Prior exercise enhances passive absorption of intraduodenal glucose

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Prior exercise enhances passive absorption of intraduodenal glucose. J Appl Physiol 95: 1132–1138, 2003. First published May 9, 2003; 10.1152/japplphysiol.01172.2002.—The purpose of this study was to assess whether a prior bout of exercise enhances passive gut glucose absorption. Mongrel dogs had sampling catheters, infusion catheters, and a portal vein flow probe implanted 17 days before an experiment. Protocols consisted of either 150 min of exercise (n = 8) or rest (n = 7) followed by basal (−30 to 0 min) and a primed (150 mg/kg) intraduodenal glucose infusion [8.0 mg·kg⁻¹·min⁻¹], time (t) = 0–90 min] periods. 3-O-[³H]methylglucose (absorbed actively, facilitatively, and passively) and L-[¹⁴C]glucose (absorbed passively) were injected into the duodenum at t = 20 and 80 min. Phloridzin, an inhibitor of the active sodium glucose cotransporter-1 (SGLT-1), was infused (0.1 mg·kg⁻¹·min⁻¹) into the duodenum from t = 60–90 min with a peripheral venous isoglycemic clamp. Duodenal, arterial, and portal vein samples were taken every 10 min during the glucose infusion, as well as every minute after each tracer bolus injection. Net gut glucose output in exercised dogs increased compared with that in the sedentary group (5.34 ± 0.47 and 4.02 ± 0.53 mg·kg⁻¹·min⁻¹). Passive gut glucose absorption increased ~100% after exercise (0.93 ± 0.06 and 0.45 ± 0.07 mg·kg⁻¹·min⁻¹). Transport-mediated glucose absorption increased by ~20%, but the change was not significant. The infusion of phloridzin eliminated the appearance of both glucose tracers in sedentary and exercised dogs, suggesting that passive transport required SGLT-1-mediated glucose uptake. This study shows 1) that prior exercise enhances passive absorption of intraduodenal glucose into the portal vein and 2) that basal and the added passive gut glucose absorption after exercise is dependent on initial transport of glucose via SGLT-1.

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EXERCISE ENHANCES THE ABILITY of insulin to stimulate skeletal muscle (25) and liver (22) glucose uptake. This increase in insulin sensitivity, however, does not uniformly lead to improved oral glucose tolerance (15, 18, 24). Work done by Hamilton et al. (9) showed that failure to improve oral glucose tolerance, despite increased insulin-stimulated glucose uptake, is due to increased absorption of glucose from the gut. The resulting enhancement in splanchnic bed glucose output counterbalances the effect of increasing muscle glucose uptake on arterial glucose levels.

The mechanism by which prior exercise enhances the absorption from the gut is unknown. Gut glucose absorption is both transporter mediated and passive. Transporter-mediated gut glucose absorption occurs via luminal sodium glucose cotransporter-1 (SGLT-1) and Na⁺−K⁺ active transporters (5, 10) and GLUT-2-mediated facilitated diffusion. Facilitated diffusion of glucose occurs when transport of glucose via SGLT-1 stimulates translocation of GLUT-2 transporters to the luminal surface of the gut (11, 16). Transporter-mediated glucose transport encompasses 90% of total gut glucose absorption in both conscious dogs (17, 23) and rats (31, 32). The remaining 10% of gut glucose absorption is due to paracellular diffusion across the intestinal wall, although this route also appears to be indirectly dependent on intestinal SGLT-1-mediated glucose transport, at least in sedentary, conscious dogs (23).

The purpose of the present study is to determine whether the increased absorption of intraduodenal glucose after exercise is due to increased transporter-mediated and/or passive glucose absorption. For this purpose, 3-O-[³H]methylglucose (absorbed via active, facilitative, and passive routes) and L-[¹⁴C]glucose (absorbed passively) were delivered in trace amounts in the duodenum to determine the contributions of transporter-mediated and passive pathways to net gut glucose absorption during an intraduodenal glucose load (3, 4).

