KRISTIE ANNE SKINNER
Effect of Three Days of Acute Resistance Exercise on Insulin and Glucose Responses in Older Men and Women
(Under the direction of KIRK J. CURETON)

This study was designed to determine whether there was a cumulative effect on several days of acute resistance exercise performed in one week on glucose and insulin responses during an oral glucose tolerance test (OGTT) in 14 healthy older adults. Participants performed three sets of 10 repetitions at 75% of the 3RM maximum on eight resistance exercises on three nonconsecutive days in 1 week. Insulin and glucose responses to an OGTT were measured at baseline, 24 hours after 1 and 3 days of exercise, and 72 hours after the third bout of exercise. The 3 days of acute exercise had no significant effects on fasting glucose or insulin responses. There also were no significant differences in glucose or insulin responses during any of the OGTTs following the exercise sessions. In conclusion, three bouts of acute resistance exercise performed on nonconsecutive days in 1 week does not have a cumulative effect on insulin or glucose responses to a glucose challenge. These findings suggest that a greater exercise stimulus is needed to improve insulin sensitivity in older adults.

INDEX WORDS: Insulin sensitivity, insulin resistance, glucose tolerance, oral glucose tolerance tests, resistance training

EFFECT OF THREE DAYS OF ACUTE RESISTANCE EXERCISE ON INSULIN AND GLUCOSE RESPONSES IN OLDER MEN AND WOMEN

by

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B.S., Virginia Polytechnic Institute and State University, 1998

A Thesis Submitted to the Graduate Faculty

of The University of Georgia in Partial Fulfillment

of the Requirements for the Degree

MASTER OF ARTS

ATHENS, GEORGIA

2001

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August 2001

DEDICATION

I dedicate this work to my friends and family. Without their love and support this study would never have been completed.

ACKNOWELEDGEMENTS

I would like to thank everyone who helped with my study. Specifically, I thank Sigurbjorn Arngrimmson and Darby Stewart for helping whenever I asked and for answering my endless supply of questions, which was usually accompanied by a smile.

As for the Exercise Science Department at The University of Georgia, I express my great appreciation for your help in learning about this field and about myself. Also, I thank Dr. Harry Duval and Dr. Richard Lewis, as my committee members, for their advice and support for this project. I would also like to thank Dr. Kirk Cureton who has guided and taught me more about the research process than I ever expected to know.

Finally, I thank all of the subjects that participated. Each of them sacrificed time and a little discomfort to help me finish this project. You will never realize how indebted I am to each of you.

This project was supported by a seed grant from the University of Georgia.

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CHAPTER I

INTRODUCTION

With advancing age, the risk of developing insulin resistance, glucose intolerance, and non-insulin-dependent diabetes mellitus (NIDDM) increases. According to NHANES II, the prevalence of diabetes is 12.8% of individuals 55-64 years of age and 17.7% of individuals 65-74 years of age (Harris et al., 1987). NIDDM increases the risk of coronary heart disease, hypertension, stroke, intermittent claudication, and microvascular disease. Complications of microvascular disease, which are prevalent in NIDDM, include retinopathy, nephropathy, neuropathy, blindness and increased risk of infection. Therefore, NIDDM is a serious chronic disease that decreases the quality and length of life (Ivy, Zderic, and Fogt, 1999).

Although the etiology of NIDDM is unknown, physical inactivity and obesity are contributing factors. Positive energy balance, adipocyte hypertrophy and an effect of physical inactivity on insulin action in skeletal muscle lead to insulin resistance in skeletal muscle and adipose tissue. Development of insulin resistance precedes, and is the hallmark of, NIDDM. Physical activity and reduction in body weight (especially visceral fat) appear to be the best tools to prevent or reverse insulin resistance (Ivy, Zderic, and Fogt, 1999). The high incidence of insulin resistance, glucose intolerance, and NIDDM in the elderly maybe more related to lifestyle changes, namely decreasing physical activity and increasing body fatness, than to aging *per se*.

Aerobic and resistance exercise can reverse and improve insulin resistance (DeFronzo et al., 1987; Hughes et al., 1993; Kahn et al.,1990; Miller et al., 1994; Miller, Sherman, and Ivy, 1984; Mourier et al., 1997; Rice et al., 1999; Ryan et al., 1996; Segal et al., 1991; Smutok et al., 1993). Insulin sensitivity, as reflected by a reduced insulin response with the same or slightly lower glucose response to a glucose challenge, is improved following a single bout of exercise in NIDDM and young controls (Fluckey et al., 1994; Kraemer et al, 1997; Mikines et al., 1988; Mikines et al., 1989). Chronic exercise training further attenuates insulin and glucose responses, although the additional gains are often modest (King et al., 1988; Mikines et al., 1989). DeFronzo, Sherwin, and Kraemer (1987) reported that short-term training of 6 weeks had the same effects on blunting glucose and insulin responses to a glucose challenge as longer training studies. The benefits of exercise on insulin and glucose responses are lost when trained subjects become inactive for as little as 5-14 days (Heath et al., 1983; King et al., 1988; Mikines et al, 1989).

Fluckey et al. (1994) examined a single bout of resistance exercise in young control subjects, older NIDDM subjects, and older age-matched controls. NIDDM and young control groups had significantly lower insulin responses post-exercise, but the age-matched controls did not. Insulin secretion was not changed, but insulin clearance was increased through hepatic and/or peripheral mechanisms. Rice et al.(1999) found resistance and aerobic training had similar effects on insulin sensitivity in healthy, obese, middle-aged men.

Although glucose and insulin responses to acute and chronic resistance exercise have been studied, the time course of changes resulting from successive exercise sessions

is not known. It is possible that adaptations reported with weeks of training may occur rapidly due to cumulative, augmented responses to successive acute bouts of exercise, as has been reported for other measures such as blood triglycerides (Gyntelberg et al., 1977; Oscai et al, 1972). If the improvement in insulin sensitivity with one week of resistance training is greater than the response to a single bout of exercise, but equal to that obtained from training longer, this would mean that even limited periods (several days) of acute resistance exercise improve health and act as preventive measure against insulin resistance and NIDDM in older men and women.

Purpose

The purpose of this study is to examine the effects of three successive bouts of acute resistance exercise performed on different days in one week on blood glucose and insulin responses in older men and women.

Hypotheses

It is hypothesized that: 1) One resistance exercise bout decreases insulin, but has no effect on glucose responses to an oral glucose tolerance test (OGTT) 24-hours post-exercise. 2) Three acute resistance exercise sessions occurring on different days in one week decrease the insulin response to an OGTT 24-hours post-exercise more than a single resistance exercise bout. 3) At 72-hours post-exercise, insulin responses are less than at 24-hours post-exercise but significantly higher than baseline. 4) And, 24-hours and 72-hours post-exercise, there is no change in glucose tolerance compared to baseline.

Significance

Insulin resistance and NIDDM are serious chronic diseases in older adults. Resistance exercise has beneficial effects on preventing or reversing insulin resistance

and NIDDM (Borghouts and Keizer, 1999; Miller et al.). However, the nature of the exercise stimulus needed to produce beneficial effects is not well understood. This study will provide new information on the value of several days of exercise on glucose tolerance and insulin resistance in older men and women.

CHAPTER II

REVIEW OF THE RELATED LITERATURE

In this section, the following domains of literature relevant to the study are discussed. The chapter starts by reviewing the effect of aerobic exercise on insulin and glucose responses. Next, studies on the effect of detraining on insulin and glucose responses are examined. Finally, a review on the effect of resistance exercise on insulin and glucose responses are discussed.

Aerobic Exercise and Insulin/Glucose Responses

Acute Exercise. Acute aerobic exercise has been used to treat NIDDM and insulin resistance for years. Benefits from acute aerobic exercise on glucose and insulin responses are seen in untrained and trained participants, at high and low intensities, and at nearly any age (Bonen, Ball-Burnett, and Russel, 1998; Mikines et al., 1989; Mikines et al., 1988).

