University of Alberta

The Effect of Exercise Intensity on Post Exercise Hexose Absorption

by

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A thesis submitted to the Faculty of Graduate Studies and Research
in partial fulfillment of the requirements for the degree of

Master of Science

Physical Education and Recreation

Spring 2010
Edmonton, Alberta

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Abstract

The effects of exercise intensity on post-exercise measures of intestinal permeability and absorption in sedentary and in active young men were examined in this study. Measures were compared bewteen rest, low intensity and high intensity interval exercise interventions. In spite of the exercise interventions being matched for work output, the high intensity interval intervention caused an increase in blood lactate and respiratory exchange ratio during the performance of exercise. No between intervention effect was found in hexose absorption. Active individuals had greater passive transcellular absorption (as measured with mannitol) than sedentary individuals after 2 hours of measurement. Significant differences in hunger measures were found between sedentary and active participants, with active participants recording increased measures of hunger. In conclusion, the hypothesis that that exercise intensity modulates post-exercise hexose absorption was not confirmed. However, measures of intestinal permeability suggest differences in digestive tract function may exist between sedentary and active individuals.

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Abbreviations

3-OMG	3-O-methyl-glucose
AUC	Area under the curve
BMI	Body mass index
GLUT2	Glucose transport protein 2
HPLC	High performance liquid chromatography
MBF	Mesenteric blood flow
OGTT	Oral glucose tolerance test
RPM	Rotations per minute
SGLT1	Sodium glucose cotransporter 1
$VO_{2\ max}$	Maximum observed oxygen consumption
$VO_{2\ max\ res}$	The resistance at which maximum observed oxygen consumption was identified

1 – Introduction

1.1 Introduction

The small intestine is a dynamic organ that has a limited capacity to respond to competing demands. It is the primary location of nutrient absorption, and, in this role, receives a significant percentage of total cardiac output (1). Blood flow to the small intestine is variable and depends on numerous factors, one of which is the presence of chyme (partly digested food). The presence of chyme causes an increase in blood flow to the small intestine to support digestion and maximize the absorption of nutrients (2; 3). The absorptive capacity of the small intestine depends on an adequate blood supply. In periods of reduced blood flow, the absorptive capacity of the small intestine is also reduced (4).

A significant reduction in blood supply to the small intestine can occur without causing regional hypoxia and tissue damage (5). This allows some capacity for reducing blood flow to the small intestine to support an increase to other tissues in times of need (5; 6). The degree to which the small intestine's blood supply will decrease to support cardiac output can be demonstrated in times when cardiac output is severely challenged. For example, in times of severe hypovolemia, blood supply to the small intestine can decrease to such an extent that damage to the small intestine can occur (7). This severe reduction in blood supply may save the individual in the short term but has been identified as a potential cause for multiple organ failure, which has an approximately 70% mortality rate (8).

This places the small intestine in two competing roles. One of these roles is as the primary location of nutrient absorption; the other role is as support for cardiac output. Both of these roles depend on the blood flow that the small intestine receives. Nutrient absorption requires adequate blood flow, but the support of cardiac output requires a sacrifice of that blood flow.

Hypovolemia is not the only cause of reduced intestinal blood flow. Exercise is a state in which a large amount of cardiac output is necessary to support the body and its increased work output. Only some of the increase in cardiac output is directed to the working muscle tissue moving the pedals (example: cycling) or hitting the ball (example: tennis). A significant portion of the increased cardiac output is diverted to support the additional work required of the heart, lungs, and respiratory muscles (6; 9). Blood flow to the small intestine is reduced to help support this increase in cardiac output (6; 10-12). The degree of the shift in blood flow depends on the intensity of exercise performed (6; 10). This presents the possibility that exercise can reduce nutrient absorption by decreasing blood flow to the small intestine, and does so in an intensity dependent fashion.

Experiments in humans have suggested (13; 14) that exercise can reduce the absorption of nutrients that are consumed during its performance. However, it is currently unknown if nutrients consumed shortly after exercise are affected in a similar way. This is important, because the vast majority of nutrients that the general population consumes are not consumed while the consumers exercise. If

a decrease in nutrient absorption continues beyond the cessation of exercise, this decrease may significantly affect nutrient absorption for the general population.

The examination of post-exercise nutrient absorption must consider numerous variables. As noted, exercise intensity may play an important role, because it influences the degree of blood-flow reduction to the intestine. Additionally, the human body can undergo significant adaptations in response to regular exercise, therefore the training status of the participants must also be considered. For example, given that a reduction in blood flow to the small intestine helps support cardiac output, active individuals may experience either reaction in response to exercise: greater reductions in blood flow than sedentary individuals to support greater cardiac output or lesser reductions in blood flow to maintain absorptive capacity.

1.2 Purpose and Hypothesis

The purpose of this study was to examine the effect of exercise intensity on post-exercise hexose absorption in sedentary and active young adult males. It was hypothesized that high-intensity exercise would cause a statistically significant reduction in post-exercise hexose absorption compared to a non-exercise (control) condition, while low-intensity exercise would cause an intermediate response. Hexose (3-O-methyl-glucose) absorption has been correlated with the absorption of glucose and other nutrients (15).

1.3 Significance of Study

Carbohydrates represent greater than 50% of the caloric intake of Canadians (16), and glucose is a primary component of these carbohydrates (17). Canada is currently experiencing an obesity epidemic; the prevalence of obesity (body mass index ≥ 30 kg•m^2) increased by 150% from 1985 to 2003 (18; 19). A reduction in carbohydrate absorption would cause a direct reduction in the calories available to the body, which, in turn, could promote a negative energy balance and, as a result, weight loss. Slowing the rate of glucose absorption and favoring a more stable blood-glucose pattern could also indirectly affect energy balance through altered feelings of hunger (20).

In addition to affecting energy balance, glucose absorption can also affect athletic performance. Glucose absorption is important in both long duration exercise performance and post-exercise recovery (21). Changing rates of post-exercise glucose absorption could then affect athletic performance and recovery from exercise.

Changes in glucose absorption can also have implications for people with type 2 diabetes. For example, the drug acarbose has been shown to prolong and decrease overall absorption of carbohydrates (primarily sucrose) (22). In subjects with impaired glucose tolerance, intake of acarbose has been shown to reduce the risk of progression to diabetes and to increase the regression to normal glucose tolerance (23). This suggests that interventions decreasing and/or slowing glucose absorption may have some protective effect against the development of diabetes.

1.4 Limitations and Delimitations

This study examines the effects of exercise intensity on post-exercise glucose absorption and tolerance. It does not, however, seek to examine the mechanisms by which exercise may decrease glucose absorption.

To accurately compare test results between sessions, the participants should be in the same nutritional state prior to testing. The diets of the participants were not recorded prior to the test sessions, though participants were asked to match their eating habits before each testing session. To limit the inconvenience of the study to the participants, diet was not specified on days before testing.

Because this is the first study to examine the effects of exercise intensity on post-exercise glucose absorption, we delimited our sample to a sample of young men (age 20-35 years) with a body mass index (BMI) of 18.5 to 30. This sample was selected for convenience of recruitment and to minimize potential confounding variables. Therefore, the results of the present study may not be generalizable to other groups, such as women or people affected by obesity or diabetes.

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Chapter 2 – Literature Review

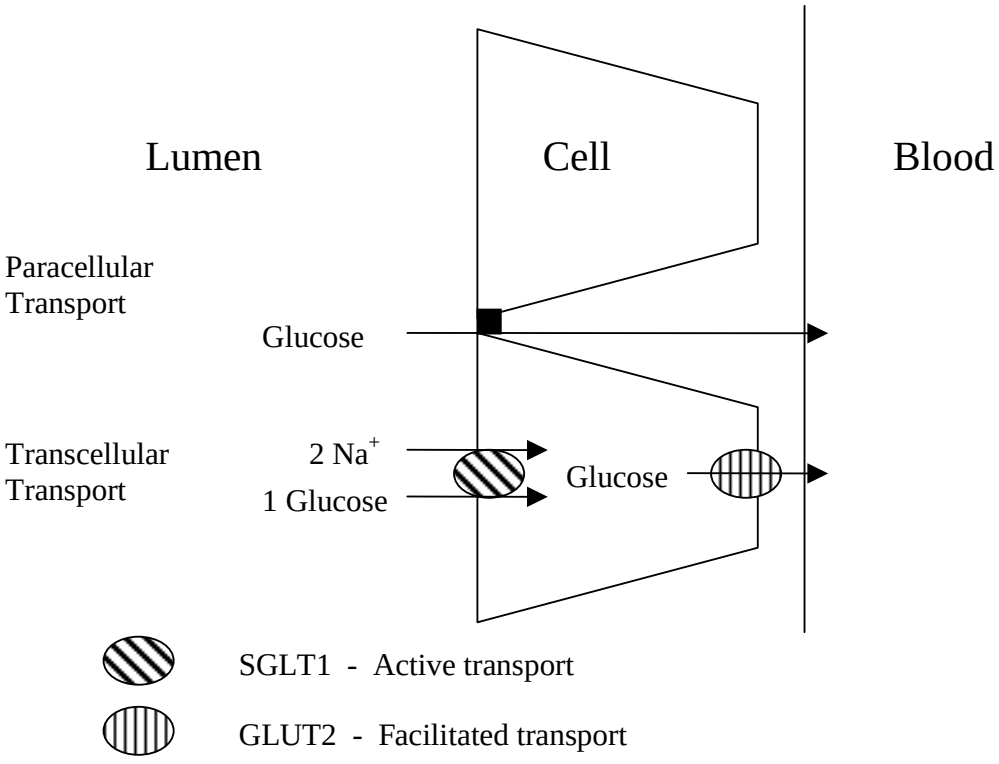
2.1 Pathways of Glucose Absorption

2.1.1 Transcellular Absorption

The human intestine must be versatile enough to handle high levels of glucose that are available post-prandially and low levels of glucose during an overnight fast. To accommodate these extremes of glucose concentration, the body has a complex set of transporters that can adapt to the large fluctuations. Glucose is transported across the cellular wall of the intestine via both transcellular (through the cells) and paracellular (between the cells) transport. Transcellular transport requires glucose to cross both the luminal and basolateral membranes of intestinal tissue. The transcellular transport of glucose uses both facilitated transport and active transport (2). Facilitated transport is the diffusion of a substance across a membrane and is facilitated by a protein transporter. Active transport requires a protein to expend energy to transport a substance from one side of a membrane to the other. In the intestine, the active transport of glucose across the luminal membrane occurs via a protein called sodium glucose cotransporter 1 (SGLT1). The SGLT1 protein derives its energy for active transport from the concentration gradient of sodium from the lumen into the cell. A separate glucose transport protein (GLUT2) then uses facilitated transport to transport glucose across the basolateral membrane from the cell to the blood (4).

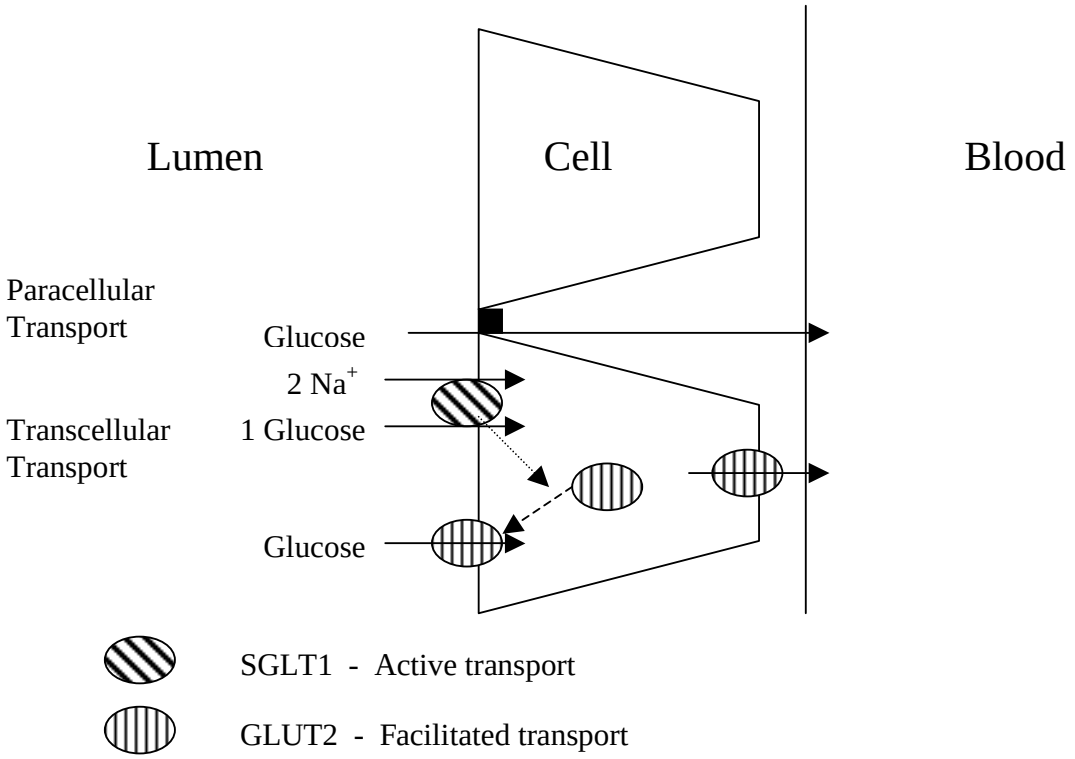
The activity of the SGLT1 protein is regulated by a variety of hormonal and metabolic signals, including insulin, gastrin, glucagon-like peptide 2, and insulin-like growth factor 1 (see Harmon and McLeod (4) for a complete review of SGLT1 activity regulators). Physical activity influences many of the hormonal and metabolic conditions which would cause SGLT1 activity to increase. An example of one hormonal change that will increase glucose absorption is the decrease in insulin that results from exercise (4). Figure 2.1 describes the pathways of glucose absorption during times of low luminal glucose.