MATERIALS AND METHODS

Animal care and surgical procedures. Fifteen mongrel dogs of either sex, with a mean weight of 23 ± 1 kg, were studied. A subset of the sedentary dogs was published previously (23). The dogs were housed in a facility that met the American Association for the Accreditation of Laboratory Animals Care guidelines. All procedures were approved by the Vanderbilt University Animal Care and Use Committee. The dogs were fed a standard diet of meat and chow (34% protein, 14.5% fat, 46% carbohydrate, and 5.5% fiber based on dry weight).

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At least 16 days before each experiment, a laparotomy was performed under general anesthesia. Two Silastic catheters (0.03 mm ID) were inserted into the inferior vena cava for indocyanine green (ICG) and glucose infusions. Silastic catheters (0.04 mm ID) were inserted into the portal vein and left common hepatic vein for blood sampling, as described previously (36). Two Silastic catheters (0.03 mm ID) were inserted into the duodenum. The first catheter was inserted just below the pyloric sphincter for administration of glucose, phloridzin, 3-O-\([^{3}H]\)methylglucose, and L-\([^{14}C]\)glucose. The second duodenal catheter was inserted just before the junction of the duodenum with the jejunum (~10 cm caudal to the first duodenal catheter). A Silastic catheter (0.03 mm ID) was inserted into the left femoral artery for blood sampling. After insertion, the vascular catheters were filled with saline containing heparin and knotted at the free ends.

Transonic flow probes (Transonic Systems, Ithaca, NY) were used to measure portal vein blood flow (PVF), as described previously (23). The flow probe lead and knotted catheter ends were stored in a subcutaneous pocket made in the abdominal region. The femoral artery catheter was stored in a pocket in the inguinal region. One week before an experiment, dogs for either protocol were trained to run on a treadmill (4 mph on a 12% grade). Training consisted of 20-, 40-, and 90-min bouts to acclimate the dogs to treadmill exercise. Dogs were not exercised 48 h before an experiment. Only those animals that met the following criteria were used in this study: a leukocyte count <18,000/mm³, a hematocrit >0.36, normal stools, and a good appetite (consuming the entire daily ration). Animals meeting these criteria were fasted 18 h before the beginning of the study to ensure that insulin, a hematocrit of 36%, normal stools, and a good appetite (consuming the entire daily ration). Animals meeting these criteria were fasted 18 h before the beginning of the study to ensure that animals were postabsorptive.