King et al. (1987) studied the effect of cycling on insulin and glucose responses in untrained and endurance trained subjects using an euglycemic clamp. The untrained group did not exercise before the clamp procedure. They found that fasting glucose and insulin levels were lower in the trained group compared to the untrained group. Insulin concentration during the clamp was not significantly different between the groups, but glucose uptake was higher in the trained group. They concluded that insulin sensitivity was improved in the trained group over the untrained group and glucose tolerance remained unchanged in both groups.

Mikines et al. (1988) examined the effect of 60 minutes of cycling (150 W) on the dose-response relationship between plasma insulin concentration and glucose uptake in seven untrained healthy young men. A hyperinsulinemic euglycemic clamp was administered after rest, immediately after exercise, 48 hours after exercise, and 5 days after exercise. Insulin-mediated glucose uptake increased immediately after and 48 hours post-exercise, but not 5 days post-exercise. Insulin concentrations were decreased after exercise. The authors suggested that the mechanisms for increased glucose disposal and increased insulin sensitivity are increased translocation of the GLUT-4 transporters initiated by muscle contraction and through the action of insulin. They concluded that moderate aerobic exercise increases insulin sensitivity by decreasing the amount of insulin needed to enhance glucose uptake.

Mikines et al.(1989) studied insulin sensitivity and responsiveness at rest and following 60 minutes of acute cycling (150 W) in seven untrained healthy men and seven endurance trained men. They used a hyperinsulinemic euglycemic clamp to measure insulin and glucose responses 15 hours post-exercise in the trained group, and 60 minutes post-exercise in the untrained group. There were no differences in fasting insulin concentration and insulin concentration during insulin infusion in trained and untrained subjects after exercise. However, basal glucose concentrations were lower in the trained group than in the untrained group, whereas glucose uptake was significantly higher in the trained group. The decreased insulin concentration during the infusion of the untrained subjects after exercise compared to at rest shows the immediate benefit of acute exercise on insulin responses in the general untrained population. Mikines et al. (1989) is the only study to examine glucose and insulin responses in untrained and trained subjects after

both groups perform an acute bout of exercise. The direct comparison between trained and untrained subjects strongly suggests the benefits of an acute bout of exercise. In conclusion, there was no reported difference between trained and untrained subjects in the improvement in insulin sensitivity, but there was increased insulin/tissue responsiveness in the trained group after an acute bout of exercise.

Kirwan et al. (1991) analyzed glucose and insulin responses after one bout of treadmill exercise to exhaustion in seven untrained young men. They found no difference in glucose disposal 12 hours after exercising to exhaustion. This finding contradicts Mikines et al. (1989), who found a significant change in glucose uptake after acute cycling exercise. Fasting glucose concentrations were not different between groups. However, they found that insulin responses were reduced after exercise compared to non-exercise groups. During the infusion of insulin, plasma insulin concentrations were significantly different immediately after exercise compared to rest. They concluded that untrained men increased insulin secretion during exhaustive treadmill running, but increased insulin clearance helped compensate decreased insulin sensitivity. This is the only study to show adverse effects of exercise on insulin sensitivity.

Cononie et al. (1994) examined the effect of 7 consecutive days of 50 minutes of endurance activity at 70% VO2 max on insulin and glucose responses in older adults. Nine men and women ranging in age from 61-82 years were given oral glucose challenges before the training began, after 1 day of endurance activity, and after 7 days of endurance activity to measure insulin and glucose responses. Fasting insulin was reduced 15% after 7 days of aerobic activity, whereas insulin responses during the glucose challenge were significantly reduced 20% after 7 days of exercise, but not after 1 day of

exercise. Glucose tolerance did not change at any point during the experiment. They concluded that fasting insulin and insulin responses can be reduced by repeated bouts of endurance exercise.

Bonen, Ball-Burnett, and Russel (1998) conducted a study on the effects of insulin and glucose responses to a single bout of low-intensity exercise (60% of age-adjusted heart rate) and a single bout of high-intensity exercise (83% of age-adjusted heart rate) on a cycle ergometer. They used 10 inactive middle-aged (40-48 years old) men and women as subjects. Insulin and glucose responses were measured by an OGTT immediately after exercise and 24 hours post-exercise. Fasting insulin concentration did not change after high- or low-intensity exercise, whereas insulin responses during an OGTT decreased after acute low-intensity exercise but not after high-intensity exercise. Glucose responses to an OGTT were reduced after high and low intensity exercise. No differences were found in fasting glucose concentrations after exercise. They concluded that high- and low-intensity aerobic exercise improve glucose tolerance and insulin sensitivity immediately after exercise, but the effects are more pronounced after 24-hours after exercise (Bonen, Ball-Burnett, and Russel, 1998).

In summary, insulin sensitivity, as reflected by reduced insulin and/or a reduced glucose response to a an OGTT, or as increased glucose uptake at a constant insulin concentration (euglycemic clamp), is improved following a single bout of exercise (Bonen, Ball-Burnett, and Russel, 1998; Mikines et al., 1988; Mikines et al., 1989; King et al., 1987). The exception to this conclusion is the study of Kirwin et al. (1991), who found no change in glucose uptake and a decrease in insulin sensitivity.

Endurance Training. Many studies have shown endurance training improves insulin sensitivity, but in most studies the effect of training has not been clearly separated from the persistent effects of acute exercise. Although, there are inconsistent results between studies, the literature suggests that as little as 6 weeks endurance training improves insulin sensitivity in lean, obese, and impaired glucose tolerant subjects (Defronzo, Sherwin, and Kraemer, 1987; Soman et al., 1979; Tonino et al., 1989; Kahn et al., 1990; Segal et al., 1991; Kirwan et al., 1993;Hughes et al., 1993; Hersey et al., 1994; Dengel et al., 1996; Kristiansen et al., 2000).

Soman et al. (1979) investigated the effect of cycling for 6 weeks on insulin sensitivity in six healthy untrained men. Each participant cycled for 1 hour, 4 days per week, for 6 weeks. They were the first to use the euglycemic insulin clamp to determine the effect of a hyperinsulinemic state on glucose metabolism after an exercise protocol. Insulin-mediated glucose uptake was increased by 30% after training. Also found was that training increases the binding of insulin to monocytes. This increase in binding was due to a 50% increase in the number of insulin receptors. However, the authors noted that a correlation between insulin sensitivity and insulin binding wasn't found. Therefore, other events occurring after the binding are contributing to the increase in insulin sensitivity after endurance training. In conclusion, the results of this study suggest that endurance training may be advantageous in the treatment of NIDDM because it increases insulin sensitivity.

Defronzo, Sherwin, and Kraemer (1987) studied insulin and glucose responses before and after 6 weeks of cycle ergometer exercise at 85% maximum heart rate in seven moderately obese women between the ages of 22-46 years. Thirty-nine men and

women served as control subjects. They initially found that obese participants were significantly more insulin resistant at baseline and continued to be so after training even though the percent decrease in fasting insulin levels was the similar to control participants. However, fasting glucose levels remained unchanged. During an OGTT there were no significant changes. However, during the hyperglycemic-euglycemic clamp, insulin responses decreased while glucose uptake increased and hepatic glucose production decreased. They concluded that cycling at a moderate intensity improved insulin sensitivity in moderately obese subjects.

Tonino (1989) examined the reversibility of insulin resistance through endurance training in 11 healthy 60- to 80-year old men. These men did not have impaired glucose tolerance, but had lower glucose uptake rates compared to younger subjects. Following 12 weeks of jogging or walking at 85% of their maximum heart rate, a hyperinsulinemic-euglycemic clamp and an OGTT was used to measure insulin and glucose responses 7 days post-exercise. Glucose uptake increased using the clamp, but insulin levels did not change. They found that fasting glucose and insulin levels did not change after training and neither did insulin or glucose responses during an OGTT. They concluded that insulin sensitivity improved following aerobic training.

Kahn et al. (1990) examined the effect of 6 months of aerobic training on insulin and glucose responses in 13 healthy older men. Using an OGTT 60 hours post-exercise, they reported a reduction in fasting insulin. They also found a significant decrease in plasma insulin responses in healthy older men, but no change in fasting glucose concentration. In conclusion, insulin sensitivity increased and glucose tolerance remained unchanged.

