ACUTE EFFECTS OF MILD EXERCISE ON POSTPRANDIAL GLUCOSE AND INSULIN RESPONSES

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ABSTRACT

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Purpose: Hyperinsulinemia is a risk factor for cardiovascular disease. Chronic exercise is established as an anti-hyperinsulinemic factor. The purpose of this study was to determine if a postprandial exercise bout (20 min walk at 70% ventilatory threshold) could reduce the insulin response to a standard meal.

Method: Healthy volunteers (n = 11) consumed a meal (982 kilocalories, 29 grams protein, 140 grams carbohydrates, 34 grams fat) on two separate days. Glucose and insulin responses were followed for 2 hours, while the subjects either rested (Control) or performed mild exercise (Exercise) between 30-50 minutes postprandial. The order of Control and Exercise was random.

Results: There was a significant suppression in serum insulin with Exercise at 60 minutes, most evident in the Insulin/Glucose ratio. Other differences were not remarkable and were consistent with reasonable regulatory-counter regulatory variations.

Conclusion: These data support the hypothesis that exercise blunts postprandial insulinemia and, accordingly, may be a strategy for reducing net insulin exposure.

COLLEGE OF HEALTH, PHYSICAL EDUCATION,

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THESIS FINAL ORAL DEFENSE FORM

Candidate: Lia Lansky

We recommend acceptance of this thesis in partial fulfillment of this candidate's requirements for the degree:

Master of Science in Adult Fitness/Cardiac Rehabilitation

The candidate has successfully completed the thesis final oral defense.

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INTRODUCTION

Insulin is a hormone that is critical for normal carbohydrate metabolism. The absence of insulin, as in Type 1 diabetes mellitus (DM), presents an acute life threatening illness. On the other hand, too much insulin, such as that occurring following exogenous insulin administration, or in individuals with insulin resistance, can also provoke major health problems. The Paris Prospective study, a long-term cardiovascular disease study, found that high plasma insulin levels were a risk factor of cardiovascular disease in obese males (1). This study also indicated hyperinsulinemia could possibly be one of the "simplest accurate indices of adiposity in man" (1). Heart disease is often preceded by insulin resistance and hyperinsulinemia (2). Hyperinsulinemia can lead to high levels of unwanted body fat and is associated with the development and progression of glucose intolerance and of Type 2 DM and eventually cardiovascular heart disease (2).

Hyperinsulinemia is becoming increasingly common and is a strong risk factor for the development of cardiovascular diseases as it contributes to the development of other risk factors. Hyperinsulinemia has been proposed to be the best predictor of a heart attack (2). Elevated triglycerides in plasma and the reduction of high density lipoprotein (HDL), two established risk factors for cardiovascular disease, have been linked with hyperinsulinemia (3). Hyperinsulinemia leads to the stimulation of the sympathetic nervous system and mediated increases in blood pressure, another risk factor for the development of cardiovascular disease (4).

A substantial volume of data points to abdominal obesity as a primary risk factor for cardiovascular disease (5). A proposed key factor in the development of Type 2 DM is a large amount of abdominal fat (6). Insulin resistance is significant when normal fluctuations of blood glucose concentrations produce abnormal release of this hormone (7). One study examining fat accumulation in men found that male abdominal obesity was positively correlated to glucose, insulin, and C-peptide levels both after a glucose load and in a fasting state (6).

An increased rate of glucose uptake in skeletal muscle can be achieved by a single exercise bout (4). The insulin-dependent glucose transporter, Glut-4, transports glucose across the plasma membrane (4). During exercise, glucose transport is increased independent of insulin, and there is enhanced insulin sensitivity. Continuous exercise training results in a decrease in insulin response and an increase in glucose tolerance (8). Benefits of exercise training have occurred in as little as seven days in obese subjects showing that exercise, independent of weight loss, has a profound effect on insulin sensitivity (9). Albright and Franz studied exercise only, diet only, diet plus exercise, and control groups of subjects with impaired glucose tolerance over a period of six years (10). Among these groups, the incidence of DM six years later was lower in the diet plus exercise group (exercise plus diet = 46%, control = 68%) (10).

Studies show that both acute (3) and chronic (10) exercise can suppress the insulin response to feeding. However, most of the acute postprandial exercise studies have been performed in athletic individuals with relatively high intensity exercise (11). Whether or not low intensity exercise performed following a meal in normal individuals

Note regarding pages 3 and 4:

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(Johnson and Johnson, Rochester, NY). Plasma was also collected in conical tubes and stored at 20°C for insulin analysis. Plasma insulin was measured using an ELISA assay kit (ALPCO®, Windham, NH). The ALPCO® two-site insulin assay kit is based on the direct antibody sandwich technique. Briefly, peroxidase-conjugated anti-insulin antibodies are bound to standard or sample insulin that has been bound to anti-insulin antibodies coating a 96-well microplate. After thorough washing, the peroxidase substrate 3,3',5,5' tetramethylbenzidine is added and the colorimetric endpoint is read spectrophotmetrically. Bichromatic absorbances at 450 and 650 nm were recorded and analyzed by a SPECTRAmax® plate reader (Molecular Devices, Sunnyvale, CA). All insulin samples were run in duplicate. Standard curve values and Lo/Hi control values were in the acceptable range as specified by the assay.

In the session that involved exercise, the subject completed a twenty-minute walk on a treadmill beginning at 30 and ending at 50 minutes into the protocol. The pace was determined from the VO_2max test administered in the first session. An intensity of 70% of the VO_2max at the ventilatory threshold was used. The Rating of Perceived Exertion (RPE) was recorded and was between 2-4 on the Borg Category Ratio Rating of Perceived Exertion Scale (12). Following completion of the exercise, blood samples were taken at 60, 90 and 120 minutes after the initial, pre-meal blood sample.

