GRAMS)


NORMALIZED WET MASS (mg/g BW)
8.0
7.0
6.0
5.0
*
PLANTAR FLEXORS
0.6
0.4
0.2
0.0
*
SOLEUS
1.8
1.2
0.6
0.0
PLANTARIS
6.0
4.0
2.0
0.0
*
GASTROCNEMIUS
3.0
2.5
2.0
DORSI FLEXORS
3.0
2.0
1.0
0.0
TIBIALIS ANTERIOR
0.9
0.6
0.3
0.0
EXTENSOR DIG. L.
■ EXERCISED (N=9)
□ CAGE CONTROL (N=8)