Segal et al. (1991) studied the effect of 12 weeks of cycle ergometer exercise on insulin and glucose responses in lean, obese, and NIDDM men. A hyperinsulinemic-euglycemic clamp and an OGTT were used 4-5 days post-exercise to measure glucose and insulin responses. NIDDM participants were found to be more insulin resistant than obese or lean participants at baseline as expected. They found that glucose uptake was lower before and after training in the obese than lean men, and that glucose uptake was lower in the NIDDM men than in the obese men. Insulin secretion decreased after training in all groups, but there was no change in plasma levels, suggesting decreased clearance after exercise. Hepatic glucose production was significantly reduced only in the NIDDM subjects. Plasma insulin and glucose responses to the clamp were not significantly changed. However, they used the euglycemic clamp 4-5 days post-exercise, which may have been too long to see any significant effects (Seals et al., 1991). This possibility is also supported by Mikines et al. (1988), who found no residual effects after 5 days post-exercise in either trained or untrained subjects. They concluded that there was no change in insulin sensitivity in lean, obese, or NIDDM men.

Kirwan et al. (1993) evaluated glucose-stimulated insulin response and glucose disposal rate after 9 months of endurance training in 12 older adults with normal glucose tolerance. The protocol consisted of 45 minutes of treadmill running at 80% of maximal heart rate. Sixteen hours after the final exercise bout, insulin levels were decreased during the hyperglycemic clamp while glucose disposal remained unchanged. The ratio between the glucose disposal rate and the plasma insulin concentration increased after exercise indicating an increase in insulin sensitivity. They also found a significant

decrease in insulin responses, but no change in glucose responses to an OGTT. They concluded, high-intensity aerobic training increases insulin sensitivity in older adults.

Hughes et al. (1993) studied the effect of 12 weeks of cycle ergometer exercise on glucose and insulin responses in older subjects with impaired glucose tolerance. They found that fasting glucose concentration decreased after training, whereas fasting insulin concentration showed no significant improvement in the impaired glucose tolerant subjects. When using a hyperinsulemic euglycemic clamp 96 hours post-exercise, they found glucose uptake increased at a high insulin concentration after training. These changes were hypothesized to be caused by the translocation of GLUT-4 transporters to the plasma membrane, which occurs following an acute exercise bout as well. However, the authors also noted that some other chronic adaptations that increase glucose uptake are increased, such as levels of the GLUT-4 protein in skeletal muscle, changes in oxidative and glycolytic enzyme activity, increased glycogen storage capability, and increased capillary density. They concluded that glucose tolerance and insulin sensitivity improved after training.

Hersey et al. (1994) examined the effect of endurance training and resistance training in improving insulin responses in healthy 70-79 year old men and women. Forty-two men and women participated in 6 months of training. The endurance group walked or jogged at 75-85% of heart rate reserve three times per week. The resistance training group did one set of 8-12 repetitions on 10 variable-resistance Nautilus machines. Glucose tolerance did not change in the control, endurance, or resistance training group. However, insulin responses improved by 16% in the endurance-trained group when compared to their own initial OGTT test. When insulin responses were compared

between the endurance group and the other two groups, there was only a significant difference at the 60-minute time point. The authors concluded that endurance training improves insulin responses after 6 months of training in healthy 70-79 year old adults, but resistance training does not.

Dengel et al. (1996) examined the effect of aerobic exercise alone, weight loss alone, aerobic exercise plus weight loss, and a control on glucose and insulin responses in 47 older obese sedentary men. The intervention lasted for 10 months. The aerobic activity consisted of 40 minutes of cycling or treadmill running at 75-85% of heart rate reserve three times per week. The weight loss intervention reduced caloric intake by 300-500 kcal/day and included a weekly visit with a registered dietitian to discuss eating behaviors. The weight-loss-alone and the aerobic/weight loss group had similar reductions in body weight and body fat, which were both significantly greater than the aerobic-exercise-alone or the control group. During an OGTT that was administered 24-36 hours post-exercise, insulin responses decreased in all groups except for the control. However, the decrease in the insulin response in the aerobic-plus-weight-loss group was significantly lower than the weight-loss-alone or the aerobic-alone groups. Glucose responses also decreased in the weight-loss-alone and aerobic/weight loss group, but not in the control or the aerobic-alone-group. Insulin-mediated glucose uptake was also significantly increased during a hyperinsulinemic euglycemic clamp in the aerobic-only and aerobic/weight loss groups compared to both the control and the weight loss alone groups. They concluded that aerobic activity and weight loss affect glucose metabolism through different mechanisms, and that both weight loss and aerobic activity are necessary to improve glucose tolerance and insulin sensitivity in older men.

Kristiansen et al. (2000) analyzed the effect of one-legged endurance training on glucose uptake in the trained and untrained leg muscles in a glycogen depleted state. During the 3 week intervention, eight healthy young males used a knee-extensor ergometer to train one leg. The final test consisted of two legged cycling followed by a non-carbohydrate meal to keep glycogen levels low. The next morning dynamic knee extensions were done simultaneously at 60, 80, and at 100% of maximal workload. Glucose uptake was almost equal at 60% of the maximal workload but significantly higher by 33% and 22% respectively, at 80% and 100% of maximal workload in the trained thigh muscle. They also found that GLUT-4 concentrations were increased in the trained leg muscle. They concluded that low glycogen levels at high work loads are conducive to increased glucose uptake in trained muscle compared to untrained muscle and that increased GLUT-4 concentrations in trained muscle may contribute to this improvement.

In summary, most endurance training studies show improvement in insulin sensitivity (Defronzo, Sherwin, and Kraemer, 1987; Soman et al., 1979; Tonino et al., 1989; Kahn et al., 1990; Kirwan et al., 1993;Hughes et al., 1993; Hersey et al., 1994; Dengel et al., 1996; Kristiansen et al., 2000), except for one study that showed no change in insulin responses (Segal et al., 1991). Since the greatest effects are seen 24-72 hours post-exercise whether with acute exercise or endurance training, Segal et al. (1991) may have seen different results if they had tested during this time frame instead of 4-5 days post-exercise. Studies that did test 48-72 hours post-exercise tended to show greater results than the studies that waited 3-7 days post-exercise (Segal et al., 1991; Tonino, 1989; Hughes et al., 1993).

Detraining

Two detraining studies have investigated insulin and glucose responses after endurance-trained athletes detrained for 10 days or 14 days (Heath et al., 1983; King et al., 1988). This short period of no exercise prevented a change in body composition even though insulin and glucose responses changed. Both studies found a decrease in insulin sensitivity (Heath et al., 1983; King et al., 1988), but only Heath et al. (1983) showed a decrease in glucose tolerance.

Heath et al. (1983) examined six men and two women that had been exercising vigorously for 5-7 days/wk for at least 6 months. The control group consisted of 18 sedentary men and women. Both groups were asked to remain inactive for 10 days. On the 11th day of inactivity, insulin and glucose measurements were taken during an OGTT. They found that the maximum rise in plasma insulin concentration during an OGTT was 100% higher following the inactivity period. They also found an increase in insulin resistance, because glucose concentrations increased 10-15%, despite the increase in plasma insulin concentration. Glucose tolerance was decreased as well. On the twelth day, subjects completed one bout of running, which King et al. (1988) did not do. They found glucose and insulin responses were returned to near initial levels. They concluded that a single bout of exercise is responsible for increases in insulin sensitivity and glucose responses because the inactivity period was too short to change VO2 max, or adiposity, or cause other training adaptations.

King et al. (1988) investigated the effect of detraining on insulin and glucose responses on 9 well-trained subjects and 12 sedentary controls. The inactivity period lasted 14 days. Physical inactivity increased insulin responses in the early and late phases

of the hyperglycemic clamp. There also was a 67% increase in insulin response to the same glucose infusion concentration. Whole-body glucose disposal did not change with inactivity, but insulin resistance increased as reflected by increases in insulin concentration. They concluded that the benefit of aerobic exercise on insulin and glucose responses is a relatively short-term effect.