A two-way repeated measures ANOVA was used to assess the main effects of Time, Condition, and Time*Condition interactions. Tukey's test was used for post hoc comparisons when significance was achieved at $p < 0.05$.

RESULTS

Heart rate was measured during the twenty-minute walk at five-minute intervals. The heart rate averaged around 80% HRmax during the walk (Fig.1). The average RPE upon completion of the twenty-minute walk was 3.5 on the 0-10 Borg Perceived Exertion scale.

Glucose (Glu) and insulin (Ins) values during each stage of the study (0,30,60,90 and 120 minutes) are presented in Table 2, along with Ins/Glu ratios for the Control and Exercise conditions. There was a striking and statistically significant suppression in serum Ins with exercise at 60 minutes, which is most evident in the Ins/Glu ratio. The temporal pattern of Glu, Ins, and Ins/Glu responses are presented in Figures 2-4. As expected, there were significant main effects of Time for both glucose and insulin in both groups ($p < 0.05$).

A significant interaction ($p < 0.05$) in time*condition for plasma glucose was also found. Pairwise comparisons revealed there was a significant ($p < 0.05$) difference in both the 60 (Control greater than Exercise) and 90 (Exercise was greater than Control) minute conditions.

A serendipitous observation was made during the testing of one subject. The subject's insulin and glucose levels were extremely high, consistent with the hyperinsulinemia and elevated fasting glucose levels observed in insulin resistance syndrome. Since the protocol specified that subjects have no known insulin disorder, we dropped this subject from data analysis. However, his results are presented in Table 3 and Figures 5-7 in comparison to the responses in the analyzed group. Table 3 shows this

subject's results including Glu, Ins, and Ins/Glu ratio for both the Control and Exercise conditions. His responses show significantly elevated glucose and (particularly) insulin values compared to the subjects with no diagnosed insulin disorder. However, as with the remainder of the subjects, at 60 minutes there was a relative decrease in insulin after exercise. Figure 7 shows the relationship of the Ins/Glu ratio in the experimental group vs subject #12. There is a significant decrease in insulin at 60 minutes with exercise in both group and subject #12, suggesting that the suppression of postprandial insulin response with exercise may occur and be useful in insulin resistance.

