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Resistance training increases glucose uptake and transport in rat skeletal muscle

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ABSTRACT

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The aim of this investigation was to determine if resistance training exercise improved glucose uptake and transport in rodent skeletal muscle. Sprague-Dawley rats were assigned to one of the three groups: control (CON), resistance trained (RT) and aerobic exercise trained (AT). Resistance trained rats were placed in a rodent squat apparatus and performed three sets of 10 repetitions at 75% of their one repetition maximum 3 days week⁻¹ for 12 weeks. Aerobic exercise training consisted of running the rats 3 days week⁻¹ for 45 min over a 12-week period on a motor-driven treadmill (32 m min⁻¹, 15% grade). Following the training period, all animals were subjected to hind limb perfusion in the presence of 500 μ U mL⁻¹ insulin. Hind limb glucose uptake was similar in the RT (9.91 \pm 0.7 μ mol g⁻¹ h⁻¹) and AT (10.23 \pm 1.0 μ mol g⁻¹ h⁻¹) animals and significantly greater than control (CON) (6.40 \pm 0.6 μ mol g⁻¹ h⁻¹). Rates of 3-O-methyl-D-glucose transport in the RT animals were elevated in the muscles utilized for RT while in the AT animals rates of 3-O-methyl-Dglucose transport were increased in those muscles recruited for running. The increased rates of 3-Omethyl-p-glucose transport in the skeletal muscles of the resistance trained and aerobic exercise trained animals appeared to be, in part, because of an increased GLUT4 protein concentration. These findings suggest that both resistance or aerobic training exercise can improve insulin-stimulated skeletal muscle glucose uptake and transport, but the training adaptations are restricted to the muscles recruited for the exercise performance.

Keywords aerobic exercise training, citrate synthase, GLUT4, glycogen, hexokinase.

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Numerous investigations have reported that aerobic exercise training improves glucose intolerance and whole body insulin action (Ivy et al. 1999). These favourable improvements from chronic aerobic training primarily result from qualitative changes that occur in the skeletal muscle. One of the primary skeletal muscle adaptations that account for improvements in glucose metabolism in response to aerobic training is an increased glucose transporter (GLUT4) protein concentration. This training induced increase in GLUT4 protein concentration has been observed in skeletal muscle of normal and insulin resistant rats, young and middle-aged adults and individuals with non-insulin dependent diabetes mellitus (Ploug et al. 1990, Banks et al. 1992, Hughes et al. 1993, Dela et al. 1994, Phillips et al. 1996). This is particularly relevant as the skeletal muscle GLUT4 protein concentration is positively related to increased rates of insulin-stimulated glucose

transport (Banks *et al.* 1992, Brozinick *et al.* 1993, Brozinick *et al.* 1996) and increased rates of blood glucose clearance as assessed by either an oral glucose tolerance test (OGTT) (Houmard *et al.* 1991) or euglycaemic clamp (Houmard *et al.* 1991, Hardin *et al.* 1995).

In contrast to aerobic exercise training, very little information is available detailing the effects of chronic resistance training on skeletal muscle glucose metabolism. However, a body of literature exists that indicates resistance training programmes will improve whole body glucose metabolism, as assessed by either OGTT or euglycaemic clamps, in young (Miller *et al.* 1984, Craig *et al.* 1989, Szczypaczewska *et al.* 1989), middle-aged (Smutok *et al.* 1993, Smutok *et al.* 1989, Dunstan *et al.* 1998) and older adults (Craig *et al.* 1989, Miller *et al.* 1994, Ryan *et al.* 2001). Miller *et al.* (1984) and Szczypaczewska *et al.* (1989) have attributed improvements in the OGTT of young resistance

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trained subjects and body builders to an increased muscle mass. Skeletal muscle is the largest insulinsensitive tissue in the body and is primarily responsible for clearing glucose following an oral glucose challenge (Katz *et al.* 1983) or intravenous glucose load (Baron *et al.* 1998). Thus, quantitative changes in muscle following a resistance training programme appear to enhance whole body glucose metabolism by increasing the mass of insulin-sensitive tissue in the body. However, the possibility exists that a resistance training programme may also result in qualitative changes that will enhance skeletal muscle glucose metabolism.

