Anabolic steroids increase exercise tolerance

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Anabolic steroids increase exercise tolerance. Am J Physiol Endocrinol Metab 280: E973–E981, 2001.—The influence of an anabolic androgenic steroid (AAS) on thymidine and amino acid uptake in rat hindlimb skeletal muscles during 14 days after a single exhaustive bout of weight lifting was determined. Adult male rats were divided randomly into Control or Steroid groups. Nandrolone decanoate was administered to the Steroid group 1 wk before the exercise bout. [3H]thymidine and [14C]leucine labeling were used to determine the serial changes in cellular mitotic activity, amino acid uptake, and myosin synthesis. Serum creatine kinase (CK) activity, used as a measure of muscle damage, increased 30 and 60 min after exercise in both groups. The total amount of weight lifted was higher, whereas CK levels were lower in Steroid than in Control rats. [3H]thymidine uptake peaked 2 days after exercise in both groups and was 90% higher in Control than in Steroid rats, reflecting a higher level of muscle damage. [14C]leucine uptake was ~80% higher at rest and recovered 33% faster postexercise in Steroid than in Control rats. In a separate group of rats, the in situ isometric mechanical properties of the plantaris muscle were determined. The only significant difference was a higher fatigue resistance in the Steroid compared with the Control group. Combined, these results indicate that AAS treatment 1) ameliorates CK efflux and the uptake of [3H]thymidine and enhances the rate of protein synthesis during recovery after a bout of weight lifting, all being consistent with there being less muscle damage, and 2) enhances in vivo work capacity and the in situ fatigue resistance of a primary plantarflexor muscle.

anabolic androgenic steroid; nandrolone decanoate; serum creatine kinase; muscle fiber damage; mitotic activity

THE ADMINISTRATION OF ANABOLIC androgenic steroids (AAS) increases skeletal muscle mass (hypertrophy) and protein synthesis (9), and these responses are enhanced when AAS is given in combination with resistance exercise (11). Skeletal muscle fibers are multinucleated, and hypertrophy is accompanied by an increase in the number of myonuclei, thereby main-

the relatively constant myonuclear domain, i.e., myonuclei per cytoplasmic volume (6, 12, 14, 21). A primary source of new myonuclei appears to be from the activation, proliferation, and incorporation of satellite cells, in that inactivation of satellite cells via irradiation prevents hypertrophy in functionally overloaded muscles (19, 20). However, there are no reports examining the relationship between protein synthesis and mitotic activity in extensor and flexor muscles after AAS treatment with and without exercise. In addition, a “membrane stabilizing effect” of AAS agents that diminishes the rise in serum creatine kinase (CK) efflux after muscle damage has been suggested (22, 23). Resistance exercise, such as weight lifting, appropriately induces muscle hypertrophy and is commonly associated with muscle damage and increased levels of serum CK in humans (5, 15, 30).

Recently, we (24, 25, 26) have reported a morphological and biochemical myogenic response associated with muscle damage and regeneration in the plantarflexor muscles after a single exhaustive session of weight lifting in previously nontrained adult rats. The severity of weight lifting-induced muscle damage was associated with the level of increase in serum CK activity after the exercise bout (24, 25). In addition, we found [3H]thymidine and [14C]leucine labeling in vivo to be useful methods to detect the mitotic activity of proliferating cells and amino acid uptake in the muscles after the exercise session (24, 26). For example, after activation of satellite cells, other stem cells, and/or fibroblasts, thymidine uptake in the nuclei of these cells is essential for DNA duplication and cell proliferation, and amino acid uptake is necessary for the differentiation of these cells. Similarly, elevations in amino acid uptake and protein synthesis are necessary for increasing the cytoplasm in hypertrophying muscle fibers.

On the basis of these findings, our primary hypothesis was that AAS would enhance the uptake of both thymidine and amino acids and thus the adaptive potential selectively in plantarflexor muscles after a

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single bout of weight lifting. There also is evidence that AAS treatment may directly improve the endurance capacity of skeletal muscles. For example, improved submaximal running capacity of rats (28) and an improved fatigue resistance of rat skeletal muscles tested via electrical stimulation (7) have been reported after AAS treatment. Thus a second hypothesis was that AAS treatment may directly improve the endurance of rat skeletal muscles tested in vivo (25) and on the in situ mechanical properties of a primary plantarflexor, i.e., the plantaris muscle.