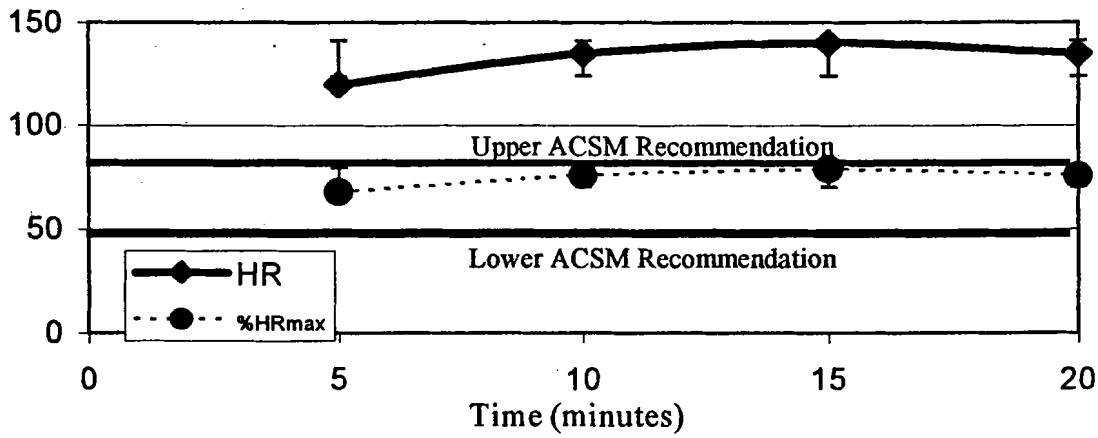

Figure 1. Heart Rate (HR) and % HRmax

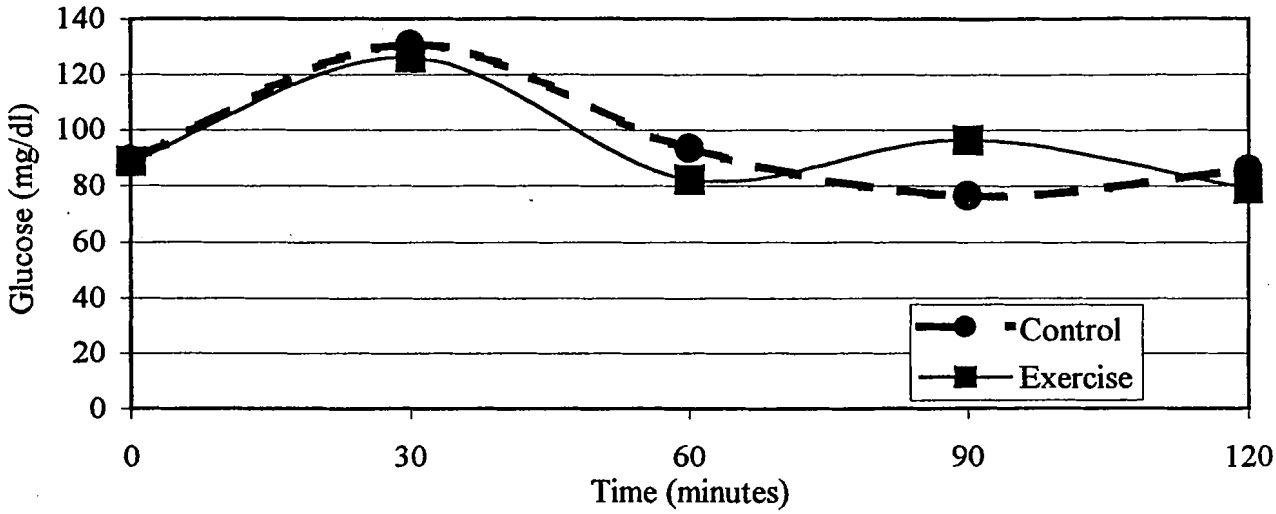

Figure 2. Time Course of Plasma Glucose Concentration in Control and Exercise Conditions

Table 2. Standard Deviations of Plasma Insulin (Ins), Glucose (Glu), and Ratio Ins/Glu

Time (min)	Glu-C	Glu-Ex	Ins-C	Ins-Ex
0	89.2 ± 6.8	88.7 ± 7.2	4.5 ± 2.8	3.4 ± 2.6
30	130.9 ± 21.7	126.2 ± 16.2	29.5 ± 11.5	29.7 ± 7.4
60	93.5 ± 21.2	82.5 ± 13.7	28.0 ± 9.1	17.3 ± 6.6
90	76.6 ± 14.2	96.6 ± 18.7	17.5 ± 6.0	24.0 ± 12.7
120	86.0 ± 15.3	79.0 ± 13.5	19.9 ± 10.3	19.8 ± 11.1

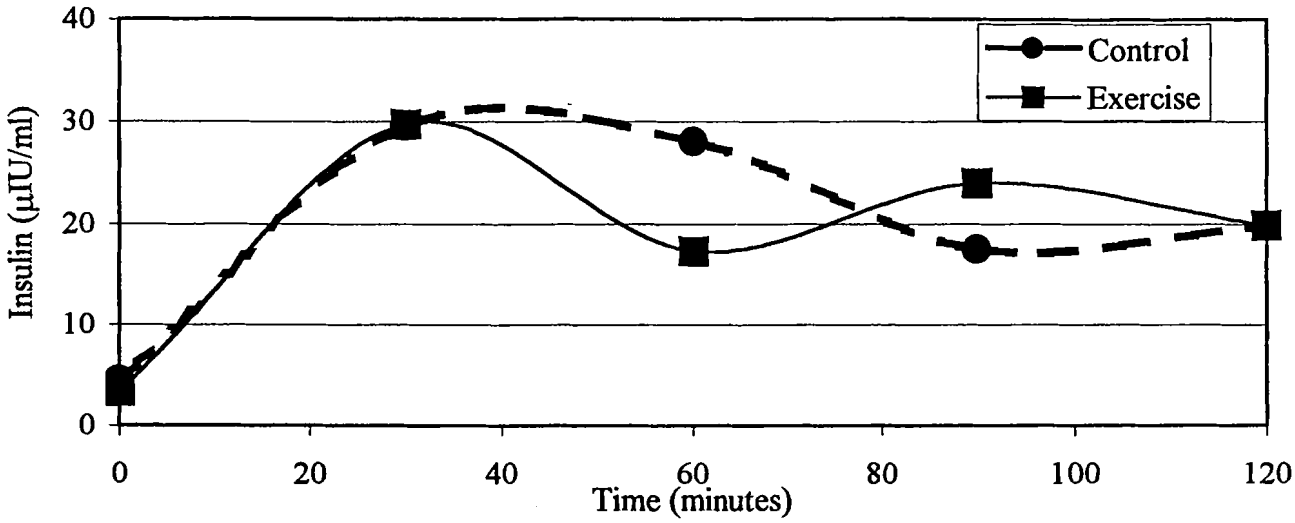

Figure 3. Time Course of Plasma Insulin Concentration in Control and Exercise Conditions

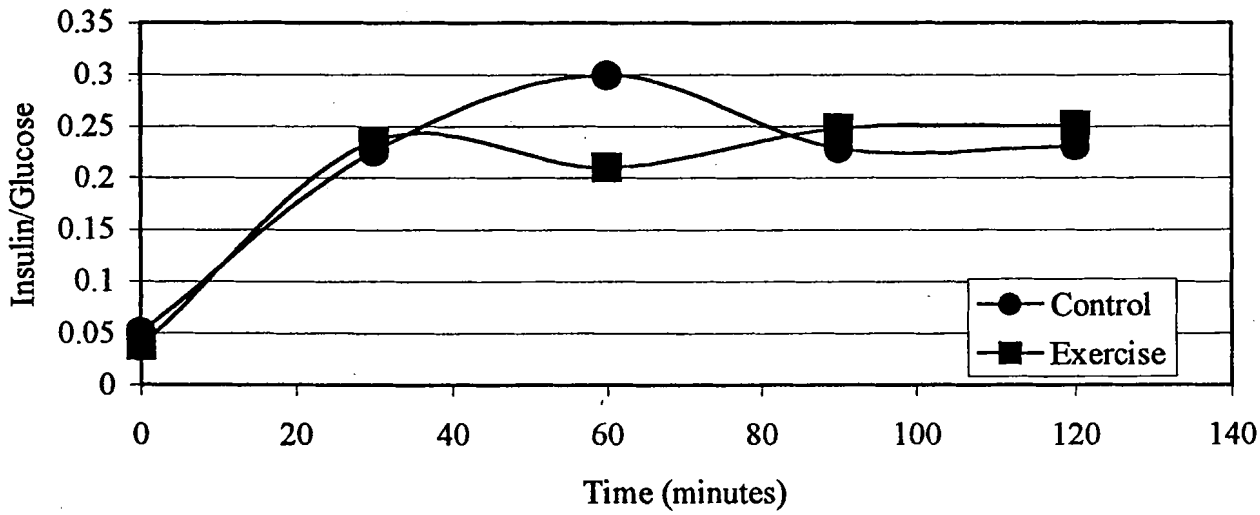

Figure 4. Time Course of Plasma Insulin/Glucose Ratio in Control and Exercise Conditions