Figure 2.1. Glucose transport in the small intestine during low intestinal glucose concentrations. Figure adapted from Harmon and McLeod (3; 4).



These pathways are supplemented during periods of high luminal glucose concentrations. A large amount of SGLT1 activity causes GLUT2 located in the cytosol to translocate to the luminal membrane. GLUT2 is a high-capacity, low-specificity transporter of glucose that, besides transporting glucose across the basolateral (blood barrier) membrane, can supplement SGLT1 in transporting glucose across the luminal barrier. In contrast to SGLT1, GLUT2 uses facilitated transport to transport glucose. This necessitates the transposition of GLUT2 to and from the luminal membrane, because in periods of low luminal glucose concentrations, GLUT2 would transport glucose out of the cell and into the lumen. See Figure 2.2 for a diagrammatic representation of glucose absorption during periods of high luminal glucose concentrations.

Figure 2.2. Glucose transport in the small intestine during high intestinal glucose concentrations. SGLT1 activates the translocation of GLUT2 from the cytosol to the luminal membrane. Figure adapted from Harmon and McLeod (3; 4)



2.1.2 Paracellular Absorption

In contrast to transcellular transport, paracellular transport moves glucose around the cell, instead of through. The quantity of glucose absorbed via the paracellular route is up for debate. Some research has stated that paracellular transport is the major route of absorption for glucose (5), but other research has disputed this point (2; 6). The proposed mechanism of paracellular absorption

begins with SGLT1. During glucose absorption, SGLT1 cotransports 2 sodium ions and a glucose molecule into the cell. This increase in cellular sodium concentration indirectly stimulates the contractile apparatus within the cytoskeleton. This contraction pulls the cell away from the tight junctions that exist between each cell. When these tight junctions open, glucose diffuses into the paracellular junction and is exposed directly to the blood vessels (5).

2.1.3 Blood Flow and Absorption

Regardless of the differences between transcellular and paracellular absorption, these pathways share a common dependency. Both transcellular and paracellular absorption benefit from a strong concentration gradient between the cell and blood stream. To maintain this concentration gradient, blood flow must move glucose away from the intestine and decrease the intestine's glucose concentration. It has been shown theoretically (via mathematical modeling) (5; 7) and experimentally (8; 9) that both transcellular and paracellular absorption depend on blood flow to attain maximal glucose absorption.

2.2 Intestinal Blood Flow

As previously indicated, blood flow is important in maintaining optimal glucose absorption. Blood flow to the small intestine branches off of the descending aorta into the superior mesenteric artery. Superior mesenteric artery blood flow is classified as part of splanchnic circulation, which encompasses all blood flow to the abdominal portion of the digestive tract (10).

2.3 Duration of Glucose Absorption

For exercise to affect post-exercise nutrient absorption, it must exert an effect on the intestines for some, if not all, of the time during which the nutrients are being absorbed. Measurements of glucose absorption have shown that, during an oral glucose tolerance test, glucose absorption occurs over approximately 4 hours, but that, during a meal, absorption occurs over an even longer period. See Figures 2.3 and 2.4, which are taken directly from Dalla Man et al., 2006 (11).

Figure 2.3. The rate of glucose absorption (Ra) during an Oral Glucose Tolerance Test (OGTT) as measured by a tracer-tracee clamp technique. The gray area indicates the range of variability with the line defining the observed mean. Figure taken directly from Dalla Man et al.(3)

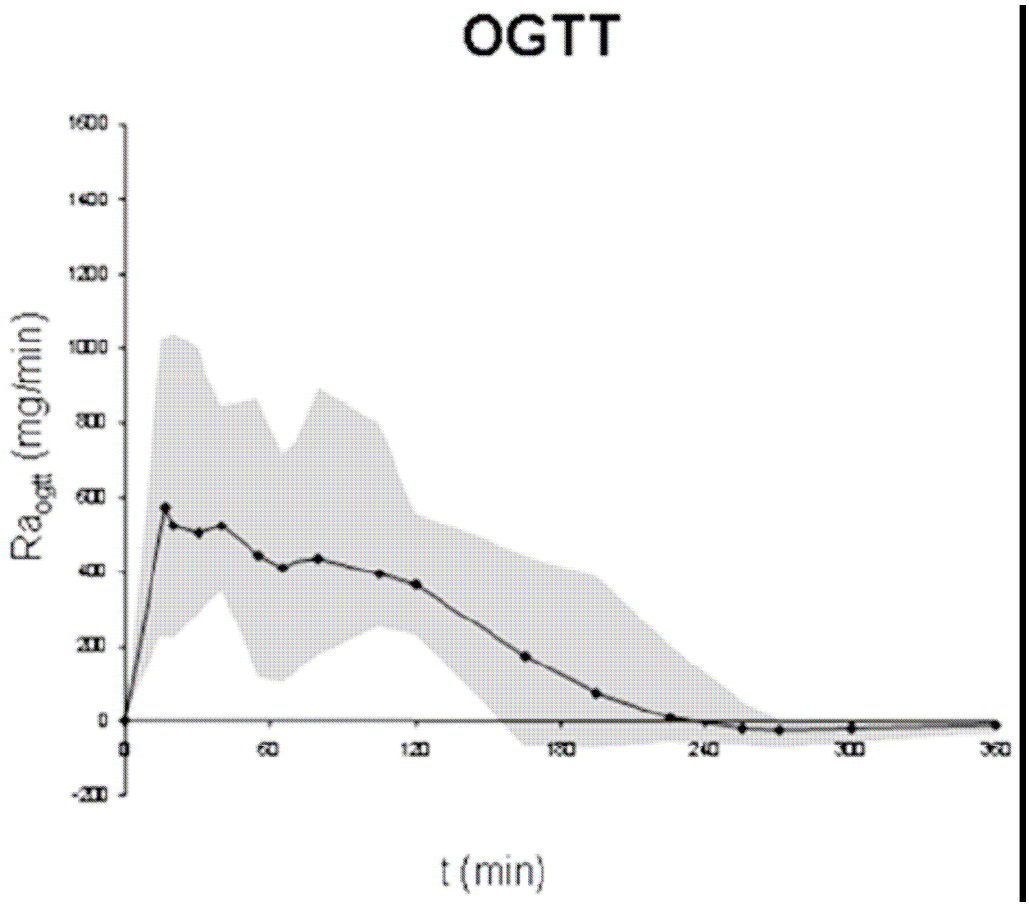
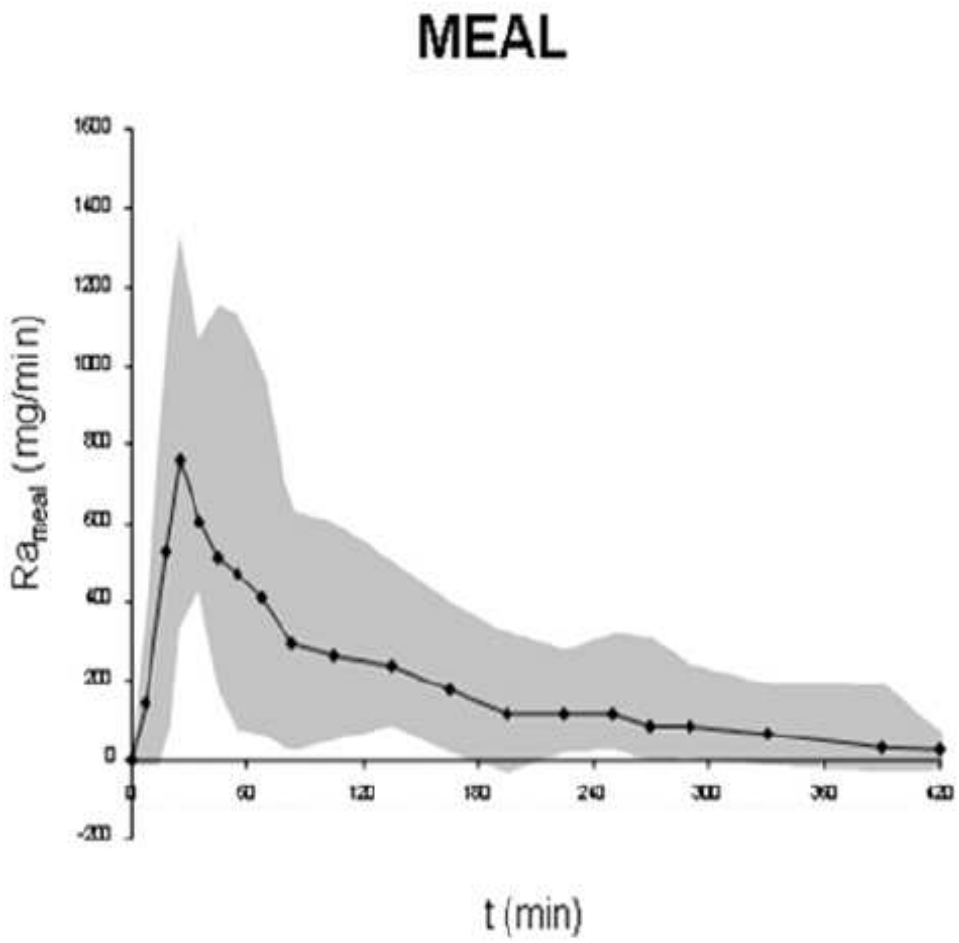


Figure 2.4. The rate of glucose absorption (Ra) immediately after consumption of a mixed meal (10 kcal/kg, 45% carbohydrate, 15% protein, and 40% fat) as measured by a tracer-tracee clamp technique. The gray area indicates the range of variability with the line defining the observed mean. Figure taken directly from Dalla Man et al. (1)



2.4 Glucose Absorption and Exercise

Pencek et. al. demonstrated that exercise creates a beneficial environment for glucose absorption (12), showing that glucose absorption increased significantly after exercise in the dog.

Contrasting the findings of Pencek et. al, van Nieuwenhoven et al. demonstrated decreased glucose absorption when consumed during exercise in man (13). The results of the Pencek experiment using the dog model cannot be generalized to humans because the physiological responses to exercise vary between species. Experiments on blood flow and exercise in the dog have yielded interesting results. Burns et al. analyzed the effects of digestion and exercise on mesenteric blood flow (MBF) in the dog (14). The findings show that dogs demonstrate little to no change in MBF during intense exercise. These findings are supported by the work of Fronek et al. (15), who examined similar variables. Scher et al. compared the sympathetic and parasympathetic responses of dogs and man (16). Scher's findings show that the sympathetic nervous system plays a reduced role in regulating blood pressure in the dog than it does in man. In humans, the sympathetic nervous system plays a role in the fight-or-flight response, shunting blood away from the viscera.

Lang et al. further investigated on human subjects. They examined the effect of exercise intensity on glucose absorption (using 3-O-methyl-glucose (3-OMG) as a marker) during exercise. They compared 3-OMG absorption during rest and during exercise at 30%, 50%, and 70% of $VO_{2\,max}$. Exercise at both 30%

and 50% of $VO_{2\ max}$ caused no statistically significant change in 3-OMG absorption as compared to rest. However, 70% $VO_{2\ max}$ decreased 3-OMG absorption during exercise as compared to rest (17).

Most calories consumed by the general population are not consumed while they are exercising at all, let alone during exercise at an intensity of 70% $VO_{2\ max}$ or greater. It is currently unknown if the reduced absorption extends to sugars consumed shortly after high-intensity exercise (a time period in which calories are more likely to be consumed).

2.4.1 Mesenteric Blood Flow, Glucose Absorption and Exercise

As stated by Scher (16), the human body experiences a significant sympathetic response to exercise, shunting blood away from the viscera to maintain blood pressure in periods of increased cardiac output. Granger et. al. found that sympathetic nervous system activity causes a decrease in intestinal capillary blood pressure and filtration (in this context, *filtration* refers to the movement of fluid in the blood through the capillary wall) (18). In humans, much research has investigated the relation between MBF and exercise. Qamar and Read (19) found that MBF decreased in response to exercise (treadmill, 5 km/h, gradient 20%, duration 15 minutes) in humans. They found a 43% decrease immediately after exercise, a 29% reduction five minutes after exercise, and a 24% reduction 10 minutes after exercise. This was corroborated in a study by Perko et al. (20), in which cycling at an intensity corresponding to 75% $VO_{2\ max}$ (30 minutes in duration) caused a 32% reduction in MBF during exercise. Pricher

et. al. (21) measured splanchnic blood flow (which includes mesenteric artery blood flow) and found a reduction that lasted for over an hour after the completion of exercise (15.9% at 1 hour post exercise, 3.9% 2 hours post exercise) though not statistically significant (cycling, 60% $VO_{2\,max}$, 60 minutes). Rowell, in 1973, published a comprehensive literature review comparing heart rate during exercise and splanchnic blood flow; this review found an inverse relationship between heart rate and splanchnic blood flow (1). Taken together, these studies suggest that MBF can be dramatically reduced during and immediately after exercise, but that the reductions are much less pronounced in the hours following exercise. This may have implications for the timing of meals (eating before, during, or after exercise) and glucose absorption.