MATERIALS AND METHODS

Experimental groups. Specific pathogen- and virus anti-
gen-free Wistar male rats (14–20 wk old; 380–520 g body wt; n = 90) were divided randomly into two groups: a Control (n = 53) and an AAS-treated (Steroid, n = 37) group. One dose of nandrolone decanoate (dea-Durabolin; Organon, 3.75 mg/kg body wt) was administered intramuscularly in the gluteus medius muscle 1 wk before the single exercise session (see Exercise protocol). This drug is a long-acting steroid ester that is hydrolyzed slowly to give a constant tissue level of steroid for >4 wk. Exercised (see Exercise protocol) and nonexercised subgroups were studied, and the nonexercised subgroups were used to obtain resting values. In addition, a subsample (n = 7) of the rats from the Control group used in the testing of the mechanical properties of the plantaris muscle (see In situ contractile properties) were administered an oil vehicle intramuscularly at the same time as the AAS treatment. The animals were housed in standard cages and were provided food and water ad libitum. The room temperature was kept at 23 ± 1°C, and a 12:12-h light-dark cycle was maintained throughout the experiment. All experimental procedures were conducted in accordance with the Japanese Physiological Society Guide for the Care and Use of Laboratory Animals as approved by the Tokai University School of Medicine Committee on Animal Care and Use and followed the American Physiological Society Animal Care Guidelines.

Exercise protocol. The hindlimbs of all exercised rats were trained for one exhaustive session of weight lifting as described in detail elsewhere (24–26). This exercise was performed preferentially by the plantarflexors, with minimal usage of the dorsiflexors. The exercise session involved multiple sets of 10 repetitions (lifts) per set with ~1 min rest between each set. The first set of lifts was with a 500-g load. In the subsequent sets, an additional 500-g load was added until the rat could not complete 10 repetitions. The load then was adjusted in 100-g increments and/or decrements until the maximum load at which 10 repetitions could be completed, i.e., the 10-repetition maximum (10RM), was determined. The 10RM was repeated until the rat could not complete the set, and then the load was decreased by 500 g. This procedure was followed until the rat failed to complete three consecutive sets even when the weight was being reduced. The total time of the exercise bout was ~30–40 min in both groups. The 10RM (g), number of sets, and total amount of load lifted (number of lifts × load lifted by different groups in absolute values expressed as kg) were recorded. A subsample of rats (n = 6 randomly selected rats from each group) also was tested for maximum weight-lifting capacity (1RM in kg).

Measurement of serum creatine kinase activity. Blood samples (0.2 ml) were obtained from the caudal vein before and 30 and 60 min after the exercise session in both the Control (n = 46) and Steroid (n = 33) groups. Serum creatine kinase (CK) activity was measured using a standard kit (Monotest CK-NAC, Boehringer Mannheim, Mannheim, Germany) and was used to estimate exercise-induced muscle damage. The activities were expressed in international units (IU)/ml.

Analyses of mitotic activity and amino acid uptake. Our previous data indicate that in vivo [3H]thymidine and [14C]leucine labeling are useful methods to detect the mitotic activity of satellite (and/or other stem) cells and amino acid uptake in muscles after the exercise session (24, 26). Analyses of mitotic activity and muscle amino acid uptake were performed at rest and 3, 6, 12, and 18 h and 1, 2, 3, 4, 7, 10, and 14 days after exercise in Control (n = 53, 3–8/time point) and Steroid (n = 37, 3–6/time point) rats. [3H]thymidine ([methyl-3H]; 15.5 MBq/kg ip; specific activity 247.9 GBq/mmol, NEN Life Science Products, Boston, MA) and [14C]leucine ([U-14C]; 1.15 MBq/kg ip; specific activity 13.6 GBq/mmol, NEN Life Science Products) were injected 1 and 3 h before sampling to label proliferating cells or proteins that use leucine during protein synthesis, respectively. The rats were overdosed with pentobarbital sodium (60 mg/kg ip), and the following muscles were removed bilaterally: primary plantarflexors [soleus (Sol), plantaris (Plt), and gastrocnemius (Gas)] and primary dorsiflexors [tibialis anterior (TA) and extensor digitorum longus (EDL)]. After excess connective tissue and fat were removed, each muscle was wet weighed and homogenized in 0.02 M phosphate buffer (pH 7.4) at a 1:20 dilution at 4°C. Then, 1 ml of the homogenate from each muscle sample was added to 5 ml of 10% trichlo-roacetic acid (TCA) and mixed well. This mixture was centrifuged (2,050 g for 10 min), and the upper solution (TCA soluble) was removed. This procedure was repeated five times, and the remaining TCA-insoluble material was collected and dried in 70% ethanol. The dried material was treated overnight with 1 ml of dissolving solution (Solvable, Packard Instruments, Meriden, CT) at 45°C, and then a 10-ml liquid scintillation cocktail (Atomlight, Packard Instruments) was added to count radioactivity (Beckman LS4800, Fullerton, CA). The total protein concentration in each homogenate was measured, and the radioactivity of each sample was expressed in disintegrations per minute per milligram of protein.