Table 3. Time Course of Glucose and Insulin in an Individual with Hyperinsulinemia

Time	Glu-C mg/dl	Glu-Ex mg/dl	Ins-C μIμ/ml	Ins-Ex μIμ/ml	Ins/Glu-C	Ins/Glu-E
0	138	96	41.1	18.3	0.30	.19
30	143	166	192.5	179.3	1.35	1.08
60	86	88	70.0	37.3	.81	.42
90	90	109	46.4	76.1	.52	.70
120	97	95	53.1	59.3	.55	.62

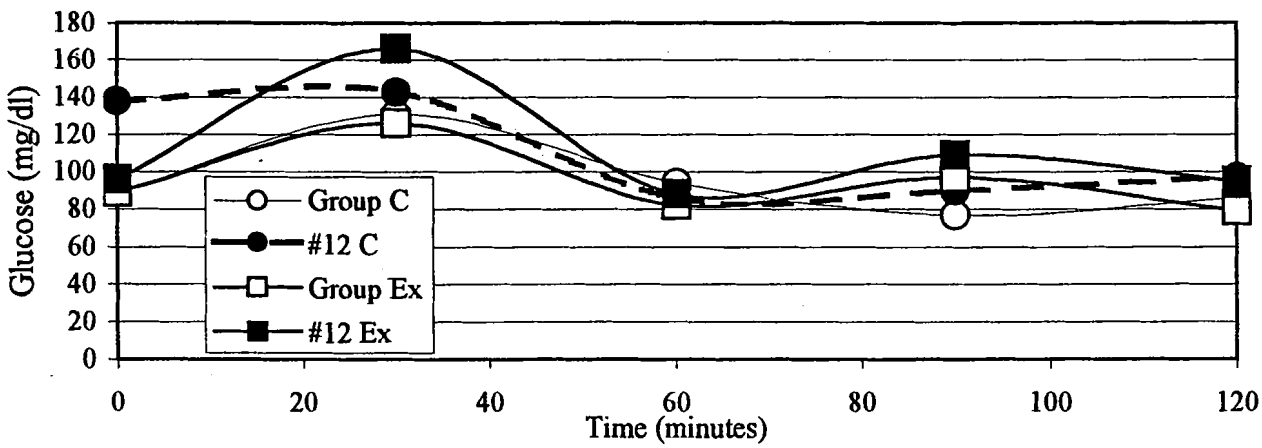

Figure 5. Time Course of Plasma Glucose Levels in the Group vs Subject #12

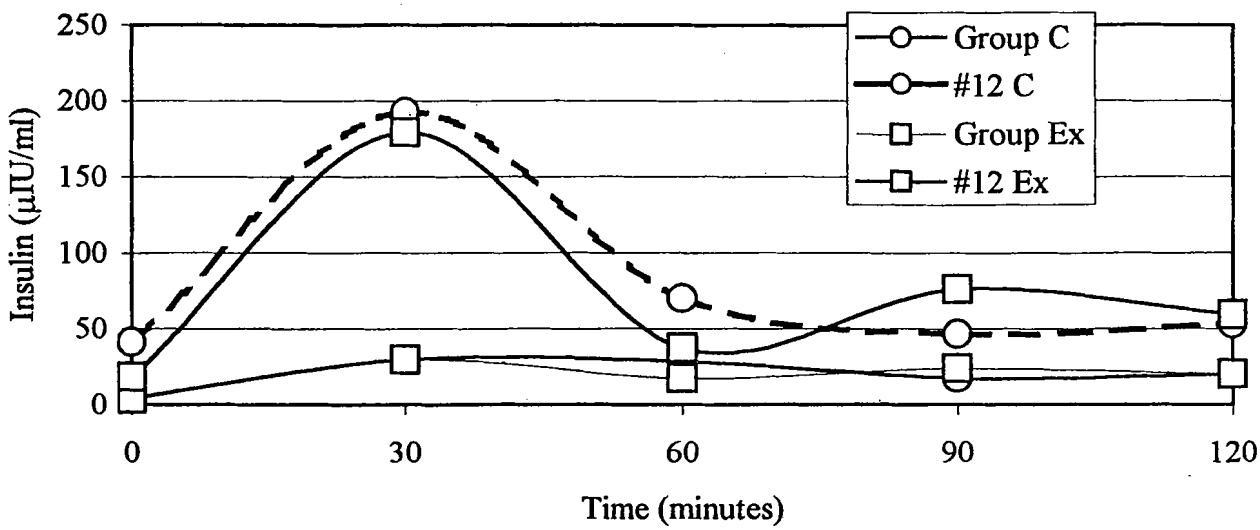

Figure 6. Time Course of Plasma Insulin Levels in the Group vs Subject #12

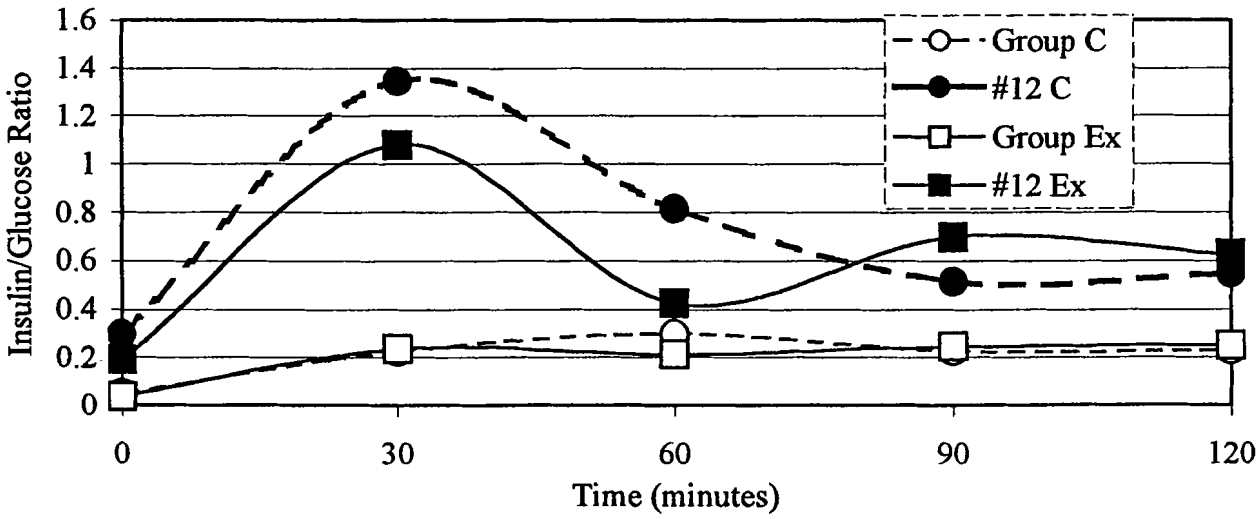

Figure 7. Time Course of Plasma Insulin/Glucose Ratio in the Groups vs Subject #12

DISCUSSION

The purpose of this study was to test the hypothesis that a moderate intensity walk after a standard meal would improve insulin sensitivity. We found that at 60 minutes (e.g. shortly following exercise) there was a significant decrease in insulin and glucose levels in the Exercise compared with the Control condition. To more simply evaluate the efficiency of insulin action after a meal, the Ins/Glu ratio was plotted. A high ratio suggests more insulin is needed relative to glucose and is indicative of less sensitivity to insulin, whereas a low ratio indicates more sensitivity to insulin. Using this ratio, an increase in insulin sensitivity in the Exercise condition was evident. There was a small, although significant, increase in both glucose and insulin following the cessation of exercise that was not evident in the Control condition, which complicates the interpretation of the data. The parallel changes in glucose and insulin simply confirms the expected regulatory response pattern of insulin to changes in plasma glucose concentration.

It has long been known that exercise improves the insulin sensitivity of tissues. This has been shown in both trained and non-trained individuals. Dela et al, found trained individuals to be more sensitive to insulin than untrained individuals (13). Exercise has also been shown to enhance insulin sensitivity in individuals with impaired glucose tolerance in several studies. In the Finnish Diabetes Prevention study, for example, it was concluded that a combination of weight reduction and an increase in physical activity improves insulin action in Type 2 DM (14).

Acute exercise has also been found to increase insulin sensitivity. A single bout or short-term exercise at different intensities and durations has consistently been shown to improve insulin sensitivity. Borghouts et al. observed increased insulin sensitivity during exercise at several levels of intensity. Heath et al. studied athletes who stopped training for 10 days (15). On the 11^{th} day they were challenged with a glucose load and either exercised or rested. It was found that with the withdrawal of exercise training, plasma insulin concentrations rose markedly, confirming that acute exercise caused an increase in insulin sensitivity.