As previously mentioned, dog and man display different changes in glucose absorption and MBF in response to exercise. However, what has not been discussed is the importance of MBF in relation to glucose absorption. Upon ingestion of food, the body increases blood flow to the intestines, via the mesenteric artery, to assist in the absorption of nutrients (22; 23). Increased blood flow allows better maintenance of the concentration gradients that drive absorption in the intestine (5). Evidence that reduced intestinal blood flow causes a reduction in glucose absorption was found in some of the first studies on this topic. Nelson and Beargie were investigating the link between sodium and glucose absorption (recall that the SGLT1 protein that is responsible for glucose absorption transports sodium and glucose in a 2:1 ratio) when they noticed that reduced blood flow in the abdominal aorta caused a reduction in glucose

absorption (24). This work on glucose absorption and blood flow was corroborated by Varro (25), who restricted blood flow directly to a section of small intestine. Lichtenstein and Winne analyzed the absorption of 3-OMG and encountered similar results (8). Ochsenfahrt found that drug absorption was also dramatically affected by blood flow (26), showing that the absorption of many substances may be negatively affected by reduced blood flow to the intestines.

However, this was not all that was found. Nelson and Beargie (24) found two notable results:

i. Reducing blood flow causes a reduction in intestinal absorption.

ii. Restoring blood flow to normal from a reduced state does not cause an immediate return to the rate of absorption that was in place before the blood-flow reduction.

Measuring absorption during reduced blood flow and then measuring absorption during progressively increasing amounts of blood flow found that absorption did not increase in proportion with the return of blood flow. This implies that the initial reduction in blood flow had a lingering effect on glucose absorption after blood flow had been restored. This contrasts with their findings on blood-flow reduction, when blood flow is reduced, there is a proportional reduction in absorption. The fact that the restoration of blood flow does not cause a simultaneously proportional return of absorption may be due to the structure of intestinal microcirculation and to its ability to distribute blood flow in parallel, rather than in series. The parallel distribution of arteries allows the intestinal wall to distribute blood flow away from the villi in times of low blood flow (27). This

implies that villus circulation, which has been shown to be key in nutrient absorption (5), may not be fully restored after upstream blood flow (such as blood flow in the mesenteric artery) has been restored.

2.4.2 The Competing Effects of Exercise and Food Consumption on Mesenteric Blood Flow

Exercise causes a decrease in MBF, which may cause a reduction in the absorption of glucose. But what about the competing effect of food intake on increasing MBF? Would that counteract the effect that exercise may have in regulating blood flow? Two of the studies previously mentioned attempted to answer this question by including a prandial session. In the previously mentioned study by Qamar and Read (19), the authors found that food consumption decreased but did not nullify the effect of exercise on MBF. (Protocol: treadmill, 5 km/h, gradient 20%, duration 15 minutes, 390 kcal provided during first 10 minutes of exercise, MBF reduction found to be statistically significant 10 minutes post exercise). The previously mentioned study by Perko also used a prandial session and confirmed a reduction in MBF while exercising in a prandial state (20). (1000 kcal 40 minutes pre-exercise, cycling, 75% $VO_{2\ max}$ for 30 minutes, 22% reduction in MBF during exercise as compared to post-prandial rest). Puvi-Rajasingham et al. found a 68% reduction in MBF during exercise in a fed state (28). (550 kcal 30 minutes pre-exercise, cycling at an incremental difficulty of 25-75 watts for 9 minutes, 68% reduction from resting post-prandial MBF). An experiment by Eriksen and Waaler (29) obtained results that

contradicted the above findings. They found that the stimulus to increase blood flow due to food consumption overcame the effect of exercise and that the effect of exercise on MBF was negligible even in the fasting state (30). (recumbent cycling, 75% $VO_{2\ max}$, 4 minute duration). These distinctly different findings could be explained by the duration of exercise used in each experiment. As Eriksen and Waaler mention in their paper, it is possible that the duration of exercise they used was not long enough to initiate a vascular response. The duration of exercise used by Eriksen and Waaler (4 minutes) was much shorter than that used by Qamar and Read (15 minutes), Perko et al. (30 minutes), and Puvi-Rajasingham et al. (9 minutes).

2.4.3 Exercise Intensity and Mesenteric Blood Flow

A reduction in glucose absorption during exercise has already been shown. However, an intensity-dependent effect has not. All of the experiments that showed a reduction in glucose absorption used a fixed intensity (19; 20; 28) and did not allow for a comparison between high- and low-intensity exercise. But other experiments compare blood flow at varying exercise intensities. Armstrong et al. explicitly measured the effect that exercise intensity has on blood flow and distribution (31). They observed an intensity-dependent decrease in blood flow to the duodenum (a section of the small intestine that immediately precedes the jejunum) during exercise. The change in blood flow was remarkable: a >90% decrease as the body shifted from rest (83ml/min/g) to exercise at VO_2 max (7 ml/min/g). Unfortunately, the experiment was performed on miniature swine and,

as described before in relation to the dog, there may be a strongly species-specific response to exercise. The results found in the miniature swine cannot be directly generalized to humans.

A study that is more applicable is a comprehensive review of literature by Rowell (1). He found a linear relationship between heart rate and reduced splanchnic blood flow in humans (1). A combination of the data that show that reduced intestinal blood flow causes a reduction in glucose absorption and the data from Rowell allows one to argue that a reduction in glucose absorption may result from an increase exercise intensity.

Figure 2.5 Effect of exercise intensity on splanchnic blood flow, as taken from Rowell (1) pg. 128

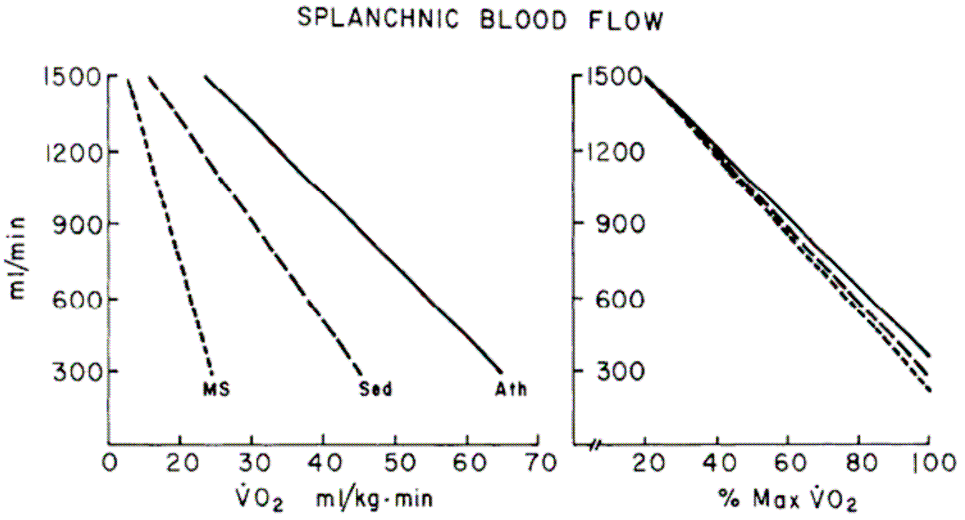


Fig.1. Decreases in splanchnic blood flow (SBF) with increasing oxygen uptake ($\dot{V}_{O_2}$) (per kg of body weight) up to maximal oxygen uptake ($\dot{V}_{O_2}$ max) in three groups: MS, patients with pure mitral stenosis; Sed, normal sedentary young men; and Ath, endurance athletes. Each line on the left ends at the average $\dot{V}_{O_2}$ max/kg of the group. On the right, lines are superimposed when data is related to per cent of $\dot{V}_{O_2}$ max. Adapted from Rowell et al. (26,29,38) and Blackmon et al. (3).

2.5 Selection of Experimental Exercise Intensities

In light of the evidence described above, to directly compare exercise intensities accurately, the effects of duration and energy expenditure must be controlled. Otherwise, any difference between the two protocols may be due not to intensity, but to differences in duration or energy expenditure. To match the duration and energy expenditure of low-intensity exercise, high-intensity exercise must be performed in intervals. Interval exercise will involve periods of high-intensity activity interspersed with periods of low-intensity activity, so that the total work performed is the same for each protocol. Both the low- and high-intensity exercise protocols must be obtainable for the given duration. Hetzler et. al. found that there was a strong relationship between blood lactate and Ratings of Perceived Exertion during exercise (32). To ensure that the low-intensity protocol is feasible for a sedentary male to perform continuously for an extended period of time, the exercise intensity must be below that individual's ventilatory threshold.

With that in mind, ventilatory threshold would be an excellent choice for deciding on the exercise intensities to use in this experiment. However, Rowell (1) found that splanchnic blood flow was inversely proportional to % VO_2 consumption. The data from Rowell (1) show that exercise intensity should be based on $VO_{2\ max}$ to ensure that a shift of blood flow occurs. This experiment will use ventilatory threshold to constrain the exercise protocols to ensure that they are feasible.

Studies investigating the intensity at which ventilatory threshold occurs in male subjects have generally reported an average ranging from 56% to 69% VO_2

$_{max}$. Inbar et. al. found ventilatory thresholds of 58.2 ± 4.5% and 68.8 ± 5.3% $VO_{2\ max}$ for healthy males 20-30 years old and 61-70 years old respectively (33). Jones et. al. found ventilatory threshold to occur at 56 ± 12% of $VO_{2\ max}$ in a sample of healthy males 15-71 years old (34). In a study of younger (age 23.4 ± 4.3) physically active men, Palka et. al. found ventilatory threshold occurring at 61.0 ± 7.8% of $VO_{2\ max}$ (35).

In a clinical study, Hansen et. al. recommended 40% $VO_{2\ max}$ as the lower limit for the non-clinical population (the population that is free from cardiovascular impairment) (36). Using an intensity of 40% $VO_{2\ max\ res}$ for the low intensity-protocol will ensure that the intensity is below the lactate threshold for the participants. Having a ventilatory threshold below 40% $VO_{2\ max}$ will be part of the exclusion criteria for this experiment.

For previously described reasons, high-intensity exercise must have a work output equal to that of low-intensity exercise while having an identical duration. Interval exercise will allow a total work output that is similar to that of the low-intensity exercise within the same duration of time, while still exposing the subject to higher exercise intensities. A previously performed pilot study uncovered two limitations on the actual implementation of high-intensity interval exercise on a mechanically braked cycle ergometer. A resistance of approximately 20% of the resistance used to achieve $VO_{2\ max}$ ($VO_{2\ max\ res}$) is the lowest functional resistance on the mechanically braked cycle ergometer; any less resistance causes inefficiencies because the wheel spins ahead of the pedals. Efficiently and consistently changing the resistance on the bike takes time;

minimizing the number of resistance changes would benefit the consistency of the study. Using this information, an exercise protocol of 20% $VO_{2\ max\ res}$ for 3 minutes, followed by 100% $VO_{2\ max\ res}$ for 1 minute was defined. The low- and high-intensity exercise protocols have an identical average work output, to help ensure that the protocols involved equivalent caloric expenditures.

Pilot testing that compared the high- and low-intensity protocols described above found similar caloric expenditures. The high-intensity protocol was found to have a higher caloric expenditure by 3.7% ± 6.7 % (n=6, p = 0.63).

All subjects were able to complete both protocols, and, anecdotally, most subjects stated that the high-intensity protocol was the more enjoyable of the two.

2.6 Summary

Glucose is absorbed both actively and passively, and, regardless of the path of absorption, glucose absorption depends on adequate blood flow to achieve maximal absorption. The absorption of glucose from a meal occurs over several hours (>4 hours). Exercise decreases blood flow to the splanchnic region in an intensity-dependent fashion. This reduction in blood flow to the intestinal region is associated with a reduction in glucose absorption. Exercise has been shown to decrease both mesenteric blood flow and glucose absorption at high exercise intensities. Blood flow to the mesenteric region does not immediately return after exercise ceases. In addition to the delay in the restoration of mesenteric blood flow, microvilli circulation may be further delayed. This microvillus circulation is key in supporting optimal glucose absorption. These delays suggest that the

decreases in glucose absorption that have been observed during exercise may continue after exercise.

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3- METHODS

3.1 Participants.

Fifteen young (20-35 years of age) men were recruited for this study. Participants had no known condition of the heart, liver, digestive tract, or endocrine system. They had not been diagnosed for diabetes or other glucose regulatory disorder, and they did not have family histories of glucose regulatory disorders. They were weight stable (no self-reported weight fluctuations of more than 5 pounds in the past 3 months) and were not taking any prescribed medications. Subjects did not currently use tobacco products and were required to abstain from consuming alcohol for 5 days before each study day.

Initially, only sedentary individuals were recruited. *Sedentary* was defined as participating in no more than 1 planned 30-minute-or-longer bout of physical activity per week. However, in preparation for this experiment, a pilot study on active individuals was conducted using an identical exercise and oral glucose tolerance test (OGTT) protocol used in this study, but did not measure intestinal permeability. This pilot work suggested a lower area under the blood-glucose curve after high-intensity exercise compared to after low-intensity exercise (1). This difference in glucose was not found between exercise protocols in the initial group of sedentary participants (2). Consequently, the inclusion criteria were modified to also include physically active males *(physically active* was defined as engaging in 2 or more 30-minute-or-longer bouts of physical activity per week). Seven participants were classified as sedentary, and eight were classified as active.