Detraining studies have shown that a continuous exercise routine is needed to maintain the improvements in glucose and insulin responses since the beneficial effects are lost within 10-14 days of inactivity (Heath et al., 1983; King et al., 1988)

Resistance Exercise and Insulin/Glucose Responses

Acute resistance exercise. Two studies have investigated the effects of acute resistance exercise on insulin and glucose (Kraemer et al.,1997; Fluckey et al., 1994). The studies used very different approaches. Since skeletal muscle is the main site of glucose uptake, resistance exercise would be expected to have an effect like aerobic exercise on glucose and insulin responses.

Fluckey et al. (1994) examined the insulin and glucose responses evoked by one bout of resistance exercise in a young control group, an older NIDDM group, and an age-matched older group. They used seven resistance exercises and performed one set at 50%, 75%, and 100% of a 10 repetition maximum for 10 repetitions. An OGTT was given 18 hours post-exercise for the measurement of insulin and glucose responses. They found fasting glucose levels were unchanged after an acute bout of resistance exercise. They also found that acute resistance exercise reduced insulin responses during an OGTT and that total insulin responses decreased in healthy, younger men and older men with NIDDM, but not in an age-matched control. However, insulin secretion remained

unchanged, as did glucose responses to an OGTT. Insulin clearance also decreased after exercise in older males with NIDDM through hepatic and/or peripheral mechanisms. Nevertheless, insulin sensitivity increased as reflected by lower insulin concentration needed for the same glucose uptake. They concluded that insulin sensitivity increased in younger men and men with NIDDM, but not in the older age-matched controls.

Kraemer et al. (1997) compared the effects of an acute bout of heavy resistance exercise on insulin and glucose concentrations post-exercise in physically active younger and older men. The lifting protocol consisted of four sets of 10 repetitions of squats at 70% of a one repetition maximum. Insulin and glucose responses were measured immediately after, and 5, 15, and 30 minutes post-exercise. No OGTT or hyperglycemic clamp was given. They found that insulin clearance decreased immediately after exercise in healthy, older male adults. Active younger men had increased plasma glucose concentration post-exercise, but active older men did not. However, the older men had a higher glucose concentration at every time point. This finding maybe explained by the fact that glucose tolerance decreases with age unless the subject remains in the trained state (Seals et al., 1984). In conclusion, insulin and glucose responses at rest and post-exercise are significantly different in young and older men.

In summary Kraemer et al. (1997) did not use any type of glucose challenge, but simply performed blood draws immediately after exercise. Fluckey et al. (1994) used an OGTT, which is common for measuring insulin and glucose responses. The insulin and glucose responses differed between the studies most likely due to the lack of a glucose or insulin stimulus in Kraemer et al. (1997).

Resistance training. An abundance of studies have shown resistance training causes physiological changes such as increased muscle mass, decreased fat mass, and increased glycogen storage. These adaptations may improve insulin sensitivity in addition to the effect observed with an acute bout of exercise. In several resistance training studies, insulin sensitivity has increased independent of age, body fat, and weight loss (Rice et al., 1999; Ryan et al., 1996; Miller JP et al., 1994; Rice et al., 1999; Smutok et al, 1994; Smutok et al, 1993; Craig, Everhart, and Brown, 1989). However, a recent study does not show that healthy older adults increase insulin sensitivity after 6 months of resistance training (Ryan et al., 2001).

Miller, Sherman, and Ivy (1984) studied the effects of 10 weeks of resistance training on 10 healthy college males. The training protocol consisted of three sets of eight repetitions of 10 different resistance exercises. An OGTT was given 2 days post-exercise to determine glucose and insulin responses. Since an OGTT was given 48 hours post-exercise, the effects observed are primarily from the last exercise bout. Glucose tolerance was not affected, but insulin responses were significantly changed. Basal insulin concentrations decreased along with a decrease in insulin response to an OGTT. Many other studies have found similar results (Ryan et al., 1996; Miller JP et al., 1994; Rice et al., 1999; Smutok et al, 1993; Craig, Everhart, and Brown, 1989). Also found was a positive relationship between increased lean body mass and decreased insulin responses. Therefore, insulin sensitivity, as reflected by a decreased insulin response while maintaining normal glucose tolerance, is often increased after resistance training (Miller, Shermin, and Ivy, 1984).

Craig, Everhart, and Brown (1989) examined insulin and glucose responses in six young and nine elderly male subjects during 12 weeks of resistance training. An OGTT was given 3 days post-exercise to measure glucose and insulin responses. Baseline glucose values were higher in the older group compared to the younger group. However, the total glucose response to an OGTT was decreased after training, but the change was not significant for either group. During an OGTT, they found that both groups had decreased fasting insulin concentrations and insulin responses after training. However, the older group had higher baseline insulin levels and a 57% higher insulin response during an OGTT after training compared to the younger group. This suggests that glucose tolerance can be improved in older men. However, aging, which is associated with decreased insulin responsiveness of tissue, may prevent older sedentary men from reaching the levels of insulin responsiveness seen in younger men. Lean body mass also improved in both groups, but the older group still had twice the body fat of the younger group. Overall, they found that glucose tolerance improved and insulin sensitivity increased, but that age- related differences could not be corrected through resistance training.

Middle-aged healthy untrained males were investigated by Smutok et al. (1993) to determine the effect of 20 weeks of aerobic and resistance training on insulin and glucose responses. They found the resistance trained group had lower fasting insulin concentration after training, whereas the aerobic trained group did not. As for insulin responses to an OGTT, both training groups had lower insulin responses. Resistance and aerobic trained groups had significant reductions in glucose during the OGTT, but the resistance trained had greater changes. They found very similar results between

participants with NIDDM or impaired glucose tolerance following training. In conclusion, both aerobic and resistance training increased glucose tolerance and insulin sensitivity in middle-aged healthy men.

Miller et al. (1994) studied insulin and glucose responses before and after 16 weeks of strength training in healthy 50- to 65-year old men. They found decreased fasting plasma insulin concentration and improved insulin responses to an OGTT and hyperglycemic clamp after resistance training. Fasting glucose concentrations and glucose responses to an OGTT remained unchanged. They tested glucose and insulin responses 24 hours after the last exercise bout, and found that chronic resistance training produced an increase in insulin sensitivity in older men. However, their findings may reflect primarily the residual effects of the last exercise bout and not training *per se*. They concluded that insulin sensitivity is increased in older men after resistance training.

Smutok et al. (1994) examined the effect of 20 weeks of aerobic or resistance exercise on insulin and glucose responses in either untrained men with NIDDM, impaired glucose tolerance, or hyperinsulinemia with normal glucose tolerance. A standard OGTT was used to measure glucose and insulin levels before and after training. Aerobic training reduced glucose tolerance by 16% while strength training reduced glucose tolerance 12%. After both types of training, all participants with impaired glucose tolerance fell into normal range. However, even though glucose tolerance improved in NIDDM participants, they were still within diabetic range. Strength training reduced fasting insulin responses, whereas aerobic training did not. Both aerobic and resistance training reduced total insulin responses during the OGTT. Aerobic training and resistance training reduced total insulin area under the curve by 21% and 22% respectively. There

were no significant differences between the effects of aerobic or resistance training on glucose or insulin responses. They concluded that middle-aged men with glucose regulation abnormalities show improvement in glucose tolerance and increased insulin sensitivity after both aerobic and resistance training.

Zachwieja et al. (1996) examined the effect of 16 weeks of heavy resistance training in 15 healthy older men on insulin sensitivity and insulin secretion. They used 64-75 year old men who participated in 4 days per week of high-intensity (70-95% of maximum strength), and low repetition (4-10) weight lifting. They alternated days between six upper body and three lower body exercises. They found that glucose tolerance was not affected when examined through an intravenous glucose tolerance test (IVGTT). An increase in insulin sensitivity in the resistance training group almost reached significance ($p=.06$). Since they waited 7 days post-exercise to perform the IVGTT, the results may have been significant if they had tested 24-48 hours earlier. Fasting insulin and glucose remained unchanged after training. They concluded that resistance training is an effective treatment to increase muscle strength and fat free mass, and shows a strong tendency to improve insulin sensitivity in older men.