The mechanism underlying the benefits of acute and chronic exercise on insulin responses is still a matter of debate. However, a large number of studies support exercise as an advantageous practice to improve glucose metabolism. Many health programs worldwide have adopted exercise in the prevention and treatment of DM. However, the best duration, intensity, and form of the exercise has still to be fully defined.

In the present study, we tested the effect of a twenty-minute moderate intensity walk and its effect on insulin sensitivity in healthy subjects. The pattern of responses including reduced glucose and insulin concentration at 60 minutes is consistent with an acute increase in insulin sensitivity and glucose transport attributable to exercise. The small, but significant, rebound in insulin/glucose following exercise is harder to understand.

Most studies have examined insulin responses to glucose loads (such as Glucola®) rather than a meal. Glucose loads are easier to standardize and therefore may allow more reproducible results than a meal, where contents of CHO, lipids, and protein

are subject to variation. However, a meal with a defined caloric content was used in this study to mimic realistic eating patterns. A realistic meal with an appreciable fat content also affects gastric emptying and the hormonal milieu differently than a glucose load making it an advantage over glucose for insulin sensitivity studies.

Although high intensity exercise has been shown to delay gastric emptying (16), this was probably not of importance in our study as the intensity of exercise was well below the ventilatory threshold. Likewise, Feldman and Nixon (17) have demonstrated that low intensity exercise, similar to that undertaken in this study, does not slow gastric emptying of a meal. Thus, the slowing of gastric emptying by exercise is intensity related and should not be a factor at the intensities of exercise used in this study.

During high intensity exercise there is significant release of catecholamines that will tend to cause glucose release from the liver and can account for significant post exercise increases in glucose, and presumably insulin in response (18). The low intensity exercise in the present study did not likely result in a significant catecholamine response.