Therefore, the aim of the present investigation was to determine if resistance-training exercise improves skeletal muscle glucose metabolism. Sprague–Dawley rats were subjected to 12 weeks of either resistance or aerobic exercise and the effects of training on insulinstimulated skeletal muscle glucose uptake and transport were evaluated using the hind limb perfusion technique. We found that both resistance and aerobic exercise training were capable of increasing insulin-stimulated hind limb glucose uptake, but the improvements in skeletal muscle glucose metabolism were exercise and fibre type specific.

MATERIALS AND METHODS

Animals

Twenty-three male Sprague–Dawley rats approximately 6 weeks of age were obtained from B & K Universal Inc. (Fremont, CA USA) and randomly divided among one of the three groups: (1) control (CON, n = 8), (2) resistance training (RT, n = 8), or (3) aerobic exercise training (AT, n = 7). The animals were housed three to a cage and provided standard laboratory chow and water *ad libitum* throughout the investigation. The animal room was maintained at 21 °C and had an artificial 12 : 12 h light–dark cycle.

Exercise training

Resistance trained animals performed three sets of 10 repetitions at 75% of one repetition maximum (1-RM) three times per week for 12 weeks in a squat apparatus modelled on a unit described by Tamaki *et al.* (1992). One repetition maximum was determined for each animal on a weekly basis. The squat training apparatus consisted of a 35-cm wooden arm fastened at one end allowing the axis of rotation to occur vertically. An acrylic holder moulded to the body shape of a rat was attached at a 65° angle to the opposite end of the wooden movement arm. Animals were strapped into a nylon vest and attached to the acrylic holder with velcro straps.

The animals were placed in a standing position using a safety stopper to support the load. A metal peg that was fixed through the wood arm 12 cm from the holder was used to load the movement arm with calibrated miniature weight plates. The safety stopper was removed from beneath the movement arm and to initiate squats a brief electrical stimulus (10 V, 0.3 s duration) was delivered by manually depressing a switch that allowed current to flow to an electrode attached to the tail. After each squat the animals were repositioned on the apparatus such that their legs were beneath the torso. A repetition was initiated by manual electrical stimulation every 15 s and repeated until 10 repetitions were completed. The animals were allowed to rest for 2 min between each set and remained attached to the apparatus in a standing position during the rest period with the safety stopper placed beneath the movement arm to support the load.

Aerobic exercise training consisted of having the rats run on a motor-driven treadmill (Quinton Instruments, Seattle, WA, USA) up a 15% grade, 3 days week⁻¹ for 12 weeks. The speed and duration of the treadmill running were rapidly increased over the first 4 weeks until the rats were running continuously for 45 min at 32 m min⁻¹. This exercise intensity was maintained for the remainder of the training period. The intensity, duration and frequency were selected to provide an adequate training stimulus (Dudley *et al.* 1982, Yaspelkis *et al.* 1999) and to subject the AT and RT animals to a similar number of exercise sessions.

All experimental procedures were approved by the Institutional Animal Care and Use Committee at California State University Northridge (Northridge, CA, USA) and conformed to the guidelines for use of laboratory animals published by the Department of Health and Human Resources, United States of America.

Hind limb perfusions

At the end of the 12-week training period and 36–40 h after the last exercise bout, animals were anaesthetized with an intraperitoneal injection of pentobarbital sodium (6.5 mg 100 g body wt⁻¹) and surgically prepared for hind limb perfusion as described previously by Ruderman *et al.* (1971) and modified by Ivy *et al.* (1989). After the surgical preparation, the soleus (Sol), plantaris (Plant), red (RG) and white (WG) gastrocnemius and red (RQ) and white (WQ) quadricep were excised from the left leg, clamp frozen in liquid nitrogen and stored at -80 °C until analysis. Total GLUT4 protein concentration and enzymatic activity were assessed in the Sol, Plant, RG, WG, RQ and WQ. Muscle glycogen content was assessed in the RQ and WQ.