Ryan et al. (1996) examined insulin and glucose responses in post-menopausal women during 4 months of resistance training. The women were divided into two groups; six obese women were enrolled in a weight-loss program along with a resistance training program while the seven remaining only participated in the resistance training. After the training period, the women in the weight loss group changed their body composition (decreased fat mass and body weight) to a level comparable to that of the resistance training only group. As in many studies, there was no change in fasting glucose or

glucose responses to a hyperglycemic clamp 24 hours post-exercise. Fasting insulin levels did not change, but the insulin response decreased 29% after the intervention. Interestingly, the resistance training-plus-weight-loss group had a reduction of 43% in insulin response to the hyperglycemic clamp. In summary, resistance training alone or with a weight loss component is a successful intervention to increase insulin sensitivity in healthy and obese postmenopausal women.

Weinstock et al. (1998) investigated the insulin and glucose responses before and after a supervised diet and exercise program in 45 obese women. They found that diet alone produced the same results as diet and resistance or aerobic training together during a span of 48 weeks. In these healthy, obese middle-aged women, a decrease in fasting insulin concentration and insulin response to an OGTT were seen, but glucose changes were not significant. They concluded that weight loss alone improves insulin sensitivity and is not further improved with exercise.

Similarly, Rice et al. (1999) investigated whether diet compared with aerobic or resistance training influenced insulin and glucose responses in obese, middle-aged men. After 16-weeks of resistance or aerobic training, an OGTT was given 5-10 days post-exercise to measure insulin and glucose responses. They found that fasting glucose and glucose responses to an OGTT were unchanged in all groups. However, fasting insulin and insulin responses during an OGTT were decreased in all groups. Furthermore, insulin responses were reduced more in the aerobic and resistance training groups than the diet alone group. This contradicts Weinstock et al. (1998) findings. They concluded that weight loss and exercise whether aerobic or resistance improved insulin sensitivity over weight loss alone.

Ryan et al. (2001) investigated the effect of 6 months of resistance exercise on insulin sensitivity in healthy older adults. Eighteen older men and women participated in the study. None of the participants were diagnosed with NIDDM, but 7 had impaired glucose tolerance. The resistance training program consisted of 11 exercises performed 3 days per week for 6 months. Insulin and glucose responses were measured by hyperinsulinemic-euglycemic clamps 24-36 hours after the last exercise session. Fasting insulin and glucose concentrations did not change. Insulin sensitivity increased 10% after resistance training, but this only approached significance ($p=0.06$). However, there was a tendency for greater improvement in the participants that had greater insulin resistance before training. In conclusion, insulin-resistant older adults show a greater improvement in insulin sensitivity after 6 months of resistance training compared to non-insulin-resistant older adults. Therefore, a resistance training program may prevent or stabilize insulin resistance in older healthy adults.

Overall, resistance training consistently shows improvement in insulin sensitivity (Ryan et al., 1996; Miller JP et al., 1994; Rice et al., 1999; Smutok et al, 1993; Craig, Everhart, and Brown, 1989), however one study only showed a trend towards improvement (Ryan et al., 2001). When aerobic and resistance training were compared directly, they equally decreased insulin responses (Rice et al., 1999; Smutok et al., 1993). Another aspect examined was the addition of a weight loss component through caloric restriction plus exercise. Both diet and exercise has each been shown to increase insulin sensitivity (Ryan et al., 1996; Weinstock et al., 1998; Rice et al., 1999). The change in body composition through weight loss causes improvements in insulin and glucose responses independent from exercise (Ryan et al., 1996; Weinstock et al., 1998; Rice et

al., 1999). However, the reverse is true as well. Exercise alone can improve insulin and glucose responses without a change in body composition (Ryan et al., 1996; Miller JP et al., 1994; Rice et al., 1999; Smutok et al, 1993; Craig, Everhart, and Brown, 1989).

CHAPTER III

THE EFFECT OF THREE DAYS OF ACUTE RESISTANCE EXERCISE ON INSULIN AND GLUCOSE RESPONSES IN OLDER ADULTS[1]

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ABSTRACT

Background. This study examined the effects of three bouts of acute resistance exercise performed on 3 days in one week on glucose and insulin responses during an oral glucose tolerance test (OGTT) in 14 healthy older adults.

Methods. Participants performed three sets of 8-10 repetitions at 75% of the 3RM maximum on eight resistance exercises on 3 nonconsecutive days in 1 week. Insulin and glucose responses to an OGTT were measured at baseline, 24 hours after 1 and 3 days of exercise, and 72 hours after the third bout of exercise.

Results. The 3 days of acute exercise had no significant effects on fasting glucose or insulin responses. There also were no significant differences in glucose or insulin responses during any of the OGTTs following the exercise sessions.

Conclusion. Three bouts of acute resistance exercise performed on nonconsecutive days in 1 week does not have a cumulative effect on insulin or glucose responses to a glucose challenge. These findings suggest that a greater exercise stimulus is needed to improve insulin sensitivity in older adults

INTRODUCTION

With advancing age, the risk of developing insulin resistance, glucose intolerance, and non-insulin-dependent diabetes mellitus (NIDDM) increases. According to NHANES II, the prevalence of diabetes is 12.8% of individuals 55-64 years of age and 17.7% of individuals 65-74 years of age (Harris et al., 1987). NIDDM increases the risk of coronary heart disease, hypertension, stroke, intermittent claudication, and microvascular disease. Complications of microvascular disease, which are prevalent in NIDDM, include retinopathy, nephropathy, neuropathy, blindness and increased risk of

infection. Therefore, NIDDM is a serious chronic disease that decreases the quality and length of life (Ivy, Zderic, and Fogt, 1999).

Although the etiology of NIDDM is unknown, physical inactivity and obesity are contributing factors. Positive energy balance, adipocyte hypertrophy and an effect of physical inactivity on insulin action in skeletal muscle lead to insulin resistance in skeletal muscle and adipose tissue. Development of insulin resistance precedes, and is the hallmark of, NIDDM. Physical activity and reduction in body weight (especially visceral fat) appear to be the best tools to prevent or reverse insulin resistance (Ivy, Zderic, and Fogt, 1999). The high incidence of insulin resistance, glucose intolerance, and NIDDM in the elderly maybe more related to lifestyle changes, namely decreasing physical activity and increasing body fatness, than to aging *per se*.

Aerobic and resistance exercise can reverse and improve insulin resistance (DeFronzo et al., 1987; Hughes et al., 1993; Kahn et al.,1990; Miller et al., 1994; Miller, Sherman, and Ivy, 1984; Mourier et al., 1997; Rice et al., 1999; Ryan et al., 1996; Segal et al., 1991; Smutok et al., 1993). Insulin sensitivity, as reflected by a reduced insulin response with the same or slightly lower glucose response to a glucose challenge, is improved following a single bout of exercise (Fluckey et al., 1994; Kraemer et al, 1997; Mikines et al., 1988; Mikines et al., 1989). Chronic exercise training further attenuates insulin and glucose responses, although the additional gains are often modest (King et al., 1988; Mikines et al., 1989). DeFronzo, Sherwin, and Kraemer (1987) reported that short-term training of 6 weeks had the same effects on blunting glucose and insulin responses to a glucose challenge as longer training studies. The benefits of exercise on insulin and

glucose responses are lost when trained subjects become inactive for as little as 5-14 days (Heath et al., 1983; King et al., 1988; Mikines et al, 1989).

Fluckey et al. (1994) examined a single bout of resistance exercise in young control subjects, older NIDDM subjects, and older age-matched controls. NIDDM and young control groups had significantly lower insulin responses post-exercise. Insulin secretion was not changed, but insulin clearance was increased through hepatic and/or peripheral mechanisms. Rice et al.(1999) found resistance and aerobic training had similar effects on insulin sensitivity in healthy, obese, middle-aged men.

Although glucose and insulin responses to acute and chronic resistance exercise have been studied, the time course of changes resulting from successive exercise sessions is not known. It is possible that adaptations reported with weeks of training may occur rapidly due to cumulative, augmented responses to several acute bouts of exercise, as has been reported for other measures such as blood triglycerides (Gyntelberg et al., 1977; Oscai et al, 1972). If the improvement in insulin sensitivity with several bouts of exercise performed in one week of resistance training is greater than the response to a single bout of exercise, but equal to that obtained from training longer, this would mean that even limited periods (several days) acute resistance exercise improve health and act as preventive measure against insulin resistance and NIDDM in older adults.