3.2. Body composition assessment.

Body composition assessment was performed by hydrostatic weighing. Vital capacity was assessed using a spirometer with the participant submerged up to the neck in water. Vital capacity measurements were taken repeatedly until 3 measurements were taken showing a range of less than of 200 mL. Vital capacity was taken to be the average of these three values. Residual volume was calculated to be 0.24 of measured vital capacity (3). Underwater weighing was done at residual volume. Body fat was calculated using the Brozek formula (4), and measurements were taken until 3 measurements showed a variation of less than 0.5% body fat. Body fat was taken to be the average of these three values.

3.3. Cardiorespiratory fitness assessment.

Participants underwent a graded exercise test on a Monark Ergomedic 884E cycle ergometer. Participants were required to maintain a cadence of 60-65 RPM throughout the test. This cadence was selected based on previous research into the preferred cadence of untrained individuals (5). Resistance began at 0.5 Kp and was increased by an additional 0.5 Kp every three minutes. Testing was terminated on volitional failure or if the subject was unable to maintain 60 RPM for any 5-second period. Metabolic data was measured using an open-circuit spirometer (a Parvomedics Truemax 2400 metabolic measurement system). Heart rate was measured using a Polar T31 heart rate monitor. VO_2 peak was taken as the highest 30-second average observed during testing. The maximum resistance

(max-res) reached and maintained for a period greater than or equal to one minute was recorded for future use during the exercise protocols.

3.4. Experimental Protocol.

Each participant was required to perform 3 different test sessions. The order in which the test sessions was performed was random. Test sessions were performed at least 4 days apart. The participants were asked to come to the lab after a 10-hour overnight fast and having not consumed any food or beverages that morning.

The participants were instructed to rest for the first 30 minutes after arriving at the lab. After this rest period, the intervention (rest, low-intensity exercise, or high-intensity exercise) was performed. The intervention lasted for 45 minutes (a 5-minute warm-up plus a 40-minute intervention). Fifteen minutes after completing the intervention, the participants were asked to void their bladders. They then consumed an oral glucose tolerance beverage (Trutol®, 75g of glucose) with added lactulose (5g), mannitol (2g), 3-O-methyl-glucose (3-OMG)(5g), and C^{13} labeled glucose (25mg). The C^{13} labeled glucose was packaged with 15g glucose, bringing the total amount of glucose consumed to 90g.

For the rest intervention, subjects sat quietly for a 45-minute period. This accounted for the 5-minute warm-up and 40-minute exercise intervention used in the other two tests. On the exercise days, the warm-up consisted of cycling at 60-65 RPM against no resistance. During the low-intensity exercise intervention, the

subject cycled at 40% of his previously recorded $VO_{2\ max\ res}$ at 60-65 RPM for 40 minutes. The high-intensity exercise intervention was composed of 10 intervals, each 4 minutes in duration. Each interval began with a resistance of 20% of $VO_{2\ max\ res}$ for 3 minutes and was then followed by 1 minute at 100% $VO_{2\ max\ res}$. Participants did not rest between intervals. The intervals of the high-intensity intervention exposed the participant to high intensities while matching the average resistance (40% $VO_{2\ max\ res}$) of the low-intensity intervention.

Subjects were given 250 mL water when they arrived at the lab and 250 mL 1 hour after they consumed the glucose beverage. Additionally, subjects were given a Chocolate Ensure® meal replacement beverage (Abbott Laboratories, Saint-Laurent, Quebec) 2 hours after they consumed the glucose beverage. The meal replacement was given to reduce hunger and to standardize food consumption, since subjects were required not to consume food or beverages outside of the lab from the morning until the final urine collection. Two participants displayed symptoms of reactive hypoglycemia as defined by having a blood glucose below 3 mmol/L 2-4 hours after a high glucose load. All incidents of hypoglycemia occurred 3.5 hours after participants consumed the OGTT beverage (1.5 hours after they consumed the meal replacement beverage). Upon identification of hypoglycemia the participants were immediately provided a meal (chosen by convenience, Sukiyaki Beef produced by Edo Japan restaurant, approximate nutritional information: 80g carbohydrate, 16g fat, 32g protein). One of these two participants (classified as active) displayed signs of reactive hypoglycemia during the rest session, and his remaining sessions were symptom

free. The other participant (classified as sedentary) displayed signs of reactive hypoglycemia for the rest session and the low-intensity session, with his high-intensity session being symptom free. Both subjects were requested to consult a physician regarding these symptoms. The participants were allowed to continue testing on the condition that they remain at our facility for observation until testing was complete and the protocol allowed them to break their fasts. Following these incidents, all participants were instructed to break the protocol and eat if they experienced signs of hypoglycemia (such as dizziness, weakness, tingling, or tremors). No other subjects reported symptoms or broke their fasts. This consumption of food during the period between leaving the lab and collection of the last urine sample would affect the 5-hour urinary lactulose / mannitol and 3-OMG measures.

Due to testing difficulties (the exclusion of 3-OMG from a limited number of test solutions, described in further detail in the examination of 3-OMG results) both of the subjects that experienced reactive hypoglycemia are excluded from 3-OMG analyses entirely. Statistical analysis of the remaining 5-hour intestinal absorption measures was done including and excluding the incidents of food consumption.

3.5. Measures.

Small intestine permeability was measured by urinary excretion of lactulose and mannitol (as well as their ratio: lactulose / mannitol). Lactulose is a reliable measure of paracellular absorption while mannitol is representative of transcellular absorption (6). Nutrient absorption can be effectively measured by

measuring 3-OMG (7; 8), particularly glucose absorption (9). However, recent research in pediatric patients with short bowel syndrome has shown that 3-OMG absorption is also correlated with fat and protein absorption (10). Another study analyzing nutrient absorption in surgically shortened rat intestine found little correlation between 3-OMG absorption and carbohydrate absorption but significant correlation between protein absorption ($r = 0.70$) and fat absorption ($r = 0.67$) (11). Urinary lactulose, mannitol, and 3-OMG were quantified via HPLC (12). Coefficients of variation for the HPLC methodology for mannitol, lactulose and 3-OMG are 2.5, 1.76 and 5.6 respectively. Briefly, urine was filtered through a 0.4μm filter. The filtrate was then diluted, deionized, and injected into a Dionex MA-1 ion exchange column. The sample was eluted with 400 to 600 mmol NaOH at a low rate of 0.4 mL/min. Detection was done using pulsed amperometric detection on a Dionex HPLC and quantified using peak areas. The intestinal permeability markers were provided alongside an oral glucose tolerance beverage. The purpose of this was to provide intestinal measurements alongside a reproducible nutrient load with the additional benefit of obtaining OGTT data. However, the addition of glucose to the intestinal permeability measures has been shown to modulate their absorption. Debru et al. (8) found that a 1.5 molar glucose solution decreased the lactulose / mannitol ratio as compared to a control (0 molar glucose) solution. Additionally, 3-OMG absorption was found to decrease in the presence of 1.5 molar glucose, but that decrease was not statistically significant (8). The solution provided in the present study had a 1.7 molar glucose concentration.

Capillary blood glucose concentrations were measured via finger prick with a One Touch Ultrasmart (LifeScan, Milpitas, CA) blood glucose meter. All blood glucose measurements were taken in duplicate, and the average was used for analysis. If the duplicate measures exhibited a difference greater than 1 mmol/L, a third measure was taken, and the average of all three measures was used for analysis. Measurements were taken immediately before the exercise or rest intervention, at 33 minutes during the intervention, and 10 minutes after the intervention. Additional measures were taken 15, 30, 45, 60, 90, and 120 minutes after consumption of the glucose solution (see Table 3.1).

Blood lactate measurements were taken with a Lactate Pro^{TM} blood lactate test meter (Arkay Inc., Shiga, Japan) via finger prick. Measurements were taken 33 minutes into the exercise or rest intervention and10 and 135 minutes after the exercise or rest intervention. All measures were taken in duplicate, and the average was used for analysis.

Average energy expenditure and RER were measured using a metabolic cart. Measures were taken to be the average over a 15 minute span. During performance of the high intensity exercise intervention the average was taken to be the average of 3 complete intervals (12 minutes). Energy expenditure was calculated using the modified Weir equation (13).

A 150mm visual analog scale was used to measure subjective ratings of desire to eat, hunger, fullness, and prospective food consumption (14; 15). Measures were taken immediately before the exercise or rest intervention, immediately before participants drank the glucose solution and 30, 60, and 120

minutes after participants consumed the glucose solution. These measures were used to identify any possible exercise-induced changes in appetite that have been identified in previous studies (16).

Immediately before subjects consumed the glucose beverage, they were requested to void their bladders (this urine was not collected). Urine was then collected 2 and 5 hours after subjects drank the beverage. Urine was collected in jugs containing 5 mL of a 10% thymol solution dissolved in isopropanol (used as an antibacterial agent). Two hours after they consumed the beverage, participants were asked to void their bladders into a collection jug. This sample was immediately weighed, then a 10 mL sample was removed and stored at -80°C. The jug containing the remaining urine was then placed on ice until 5 hours post beverage consumption. At 5 hours after the participants had consumed the beverage, they were again asked to void their bladder into the collection jug. Again, the weight of the jug was recorded and a 10 mL sample was stored at -80°C.

Table 3.1. Experimental Session Timeline

Time	**Activity**	**Measures**				
		Blood glucose	Blood lactate	Metabolic cart data collected (15 min.)	Hunger and appetite	Urine collection
0	Subject given 250mL water, rests					
30 min.	Begins warm-up/rest	X			X	
35 min.	Begin exercise/rest intervention					
60 min.				X		
68 min.		X	X			
75 min.	End exercise / rest intervention					
85 min.		X	X		X	
90 min.	Void bladder. Consume glucose solution					
105 min.		X				
120 min.		X			X	
135 min.		X				
150 min.	Consume water (250 mL)	X		X	X	
180 min.		X				
210 min.	Provide meal replacement beverage	X	X		X	X
390 min.						X

3.6. Statistical analyses

Students' T-Tests (independent) were used to identify statistically significant differences in baseline characteristics between the two groups (sedentary vs. active). A mixed between-within subjects ANOVA(split plot ANOVA) was done to compare the effects of exercise interventions and participant groups on exercise measures.

To analyse the relationships between experimental data from all three interventions, a mixed between-within subjects ANOVA (split-plot ANOVA) was

used. This allowed the simultaneous analysis of between-subject (sedentary vs. active) and within-subject effects (rest vs. low-intensity vs. high-intensity) and the analysis of any possible interaction effects between experimental condition and participant group. Pearson correlation coefficients were calculated to measure the strength of the associations among variables.

Statistical analysis was performed using Statistical Analysis System (SAS) software (version 9.1.3) using the proc glm function. An α of 0.05 was used to identify statistical significance.

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4- RESULTS

4.1 Participants

The participants who were considered physically active achieved a significantly higher VO_2 peak and a higher workload during initial subject testing ($p < 0.05$). No other differences, including height, weight, and % body fat, reached statistical significance (Table 4.1).

Table 4.1 Participant characteristics

	Sedentary n = 7	Active n = 8	p value
Age (years)	29 ± 5.2	26.6 ± 4.6	0.696
Body mass (kg)	77.2 ± 12.0	78.4 ± 8.8	0.748
Height (cm)	179.2 ± 4.5	179.8 ± 7.7	0.832
BMI (kg/m^2)	24.0 ± 2.9	24.3 ± 2.0	0.726
% Body fat	16.4 ± 6.9	12.4 ± 6.3	0.204
Fat free mass (kg)	63.5 ± 9.9	68.6 ± 5.3	0.230
VO_2 peak (mL $O_2 \cdot kg^{-1} \cdot min^{-1}$)	39.5 ± 6.9	52.2 ± 5.6	**0.005**
Resistance at VO_2 peak (kp)	3.7 ± 0.6	5.1 ± 0.7	**0.0004**

BMI= body mass index
Results shown as mean ± SD

4.2 Comparison of Exercise Interventions

A comparison between the high-intensity and low-intensity interventions (Table 4.2) found that the high-intensity session produced a higher level of blood lactate during and 10 minutes after exercise ($p < 0.05$), but not 2 hours 15 minutes after exercise. There were no statistically significant differences in blood lactate between active and sedentary subjects at any of the three times; consequently, their results have been pooled in Figure 4.1. A significant group-by-intervention interaction was observed for blood lactate 2 hours 15 minutes after exercise ($p < 0.05$): blood lactate concentrations were higher in the active subjects following low-intensity exercise but were lower following high-intensity exercise (as compared to measures of sedentary participants) (Table 4.2).