A decline in plasma insulin is crucial for the rise in glucose production during exercise. With a low intensity exercise, as used in the present study, Levitt et al (19) described a reduction in peripheral insulin concentrations and attributed that observation to a decrease in insulin secretion.

After consuming a standard meal both insulin and glucagon are increased. Insulin acts to increase glucose uptake, utilization, and storage, while glucagon mobilizes glucose by increasing hepatic gluconeogenesis and glycogenolysis. Kreisman et al.

studied the glucoregulatory responses to intense exercise after eating and found that exercise hyperglycemia in the postprandial state was delayed and diminished (19).

Moderate intensity exercise suppression of standard meal-induced insulin secretion may explain the observed decreases in insulin at 60 minutes postprandial with exercise. A well documented increased in glucose disposal and insulin sensitivity with exercise may explain the observed decreased in glucose at 60 minutes postprandial, despite decreased insulin. The blunted insulin response with exercise may result in a reduced response to the mixed meal-induced glucagon secretion and therefore explain the observed increase in insulin and glucose with exercise at 90 minutes postprandial.

Clinical Implications

From the present data we can conclude that a moderate intensity walk has a potentially beneficial effect on the insulin response to a meal, supporting our hypothesis. Regular exercise-induced increases in insulin sensitivity and associated blunting of postprandial hyperinsulinemia could potentially reduce net insulin exposure, which is a goal in the treatment of insulin resistance and DM.

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APPENDIX A

INFORMED CONSENT

ACUTE EFFECTS OF MILD EXERCISE ON POSTPRANDIAL GLUCOSE AND INSULIN RESPONSES

I, _____, give my informed consent to participate in a research study designed to determine the effect of postprandial (after a meal) exercise (a twenty minute walk) on insulin. I consent to presentation and publication of this study so long as the information is anonymous and disguised so that no personal identification can be made. I have been informed that although a record will be kept of my having participated in the study, all experimental data collected from my participation will be identified by number only.

(1) I have been informed that I will be required to perform a maximal exercise test on a treadmill before the actual testing begins. I have been informed that I will be required to eat two meals during the testing protocol which consists of a chicken sandwich, french fries and a coke. I have been informed that during one of the testing protocols a twenty minute walk will be required. I also have been informed that throughout testing blood draws will be performed in the Human Performance Lab in Mitchell Hall at University of Wisconsin- La Crosse by a trained phlebotomist.
(2) I have been informed that the general purpose of this study is to study the effects of insulin and how an after dinner walk affects these levels.
(3) I have been informed that with any exercise, the possibility of dizziness, fatigue, difficulty in breathing, and in rare instances, cardiac arrest, stroke, or even death. The risk of exercise related complication is approximately 6/10, 000 tests for all complications and 1/10,000 tests for serious complications. I declare that I am not aware of any pre-existing conditions such as heart disease, lung/respiratory conditions, prone to fainting or seizures, and blood-borne contagious diseases. I may become fatigued during the exercise session on the treadmill. I may also have a sore arm due to the drawing of blood samples.
(4) I have been informed that there are not "disguised" procedures in this study. All procedures can be taken at face value.
(5) I have been informed that the investigator will answer questions regarding the procedures of this study. I have been informed that I am free to withdraw at any time without penalty.

(6) I have been informed that Lia Lansky, a graduate student in the Cardiac Rehab/Adult Fitness program at UWL will conduct the tests. She may be reached at (608) 782-2059. The thesis chairperson will be Carl Foster, PhD (608) 785-8687. Questions regarding the protection of human subjects may be addressed to Dr. Dan Duquette, Chair, University of Wisconsin-La Crosse Institutional Review Board for the Protection of Human Subjects, (608) 785-8124.

_____ _____

Participant Signature Date
(I have received a copy of this Informed Consent Form)

_____ _____

Witness Signature Date

APPENDIX B

AHA/ACSM HEALTH/FITNESS FACILITY PREPARTICIPATION SCREENING QUESTIONNAIRE

AHA/ACSM Health/Fitness Facility Preparticipation Screening Questionnaire

Assess your health needs by marking all *true* statements.

History
You have had:
__ a heart attack
__ heart surgery
__ cardiac catheterization
__ coronary angioplasty (PTCA)
__ pacemaker/implantable cardiac defibrillator/rhythm disturbance
__ heart valve disease
__ heart failure
__ heart transplantation
__ congenital heart disease

If you marked any of the statements in this section, consult your healthcare provider before engaging in exercise. You may need to use a facility with a medically qualified staff.

Symptoms:
__ you experience chest discomfort with exertion.
__ you experience unreasonable breathlessness.
__ you experience dizziness, fainting, blackouts.
__ you take heart medications.

Other health issues:
__ you have musculoskeletal problems.
__ you have concerns about the safety of exercise.
__ you take prescription medication(s)
__ you are pregnant.

Cardiovascular risk factors:
__ you are a man older than 45 years.
__ you are a woman older than 55 years or you have had a hysterectomy or you are postmenopausal.
__ you smoke.
__ your blood pressure is greater than 140/90.
__ you don't know your blood pressure.
__ you take blood pressure medication.
__ your blood cholesterol level is >240 mg/dL.
__ you don't know your cholesterol level.
__ you have a close blood relative who had a heart attack before age 55 (father or brother) or age 65 (mother or sister).