The purpose of this study is to examine the effects of three bouts of acute resistance exercise performed on nonconsecutive days in one week on blood glucose and insulin responses in older men and women.

METHODS

Subjects

Three males and 11 females aged 55-75 years participated in this study. Their physical characteristics are presented in Table 1. Participants were not engaged in any systematic aerobic or resistance exercise in the last 6 months. None of the subjects had cardiovascular, pulmonary, or metabolic disease. All participants received physician clearance before they began the study to assure that they were healthy enough to complete the protocol required. After the initial OGTT, six participants were classified as having impaired glucose tolerance while the remaining eight participants had normal glucose tolerance. Following an explanation of procedures, subjects gave written informed consent. This study was approved by the Institutional Review Board at the University of Georgia.

Table 1. *Subject Physical Characteristics*

	Men (n=3)	Women (n=11)
Age	59.3 ± 2.3	60.7 ± 5.7
Weight (kg)	99.5 ± 28.7	69.6 ± 12.3
% Body fat	32.3 ± 7.5	35.3 ± 7.6
BMI	32.7 ± 6.4	26.4 ± 4.1

[1]All physical characteristic values are 0 ± SD

Design

A repeated-measures design in which subjects served as their own control was used. Subjects completed three bouts of resistance exercise on nonconsecutive days within 1 week to determine if there is an additive effect on blood glucose and insulin responses, compared to baseline values and a single bout of exercise. Fasting oral glucose

tolerance tests (OGTT), in which glucose and insulin to a glucose challenge were administered: 1) after a 12-hour fast (control), 2) 24-hours after the first and third exercise sessions to assess the responses to a single bout, and three successive bouts, of acute resistance exercise and, 3) 72-hours after the third exercise session, to assess more-persistent training adaptations.

Protocol and Procedures

Subjects attended ten testing sessions over a period of 3-5 weeks. At the first session, they completed necessary paperwork and were oriented to procedures. During this session a 3 day dietary food log was completed to assess if at least 150 grams of carbohydate were being consumed each day. At the second testing session, subjects were given a 75-gm OGTT following a 12-hour fast. At the third testing session, the subjects were taught how to perform resistance exercises and skinfold measurements were taken using Lange skinfold calipers. Total body fat was estimated using the Jackson and Pollock 7-site equation for men and women. After the participants were comfortable with the equipment, 3-repetition maximum (3RM) strength tests were performed. Strength for the eight exercises are summarized in Table 2.

Resistance Exercise Protocol

The eight resistance exercises performed were leg extension, leg press, biceps curl, shoulder press, triceps extension, latissmus pull-down, rear deltoid flys, and bench press. All exercises were performed on Cybex© equipment except for bicep curls in which dumbbells were used. The resistance exercise protocol consisted of three exercise sessions performed within 1 week. Each subject performed three sets of ten repetitions at

75% of the 3RM. A 5-minute warm-up was performed on a cycle ergometer and a 5-minute stretching session was done after the resistance exercise.

The bouts of acute resistance exercise commenced at least one week after the 3RM was determined to assure that there were no residual effects of the maximal effort given and to allow the normal rate of glycogen synthesis to be restored (MacDougall, Ward, and Sutton, 1977). The resistance exercise protocol was on days five, seven, and eight. On the sixth, ninth, and tenth day of attendance, an OGTT was given 24 hours after the first and third resistance exercise session, and 72 hours after the third exercise session.

Table 2: *Subject 3RM Strength*

	Bicep Curls (lbs)	Tricep extension (lbs)	Leg extension (lbs)	Leg Press (lbs)	Shoulder Press (lbs)	Bench Press (lbs)	Lat Pulldown (lbs)	Rear Deltoid Flys (lbs)
Men	28.3± 2.9	78.3± 20.2	91.7± 16.07	203.3± 30.6	56.7± 11.6	103.3± 23.1	150.0± 34.6	116.7± 11.6
Women	15.0± 3.9	52.7± 11.0	66.4± 18.9	145.5± 67.7	29.6± 10.4	45.9± 14.5	91.4± 18.5	72.3± 15.6

[1]all resistance exercises were performed on Cybex® equipment except for bicep curls.
[2]Strength was assessed using a 3RM. All strength values are 0 ± SD

OGTT. Subjects fasted for 12-hours before each OGTT. After a baseline blood sample was drawn through a catheter in a forearm vein, a 75-g load glucose solution was consumed within 5 minutes. A blood sample was drawn every 30 minutes for 2 hours after ingestion and analyzed for glucose and insulin concentration. Glucose concentrations were determined using a YSI 2300 STAT PLUS (Yellow Springs, OH) glucose analyzer. Radioimmunoassays (RIA) (ICN #0720102, Costa Mesa, CA) were used to determine insulin concentrations. The intra-assay coefficient for duplicate samples was 0.04% for glucose and 2.1% for insulin. Mean replacement was used if a

duplicate sample was not within 1 standard deviation. Area under the curve (AUC) for insulin and glucose responses were calculated using the trapezoidal rule (Matthews et al.,1990).

Nutritionalist V was used to assess the carbohydrate intake from 3-day dietary logs to assure that 150 grams of carbohydrate, which is the minimal amount needed to have a valid OGTT, was being consumed.

Statistical Analysis. The significane of mean differences among trials for the insulin and glucose AUC were analyzed using a repeated measures one-way ANOVA. A two-way (Trial x Time) ANOVA was used to determine whether there were differences among means for insulin and glucose responses at different points in time during the OGTTs. An alpha level of 0.05 was used for all significance tests.

RESULTS

Glucose tolerance. In the two-way ANOVA on blood glucose, there was no significant Trial or Trial x Time interaction effects. Thus, the blood glucose concentration prior to and during OGTTs following one or three bouts of resistance exercise were not different from those from the OGTT administered prior to exercise or from one another (Table 3, Figure 1). Similarly, in the one-way ANOVA, there was no significant difference in the glucose AUC among the four trials (Figure 2).

Table 3: *Glucose Concentration (mmol/L) at time points during the OGTTs*

	Fasting	30 min	60 min	90 min	120 min
OGTT 1 (n=14)	5.3± 1.0	8.4± 1.7	8.5± 2.5	7.6± 3.2	7.2± 3.1
OGTT 2 (n=14)	5.9± 1.1	8.9± 2.4	8.7± 3.7	8.5± 4.1	7.6± 3.8
OGTT 3 (n=14)	5.4± 1.2	8.7± 2.3	8.1± 2.6	7.9± 2.7	6.8± 2.2
OGTT 4 (n=14)	5.5± 1.0	9.0± 2.1	8.2± 2.2	7.5± 2.7	7.4± 2.7

[1]OGTT 1 is the baseline test, OGTT 2 is 24 hrs after the 1st exercise session, OGTT 3 is 24 hrs after the 3rd exercise session, OGTT 4 is 72 hrs after the 3rd exercise session
[2]All values are listed with 0 ± SD

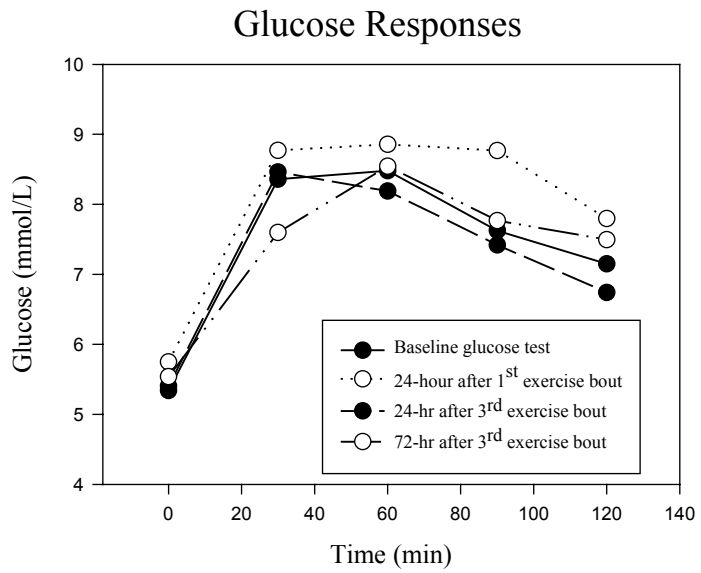

Figure 1. Plasma glucose concentration at baseline (fasting) and 30, 60, 90, and 120 minutes after glucose ingestion.