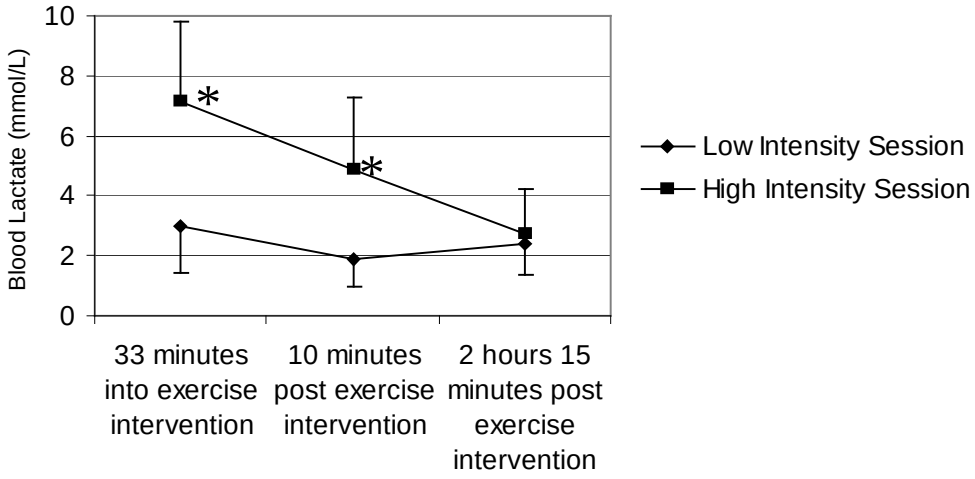

Figure 4.1 Blood Lactate (Error bars = SD)
* = statistical difference between exercise interventions (low intensity vs. high intensity) ($p < 0.05$)
Groups pooled in figure

Table 4.2 Comparison of Exercise Interventions

Measure and session		Sedentary n = 7	Active n = 8	Overall n = 15	Between-Groups Effect	Within-Subject Effect	Interaction Effect
Blood lactate during exercise intervention (mmol / L)	Low	3.06 ± 1.56	2.86 ± 1.66	2.96 ± 1.56	0.4913	<**0.0001**	0.7146
	High	7.59 ± 3.18	6.26 ± 2.5	7.11 ± 2.71			
Blood lactate 10 minutes post exercise intervention (mmol / L)	Low	1.85 ± 1.17	1.94 ± 0.78	1.90 ± 0.95	0.6400	<**0.0001**	0.2519
	High	5.39 ± 2.94	4.46 ± 1.86	4.89 ± 2.38			
Blood lactate 2 hours 15 minutes post exercise intervention (mmol / L)	Low	2.31 ± 1.03	2.43 ± 1.09	2.38 ± 1.03	0.2440	0.1734	**0.0117**
	High	3.51 ± 1.88	2.02 ± 0.61	2.72 ± 1.51			
Mean respiratory exchange ratio during exercise intervention (CO_2 L / O_2 L)	Low	0.92 ± 0.06	0.93 ±0.02	0.92 ± 0.04	0.6408	<**0.0001**	0.3461
	High	1.00 ± 0.04	0.98 ± 0.06	0.99 ± 0.05			
Mean respiratory exchange ratio 1 hour 15 minutes post exercise intervention (CO_2 L / O_2 L)	Low	0.91 ± 0.07	0.93 ± 0.04	0.92 ± 0.05	0.5821	**0.0136**	0.9904
	High	0.87 ± 0.04	0.89 ± 0.06	0.88 ± 0.05			
Average energy expenditure during exercise intervention (Kcal / min)	Low	7.35 ± 1.41	9.27 ± 1.21	8.38 ± 1.60	**0.0015**	**0.0405**	0.4260
	High	7.74 ± 0.88	10.11 ± 1.09	9.00 ± 1.55			
Average energy expenditure 1 hour 15 minutes post exercise intervention (Kcal / min)	Low	1.53 ± 0.24	1.57 ± 0.17	1.55 ± 0.20	0.2471	0.4203	0.6716
	High	1.50 ± 0.19	1.58 ± 0.12	1.55 ± 0.15			

Results shown as mean ± SD

In spite of being matched for work output, a within subjects effect was found when examining average exercise intervention energy expenditure ($p < 0.05$), with low intensity exercise found to have a 6.9% lower energy expenditure (Table 4.2). A between-subjects effect of 28% was also found when we examined intervention energy expenditure ($p < 0.05$) (Table 4.2). A difference in intervention energy expenditure between subject groups was expected, given that there was a 37% difference in resistance at VO_2 peak between groups ($p < 0.05$) (Table 4.1), which is the measure by which the exercise interventions' intensities were calculated. No statistically significant difference was found for average energy expenditure 1 hour 15 minutes post exercise. The average energy expenditure was averaged from the 15 minutes the subject was on the metabolic cart, and therefore does not take into consideration excess post-exercise oxygen consumption and if there was greater efficiency at the beginning of the intervention. The respiratory exchange ratio was found to be higher during high-intensity exercise ($p < 0.05$), but lower 1 hour 15 minutes after ($p < 0.05$) high-intensity exercise as compared to after low-intensity exercise (Figure 4.3).

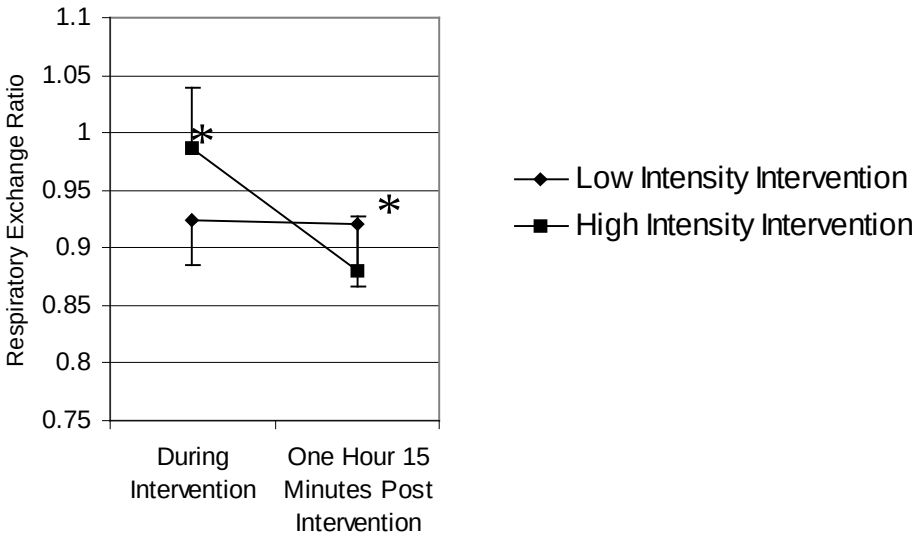

Figure 4.2 Respiratory exchange ratio, comparison of exercise sessions (Error bars = SD).
* = statistically significant difference between sessions ($p < 0.05$)

4.3 Primary Outcomes

The statistical analysis of intestinal absorption measurements was done twice: once including the subjects (one sedentary and one active) who displayed reactive hypoglycemia during testing and once excluding these subjects (Tables 4.3 and 4.4, respectively). There was no change in findings between the two statistical analyses.

No statistical difference was found for percent lactulose excretion (Figures 4.4 and 4.5) between interventions or subject groups. A between-subjects effect was found for 2-hour percent mannitol excretion ($p < 0.05$): active participants had an approximately 50% (range: 31-66%) higher mannitol excretion in all three sessions (Figure 4.6). No statistically significant differences were found for the lactulose / mannitol ratio (Figures 4.7 and 4.8).

Due to an error during the preparation of the beverages, 3-OMG was not consumed for 8 of the 45 test sessions. This excluded 4 subjects (1 classified as sedentary, 3 classified as active) from 3-OMG analysis. The participants who had observed symptoms of hypoglycemia are part of these 4 subjects, thus a secondary analysis excluding this population was not required.

No statistically significant between-groups or within-subject differences were found in our measurements of 3-OMG. However, a group-by-intervention interaction was found for the 5-hour 3-OMG measure ($p < 0.05$) (Table 4.5, Figure 4.9).

Table 4.3 Intestinal Permeability Measures (urinary lactulose and mannitol) Including Subjects with Observed Hypoglycemia

			Sedentary n = 7	Active n = 8	Overall n = 15	Between Groups Effect	Within Subject Effect	Interaction Effect
Urinary lactulose (percent excretion)	2 hour	Rest	0.381 ± 0.192	0.545 ± 0.366	0.468 ± 0.300	0.4558	0.2169	0.5038
		Low	0. 348 ± 0.274	0.442 ± 0.209	0.398 ± 0.237			
		High	0.349 ± 0.272	0.381 ± 0.278	0.366 ± 0.266			
	5 hour	Rest	0.741 ± 0.361	0.863 ± 0.721	0.806 ± 0.565	0.5001	0.8524	0.6980
		Low	0.634 ± 0.455	0.898 ± 0.575	0.775 ± 0.522			
		High	0.693 ± 0.415	0.797 ± 0.396	0.748 ± 0.394			
Urinary mannitol (percent excretion)	2 hour	Rest	3.882 ±1.436	6.455 ± 2.609	5.254 ± 2.460	**0.0404**	0.3321	0.2831
		Low	3.820 ± 0.985	5.787 ± 2.681	4.869 ± 2.245			
		High	3.929 ± 0.847	5.141 ± 1.550	4.575 ± 1.379			
	5 hour	Rest	12.722 ± 4.029	19.351 ± 8.848	16.258 ± 7.604	0.1568	0.1403	0.1787
		Low	13.310 ± 3.516	17.007 ± 8.064	15.282 ± 6.438			
		High	12.537 ± 3.130	14.885 ± 4.926	13.789 ± 4.219			
Urinary lactulose / mannitol ratio	2 hour	Rest	0.10310 ± 0.04317	0.08408 ± 0.04514	0.09296 ± 0.04374	0.4429	0.5647	0.8788
		Low	0.09206 ± 0.06930	0.08272 ± 0.04114	0.08708 ± 0.05411			
		High	0.09042 ± 0.06247	0.06794 ± 0.04131	0.07843 ± 0.05158			
	5 hour	Rest	0.06035 ± 0.02459	0.04667 ± 0.02808	0.05305 ± 0.02652	0.6439	0.4858	0.5403
		Low	0.04800 ± 0.03057	0.05032 ± 0.02440	0.04924 ± 0.02645			
		High	0.06137 ± 0.04347	0.05439 ± 0.02386	0.05765 ± 0.03328			

Results shown as mean ± SD

Table 4.4 Intestinal Permeability Measures (urinary lactulose and mannitol) Excluding Subjects with Observed Hypoglycemia

			Sedentary n = 6	Active n = 7	Overall n = 13	Between Groups Effect	Within Subject Effect	Interaction Effect
Urinary lactulose (percent excretion)	2 hour	Rest	0.347 ± 0.186	0.575 ± 0.384	0.470 ± 0.320	0.1961	0.1841	0.4083
		Low	0.284 ± 0.237	0.453 ± 0.223	0.375 ± 0.236			
		High	0.277 ± 0.212	0.397 ± 0.296	0.342 ± 0.258			
	5 hour	Rest	0.703 ± 0.379	0.982 ± 0.690	0.853 ± 0.564	0.2085	0.4877	0.6394
		Low	0.585 ± 0.478	0.908 ± 0.620	0.758 ± 0.562			
		High	0.580 ± 0.314	0.808 ± 0.426	0.703 ± 0.382			
Urinary mannitol (percent excretion)	2 hour	Rest	3.782 ± 1.547	6.457 ± 2.818	5.222 ± 2.626	**0.0399**	0.3055	0.2918
		Low	3.620 ± 0.911	5.518 ± 2.777	4.642 ± 2.274			
		High	3.886 ± 0.920	5.225 ± 1.655	4.607 ± 1.485			
	5 hour	Rest	12.486 ± 4.361	18.326 ± 9.030	15.631 ± 7.608	0.1854	0.2897	0.3515
		Low	13.760 ± 3.624	16.309 ± 8.445	15.133 ± 6.548			
		High	12.918 ± 3.246	14.654 ± 5.274	13.853 ± 4.371			
Urinary lactulose / mannitol ratio	2 hour	Rest	9.852 ± 4.539	8.882 ± 4.656	9.329 ± 4.436	0.8562	0.5172	0.7874
		Low	8.314 ± 7.137	8.774 ± 4.172	8.561 ± 5.476			
		High	7.435 ± 5.011	6.918 ± 4.447	7.156 ± 4.519			
	5 hour	Rest	0.05897 ± 0.02664	0.05315 ± 0.02300	0.05583 ± 0.02386	0.8320	0.5586	0.7313
		Low	0.04139 ± 0.02744	0.05211 ± 0.02579	0.04716 ± 0.02603			
		High	0.04931 ± 0.03231	0.05594 ± 0.02534	0.05288 ± 0.02771			

Results shown as mean ± SD

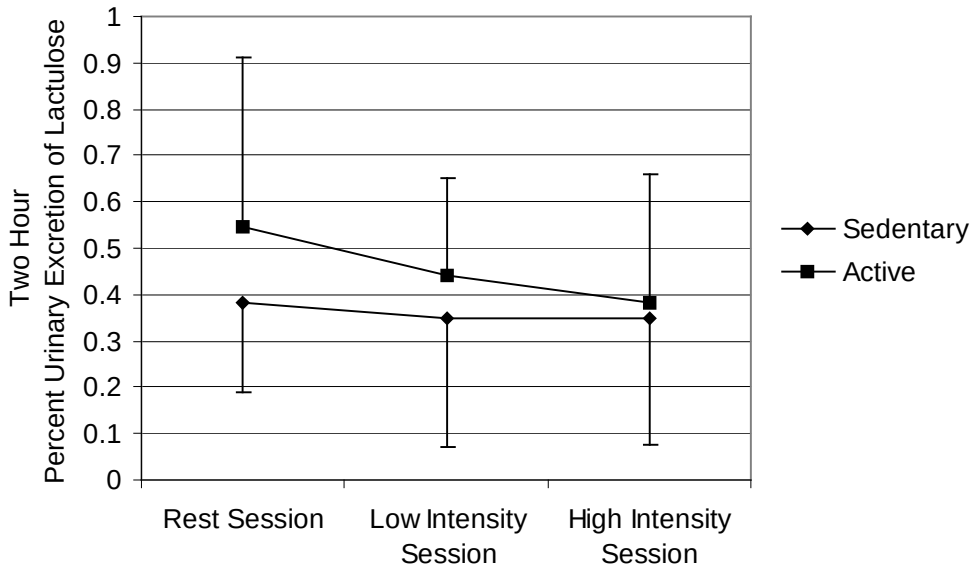

Figure 4.4 Two-hour percent urinary excretion of lactulose (Error bars = SD)