__ you are diabetic or take medicine to control your blood sugar. __ you are physically inactive (i.e. you get less than 30 minutes of physical activity on at least 3 days per week). __ you are more than 20 pounds overweight.	*If you marked two or more of Statements in this section, you should consult your healthcare provider before engaging in exercise. You might benefit by using a facility with a professionally qualified exercise staff to guide your exercise program.*
__ None of the above is true.	*You should be able to exercise safely without consulting your healthcare provider in almost any facility that meets your exercise program needs.*

AHA/ACSM indicates American Heart Association/American College of Sports Medicine.

APPENDIX C

REVIEW OF LITERATURE

Association of Type 2 Diabetes Mellitus with Hyperinsulinemia and Insulin Resistance

Controlling fuel homeostasis following a meal (in the net anabolic state) is the paramount role of insulin. Three main tissues, including the liver, adipose tissue, and muscle, respond vigorously to insulin (1). Insulin stimulates uptake, utilization, and storage of glucose and other energy substrates by cells (2). After a meal, blood glucose concentrations increase, reaching a peak after thirty minutes to one hour. Blood glucose returns to normal (90-110 mg/dl) within 2 or 3 hours after ingesting the meal (2) due to pancreatic insulin release to the circulation. Insulin promotes conversion of glucose to glycogen, storage of amino acids as protein, and synthesis of triglycerides while inhibiting lipolysis (2). Opposite actions occur in the fasting (net catabolic) state, and these effects are mediated by the sympathetic nervous system and the pancreatic hormone glucagon. Glucose levels are low while in the fasting state resulting in low insulin levels. In this situation, the body uses fat as the source of energy and both glycogen and protein breakdown eventually provide glucose to glucose dependent organs such as the brain.

Major problems arise when glucose homeostasis is impaired leading to the disorder known as diabetes mellitus (DM). DM can be classified as two rather different disorders: Type 1 (formerly called insulin-dependent DM) and Type 2 (formerly called non-insulin-dependent DM) (1). These are caused, respectively, by a deficiency of insulin or a resistance to insulin action, both which lead to hyperglycemia. Type 1 DM is characterized by a deficiency of insulin and is treated with insulin to control hypoglycemia. However, Type 2 DM, which may be associated with low, adequate, or

even elevated insulin but still inappropriate hyperglycemia, accounts for 90-95% of DM cases in the United States (3).

Insulin resistance is found among Type 2 patients and may occur as normal or high amounts of insulin produce subnormal biological responses (4). It has been found that insulin resistance initially leads to hyperinsulinemia, defined as plasma insulin higher than expected for a given plasma glucose concentration (4). Even without overt Type 2 diabetes, hyperinsulinemia has been found frequently in individuals with coronary artery disease and is believed to affect 25% of the population (5). Hales and Randle reported high ratios of plasma insulin to glucose in Type 2 DM patients (6). Over the following years there were numerous studies confirming hyperinsulinemia as the primary defect in Type 2 DM patients. It is now evident that most Type 2 DM patients are insulin resistant and this promotes exaggerated responses to glucose loads causing hyperinsulinemia (7).

Relationships Among Hyperinsulinemia, Hyperlipidemia, and Endothelial Damage

Hyperlipidemia is an established risk factor for cardiovascular disease. Elevated triglycerides and reduced high-density lipoprotein (HDL) cholesterol levels occur in parallel with hyperinsulinemia (8). The San Antonio Heart Study showed that fasting insulin levels could predict decreased levels of HDL and high levels of triglycerides in blood (8). Other studies have found that insulin resistance and hyperinsulinemia are associated with the occurrence of smaller, denser low-density lipoproteins (LDL). In a study by Reaven et al., 100 normal adults were examined to look at the changes in triglycerides, and high density lipoprotein cholesterol. The purpose of the study was to

see if the subjects who were identified as having small low-density lipoprotein particles were also insulin resistant. It was found that individuals with a small, dense LDL particle profile were more likely to be insulin resistant, glucose intolerant, hyperinsulinemic, hypertensive, and have a lower HDL cholesterol concentration (9).

An excess of circulating LDL and its cholesterol content has been directly linked with the initial stages of atherosclerosis development. Oxidized LDL particles damage the endothelium which in turn attracts immune cells to infiltrate the blood vessel walls. Therefore, the increase in small, dense LDL particles, triglycerides, and low HDL are compatible with Type 2 diabetics being at risk for atherosclerosis and subsequent cardiovascular disease.

Microvascular complications are also well known features of DM. Coronary heart disease and stroke are also more frequent in diabetics than in non-diabetics accounting for the major causes of mortality in DM. The recent study by Despres et al establishes a link showing that hyperinsulinemia is an independent risk factor of cardiovascular disease (10). In this case control study an extensive array of plasma lipid and lipid proteins were measured and associated with cardiovascular risks and hyperinsulinemia.

In the Paris Prospective Study, a long term study on cardiovascular disease, it was found that plasma insulin levels predicted mortality due to cardiovascular disease in groups with similar levels of risk factors (11). Although in non-obese males blood pressure was a good predictor of heart disease, in obese males plasma insulin was a more reliable marker for cardiovascular disease.

Effect of Acute Exercise on Insulin Responses

Exercise has a favorable effect on insulin sensitivity in both healthy and diabetic populations. Differences between the effects of acute and chronic exercise on insulin sensitivity have been noted. Up to two hours after exercise the increase in postprandial glucose uptake by cells is due to both insulin dependent and independent mechanisms. A single bout of exercise enhances uptake of glucose into muscle cells by upregulating glucose transporter placement in the plasma membrane (12). Moreover, acute exercise has been shown to increase the binding of insulin to erythrocytes and the sensitivity of muscle to insulin.