The right iliac artery was catheterized to the tip of the femoral artery to limit perfusate flow to the right hind limb. Catheterization of the lower abdominal vena cava to the tip of the iliac vein permitted the collection of effluent perfusate. Immediately after catheterization of the vessels, rats were sacrificed via an intracardiac injection of pentobarbital as the hind limbs were washed out with 10 mL of Krebs-Heinseleit buffer (KHB). The catheters were then placed in line with a non-recirculating perfusion system and the hind limb was allowed to stabilize during a 5-min washout period. The perfusate was continuously gassed with a mixture of 95% O₂-5% CO₂ and warmed to 37 °C. Perfusate flow rate was set at 5 mL min⁻¹ during the 5-min stabilization and the subsequent perfusion, during which the rates of muscle glucose uptake and glucose transport were determined.

Perfusions were carried out in the presence of 500 μ U mL⁻¹ insulin for all experimental groups. The basic perfusate medium consisted of 30% washed timeexpired human erythrocytes (HemaCare Corp., Van Nuys, CA, USA), KHB (pH 7.4), 4% dialysed bovine serum albumin (Fraction V; Catalog # BP1605-100, Fisher Scientific, Fair Lawn, NJ, USA) and 0.2 mM pyruvate. Over the first 20-min glucose uptake was measured across the hind limb using perfusate that contained 8 mM glucose. Subsequent to the determination of glucose uptake, the hind limb was washed out with glucose-free perfusate for 1 min in preparation for the measurement of glucose transport. Glucose transport was measured over an 8-min period using an 8-mM concentration of the non-metabolizable glucose analogue 3-O-methylglucose (3-MG) (32 μ Ci 3-[³H] MG mmol⁻¹) and 2 mM mannitol (60 μ Cid-[1-¹⁴C] mannitol mmol⁻¹). Rates of 3-MG transport have previously been found to be linear under these conditions (Sherman et al. 1988). Immediately at the end of the transport period the Sol, Plant, RG, WG, RQ and WQ were excised from the right leg, blotted on gauze dampened in cold KHB and clamp frozen in tongs cooled in liquid N2. The muscles were stored at -80 °C until analysed for rates of insulin-stimulated 3-MG transport.

Skeletal muscle glucose uptake

Glucose uptake was determined over a 20-min nonrecirculating perfusion by collecting arterial perfusate samples before perfusion and collecting the total venous effluent. Well-mixed aliquots of the arterial perfusate and venous effluent were analysed for glucose concentration by a glucose oxidase method on a model 2300 STAT Plus glucose analyzer (Yellow Springs Instruments, Yellow Springs, OH, USA). Muscle glucose uptake, expressed in micromoles per gram of muscle per hour, was calculated from the arteriovenous difference, the perfusate flow rate and the weight of the muscle perfused. The weight of the perfused muscle was determined by dissection of the rat hind limb (Sherman *et al.* 1988).

3-MG Transport

Muscle samples were weighed, homogenized in 1 mL of 10% trichloroacetic acid (TCA) at 4 °C with a Pyrex tissue grinder and centrifuged at 5254 g (Micro H microcentrifuge, Fisher Scientific, Pittsburgh, PA, USA) for 10 min. Duplicate 300 µL samples of the supernatant were transferred to 7 mL scintillation vials containing 6 mL of Bio-Safe II scintillation counting cocktail (Research Products International Corp., Mount Prospect, IL, USA) and vortexed. For determination of perfusate specific activity, 200 µL of the arterial perfusate was added to 800 μ L of 10% TCA and treated the same as the muscle homogenates. The samples were counted for radioactivity in a LS 1801 liquid scintillation spectrophotometer (Beckman Instruments, Fullerton, CA USA) set for simultaneous counting of ³H/¹⁴C. The accumulation of intracellular 3-[³H]MG, which is indicative of muscle glucose transport, was calculated by subtracting the concentration of 3-[³H]MG in the extracellular space from the total muscle 3-[³H]MG concentration. The 3-[³H]MG in the extracellular space was quantified by measuring the concentration of [¹⁴C]mannitol in the homogenate. Extracellular space of the muscles assessed was not different among groups (data not shown).