**Experimental protocol.** The experimental protocol is shown in Fig. 1. On the day of the experiment, the catheters and flow probes were freed from subcutaneous pockets by using 2-cm incisions made after application of 2% lidocaine. Saline was infused into the arterial sampling catheter throughout the duration of the study. Dogs were submitted to 150 min of moderate treadmill exercise (n = 8; 4 mph, 12% grade) or an equivalent period of rest in a Pavlov stand (n = 7; time (t) = –190 to –40 min). At t = –110 min, a venous infusion of ICG was initiated and was continued for the duration of the study. This infusion served as a backup measurement of splanchnic blood flow in case the transonic flow probes did not function properly. It was assumed, based on previous work (9), that PVF is ~80% of splanchnic blood flow, whereas hepatic artery blood flow represents the other 20%. ICG was used as a substitute for transonic flow probes in 3 of the 15 experiments. At t = –40 min, exercised dogs were transferred to a Pavlov harness for the remainder of the study. From t = –30 to 0 min, blood samples were taken for baseline measurements. Because the duodenum was empty during this period, no duodenal sample could be obtained. The experimental period (t = 0–90 min) began with the injection of a 150 mg/kg body wt glucose primer (20% dextrose) into the duodenum, followed by a continuous intraduodenal glucose infusion of 8 mg·kg\(^{-1}\)·min\(^{-1}\) (20% dextrose) until t = 90 min. The rate of the intraduodenal glucose infusion was chosen to reproduce glucose levels commonly seen in the portal vein after feeding. At t = 20 min, a bolus containing trace amounts of 3-O-\([^{3}H]\)methylglucose and L-\([^{14}C]\)glucose (25 μCi of each isotope) was injected into the duodenum. At t = 60 min, an intraduodenal bolus of phloridzin (1.97 mg/kg) was given, followed by a continuous intraduodenal phloridzin infusion of 0.1 mg·kg\(^{-1}\)·min\(^{-1}\) for the remainder of the study. At the start of the phloridzin infusion, an isoglycemic clamp was initiated to maintain the arterial glucose concentration at the level seen before phloridzin infusion. At t = 80 min, a second bolus of 3-O-\([^{3}H]\)methylglucose and L-\([^{14}C]\)glucose (100 μCi of each isotope), fourfold larger than the first, was introduced into the duodenum. During the experimental period, blood and duodenal samples were taken every 10 min. In addition to these samples, blood and duodenal samples were taken every minute for 5 min after administration of each tracer bolus. Because \( \Delta \)-glucose and 3-O-methylglucose are transported out of the lumen, less of these sugars makes it to the paracellular gaps, compared with \( \Delta \)-glucose. Consequently, gradients in the ratios of 3-O-\([^{3}H]\)methylglucose to L-\([^{14}C]\)glucose exist. Although these gradients are impossible to measure directly, evidence suggests that they are minimal during the period immediately after the bolus, as direct and indirect measures of luminal sugar ratios give the same result (23). It has been shown in our previous work (23) that determination of the passive fraction of gut glucose absorption using this technique is quantitatively the same as is seen in the work of Lane et al. (17), which measured the absorption of \( \Delta \)-glucose isotopes in isolated perfused jejunal sections over a 2-h period. At the end of the experiment, animals were euthanized with pentobarbital sodium, and an autopsy was performed to confirm catheter and flow probe placement.

**Blood and intraduodenal sample analyses.** Plasma and intraduodenal glucose levels were determined on the day of the experiment by using the glucose oxidase method with a Beckman Glucose Analyzer II (Beckman Instruments, Fullerton, CA). ICG absorption was assessed in arterial and hepatic vein plasma samples at 810 nm after centrifugation (3,000 ×g, 30 min). Those plasma samples that were not immediately analyzed were stored at –70°C for later analysis. Whole blood and intraduodenal samples were deproteinized with barium hydroxide and zinc sulfate to assess the radioactivity of 3-O-\([^{3}H]\)methylglucose and L-[\(^{14}C\)]glucose in blood and duodenal samples. After centrifugation (3,000 ×g, 30 min), the supernatant was dried and reconstituted in 1 ml of water and 10 ml Ultima Gold scintillant (Packard, Meriden, CT). Radioactivity was determined by using a Packard TRI-CARB 2900TR liquid scintillation counter. Plasma insulin

![Fig. 1. Experimental protocol. Arrows indicate the injection of a tracer bolus [25 μCi at time (t) = 20 min and 100 μCi at t = 80 min] of 3-O-[\(^{3}H\)]methylglucose and L-\([^{14}C]\)glucose into the duodenum. Arterial plasma glucose levels were clamped from t = 60–90 min to match concentrations from t = 20–60 min.](http://jap.physiology.org/content/95/3/1133/F1)

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*Glucose 8.0 mg·kg\(^{-1}\)·min\(^{-1}\)*
† Phloridzin 0.1 mg·kg\(^{-1}\)·min\(^{-1}\)
‡ Variable peripheral glucose infusion

**Figure 1.** Experimental protocol. Arrows indicate the injection of a tracer bolus [25 μCi at time (t) = 20 min and 100 μCi at t = 80 min] of 3-O-[\(^{3}H\)]methylglucose and L-[\(^{14}C\)]glucose into the duodenum. Arterial plasma glucose levels were clamped from t = 60–90 min to match concentrations from t = 20–60 min.
and glucagon and blood glucose were measured as described previously (9).