We have reported previously (24, 26) that the uptake of thymidine and leucine into individual muscles within a rat and for individual muscle across rats varies widely, most likely reflecting varying levels of recruitment of each muscle during the weight-lifting task. However, in all cases, the pooled values for the plantarflexors (Sol, Plt, and Gas) had a higher amino acid uptake than the pooled values for the dorsiflexors (TA and EDL). Thus, to minimize the impact of the intra- and intermuscle variability on the effects of exercise on thymidine and leucine uptake, the difference in the uptake between the plantarflexor and dorsiflexor muscles in both legs of each rat is reported along with the absolute values.

Analysis of myosin synthesis. The determination of myosin synthesis was performed at the same time points and for the same groups as for the analysis of mitotic activity and amino acid uptake. Myosin was extracted with 0.6 M KCl solution (50 ml) from a 1-ml homogenate for 15 min at 4°C and filtered with three sheets of gauze. The myosin-extracted KCl solution was diluted with cool, distilled water (1:20), which resulted in the reappearance of myosin deposits. The diluted solution was passed through an omniflow nondissolving membrane filter (10-µm aperture and 47-mm diameter; Niton Millipore, Yonezawa, Japan). The membrane containing...
the deposits was dried, cut into several pieces, and soaked in a dissolving solution overnight at 45°C. The radioactivity was counted using the same procedures employed for the mitotic activity and protein synthesis analyses. Values were expressed in disintegrations per minute per milligram of protein.

**In situ contractile properties.** The in situ isometric mechanical properties of the Plt muscle were determined under urethane anesthesia (800 mg/kg ip) 1 wk after the single AAS or oil vehicle treatment. Twenty-seven rats (Control, n = 11; Vehicle, n = 7; Steroid, n = 9) were studied for this portion of the study. The body (rectal) temperature was maintained at \(36 \pm 1^\circ\text{C}\) using a heating pad, and atropine sulfate (0.05 mg/kg sc) was administered to avoid parasympathetic secretory hyperfunction. A tracheal tube was inserted. The jugular vein was cannulated, and warm Ringer's solution containing 5% glucose was administered intravenously, as necessary, i.e., based on changes in heart rate (monitored via electrocardiogram) and breathing rate and depth.

The rat was placed in a prone position on a custom-made operation table that allowed stabilization of the head and limbs with surgical tape. A mid sagittal incision was made extending from the popliteal area to the base of the calcaneus to expose the posterior aspect of the lower hindlimb. The right Plt muscle was exposed and freed from surrounding tissues, care being taken to avoid any interference with the normal blood and nerve supplies. The distal tendon of the Plt muscle was cut and attached to a transducer (TB-611T, Nihon Kohden). The surrounding skin was used to mine the relationship between \([3H]\)thymidine uptake and CK activity. Differences were considered statistically significant at \(P \leq 0.05\).

**RESULTS**

**Body and muscle mass.** The mean final body mass and mass of each muscle studied (TA, EDL, Sol, Plt, and Gas) were similar for the two groups (Table 1).

**Exercise capacity.** The weight-lifting performance during the single exercise session was significantly better in the Steroid than in the Control group (Table 2). The total amount of weight lifted, the total number of sets, 10RM, and number of complete sets at 10RM were 47, 12, 22, and 81% higher in the Steroid than in the Control group, respectively. In addition, there was no difference in the 1RM between the subsamples of rats tested in the Control and Steroid groups, i.e., 4.0 ± 0.3 and 4.1 ± 0.1 kg, respectively.