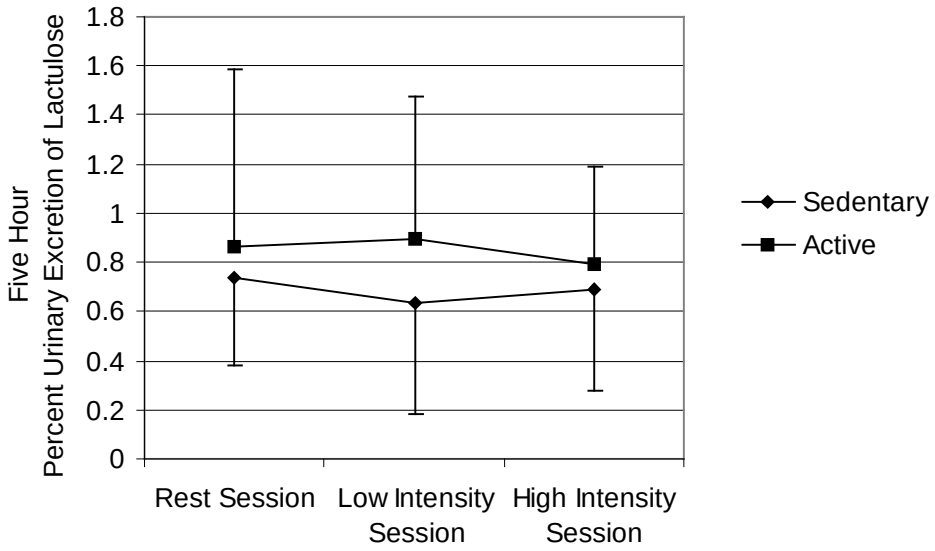

Figure 4.5 Five-hour percent urinary excretion of lactulose (Error bars = SD)

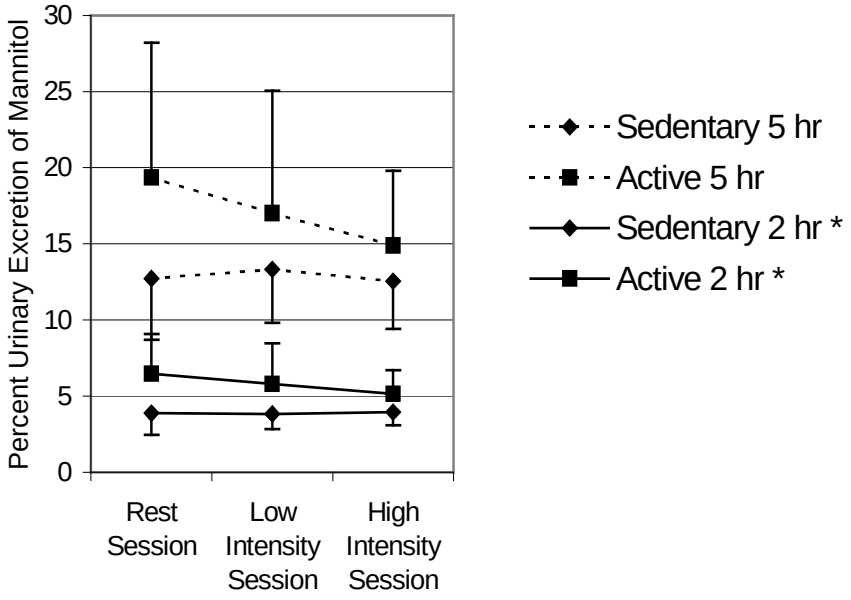

Figure 4.6 Percent urinary excretion of mannitol (Error bars = SD)
* = statistically significant between group (sedentary vs. active) difference for 2-hour measurements (repeated measures ANOVA, $p < 0.05$)

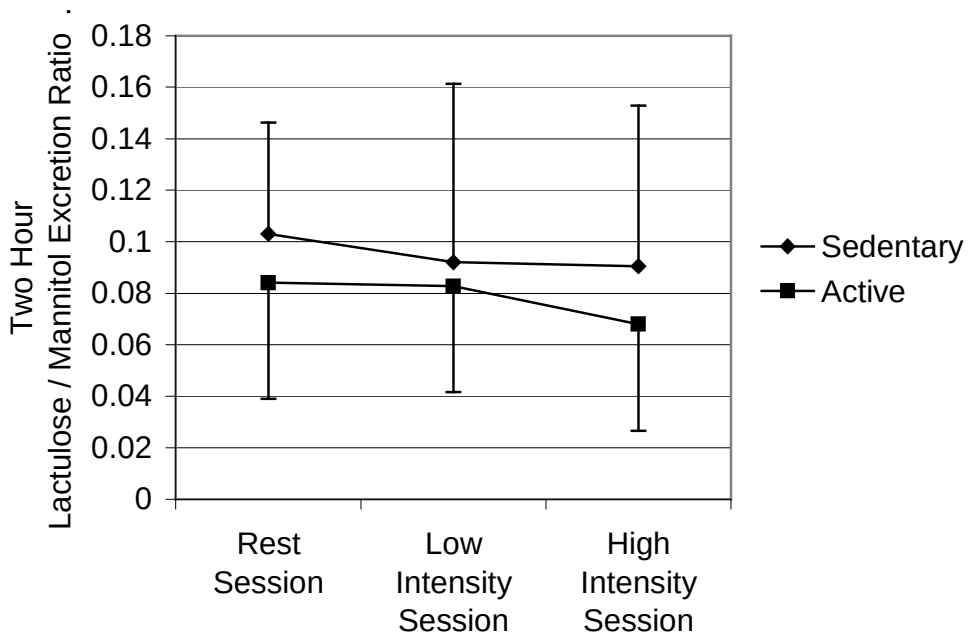

Figure 4.7 Two-hour lactulose / mannitol urinary excretion ratio
(Error bars = SD)

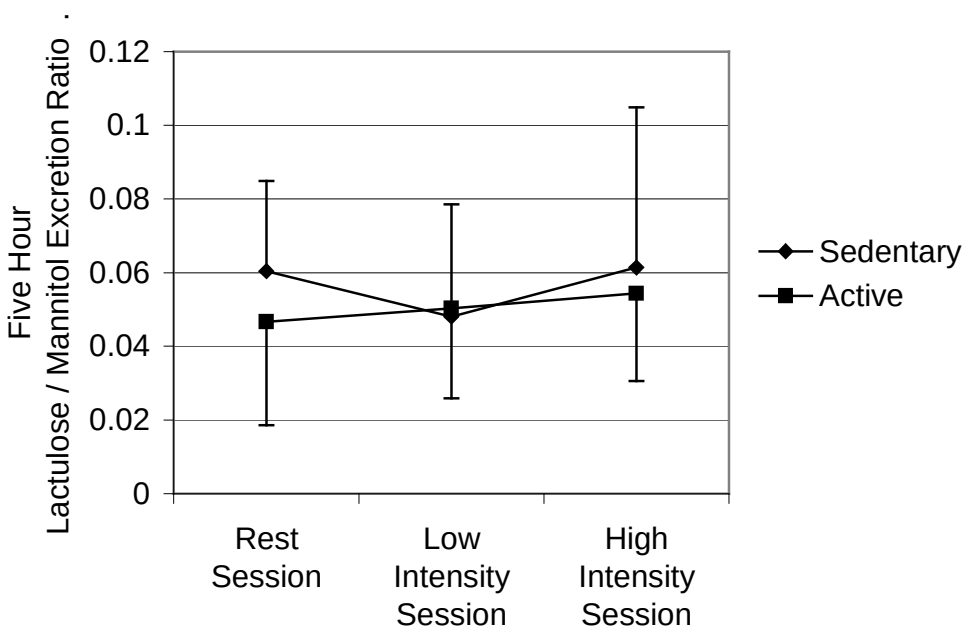

Figure 4.8 Five-hour lactulose / mannitol urinary excretion ratio
(Error bars = SD)

Table 4.5 3-O-methyl-glucose (percent excretion)

		Sedentary n = 6	Active n = 5	Overall n = 11	Between Groups Effect	Within Subject Effect	Interaction Effect
2 hour	Rest	7.185 ± 3.772	9.748 ± 1.631	8.350 ± 3.157	0.2285	0.9806	0.4929
	Low	8.083 ± 3.002	8.805 ± 2.576	8.411 ± 2.702			
	High	7.489 ± 2.507	9.695 ± 2.575	8.492 ± 2.669			
5 hour	Rest	25.293 ± 7.037	30.076 ± 3.921	27.467 ± 6.095	0.7551	0.3790	**0.0104**
	Low	28.954 ± 3.792	24.467 ± 8.247	26.915 ± 6.315			
	High	27.526 ± 3.482	29.885 ± 2.965	28.598 ± 3.331			

Results shown as mean ± SD

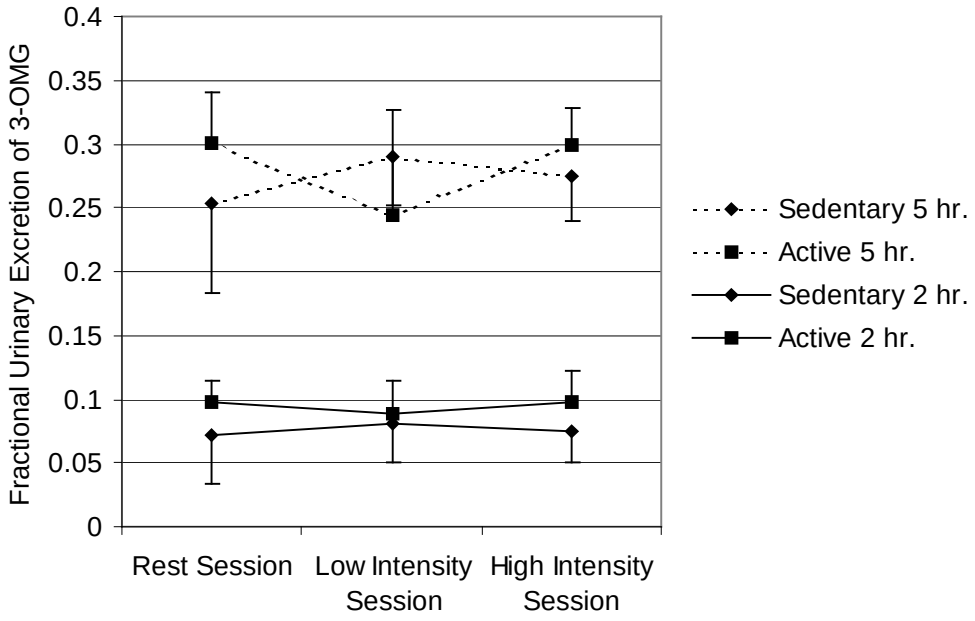

Figure 4.9 3-OMG percent urinary excretion (Error bars = SD) statistically significant interaction effect for 5-hour measurements (repeated measures ANOVA, $p < 0.05$)

Because differences in urinary volumes between sessions were found ($p < 0.05$) (Table 4.6), cross-sectional analysis was done to investigate whether intestinal permeability and absorption measurements were correlated with urinary volume during the resting session. No statistically significant correlation was found between urinary volume and measurements of intestinal permeability and absorption (Table 4.7).

Table 4.6 Total 5-Hour Urinary Volume

5-hour urinary volume	Sedentary n = 7	Active n = 8	Overall n = 15	Between Groups Effect	Within Subject Effect	Interaction Effect
Rest	657.4 ± 254.9	728.0 ± 326.7	695.1 ± 287.3	0.6310	**0.0040**	0.3445
Low	514.9 ± 243.3	449.3 ± 161.4	479.9 ± 198.9			
High	385.5 ± 121.6	525.2 ± 290.7	460.0 ± 231.9			

Results shown as mean ± SD

Table 4.7 Pearson Correlation of Urinary Volume with Measures of Intestinal Absorption (measurements as taken 5 hours after subjects' consumption of glucose beverage, for the rest sessions only)

n = 15		3-OMG fractional excretion	Lactulose fractional excretion	Mannitol fractional excretion	Lactulose / Mannitol ratio
Urinary volume	r	0.2344	0.1427	0.2623	-0.1697
	p	0.4003	0.6120	0.3449	0.5454
3-OMG fractional excretion	r		0.06123	-0.4872	0.3017
	p		0.8284	0.0655	0.2745
Lactulose fractional excretion	r			0.4746	0.6476
	p			0.0739	0.0090
Mannitol fractional excretion	r				-0.2994
	p				0.2783

4.4 Secondary Outcomes

No statistical difference between groups and interventions was found for peak or area-under-the-curve measurements of blood glucose (Table 4.8, Figure 4.10). As shown in table 4.8, the active subjects tended to have lower peak

glucose levels and glucose areas under the curve, but the difference failed to reach statistical significance.