Skeletal muscle GLUT4 protein concentration

Total skeletal muscle GLUT4 glucose transporter content was determined by Western blotting as described previously (Yaspelkis et al. 2001). Briefly, portions of the freeze clamped muscles from the left hind limb were weighed frozen and then homogenized (PT 2100 Polytron homogenizer, Kinematica AG, Littau/Luzern, Switzerland) in Hepes-ethylenediaminetetraacetic acid (EDTA)-sucrose (HES) buffer (pH = 7.4). The protein concentration of the homogenate was determined by the Bradford (1976) method. A 100- μ L sample of the tissue homogenate was diluted 1:1 with Laemmli (1970) sample buffer. An aliquot of the diluted homogenate sample containing 75 μ g of protein was subjected to sodium dodecyl sulphatepolyacrylamide gel electrophoresis (SDS-PAGE) run under reducing conditions on a 12.5% resolving gel on a Mini-Protean II dual slab cell (Bio-Rad, Richmond, CA, USA). Resolved proteins were transferred to polyvinylidene difluoride (PVDF) sheets (Bio-Rad, Richmond, CA, USA) by the method of Towbin et al. (1979) using a Bio-Rad semidry transfer unit. The membranes were incubated with an affinity purified polyclonal GLUT4 antibody (donated by Dr Samuel W. Cushman, NIDDK, Bethesda, MD, USA) followed by incubation with Protein A conjugated HRP (Amersham Life Science, Arlington Heights, IL, USA). Antibody binding was visualized using enhanced chemiluminescence autoradiography in accordance with the manufacturer's instructions (Amersham Life Science). Bands were quantified by capturing images of the autoradiographs in a Macintosh G4 computer. The captured images of the autoradiographs were produced by an image scanner (ScanJet 4C, Hewlett Packard, Palo Alto, CA, USA) equipped with a transparency module. The captured images were digitized and imported into the public domain NIH image program (developed at the US National Institutes of Health and available on the Internet at http://rsb.info.nih.gov/nih-image/). The density of the labelled bands was calculated, corrected for background activity and expressed as a percentage of a standard (30 μ g of heart homogenate protein) run on each gel.

Enzymatic activity

Aliquots of muscle samples that were homogenized 1:20 in HES buffer were utilized for enzymatic analysis. Hexokinase, an enzyme required for glucose metabolism, was measured as described by Uyeda & Racker (1965). Citrate synthase, a marker of the tricarboxylic acid cycle, was measured spectrophotometrically (Srere 1969) after dilution of the initial homogenate 1:10 in 1 M Tris–HCl + 0.4% Triton X (pH 8.1).

Glycogen concentration

Muscle glycogen concentration was determined in the RQ and WQ using a modification of the Passonneau and Lauderdale procedure (Passonneau & Lauderdale 1974). Approximately 50 mg of muscle was dissolved in 1 mL of 1 N KOH at 70 °C for 30 min. One hundred microliters of the dissolved homogenate was removed and neutralized with 250 μ L of 0.3 M sodium acetate buffer (pH 4.8) and 10 μ L of 50% glacial acetic acid. The homogenate was then incubated for 2 h at 100 °C after the addition of 200 μ L of 2 N HCl. Following the incubation, the reaction mixture was neutralized with 2 N NaOH. Samples were then analysed by measuring glucosyl units by the Trinder reaction (Catalog #315–100, Sigma, St Louis, MO, USA).

Statistical analysis

A one-way analysis of variance (ANOVA) was used on all variables to determine whether significant differences existed between the CON, AT and RT groups. When a significant *F*-ratio was obtained, a Fisher's protected least significant difference post hoc test was employed to identify statistically significant differences (P < 0.05) among the mean values.