**Serum CK activity.** The mean preexercise serum CK levels were similar in the Steroid and Control groups (Fig. 1). These levels were increased significantly in

| Table 1. Mean body and muscle mass of Control and Steroid-treated rats |
|--------------------------|--------|--------|--------|--------|
|                         | Body Mass, g | Muscle Mass, mg |
|                         | TA      | EDL    | Sol    | Plt    | GAS    |
| Control (n = 53)        | 408 ± 11 | 778.4 ± 19 | 185.4 ± 5 | 202.9 ± 6 | 415.6 ± 10 | 2037.3 ± 48 |
| Steroid (n = 37)        | 412 ± 6  | 756.7 ± 17 | 180.5 ± 4 | 197.1 ± 5 | 416.3 ± 5  | 2047.1 ± 33 |

Values are means ± SE. TA, tibialis anterior; EDL, extensor digitorum longus; Sol, soleus; Plt, plantaris; Gas, gastrocnemius.
both groups 30 and 60 min after the exercise session. The postexercise values were significantly lower in the Steroid than in the Control group at both time points.

**Thymidine and amino acid uptake rates.** Compared with the Control group, both the plantarflexor (Sol, Plt, and Gas) and dorsiflexor (TA and EDL) musculature of the Steroid group had significantly lower uptakes of [3H]thymidine (−16% in the dorsiflexors and −26% in the plantarflexors) and higher uptakes of [14C]leucine (+64% in the dorsiflexors and +90% in the plantarflexors) in the resting state (Fig. 2, A and B). The mean uptake values of both amino acids also were significantly higher in the plantarflexors than in the dorsiflexors in both groups.

Compared with resting levels, the absolute [3H]thymidine uptake in the plantarflexors was significantly higher after 1–3 days in Control and after 2 days in Steroid rats (Fig. 3, A and B). In contrast, there were no significant changes in the dorsiflexor muscles of either group during the 2-wk postexercise period. A significant increase in [14C]leucine uptake was observed at 10 days after exercise in the plantarflexors of Control rats (Fig. 4A). No significant changes were observed in the dorsiflexors of the Control group or in either muscle group of the Steroid rats (Fig. 4, A and B).

Because there was no exercise effect on the overall mean uptakes of these thymidine and amino acids for the dorsiflexor muscles of either group, we then normalized the exercise effects of the plantarflexors to the dorsiflexor muscles (Fig. 5). In effect, this procedure minimized the intra-animal variability. The relative uptake of [3H]thymidine increased significantly 1–3 days after exercise and showed a peak at 2 days after

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**Table 2. Record of weight-lifting exercise**

<table>
<thead>
<tr>
<th></th>
<th>Body Mass, g</th>
<th>Total Weight Lifted, kg</th>
<th>Total Number of Sets</th>
<th>10RM, g</th>
<th>Number of Sets at 10RM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n = 46)</td>
<td>403 ± 12</td>
<td>427 ± 18</td>
<td>22.5 ± 0.4</td>
<td>2474 ± 59</td>
<td>4.3 ± 0.7</td>
</tr>
<tr>
<td>Steroid (n = 33)</td>
<td>411 ± 7</td>
<td>628 ± 16b</td>
<td>25.2 ± 0.4</td>
<td>3024 ± 42*</td>
<td>7.8 ± 0.9*</td>
</tr>
</tbody>
</table>

Values are means ± SE. 10RM, 10-repetition maximum. *Significant difference between Control and Steroid groups at P ≤ 0.05.
Exercise in both groups (Fig. 5A). The peak value at 2 days after exercise, however, was significantly lower in the Steroid than in the Control group. There was a tendency for the [14C]leucine uptake in the Control group to be elevated compared with rest values from 1 to 10 days after exercise, with significant peaks at 3 and 10 days postexercise (Fig. 5B). In the Steroid group, however, there was a tendency for the [14C]leucine uptake to be higher than rest values from 6 h to 3 days after exercise, with a significant peak at 1 day postexercise. Significant differences in the [14C]leucine uptake levels between the Control and Steroid groups were observed at rest, at 6 and 12 h, and at 1 and 10 days after exercise. Interestingly, the uptake levels of [14C]leucine at 3 h after exercise tended to be lower than rest levels in both groups \((P \leq 0.05)\) in the Steroid group.