A statistically significant ($p < 0.05$) within-subject effect was found in the respiratory exchange ratio during and post interventions. (Table 4.8). No statistically significant difference (group or intervention) was found in energy expenditure as measured 1 hour 15 minutes post intervention (Table 4.8).

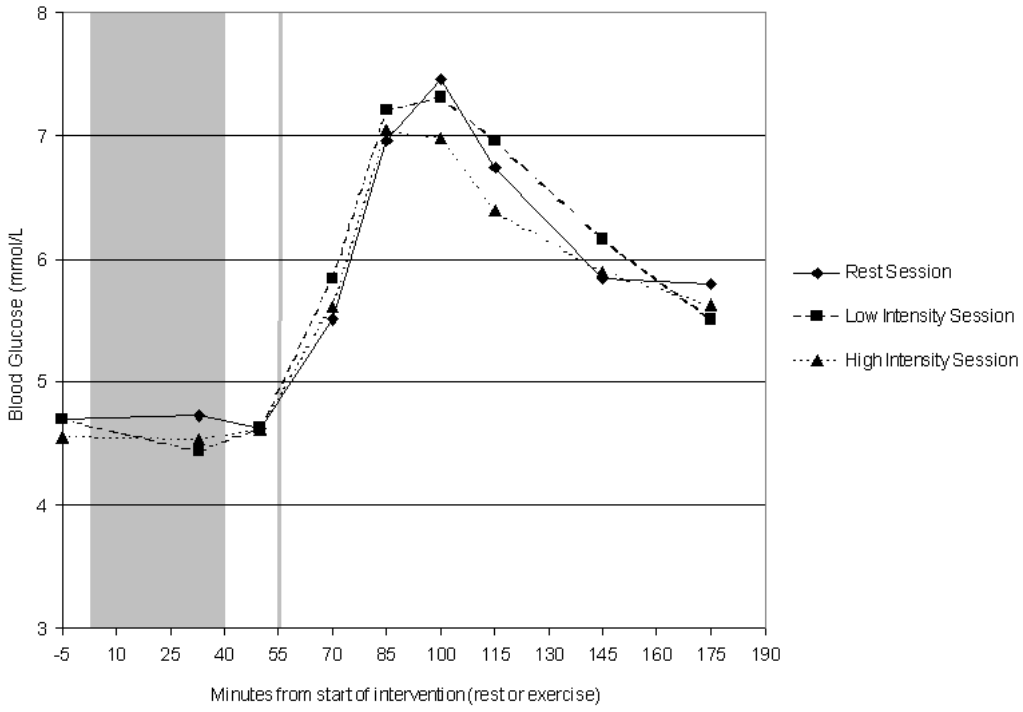

Figure 4.10 Blood glucose (sedentary and active groups pooled)
shaded section = 40 minute rest, low intensity or high intensity exercise interventions
vertical line = consumption of glucose beverage

Table 4.8 Metabolic Measures

		Session	Sedentary n = 7	Active n = 8	Overall n = 15	Between-Groups Effect	Within-Subject Effect	Interaction Effect
Blood glucose	Peak (mmol/L·min)	Rest	8.1 ± 1.0	7.3 ± 1.0	7.7 ± 1.0	0.0557	0.441	0.4306
		Low	8.5 ± 2.1	7.0 ± 0.9	7.7 ± 1.7			
		High	7.8 ± 0.7	7.0 ± 0.5	7.4 ± 0.7			
	AUC (mmol/L·min)	Rest	812.0 ± 112.5	733.0 ± 99.8	769.9 ± 109.9	0.0569	0.3934	0.3318
		Low	866.0 ± 179.2	723.8 ± 89.7	790.1 ± 152.2			
		High	802.0 ± 65.2	722.6 ± 60.8	759.7 ± 73.2			
Average energy expenditure (Kcal/min)	During intervention	Rest	1.30 ± 0.13	1.33 ± 0.13	1.32 ± 0.13	**0.0021**	**<0.0001**	**0.0006**
		Low	7.35 ± 1.40	9.27 ± 1.21	8.37 ± 1.60			
		High	7.74 ± 0.87	10.10 ± 1.08	9.00 ± 1.55			
	Post intervention	Rest	1.49 ± 0.25	1.54 ± 0.13	1.52 ± 0.19	0.2099	0.2702	0.8630
		Low	1.52 ± 0.23	1.57 ± 0.16	1.55 ± 0.19			
		High	1.50 ± 0.18	1.58 ± 0.12	1.54 ± 0.15			
Respiratory exchange ratio	During intervention	Rest	0.82 ± 0.05	0.83 ± 0.03	0.83 ± 0.04	0.7983	**<0.0001**	0.6596
		Low	0.92 ± 0.05	0.92 ± 0.02	0.92 ± 0.03			
		High	0.99 ± 0.41	0.97 ± 0.06	0.98 ± 0.05			
	Post intervention	Rest	0.88 ± 0.03	0.90 ± 0.02	0.90 ± 0.03	0.3766	**0.0306**	0.9658
		Low	0.90 ± 0.06	0.93 ± 0.03	0.92 ± 0.05			
		High	0.87 ± 0.03	0.88 ± 0.05	0.88 ± 0.04			

Results shown as mean ± SD
AUC = area under the cuve

Between-groups differences were found in regard to various subjective appetite ratings. Statistically significant differences were found between groups for peak desire to eat ($p < 0.05$), area-under-the-curve desire to eat ($p < 0.05$), peak hunger ($p < 0.05$), area-under-the-curve hunger ($p < 0.05$), peak prospective food consumption ($p < 0.05$), and area-under-the-curve prospective food consumption ($p < 0.05$) (Table 4.9). Means for the previously mentioned measurements of hunger were found to be higher in the active group for all conditions (Table 4.8).

Table 4.9 Subjective Appetite Ratings

			Sedentary n = 7	Active n = 8	Overall n = 15	Between-Groups Effect	Within-Subject Effect	Interaction Effect
Desire to eat	Peak (cm)	Rest	7.02 ± 2.33	10.78 ± 2.73	9.03 ± 3.13	**0.0051**	0.4589	0.6725
		Low	6.60 ± 2.04	9.40 ± 2.52	8.09 ± 2.66			
		High	6.04 ± 2.49	10.19 ± 3.54	8.26 ± 3.68			
	AUC (cm·min)	Rest	1028.23 ± 414.31	1600.20 ± 549.74	1333.28 ± 558.49	**0.0303**	0.1157	0.6958
		Low	892.60 ± 348.55	1297.65 ± 597.85	1108.63 ± 523.95			
		High	774.62 ± 408.64	1374.12 ± 579.26	1094.36 ± 578.95			
Hunger	Peak (cm)	Rest	7.53 ± 2.09	10.45 ± 2.60	9.09 ± 2.74	**0.0018**	0.7771	0.4789
		Low	7.71 ± 1.56	10.48 ± 1.73	9.19 ± 2.14			
		High	6.59 ± 1.88	10.75 ± 2.57	8.81 ± 3.07			
	AUC (cm·min)	Rest	1092.56 ± 345.48	1509.87 ± 526.50	1315.13 ± 486.00	**0.0200**	0.3285	0.3591
		Low	1035.55 ± 298.44	1368.19 ± 443.04	1212.96 ± 407.21			
		High	803.52 ± 346.74	1455.15 ± 495.96	1151.06 ± 536.42			
Fullness	Peak (cm)	Rest	5.60 ± 2.44	5.12 ± 3.95	5.35 ± 3.23	0.5271	0.9520	0.8503
		Low	6.00 ± 1.35	4.99 ± 2.94	5.47 ± 2.32			
		High	6.10 ± 2.95	4.98 ± 2.90	5.50 ± 2.87			
	AUC (cm·min)	Rest	756.48 ± 412.35	577.22 ± 589.21	660.88 ± 505.00	0.2032	0.9498	0.7214
		Low	821.13 ± 327.86	535.86 ± 384.89	668.99 ± 376.61			
		High	808.78 ± 484.89	491.45 ± 266.77	639.54 ± 403.98			
Prospective food consumption	Peak (cm)	Rest	8.27 ± 1.43	11.60 ± 1.89	10.05 ± 2.37	**0.0005**	0.1724	0.3531
		Low	8.38 ± 1.01	11.52 ± 2.04	10.05 ± 2.26			
		High	7.43 ± 0.84	11.43 ± 1.95	9.56 ± 2.54			
	AUC (cm·min)	Rest	1297.35 ± 199.39	1834.62 ± 442.67	1583.89 ± 438.17	**0.0108**	0.1069	0.7271
		Low	1230.48 ± 182.80	1721.98 ± 509.11	1492.61 ± 456.44			
		High	1132.97 ± 177.48	1725.42 ± 501.51	1448.94 ± 482.55			

Results shown as mean ± SD
AUC = area under the curve

5. DISCUSSION

5.1 Discussion

The study presented in this thesis is the first to examine the effect of exercise intensity on intestinal permeability and the absorption of a glucose solution after exercise. Our primary hypothesis was not confirmed; no significant changes were found in 5-hour urinary lactulose, mannitol, lactulose / mannitol ratio, or percent 3-OMG excretion following low- or high-intensity exercise compared to a resting condition.

Previous studies have shown that markers of glucose absorption and intestinal permeability can be reduced by exercise of a sufficient intensity (1; 2). However, there are important differences between those studies–in which a reduction was found–and the current study. In this study, the solution in which the intestinal markers were provided was different than in previous studies. Lang et. al. (2) provided the absorption markers in water, not alongside additional nutrients. In the van Nieuwenhoven study, absorption markers were dissolved in a carbohydrate-electrolyte solution that provided a small quantity of additional nutrients (0.14g carbohydrate kg^{-1} bodyweight, 0.42mg amino acids kg^{-1} bodyweight) (1). In our experiment, the absorption markers were provided in an OGTT beverage (90g glucose). A glucose load of this magnitude can affect measurements of intestinal absorption. Debru et. al found that a 1.5 Mol glucose solution decreased the lactulose / mannitol ratio and caused a small, statistically insignificant decrease in 3-OMG absorption in the rat (3). The absorption

markers in this study were provided in a 1.7 Mol glucose solution. There is a sharp contrast in the percent excretion of 3-OMG between Lang et. al. (45.4%) (2), van Nieuwenhoven et. al. (46.6%) (1), and this study (27.5%) (all values are from the rest condition of the respective experiments and were collected over 5 hours). The scale of these differences is similar to that found by Debru et. al, who found a ~50% percent excretion in relation to a 0 Mol glucose solution and a ~34% percent excretion in relation to a 1.5 Mol glucose solution; however, as mentioned previously, these differences were not found to be statistically significant (please note that 3-OMG measurements were only provided in figure format in that paper, and thus the numbers provided here are estimations based on that figure) (3). Given that additional glucose can modify intestinal absorption measurements, it is unknown if this effect would modulate the effect that exercise has on intestinal absorption measurements.

The exercise intensities used in our experiment differ dramatically from those used in Lang et. al. (2) and van Nieuwenhoven et. al. (1). Both the Lang and van Nieuwenhoven studies involved continuous exercise and, in that aspect, are comparable to this study's low-intensity intervention. The highest-intensity exercise protocol used by Lang et. al. involved exercise at 70% $VO_{2\ max}$ for 60 minutes. The exercise protocol in the van Nieuwenhoven study was exceptionally difficult, representing a greater than 80% $VO_{2\ max}$ intensity for 90 minutes. No participants in the van Nieuwenhoven study were able to maintain the prescribed intensity; participants required an average reduction in intensity of 11% to complete the 90 minute protocol. The duration and intensity in our experiment

were restricted to ensure their successful completion by sedentary individuals. The low-intensity / continuous intervention used in our experiment involved exercise at 40% $VO_{2\ max}$ for 40 minutes. The high-intensity intervention was constrained to match both the work output and duration of the low-intensity session and was thus composed of intervals. The interval nature of the high-intensity intervention does not allow for an easy comparison to the continuous protocols found in other experiments. The high-intensity intervention was 40 minutes long and switched between 20% and 100% $VO_{2\ max}$ intensity. During the high-intensity intervention, participants accumulated 10 minutes of activity at 100% $VO_{2\ max}$ intensity. Few, if any, of the studies reviewed in this thesis approached a relative intensity this high. This exposure was expected to reduce mesenteric blood flow. Both the Lang and van Nieuwenhoven studies involved exercise interventions of much greater duration and work output, both of which may affect mesenteric blood flow and intestinal absorption capacity. The workload and durations were lower in our study, but allowed low-intensity and high-intensity to be matched for duration and work output.

An additional difference between this study and previous studies (1; 2) is the time at which the intestinal absorption markers were consumed in relation to exercise. Both Lang (2) and van Nieuwenhoven (1) administered the intestinal absorption markers at the onset of exercise and collected urine for the subsequent 5 hours, thus measuring intestinal absorption both during and post exercise. The durations of these exercise sessions were 60 and 90 minutes respectively; during these sessions, exercise was being performed while intestinal absorption was

being measured. The study presented in this thesis administered the intestinal absorption markers post exercise, thus excluding the effect that exercise may have on absorption during its performance, measuring only a residual effect that exercise may have after its cessation. To our knowledge, the study presented in this thesis is the first to investigate whether the effects of exercise on glucose absorption and intestinal permeability extend beyond the cessation of exercise.