RESULTS

Body and muscle mass

The body mass of the CON $(237.9 \pm 4.3 \text{ g})$, AT $(233.7 \pm 3.5 \text{ g})$ and RT $(240.7 \pm 2.5 \text{ g})$ animals were similar at the onset of training (Fig. 1a). Although the body mass of all groups increased throughout the training period, the AT animals were significantly lighter than the CON animals at week 4 and maintained this reduced body mass for the remainder of the training period (Table 1). The AT animals were also significantly lighter than the RT animals at week 8. No differences in body mass existed between the CON and RT animals. Muscle masses were similar across groups (Table 1). The variability in the mass of the plantaris in



Figure 1 (a) Body mass of control (CON), aerobically trained (AT) and resistance trained (RT) rats during the training period. *, Significantly different from CON (P < 0.05); †, Significantly different from RT (P < 0.05). (b) Weight used zby the RT animals for one weekly repetition maximum (1-RM) and training (75% 1-RM). Resistance training required the RT animals to perform 3 sets \times 10 repetitions of squats three times per week. Values are mean \pm SE.

Tab	le	1	Final	body	and	muscle	e mass
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	$\begin{array}{l} \text{CON} \\ n = 8 \end{array}$	$\begin{array}{l} \mathrm{AT} \\ n = 7 \end{array}$	$\begin{array}{l} \text{RT} \\ n = 8 \end{array}$
Body mass (g)	487.0 ± 17.1	439.1 ± 8.6*	451.2 ± 12.7
Muscle mass Soleus (mg) Plantaris (mg) Total hind limb (g)	$\begin{array}{c} 191.8 \pm 8.8 \\ 437.0 \pm 20.3 \\ 24.63 \pm 0.9 \end{array}$	190.7 ± 8.3 417.5 ± 13.0 24.12 ± 1.0	171.5 ± 10.6 504.9 ± 66.1 25.40 ± 0.6

Values are mean \pm SE. CON, control; AT, aerobic trained; RT, resistance trained. Total hind limb muscle mass was the sum of all muscle dissected from the right hind limb. *, Significantly different from CON (P < 0.05).

the RT animals was likely because of the strategy employed to perform a squat. Some of the animals completed a squat by keeping their feet flat while others rose up on their toes.

Resistance training performance

The initial 1-RM of the RT animals averaged 528.1 \pm 4.2 g (Fig. 1b). Over the 12-week training period the 1-RM increased such that by the end of the training period the average 1-RM was 2626.9 \pm 188.7 g (~5.8× body mass). The RT animals trained using 75% of their 1-RM. During the first week of training the animals lifted 396.2 \pm 3.2 g and by the twelfth week were using a training weight of 1969.4 \pm 141.4 g (Fig. 1b). For comparative purposes, during the first week the animals were training with a weight that was ~1.6× body mass and by the final week they were training with a weight that was ~4.3× body mass.

We did not however, assess 1-RM of the CON animals at the twelfth week of the investigation and cannot exclude the possibility that the increased 1-RM of the RT animals was solely because of maturation. To address this concern, we obtained six additional male Sprague–Dawley rats that had a body mass (472.1 \pm 35.7 g) similar to the CON animals at the twelfth week of the investigation. These animals were familiarized with the squat training apparatus and their 1-RM was determined to be 1116.0 \pm 103.4 g or 2.4× body mass. As the 1-RM was significantly less than that of the RT animals, it suggests that the increased 1-RM of the RT animals resulted from the resistance training.

Skeletal muscle glucose uptake

The rates of insulin-stimulated skeletal muscle glucose uptake were increased by $\sim 60\%$ and $\sim 55\%$ in the AT and RT animals, respectively, when compared with the CON group (Fig. 2). In contrast, rates of insulin-stimulated glucose uptake were not different between the AT and RT animals.



Figure 2 Glucose uptake in hind limbs of control (CON), aerobically trained (AT) and resistance trained (RT) rats during perfusion with 8 mM glucose and 500 μ U mL⁻¹ insulin. Values are mean ± SE. *, Significantly different from CON (P < 0.05).