Fraction of amino acid uptake for myosin. For the Control group, the uptake of [14C]leucine for the myosin fraction in the plantarflexor muscles was significantly elevated from rest values at 10 days after exercise, whereas the uptake rates were similar to rest values at all other recovery time points (Fig. 6). For the Steroid group, significant decreases were observed at 3, 6, and 12 h and at 3 days after the exercise bout. No other significant changes were observed throughout the 14-day postexercise period (Fig. 6). The levels of [14C]leucine uptake of the Steroid group, however, were significantly higher than Control values at rest, from 3 h to 2 days, and at 14 days after exercise.

In situ mechanical properties of the Plt muscle. Body and muscle mass, and all mechanical properties of the Plt muscle except for the fatigue index, were similar among the three groups (Table 3). The Plt in the Steroid group was more resistant to fatigue than in the other two groups. Note that there were no differences between Control and Vehicle groups.

**DISCUSSION**

**Ergogenic effects on the in vivo and in situ conditions.** The mean body and muscle weights were similar in the Control and Steroid groups (Table 1). These results
were expected, because the rats were maintained for only 1–3 wk after the single dose of AAS and were subjected to a single bout of exhaustive weight lifting 1 wk after AAS treatment.

In the present study, the rats were subjected to an exhaustive submaximal weight-lifting regimen, i.e., 10RM corresponding to 70–80% of the maximum capacity (1RM), and the Steroid group lifted 47% (P < 0.05) more total weight than the Control group. This large difference reflects a higher number of sets and a higher load at 10RM in the Steroid than in the Control group (Table 2). These data suggest the possibility of an improvement in the capacity of 1RM itself. However, there was no difference in the 1RM between the two groups. Thus AAS treatment improved repetitive lifting capacity at a relatively high load, a finding consistent with athletes using AAS being able to withstand an enhanced work volume (weight lifting) (11).

Suggested mechanisms for the ergogenic effects of AAS include the possibility that these agents 1) act through the central nervous system, allowing the subjects to train harder (2) or 2) may improve skeletal muscle function directly by increasing protein synthesis (8, 9, 17) or membrane stabilization (22, 23). We have made preliminary examinations of the effects of AAS on the level of various neurotransmitters of the central nervous system of these same rats (unpublished observations). The level of norepinephrine and its metabolite 4-hydroxy-3-methoxyphenylglycol appears to be higher in the hypothalamus of Steroid than of Control rats. Thus we are hypothesizing that this hyperadrenergic state may have resulted in an increased cardiac output, a reduced peripheral resistance, and an enhanced muscle blood flow, thus contributing to the enhanced endurance capacity observed in the AAS-treated rats.

This interpretation is consistent with the in situ isometric mechanical properties of the Plt muscle, a primary plantarflexor muscle. The maximum isometric twitch and tetanic forces and the conduction-transmission time of the nerve/muscle were unaffected by the AAS treatment (Table 3). These data suggest that the AAS treatment had little direct effect on the function of the neuromuscular unit, including the motoneuron, peripheral nerve, and muscle. However, the fatigue resistance as tested by continuous 12-Hz trains of impulses was enhanced significantly by the AAS treatment (Table 3). This enhanced muscle fatigue resistance in the Steroid group is consistent with the enhanced work capacity observed during the weight-lifting task. These results also are consistent with the reported improvement in the fatigue resistance of the rat EDL muscle to a continuous 4-Hz stimulation train after subcutaneous injection of 1 mg of nandrolone phenylpropionate on alternate days for 5–6 wk without a change in the mean fiber cross-sectional area (7). Furthermore, greater submaximal running endurance has been reported in AAS-treated rats (0.5 mg nandrolone phenylpropionate injection for 4 wk every other day), despite the observation that the training intensity and skeletal muscle oxidative capacities were similar in AAS- and saline-treated rats (28). These latter reports suggest that the increased muscle fa-
mitotic activity (uptake of \(^{3}\text{H}\)thymidine) in the exercised regions (24, 26). We also have reported that the model has been confirmed morphologically in histological sections (24, 26). Using the same weight-lifting model, we have shown that the degree of CK leakage is associated with the severity of damage in the exercised muscles (24). Figure 1 depicts the relationship between serum CK activity and uptake of \(^{3}\text{H}\)thymidine in the resting state. The uptake of \(^{3}\text{H}\)thymidine was lower and that of \(^{14}\text{C}\)leucine higher in the Steroid than in the Control group (24). A lower \(^{3}\text{H}\)thymidine uptake indicates reduced cell proliferation, i.e., DNA level, in the resting muscles, suggesting that AAS inhibits DNA replication in skeletal muscles. Increased leucine incorporation, an indicator of increased protein synthesis rates, into the muscles after the administration of AAS has been observed previously in humans (9) and rats (17). It also has been reported that AAS have a high affinity for glucocorticoid receptors and thus may counteract the catabolic effect of high circulating glucocorticoid concentrations resulting from training (3, 13, 18, 29). The present study does not provide direct evidence of the effects of AAS on muscle protein catabolism. However, because the final muscle weights of the Steroid group were similar to those of the Control group (Table 1), it seems reasonable to assume that the rate of muscle protein degradation must have increased in proportion to the increase in the rate of protein synthesis.