Though no statistically significant within subject-effect was found, an interaction effect was found in 5-hour 3-OMG percent excretion. This effect is primarily due to one outlying value. The 5-hour percent excretion of 3-OMG for active individuals for the low intensity session was 0.24467 ± 0.08247. This is the lowest average value reported for 5-hour 3-OMG percent excretion regardless of session type or group. The 5-hour measures for active individuals for the low-intensity session contain an exceptionally low value (0.12745). Removing this one outlying value (0.12745) changes this group-session mean ± SD from 0.24467 ± 0.08247 to 0.27398 ± 0.05781, bringing the group-session mean in line with other means and reducing the reported standard deviation for that group-session. However, the removal of this value does not eliminate the statistically significant group-session interaction; the statistically significant interaction effect remains ($p = 0.0415$).

Active individuals had higher percent excretion of mannitol than sedentary individuals for all sessions (rest, low, and high) and for all time periods (2-hour and 5-hour); with the differences for 2 hour measures being statistically significant. Percent excretion of mannitol was higher in active individuals after 5

hours for all sessions but did not reach statistical significance ($p = 0.16$). One noticable but statistically non-significant observation was that lactulose measurements were also higher in active individuals than in sedentary individuals for all time periods and sessions. These general trends observed in intestinal permeability measurements when comparing sedentary and active participants suggest that numerous statistically significant findings might be identified in a sample of sufficient size. The lactulose and mannitol observations suggest that active individuals have greater transcellular (mannitol) and paracellular (lactulose) transport than sedentary individuals. The lactulose / mannitol ratio is used to measure intestinal permeability. The proposed increase in transcellular and paracellular transport cannot be explained by increased permeability because no statistical difference was found in the lactulose / mannitol ratio between groups (5-hour measurements, $p = 0.8320$).

One possible explanation of these findings is a difference in segmentation contractions occurring in the small intestine between groups. Segmentation contractions are contractions of the small intestine that mix the chyme and improve the chyme's exposure to the intestinal wall. Increased exposure of the chyme to the intestinal wall would increase absorption in the absence of increased intestinal permiability (4). One explanation of these findings could be that the active participants had a greater number of segmental contractions than the sedentary participants, thus causing an increase in chyme exposure and absorption in the absence of increased intestinal permeability.

Numerous between-groups differences were found in measurements of appetite. This may be partially explained by the previously mentioned difference in intervention energy expenditure between the two groups. However, measurements of appetite were also greater in the active group during the rest session. Basal metabolic rate might offer an explanation, but there was a negligible difference in resting metabolic rate (sedentary: 1.30 ± 0.13 Kcal/min, active: 1.33 ± 0.13 Kcal/min).

A possible explanation for the differences in intestinal absorption (as measured by mannitol and lactulose) and in appetite between groups is differences in gastrointestinal hormones between the two populations. For example, the hormone ghrelin has been shown to increase both appetite and gut motility (5); however, further experimentation would be necessary to ascertain its influence on these experimental measurements.

5.2 Future Areas of Research

The primary hypothesis that high-intensity exercise would cause a reduction in post-exercise hexose absorption was not confirmed. However, numerous areas for future experimentation have been identified. Trends observed in transcellular and paracellular absorption (though most of these trends did not reach statistical significance) suggest that there may be differences in gut motility between sedentary and active individuals. The significant differences in appetite suggest that an experiment comparing the resting ghrelin levels between sedentary and active individuals may yield interesting results.

The long duration in which nutrients are absorbed post-prandially invites a modification of the current experiment. Could the absorption of a meal be reduced by exercise performed post-prandially? (Both Lang (2) and van Nieuwenhoven (1) have shown that exercise can significantly influence the absorption that occurs immediately after the consumption of absorption markers, but they did not examine the the effects of a delay between the consumption of absorption markers and the performance of exercise). The long duration of absorption of a meal (4 hours or more) (6) presents an opportunity for the absorption of nutrients to be directly affected during the performance of post-prandial exercise. More than 50% of the nutrients consumed have yet to be absorbed 1 hour after a person has consumed an oral glucose tolerance beverage (estimation based on data from Dalla Man et. al. (6)).

5.3 Conclusion

A reduction in hexose absorption after the performance of high-intensity exercise cannot be confirmed from this study; however, future areas of research have been identified. The hypothesized (but not tested) method by which this reduction in intestinal absorption would occur was by an exercise-intensity-dependent reduction of blood flow (7) to the intestinal tract causing a reduction in nutrient absorption (8; 9). It has been shown that glucose absorption for an oral glucose tolerance beverage occurs over approximately 4 hours. The exercise interventions used in this experiment may have affected superior mesenteric artery blood flow and intestinal absorption; however, there exists a 4-hour

window in which intestinal absorption capacity can be restored. This long duration of absorption may allow for the compensation for a temporary decrease in capacity.

Outside of the main hypothesis, possible differences in intestinal motility and absorption have been suggested between sedentary and active individuals.

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Information Sheet

Title: The effects of exercise intensity on sugar absorption.
Principal Investigator: Normand Boulé (Ph.D.), nboule@ualberta.ca, 492-4695.
Co-Investigator: Jason Howard (M.Sc. Candidate), jmhoward@ualberta.ca, 492-7394.

Dear Participant.

I (Jason Howard) am a graduate student in the Faculty of Physical Education and Recreation under the supervision of Dr. Normand Boulé. I am conducting a study on the effects of exercises on sugar absorption.

To be a subject in our study, you must be a healthy male between 20 and 35 years of age. Also, you must be free of medical conditions that influence blood glucose (e.g. diabetes). We will ask you a series of questions to ensure you can perform exercise with minimal little risk to your health.

You will be asked to come to the exercise physiology laboratory for **5 visits**. The total time commitment of the sessions is approximately 21.75 hours (12.75 hours in lab, 9 hours out). During the **first visit**, you will be given more information about the study. During the **second visit** we will measure your physical fitness. The test requires you to cycle on a stationary bike for about 15 minutes. The difficulty is easy to begin with. However, the difficulty will be increased gradually every 3 minutes until you can no longer continue. During this test, your heart and your breathing will be monitored. To monitor your heart, we use a heart rate monitor which is placed around your chest. To monitor your breathing, you will be asked to breath into a mouthpiece (similar to a snorkel) while wearing a nose clip. During the **second visit**, we will also measure body fat. This test requires us to measure your body weight while you are under water. You need to bring a swimsuit.

After the measurement of your fitness and body composition, the **next three sessions** will be scheduled. Please refrain from consuming alcohol for 5 days prior to each test day. These sessions will occur from approximately 8AM to 3PM on three separate days. They will involve rest or exercise, and drinking a very sweet beverage. You will be asked to consume a similar diet (of your own choosing) and refrain from eating past 10PM the day before each testing session. On the morning of testing, please do not consume food or fluids. Also, please do not exercise the morning of each testing day. This includes walking (>15 minutes) or bicycling to the laboratory. If some activity must be performed, please ensure that it is light, and is performed before each test session.

During 2 of your last 3 sessions, exercises will be performed on an exercise bicycle. One of the sessions will include exercise of a low-to-moderate intensity for 40 minutes. The other will be composed of 3 minutes at a very low intensity followed by 1 minute at a higher intensity. During this session, you will alternate between low and high intensity exercise for a total of 40 minutes. The difficulty of these exercises will be based on the resistance you reached during your fitness test. We will also ask you to do a third session in which there is no exercise. The order of these 3 sessions will be randomly determined (in a manner

similar to flipping a coin). Two drops of blood will be taken during each exercise session. Blood samples will be used to measure glucose and lactate.

Fifteen minutes after performing the exercise, you will be required to drink a sweet beverage. This sweet beverage will contain four markers. These markers are called 3-OMG, mannitol, lactulose, and C^{13} labeled glucose. Three of these markers are inactive sugars. This means that the body absorbs them, but can not use them for energy. They are excreted in urine, which will be collected for measurement. The only side-effect of these three markers may be minor digestive upset. The fourth marker is a different version of the sugar glucose. This is a naturally occurring stable version and is very safe. Drinking the sweet beverage will be followed by 9 blood sugar and blood lactate measures over the next 2 hours. Blood samples will be taken by finger pricks performed with a small needle. This is the same method used by diabetics to monitor blood sugar. Each blood sample will require less than a drop of blood. Four other blood samples will be taken with a needle to measure insulin response. Breath samples will be taken at the same time as these measures. These breath samples will be used to measure one of the markers that was consumed. You will also be asked questions regarding your hunger and appetite.

Two hours after completion of the exercise or rest protocol you will be given a commercial meal replacement beverage to ease any feelings of hunger. You will then be allowed to leave the lab, and will be required to collect your urine for three hours. You will be provided with a sealable container and only require to refrigerate the sample until it is convenient to bring it to the lab.

All biological samples will be destroyed after publication of the data gathered (up to 2 years after completion of the study).

Risks: All blood samples will be taken with sterile equipment by trained individuals. However, a very small risk of infection exists. The finger prick procedure is performed by diabetics multiple times per day and represents a minimal risk.

There may be some health risk with exercise, particularly during the maximal fitness test. During and following the test, it is possible to experience symptoms such as abnormal blood pressure, fainting, lightheadedness, muscle cramps or strain, nausea and, in very rare cases (0.5 per 10,000 in testing facilities such as exercise laboratories, hospitals and physician offices), heart rhythm disturbances or heart attack. While serious risk to healthy participants is highly unlikely, they must be acknowledged and participants willingly assume the risks associated with very hard exercise. The exercise test will be administered by qualified personnel under the supervision of Dr. Boulé. Personnel are trained to handle identifiable risks and emergencies, and have certification in CPR. Certifications can be produced if requested.

Benefits: Your fitness and body fat levels can be provided to you. You will also be advancing research in the area of exercise and nutrient absorption. On completion of this study you will be provided a free one hour session with a personal trainer.

Time Commitment:

Information Assessment:	1 hour
Fitness Assessment:	2 hours
Exercise sessions:	6.75 hours X 3
Total time commitment	23.25 hours

Confidentiality: To ensure confidentiality, personal data will be coded and stored in a locked file cabinet to which only the investigators will have access. Normally data is retained for a period of five years post-publication, after which it may be destroyed. Any presentation of data will contain no personal information and will have no way to identify individual participants.

Freedom to Withdraw: You will be allowed to withdraw at any time without question or consequence. You can withdraw from the study by informing one of the investigators verbally, by phone, or by email. All information regarding your participation in the study will be deleted at your request.

Additional contacts: If you have concerns about the study and wish to speak with someone who is not involved with this study, please call Dr. Marcel Bouffard, Associate Dean of Research and Chair of Research Ethics Board, Faculty of Physical Education and Recreation at 492-5910.

Thank you,

Normand Boulé, Ph.D. **Jason Howard**

INFORMED CONSENT FORM

Part 1 (to be completed by the Principal Investigator)

Title: The effects of exercise intensity on sugar absorption.
Principal Investigator: Normand Boulé (Ph.D.), nboule@ualberta.ca, 492-4695.
Co-Investigator: Jason Howard (M.Sc. Candidate), jmhoward@ualberta.ca, 492-7394.

Part 2 (to be completed by the research participant)

Do you understand that you have been asked to be in a research study?	Yes	No
Have you read and received a copy of the attached Information Sheet	Yes	No
Do you understand the benefits and risks involved in taking part in this research study?	Yes	No
Have you had an opportunity to ask questions and discuss this study?	Yes	No
Do you understand that you are free to refuse to participate, or to withdraw from the study at any time, without consequence, and that your information will be withdrawn at your request?	Yes	No
Has the issue of confidentiality been explained to you? Do you understand who will have access to your information?	Yes	No

This study was explained to me by: _____

I agree to take part in this study:

_____ _____ _____

Signature of Research Participant Date Witness

_____ _____

Printed Name Printed Name

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

_____ _____

Signature of Investigator or Designee Date

The information sheet must be attached to this consent form and a copy of both forms given to the participant.

The effects of exercise intensity on sugar absorption

Participant Screening and Medical Information Form

1. To the best of your knowledge, has your weight fluctuated more than 5 pounds in the past 3 months?

   Yes **No**

2. Do you participate in planned bouts of physical activity for more than 30 minutes twice per week?

   Yes **No**

3. Do you plan to change your activity level in the next month?

   Yes **No**

4. Do you have any limitations to intense physical activity? (Examples: orthopedic (joint pain), metabolic (diabetes), asthma)

   Yes **No**

5. Have you been previously diagnosed with cardiovascular disease or hypertension?

   Yes **No**

6. Have you been previously diagnosed with a disease or disorder effecting the central nervous system, renal system, liver, endocrine, gastrointestinal systems?

   Yes **No**

7. Have you had a history of alcohol or drug addiction, or regular (>= once per day) tobacco use?

   Yes **No**

Participant Screening and Medical Information Form (continued)

8. Are you currently receiving any prescribed medications?

   Yes **No**

9. Have you been previously diagnosed with diabetes or other glucose regulatory disorder or have a family history of diabetes?

   Yes **No**

Name: _____

Current address:
_____

Postal Code: _____

Phone numbers:

Home: _____ Cell: _____ Work: _____

Family physician's name: _____ Phone: _____

Emergency contact: _____

Emergency contact phone numbers:

Home: _____ Cell: _____
Work:_____

_____
_____
Participant's signature Date