3-MG transport

Rates of glucose transport were determined in the Sol, Plant, RG, WG, RQ and WQ under insulin-stimulated conditions using the glucose analogue 3-MG (Fig. 3). The 3-MG is carried by the glucose transporter but is not phosphorylated, which results in its intracellular accumulation representing the glucose transport process independent of intracellular disposal. Rates of 3-MG transport in the Sol, Plant and RG of the AT animals were significantly greater than the CON and RT animals. The 3-MG transport in the WG of the AT and RT animals was greater than that of the CON animals. No differences in 3-MG transport rates were found in WG and RQ between the AT and RT animals. While 3-MG transport rates in the RQ of the RT group



Figure 3 The 3-O-methylglucose (3-MG) transport in the presence of 500 μ U mL⁻¹ insulin in hind limb muscles of control (CON), aerobically trained (AT), and resistance trained (RT) rats. Sol, soleus; Plant, plantaris; RG, red gastrocnemius; WG, white gastrocnemius; RQ, red quadricep; WQ, white quadricep. Values are means \pm SE. *, Significantly different from CON (P < 0.05); †, Significantly different from RT (P < 0.05).

were not different from the CON animals, there was a trend for it to be increased in the RT animals (P = 0.10). 3-MG transport in the WQ was similar between the CON and AT animals. However, the RT animals exhibited rates of 3-MG transport in the WQ that were significantly greater than both the CON and AT groups.

GLUT4 protein concentration

The AT animals had a significantly greater GLUT4 protein concentration in all muscles evaluated compared with CON animals (Fig. 4). In addition, the GLUT4 protein concentration in the Sol, Plant and RG of the AT animals were greater than that of the RT group. The GLUT4 protein concentration in the WG, RQ and WQ of the RT animals was greater than the CON group, but was not different from the AT animals.

Citrate synthase and hexokinase activity

Citrate synthase activity was similar in all muscles evaluated from the CON and RT animals with the exception of the WQ (Fig. 5). The AT animals exhibited a greater citrate synthase activity in the Sol, Plant and RG compared with the CON group. The AT animals also had greater rates of activity in the Sol and Plant in comparison to the RT animals. No differences existed among groups in the WG and RQ.

Hexokinase activity was similar in all muscles of the CON and RT animals except for the WQ (Fig. 6). The AT animals had elevated hexokinase activity in the Sol, RG and RQ compared with both the CON and RT



Figure 4 The GLUT4 protein concentration, expressed as a percentage of a heart standard, in skeletal muscles from rats that were divided among one of three groups: control (CON), aerobically trained (AT) and resistance trained (RT). Sol, soleus; Plant, plantaris; RG, red gastrocnemius; WG, white gastrocnemius; RQ, red quadricep; WQ, white quadricep. Representative autoradiographs for each muscle are presented above the bars. Values are mean \pm SE. *, Significantly different from CON (P < 0.05). †, Significantly different from RT (P < 0.05).



Figure 5 Citrate synthase activity in skeletal muscles from rats that were divided among one of three groups: control (CON), aerobically trained (AT) and resistance trained (RT). Sol, soleus; Plant, plantaris; RG, red gastrocnemius; WG, white gastrocnemius; RQ, red quadricep; WQ, white quadricep. Values are mean \pm SE. *, Significantly different from CON (P < 0.05); †, Significantly different from RT (P < 0.05).

groups. Hexokinase activity in the Plant and the WQ of the AT animals differed only from the CON animals. No differences in hexokinase activity existed in the WG among the groups.

Muscle glycogen

Following 12 weeks of training, muscle glycogen was elevated in the RQ of both the AT and RT animals when compared with the CON group (Table 2). In contrast, resistance training, but not aerobic training,



Figure 6 Hexokinase activity in skeletal muscles from rats that were divided among one of three groups: control (CON), aerobically trained (AT) and resistance trained (RT). Sol, soleus; Plant, plantaris; RG, red gastrocnemius; WG, white gastrocnemius; RQ, red quadrice; WQ, white quadricep. Values are mean \pm SE. *, Significantly different from CON (P < 0.05). †, Significantly different from RT (P < 0.05).

Table 2	Muscle	glycogen	concentration
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	$\begin{array}{l} \text{CON} \\ n = 8 \end{array}$	$\begin{array}{l} \mathrm{AT} \\ n = 7 \end{array}$	$\begin{array}{l} \mathrm{RT} \\ n = 8 \end{array}$
Glycogen, glucosyl (μ mol g wet wt ⁻¹)	units		
RQ	35.12 ± 3.4	48.11* ± 2.5	$51.80 \pm 2.9^*$
WQ	43.99 ± 4.2	52.08 ± 3.48	61.05 ± 4.3*

Values are mean \pm SE. CON, control; AT, aerobic trained; RT, resistance trained. RQ, red quadricep; WQ, white quadricep. *, Significantly different from CON (P < 0.05).

resulted in WQ glycogen levels increasing above that of the CON animals.