Borghouts, et al. examined the role of exercise intensity on the improvement in insulin sensitivity. Eighteen untrained subjects, male and female participated in a one hour bicycle session with a duration of four weeks, five times per week. The training incorporated 3-minute bouts interspersed with 2 minutes at a lower exercise intensity. The high range intensities were 80% and 40% and the low range intensities were 40% and 20%. The results showed improvements in insulin sensitivity in high intensity training as opposed to low intensity training.

It is believed that the total amount of work is more important than the intensity of the exercise with regard to exercise-induced increases in insulin sensitivity. A study was conducted on the effects of exercise intensity on insulin sensitivity in women with non-insulin-dependent DM (13). Eight women participated in three groups of training: low intensity which consisted of treadmill walking at 50% of maximal oxygen consumption, high intensity, which consisted of treadmill walking at 75% of maximal oxygen

consumption, and a no exercise group. The energy expenditure was equal at both intensities due to adjustments of the duration during each exercise session. Plasma glucose response after a meal was the same among the three groups however plasma insulin was lower in both the high intensity and low intensity groups as compared with the no exercise group. Therefore, low and high intensity exercise were equally effective in improving insulin sensitivity.

Another study of the effects of exercise on glucose tolerance and insulin sensitivity was performed in trained individuals (14). Physically trained subjects stopped training for 10 days, on the 11^{th} day there was no change in VO_2max, body fat, or body weight. The peak rise in plasma insulin concentration in response to a 100-g oral glucose load was twice that in the group without the exercise as compared to normal exercising. Blood glucose concentrations also became elevated with no exercise. During the period of inactivity, insulin binding to monocytes were decreased. One exercise bout was performed on the 11^{th} day and the insulin binding returned to levels similar to the exercised state. The plasma insulin concentration was 55% higher and after a period of 10 days without exercise it rose to 120%. Consequently this study confirmed that acute exercise caused a blunted insulin response to a glucose load and, thus, an increased sensitivity to insulin.

A study that examined morbidly obese men found that after 7 days of exercising at 65% of their VO_2 peak for sixty minutes each day there were no changes in VO_2 peak or body composition with training. However, the fasting plasma insulin decreased significantly ($p < .05$) and the total area under the insulin curve from 0-2 hours, 75-g

glucose load was reduced by 23% (15). The main observation from this study is that exercise is indeed an effective way to improve insulin resistance even in obese individuals (15).

An enhancement of insulin stimulation of glucose entry into skeletal muscle is also seen during acute exercise in diabetic patients (16). However, the benefit of a single bout of exercise is short lived and the enhancement of insulin action is lost within a few days (3). Regular physical activity in patients with Type 2 diabetes is essential in lowering insulin and glucose (3). At around 72 hours after the last exercise session, the positive effects of exercise on glucose tolerance decline and another exercise session is recommended. A minimum of 1000 $kcal*wk^{-1}$ should be achieved through physical activity in patients with Type 2 diabetes (3).

Effect of Chronic Exercise on Insulin Responses

Physical training potentiates the beneficial effects of exercise on insulin sensitivity and it produces favorable changes in lipid and glucose metabolism which are relevant to Type 2 DM (12). Studies comparing trained with untrained individuals showed that trained subjects had a decreased insulin response to a glucose load, a lower basal insulin level, and a better insulin response during glucose infusion (12).

Six obese subjects with non-insulin-dependent DM underwent a series of tests to examine if there was an improvement of glucose homeostasis after exercise training. Before and after six to ten weeks of aerobic training sessions the subjects completed glucose tolerance, insulin secretory capacity, and insulin-induced glucose disposal tests.

The fasting plasma glucose declined in every subject and oral glucose improved in five out of the six subjects with training (17). The insulin-induced glucose disposal rates did not improve. Positive changes in glucose homeostasis and insulin secretion most likely occurred because of changes in fuel utilization during exercise. The continuous lowering of plasma glucose by acute exercise may have correlated directly with reductions in insulin secretion. In this study, it was concluded that regular aerobic activity is responsible for reducing fasting plasma glucose concentration and insulin secretion in obese and non-insulin dependent diabetics and improving glucose tolerance.

In a 6-year diabetes prevention study in China, 577 individuals with impaired glucose tolerance were divided into four groups: exercise only, diet only, diet plus exercise, and control. The individuals in the exercise only group were asked to increase their physical activity to one unit, which is similar to a 20-minute brisk walk. The occurrence of diabetes after six years was much lower in both exercise intervention groups. The results were exercise only = 41%, exercise plus diet = 46%, diet only = 44% and control = 68% (3).

The ongoing Finnish Diabetes Prevention study to assess the efficacy of a diet and exercise program in preventing or delaying Type 2 DM, provides evidence that a combination of weight reduction and increased physical activity can improve insulin action in Type 2 DM patients and delays the onset of Type 2 DM in patients with impaired glucose tolerance (18). Exercise also has a major role in improving insulin sensitivity, positively changing lipid abnormalities and reducing hypertension (3).

Physical training thus causes multiple adaptations in skeletal muscle that contribute to an increase in insulin sensitivity. This helps to control glucose homeostasis and induces positive changes in blood lipid profiles and lipid metabolism which lowers the risk of obesity and cardiovascular disease. However, differences in insulin sensitivity, age, degree of obesity, metabolic control, and cardiovascular health, among other factors, make the DM population heterogeneous. Recent studies have improved our understanding of the acute and chronic benefits of physical exercise regarding improvements in although the duration, intensity and type of exercise that best increases insulin action must be studied.

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