Serum CK activity and uptake of \(^{3}\text{H}\)thymidine. Serum CK activities were increased in both the Steroid and Control groups 30–60 min after the exercise bout (Fig. 1). Using the same weight-lifting model, we have shown that the degree of CK leakage is associated with the severity of damage in the exercised muscles (24). Weight lifting-induced muscle damage by use of this model has been confirmed morphologically in histological sections (24, 26). We also have reported that the intensity of weight lifting (amount of work), the degree of muscle damage, the serum CK activity, and the mitotic activity (uptake of \(^{3}\text{H}\)thymidine) in the exercised muscles are closely related events in this model (24, 25).

In the present study, the serum CK activities were lower in the Steroid than in the Control group 30–60 min after the exercise bout, whereas the total amount of weight lifted was higher in the Steroid group. Similarly, a diminished CK response in humans using AAS has been reported after a single bout of heavy-resistance exercise (4). Evidence suggests that AAS agents may have a membrane-stabilizing effect (22, 23) and that this may blunt the rise in serum CK efflux after muscle damage. In a similar manner, vitamin E also has the potential to stabilize muscle fiber membrane (16), and the vitamin E treatment of rats diminishes CK leakage from contraction-induced damage of the muscle (27). However, vitamin E treatment does not ameliorate the induction of muscle injury itself (27). In the present study, it is highly likely that muscle damage in the Steroid group, as reflected by the serum CK levels and \(^{3}\text{H}\)thymidine uptake rates, was minimized by AAS treatment.

After muscle damage, skeletal muscle fibers can regenerate, with the satellite cells playing a primary role (1, 10). Damage of parent fibers activates normally dormant satellite cells, which then begin to proliferate. Peak proliferation is observed ~48 h after muscle damage.

Table 3. Body mass, plantaris mass, and contractile properties

<table>
<thead>
<tr>
<th></th>
<th>Control ((n = 11))</th>
<th>Vehicle ((n = 7))</th>
<th>Steroid ((n = 9))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass, g</td>
<td>415 ± 14</td>
<td>400 ± 11</td>
<td>421 ± 15</td>
</tr>
<tr>
<td>Muscle mass, mg</td>
<td>445.8 ± 11.1</td>
<td>436.6 ± 11.5</td>
<td>448.3 ± 10.4</td>
</tr>
<tr>
<td>Maximum twitch tension, N</td>
<td>0.74 ± 0.03</td>
<td>0.75 ± 0.04</td>
<td>0.72 ± 0.02</td>
</tr>
<tr>
<td>Maximum tetanic tension, N</td>
<td>2.86 ± 0.08</td>
<td>2.8 ± 0.07</td>
<td>2.86 ± 0.09</td>
</tr>
<tr>
<td>Relative twitch tension, N/g</td>
<td>1.66 ± 0.06</td>
<td>1.71 ± 0.07</td>
<td>1.62 ± 0.06</td>
</tr>
<tr>
<td>Relative tetanic tension, N/g</td>
<td>6.47 ± 0.24</td>
<td>6.65 ± 0.28</td>
<td>6.43 ± 0.22</td>
</tr>
<tr>
<td>Time-to-peak tension, ms</td>
<td>29.6 ± 0.7</td>
<td>29.2 ± 0.6</td>
<td>30.0 ± 0.9</td>
</tr>
<tr>
<td>Half relaxation time, ms</td>
<td>14.2 ± 0.7</td>
<td>13.9 ± 0.6</td>
<td>14.1 ± 0.8</td>
</tr>
<tr>
<td>Contraction time, ms</td>
<td>95.3 ± 2.0</td>
<td>94.3 ± 2.1</td>
<td>96.4 ± 1.9</td>
</tr>
<tr>
<td>Fatigue test, s</td>
<td>36 ± 16</td>
<td>32 ± 14</td>
<td>56 ± 11</td>
</tr>
<tr>
<td>Conduction-transmission time, ms</td>
<td>1.66 ± 0.03</td>
<td>1.65 ± 0.06</td>
<td>1.66 ± 0.05</td>
</tr>
</tbody>
</table>