DISCUSSION

While aerobic exercise training has traditionally been prescribed as the ideal mode of exercise to improve whole body and skeletal muscle glucose metabolism, it appears that resistance training may also be an effective mode of training. A number of studies have found resistance training programmes to improve whole body glucose tolerance in human subjects of various ages and genders (Miller et al. 1984, Craig et al. 1989, Szczypaczewska et al. 1989, Smutok et al. 1993, Miller et al. 1994, Smutok et al. 1994, Dunstan et al. 1998, Ryan et al. 2001). It has been suggested that the improvements in whole body glucose tolerance are a result of the increased lean body mass serving to enhance the glucose disposal area of the body. However, it is plausible that resistance training programmes may also facilitate qualitative changes in skeletal muscle that contribute to the improvements in glucose metabolism. In the present investigation we chose to investigate resistance training using a rodent model that enabled us to evaluate the training effects on skeletal muscle glucose uptake and transport across the different muscle fibre types. Furthermore, by including an AT group we envisioned that it might be possible to characterize the training specific adaptations on skeletal muscle glucose metabolism that occur in response to either resistance or aerobic exercise.

Our first line of enquiry was to determine if a resistance training programme increased insulin-stimulated skeletal muscle glucose uptake. When compared with the CON animals, we found that hind limb glucose uptake was increased in the RT animals. While we had hypothesized that resistance training would increase hind limb glucose uptake compared with CON animals, we expected the improvement on glucose uptake to be less than what would occur with aerobic training. However, an unexpected, but most intriguing finding was that the resistance and aerobic training programmes were equally effective on increasing rates of insulin-stimulated hind limb glucose uptake. Of interest, Fluckey et al. (1999) have reported that resistance training reduces insulin-stimulated glucose uptake in rodent skeletal muscle. However, these contrasting findings are likely a result of methodological differences between investigations. Fluckey et al. (1999) evaluated skeletal muscle glucose metabolism after subjecting rodents to four bouts of resistance training (2 sets \times 50 repetitions per training session) over an 8-day period. In the present investigation skeletal muscle glucose metabolism was evaluated following 12 weeks of resistance training during which animals trained 3 days week⁻¹ and performed three sets of 10 repetitions. Fluckey et al. (1999) speculated that their results may reflect the adaptations that occur at the onset of a resistance training programme and that reductions in insulin-stimulated glucose uptake may dissipate with additional training, which appear to be supported by our observations.

Previous investigations that have evaluated the effects of aerobic exercise training on hind limb glucose uptake have typically used training programs of greater duration (1-2 h) and frequency $(5-6 \text{ days week}^{-1})$ (Ivy et al. 1983, Cortez et al. 1991, Etgen et al. 1993). Thus it is possible that the rates of insulin-stimulated glucose uptake were similar in the RT and AT animals due to the AT animals having been exercised for only 45 min three times per week. Our observation that the AT animals had rates of insulin-stimulated (500 μ U mL⁻¹) hind limb glucose uptake that were 60% above CON is in agreement with that of Cortez et al. (1991). These investigators reported that rates of insulin-stimulated $(500 \ \mu \text{U mL}^{-1})$ hind limb glucose uptake were increased by 63% in obese Zucker rats that were aerobically trained for 2 h day⁻¹, 5 days week⁻¹ for 6-8 weeks. While not an aim of the present investigation, our finding that 45 min of aerobic exercise performed only three times per week for 12 weeks increased hind limb glucose uptake similar to other training protocols of greater frequency and duration raises a provocative question relative to the weekly volume of aerobic exercise necessary to improve skeletal muscle glucose uptake in a rodent model.