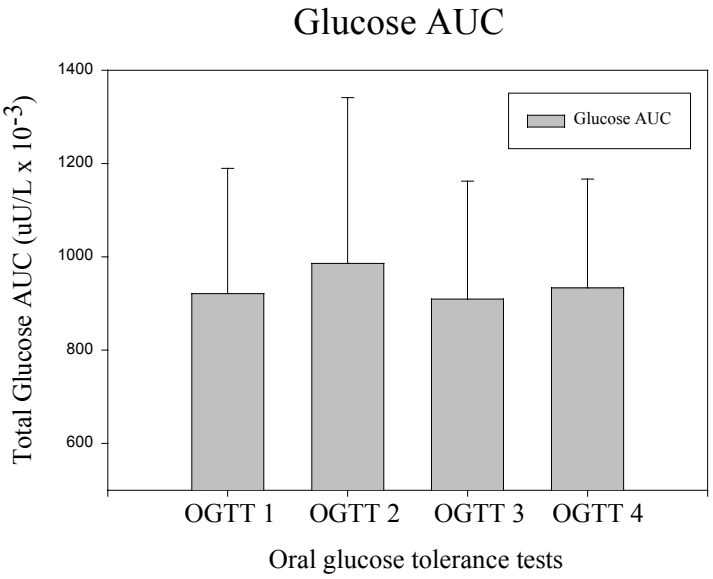

Figure 2. Area under the curve for glucose during each of the four OGTTs. OGTT 1 is the baseline test, OGTT 2 is 24-hrs after the 1st exercise bout, OGTT 3 is 24-hrs after the 3rd exercise bout, OGTT 4 is 72-hrs after the 3rd exercise bout.

Insulin responses. In the two-way ANOVA on blood insulin, there was no significant Trial or Trial x Time interaction effects. Thus, the blood glucose concentration prior to and during OGTTs administered following one or three bouts of resistance exercise were not different from those from the OGTT administered prior to the exercise or from one another (Table 4, Figure 3). Similarly, in the one-way ANOVA, there was no significant difference in the insulin AUC among the four trials (Figure 4).

Table 4: *Insulin concentration (uU/L) at time points during the OGTTs*

	Fasting	30 min	60 min	90 min	120 min
OGTT 1 (n=14)	10.7± 5.4	91.9± 42.5	106.4± 51.7	95.4± 48.5	71.1± 39.8
OGTT 2 (n=14)	11.1± 6.1	80.1± 42.0	91.6± 56.5	89.0± 48.7	85.9± 53.0
OGTT 3 (n=14)	13.7± 9.0	93.8± 60.3	113.9± 65.1	94.1± 55.9	85.6± 43.7
OGTT 4 (n=14)	12.7± 8.1	93.0± 49.1	102.9± 51.3	89.6± 48.5	86.5± 58.9

[1]OGTT 1 is the baseline test, OGTT 2 is 24 hrs after the 1st exercise session, OGTT 3 is 24 hrs after the 3rd exercise session, OGTT 4 is 72 hrs after the 3rd exercise session
[2]All values are 0 ± SD

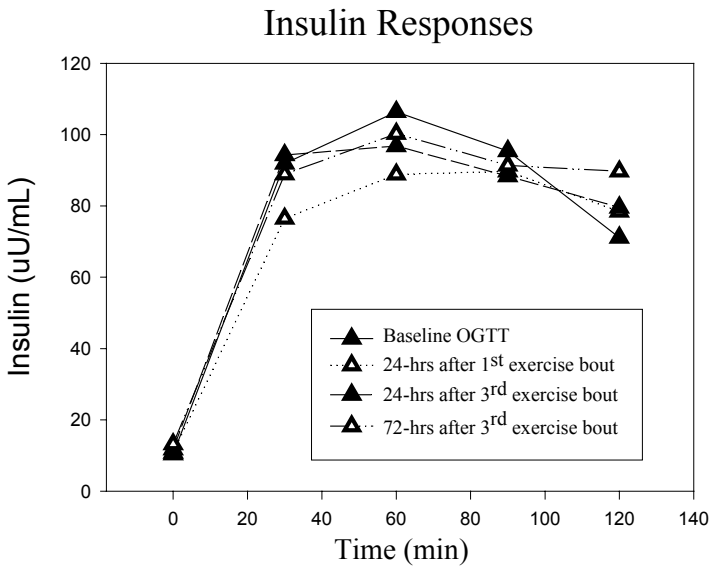

Figure 3. Plasma insulin concentration at baseline (fasting) and 30, 60,90, and 120 minutes after glucose ingestion.

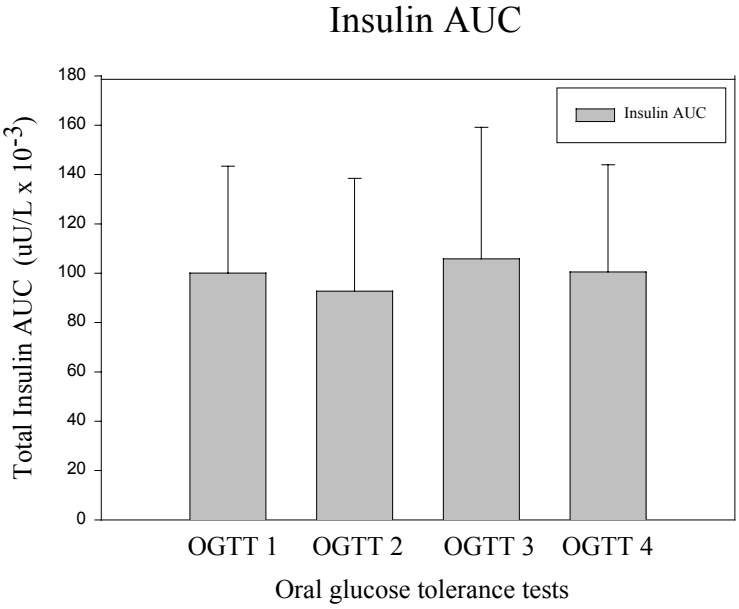

Figure 4. Area under the curve for insulin during each of the four OGTTs. OGTT 1 is the baseline test, OGTT 2 is 24-hrs after1st exercise bout, OGTT 3 is 24-hrs the 3rd exercise bout, and OGTT 4 is after 72-hrs after the 3rd exercise bout

DISCUSSION

This study is, to our knowledge, the first to examine the effect of 3 days of acute resistance exercise on insulin and glucose responses to an OGTT in healthy older adults. Our major findings were that acute resistance exercise did not improve glucose tolerance or insulin sensitivity after 1 or 3 days of resistance exercise in healthy older adults. Therefore, we found no cumulative effect across days of resistance exercise.

Glucose tolerance was not changed after 1 day or 3 days following acute resistance exercise. There also was no effect 72 hours after the last bout of exercise. This finding was consistent with most of the literature on the effect of aerobic and resistance exercise. In general, glucose tolerance does not change with acute or chronic exercise if glucose tolerance is already normal (Zachwieja et al., 1996; Cononie et al., 1994; Kirwin et al., 1993; Tonino, 1989; Ryan et al., 2001; Ryan et al., 1996; Miller JP et al., 1994; Rice et al., 1999; Smutok et al, 1993), although there are exceptions (Bonen, Ball-Burnett, and Russel, 1998; Hughes et al., 1993). Furthermore, acute resistance exercise is not enough to change glucose tolerance even in NIDDM or impaired glucose tolerant adults (Fluckey et al., 1994).

Following a single bout of resistance exercise, there was no difference in insulin responses to an OGTT 24-hours post-exercise. Cononie et al. (1994) obtained similar results; they did not find a significant difference in the insulin response to an OGTT after 1 day of aerobic exercise compared to a control day with no exercise. Flucky et al. (1994) did not see any change in the insulin response to an OGTT in a healthy older control group after one day of resistance exercise, but did see a significant decrease in older NIDDM patients and younger healthy subjects. However, other studies have

reported a decrease in the insulin response to an OGTT or an increase in insulin sensitivity after a single bout of aerobic exercise (Bonen, Ball-Burnett, and Russel, 1998; Mikines et al., 1988; Mikines et al., 1989; King et al., 1988).