Values are means ± SE. *Significantly different from Control and Vehicle groups at \(P < 0.05\).
age, at which time the satellite cells begin to fuse and form multinucleated myotubes to repair the damaged portions of the parent fibers (1, 10). Skeletal muscle fibers are long, multinucleated cells, and there is a relatively constant amount of cytoplasm supplied by each myonucleus, i.e., the myonuclear domain concept (12, 14). This concept suggests that, after muscle damage, satellite cells proliferate and provide additional myonuclei, thus reestablishing a normal myonuclear domain size. In turn, the mitotic activity (uptake of \[^{3}H\]thymidine) at 2 days after exercise has been associated with muscle damage. We observed a significantly lower peak uptake of \[^{3}H\]thymidine 2 days after exercise in the Steroid group (Fig. 5A), suggesting that AAS treatment diminished the level of muscle disruption in the Steroid group. This view is further supported by the following observation. A significant correlation between CK activity (the degree of muscle damage) 30–60 min after the exercise bout and the uptake of \[^{3}H\]thymidine (mitotic activity) 2 days after the exercise bout was evident in both groups (Fig. 7). However, for any \[^{3}H\]thymidine uptake rate, the serum CK values for the Steroid group were consistently lower than those of the Control group. Together, these data suggest that AAS diminished CK leakage and minimized muscle fiber damage after a single bout of exhaustive resistance exercise.

**Total and muscle protein synthesis.** The Control group showed a biphasic response in \[^{14}C\]leucine uptake, i.e., peaks at 3 and 10 days after the exercise bout (Fig. 5B). We recently reported that this first peak most likely reflects increased protein synthesis (hyper trophy) in the primary tissues (contractile proteins, connective tissue, revascularization, activation of satellite cells, etc.), whereas the second peak may reflect the synthesis of the contractile components of regenerated and/or de novo muscle fibers (hyperplasia) (24). In the Steroid group, in contrast, there was a tendency for an earlier increased uptake, i.e., at 6 h to 3 days after the exercise bout, with a single peak at 1 day after the exercise bout (Fig. 5B). Thus the increase in protein synthesis associated with the weight-lifting exercise bout occurred more rapidly and in a shorter time period in the AAS-treated than in the Control rats. However, it is also clear that the cell cycle of proliferating cells (including satellite cells) in the muscles of the Steroid group was not affected by AAS treatment, because the peak uptake of \[^{3}H\]thymidine was observed 2 days after exercise in both groups (Fig. 5A).

\[^{14}C\]leucine uptake for myosin in the plantarflexor muscles of the Steroid group (Fig. 6) was significantly lower at 3–12 h and 3 days after exercise than at rest, whereas the absolute total uptake levels were similar except for the level at 3 h (Fig. 4B). Moreover, the total uptake level of \[^{14}C\]leucine was significantly higher in the Steroid than in the Control group (Figs. 2B and 5B). Together, these data indicate that AAS treatment enhanced protein synthesis in the noncontractile (i.e., connective tissue and/or membrane proteins) in addition to the contractile components of the muscle.

In conclusion, the present data indicate that AAS treatment before a single bout of exhaustive weight-lifting exercise 1) enhances the total in vivo work capacity of the muscles, 2) reduces the CK leakage and the uptake of \[^{3}H\]thymidine of the muscle fibers, consistent with there being less muscle fiber damage induced by weight lifting, 3) enhances the fatigue resistance of a primary plantarflexor muscle, and 4) increases the protein synthesis of both the contractile and noncontractile components of the muscles. These results demonstrate an improved adaptability of the muscle to overload and an elevated threshold at which an unusual exercise intensity can initiate a “muscle damage syndrome.”

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