To more fully evaluate the training effects in specific muscle fibres, we assessed rates of insulin-stimulated 3-MG transport. Improvements in 3-MG transport are fibre type specific in response to aerobic training and occur only in those muscles that are recruited to perform the exercise training (Cortez *et al.* 1991, Banks *et al.* 1992). In light of these previous findings, we had hypothesized that the two forms of exercise training would increase insulin-stimulated 3-MG transport when compared with the CON animals, but in an exercise and fibre type specific manner. Consistent with this premise, we found rates of 3-MG transport to be elevated in the Sol, Plant, RG and RQ of the AT animals, but not in the RT animals. In contrast, 3-MG transport was elevated in the WQ of the RT animals compared with both CON and AT animals and was similar in the WG and RQ of the AT and RT animals.

Rates of insulin-stimulated 3-MG transport are related to the total skeletal muscle GLUT4 protein concentration (Henriksen et al. 1990, Banks et al. 1992, Brozinick et al. 1993). Consequently, it was likely that if both aerobic and resistance training increased rates of 3-MG transport then it would be in part because of the total skeletal muscle GLUT4 protein concentration being elevated. In agreement with previous investigations (Banks et al. 1992, Rodnick et al. 1992, Etgen et al. 1993), we observed that aerobic training increased citrate synthase activity and GLUT4 protein concentration in the Sol, Plant, RG and RQ and that these alterations in oxidative capacity and GLUT4 concentration compared favourably with the improvements in 3-MG transport. In contrast, resistance training did not alter oxidative capacity or GLUT4 protein concentration in the Sol, Plant or RG and provides a basis for 3-MG transport rates not being increased in these muscles. While both aerobic and resistance training increased skeletal muscle GLUT4 protein concentration and 3-MG transport in the RQ and WG, this relationship was not consistent in the WQ. Despite the RT and AT animals exhibiting similar increases in GLUT4 protein concentration in the WQ, the RT animals had rates of 3-MG transport that were greater than that of the AT group. Why this difference existed between the RT and AT groups in the WQ is not readily apparent but may be related to the increased oxidative capacity in the muscle from the RT animals. However, the possibility exists that resistance training, in addition to increasing the GLUT4 protein concentration, may be improving other components of the glucose transport pathway (i.e. insulin signalling cascade, transporter translocation, intrinsic activity of the transporter) in a manner that is unique to this mode of training.

While the optimal programme design to induce muscle hypertrophy with resistance training in rodents has not been established, we based the sets and repetitions that the animals performed to more closely parallel the general recommendations for resistance training in humans. It is possible that this volume of resistance training exercise and the use of only one exercise (i.e. squat training) may not have been of a sufficient stimulus to significantly increase the mass of each hind limb muscle in this rodent model. Nevertheless, the resistance training programme appeared to positively affect the WQ, WG and RQ, as evidenced by increased rates of 3-MG transport and GLUT4 protein concentration. This finding suggests that RT does not necessarily need to induce significant increases in skeletal muscle mass to improve skeletal muscle glucose metabolism. While both aerobic and resistance training improved skeletal muscle glucose metabolism, the improvements were restricted to only those muscles that appeared to be recruited for performance of the specific mode of training. In light of the these findings, it is plausible to suggest that fibre type specific training improvements in skeletal muscle glucose metabolism are a direct result of increased contractile activity in those muscles recruited to perform the exercise, regardless of the mode of the activity.

In summary, we have shown that either resistance or aerobic exercise training can increase insulin-stimulated skeletal muscle glucose uptake. However, the improvements in hind limb glucose metabolism were exercise and fibre type dependent as glucose transport was increased in only those muscles that were recruited for the exercise performance. The improvements in skeletal muscle glucose transport appeared to be, in part, because of elevations in the skeletal muscle GLUT4 protein concentration regardless of the mode of exercise training. These results suggest that resistance exercise training can be effectively used as an exercise intervention to improve skeletal muscle glucose metabolism. Furthermore, as the resistance and aerobic training resulted in exercise specific skeletal muscle adaptations, it is possible that by incorporating both modes of training into a comprehensive exercise programme that skeletal muscle glucose metabolism might be improved to a greater extent than when these exercise modes are used independently.

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