Another major finding was that there was no change in the insulin response to an OGTT after 3 days of resistance exercise in healthy men and women. Since no other studies have examined the effect of 3 days of resistance exercise on healthy older adults, no direct comparisons with other studies can be made. However, supporting our finding are two studies that show that acute or chronic resistance exercise does not affect insulin sensitivity in older people with normal glucose tolerance (Ryan et al., 2001; Fluckey et al., 1994). A recent study by Ryan et al. (2001) found no significant differences in insulin and glucose responses to a hyperglycemic clamp in normal or impaired glucose tolerant men and women after 6 months of resistance training, but a trend was seen for decreasing insulin responses. Once again, Fluckey et al. (1994) did find a significant reduction in insulin response during an OGTT in older NIDDM patients and in healthy younger controls, but not in healthy older-aged matched controls. In contrast to our data is a study by Cononie et al. (1994), which found seven consecutive days of aerobic exercise improved insulin sensitivity using a 3 hour OGTT, whereas 1 day did not. Furthermore, most training studies involving either aerobic or resistance exercise have found a significant increase in insulin sensitivity (Zachwieja et al., 1996; Cononie et al., 1994; Tonino, 1989; Ryan et al., 1996; Miller JP et al., 1994; Rice et al., 1999; Smutok et al., 1993).

Interestingly, Tonino (1989) did not find any significant effects of 12 weeks of endurance training on oral glucose tolerance, but did see insulin sensitivity improve when

tested with an euglycemic clamp. It is a possibility that if we had used an euglycemic-hyperinsulinemic clamp along with our OGTT that our results may have been different.

There also were no significant differences in glucose or insulin responses 72 hours after the last exercise bout. This result was plausible due to the fact that there were no significant results 24 hours post-exercise which is when the greatest effects are seen (Mikines et al., 1989; Fluckey et al., 1994).

Even though this study did not find a significant improvement in insulin sensitivity, there were five participants who did improve their insulin profiles. These five participants had normal glucose tolerance and tended to have a lower BMI. This finding contradicts some of the resistance training studies that have found greater results in insulin resistant and impaired glucose tolerant participants (Ryan et al., 1996; Ryan et al. 2001). One possible explanation could be that healthier adults respond faster during acute exercise then plateau with training, whereas adults with insulin resistance or impaired glucose tolerance may take longer to show an effect but continue to improve with training.

We hypothesized that insulin sensitivity would be improved after 1 day of acute resistance exercise and that a larger cumulative effect would be observed following 3 days of resistance exercise because when training studies have directly compared aerobic and resistance training they have found similar results between the two. Smutok et al. (1994) found that 20 weeks of resistance exercise or aerobic exercise decreased insulin responses equally in men with NIDDM, impaired glucose tolerance, and in hyperinsulemia with normal glucose tolerance. Rice et al. (1999) also found that aerobic and resistance training produced similar results in insulin responses in middle-aged obese

men. Since these studies found similar results in improving insulin responses between aerobic and resistance training, we expected to see similar findings between acute aerobic and resistance exercise.

One possibility for the lack of significant effects of 1 or 3 days of resistance exercise on glucose and insulin responses is that our exercise protocol was not hard enough. Our resistance exercise protocol involved performing eight exercises at an intensity of 75% of a 3RM for three sets of 10 repetitions. This protocol was very hard for most participants. Therefore, because performing resistance exercise at a higher intensity or for a longer duration would not have been feasible for this sample, it is unlikely that inadequate resistance exercise was the cause of the lack of significant responses in glucose and insulin. It may be that untrained older adults do not have the capacity to perform the amount of exercise needed for an effect.

In healthy adults, acute aerobic exercise appears to cause an improved insulin profile while acute resistance exercise does not in healthy adults. This suggests that the greater number of muscle contractions and perhaps the greater total amount of muscle activated in large-muscle aerobic activity such as walking, running and cycling may provide a greater stimulus for changes in insulin and glucose than the fewer number of more intense contractions in a more limited muscle mass involved in resistance exercise.

An improvement in insulin sensitivity may be dependent on the amount of work done (Borghouts and Keizer, 1999; Braun et al., 1995). The work done or the caloric expenditure in one hour of resistance exercise is probably less than that performed during one hour of aerobic activity. The amount of work done would affect the depletion of glycogen stores. If glycogen stores are decreased sufficiently, the muscle becomes more

sensitive to insulin stimulated glucose uptake after exercise has stopped (Douen et al., 1990; Cartee et al., 1986). Therefore, the resistance exercise protocol may not have depleted glycogen levels enough. Unfortunately, no muscle biopsies were taken to assess this. This suggests that it may be more important to lower the intensity of the resistance exercise and increase the number of sets and repetitions to increase the amount of work done, and to deplete glycogen stores.

Another reason that acute resistance exercise may not show an improvement in insulin sensitivity is muscle damage caused by eccentric contractions that can interfere with glycogen resynthesis (King et al., 1993; Doyle, Shermin, and Strauss, 1993). Studies show that glycogen resynthesis is slower in muscles that have muscle injury due to eccentric contractions. This interference in glycogen resynthesis appears to last 1-4 days post-exercise (Widrick et al., 1992; Asp, Daugaard, and Richter, 1995). Since resistance exercise involves more intense eccentric contractions likely to cause muscle damage compared to aerobic activity, this could be a mechanism that differentiates between the immediate improvements in insulin sensitivity seen from acute aerobic exercise compared to acute resistance exercise (Pascoe et al., 1996).

Other adaptations to training, such as increased muscle mass, increased insulin signaling, or decreased hepatic glucose output do not occur after an acute bout of exercise (Coggan et al., 1995; Defronzo et al., 1987). Therefore, resistance training and aerobic training may both add these benefits after weeks of training along with other mechanisms to increase insulin sensitivity equally.

In conclusion, we found that glucose tolerance did not change with acute resistance exercise. Furthermore, insulin responses and/or insulin sensitivity did not

change after 1 day of resistance exercise or after 3 days of resistance exercise in older healthy adults. Therefore, there was no cumulative effect in 1 week of acute resistance exercise on insulin responses.

ACKNOWLEDGEMENTS

We thank the participants for their time and participation in this study. We also thank the Georgia Gerontology Seed Grant for financially supporting this study.

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CHAPTER IV

SUMMARY AND CONCLUSIONS

This study examined the effect of 3 days of acute resistance exercise on insulin and glucose responses in older adults. The main purpose was to investigate whether there was a cumulative effect of a multiple days of exercise in healthy untrained older adults. We also investigated whether there was a persistent effect on insulin or glucose responses 72 hours after the third resistance exercise session.

Fourteen older men and women participated in this study. Eight participants had normal glucose tolerance and 6 participants had impaired glucose tolerance. None of the participants were currently involved in a structured exercise program. The resistance exercise protocol consisted three sets of 10 repetitions of eight whole-body exercises performed at 75% of a 3RM. The resistance exercise regimen consisted of bicep curls, tricep extension, shoulder press, chest press, leg press, leg extension, lat pull-downs, and rear deltoid flys. All subjects were able to complete the protocol.

Four fasting OGTT were given to assess insulin and glucose responses throughout the duration of the study. The OGTT were administered 1) after a 12 hour fast (control), 2) 24 hours after the first and third exercise sessions to assess the responses to a single bout, and three successive bouts, of acute resistance exercise and, 3) 72 hours after the third exercise session to assess more-persistent training adaptations. Our major findings were that there was no change in insulin or glucose responses after 1 or 3 days of resistance exercise. Therefore, there was no cumulative effect on insulin responses after

1 week of resistance exercise. Also found was that there no change in glucose tolerance, and no persistent effects after 72-hours after the third exercise session.

We conclude, three bouts of acute resistance exercise performed on nonconsecutive days in one week does not have an cumulative effect of glucose and insulin responses to a glucose challenge.

CHAPTER V

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