Calculations. Total net gut glucose output (NGGO) was calculated as described by Eq. 1

\[
\text{NGGO} = ([P] - [A]) \cdot \text{PVF} 
\]

where [P] and [A] are portal vein and arterial glucose concentrations, respectively. NGGO during the duodenal glucose infusion is represented as the average NGGO from \( t = 20 \) to 60 min. Calculations of the transporter-mediated and passive components of gut glucose absorption are based on tracer data obtained during the 5 min of sampling after administration of the tracer bolus. Previous work has shown that the calculation of the passive fraction of gut absorption via both direct and indirect assessment of intraduodenal radioactivity yields the same results (23). The direct approach was used in the present study (Eq. 2) to calculate the passive fraction of gut glucose absorption.

\[
\text{Fraction of gut glucose absorption that is passive} = \frac{(1-\text{Glcp} - \text{Glca}) \cdot \text{MGD}}{\text{MGp} - \text{MGa}} \cdot \text{L-GlcD} \quad (2)
\]

where Glcp and Glca are the portal venous and arterial radioactivity of \( ^{14} \text{C} \)-glucose, respectively; MGP and MGA are the radioactivities of 3-O-\(^3\text{H}\)-methylglucose in the portal vein and the artery, respectively; and MGD and MGD are the duodenal concentrations of 3-O-\(^3\text{H}\) methylglucose and \(^{14} \text{C} \)-glucose, respectively. The rates of transporter-mediated and passive absorption were calculated by multiplying the fraction of passive and transporter-mediated absorption by NGGO (Eqs. 3 and 4, respectively).

Net rate of transporter-mediated absorption

\[
\text{Net rate of transporter-mediated absorption} = (1 - \text{Passive fraction}) \cdot \text{NGGO} \quad (3)
\]

Net rate of passive absorption

\[
\text{Net rate of passive absorption} = \text{Passive fraction} \cdot \text{NGGO} \quad (4)
\]

Statistics. All data presented herein are means \( \pm \) SE. ANOVA was performed to assess differences between gut absorption, hormone, and substrate concentrations in sedentary and exercised dogs. Differences were considered significant if \( P < 0.05 \).

RESULTS

Arterial blood glucose, glucose infusion rates, plasma hormones, and PVF. Arterial blood glucose concentrations were not significantly different in exercised (75 \( \pm \) 3 mg/dl) and sedentary (82 \( \pm \) 2 mg/dl) dogs during the basal period (Fig. 2). Arterial blood glucose levels rose to similar levels in both exercising (110 \( \pm \) 7 mg/dl) and sedentary (113 \( \pm \) 5 mg/dl) dogs during the intraduodenal glucose infusion. After the administration of phloridzin, arterial blood glucose levels were maintained at levels seen before phloridzin administration with the peripheral glucose clamp (107 \( \pm \) 6 exercised vs. 107 \( \pm \) 5 mg/dl sedentary). The glucose infusion rate required to maintain isoglycemia was not different in exercised and sedentary dogs (5.19 \( \pm \) 0.70 vs. 4.67 \( \pm \) 0.48 mg.kg\(^{-1} \).min\(^{-1} \)).

Arterial plasma insulin was significantly less in exercised compared with sedentary dogs (4 \( \pm \) 1 vs. 7 \( \pm \) 1 \( \mu \text{U/ml} \)) during the baseline period, whereas glucagon was significantly higher (50 \( \pm \) 5 vs. 33 \( \pm \) 6 ng/ml). During intraduodenal glucose infusion in the absence of phloridzin, insulin rose approximately threefold in each group but remained significantly lower in exercised compared with sedentary (15 \( \pm \) 3 vs. 24 \( \pm \) 5 \mu U/ml) dogs. Arterial plasma glucagon in exercised and sedentary dogs was not different during intraduodenal glucose infusion (40 \( \pm \) 6 vs. 30 \( \pm \) 5 ng/ml). Plasma cortisol levels were significantly higher in the baseline period in exercised dogs (5.4 \( \pm \) 0.9 vs. 2.4 \( \pm \) 1.7 pg/ml). During the intraduodenal glucose infusion, plasma cortisol levels were similar between groups (3.8 \( \pm \) 0.9 vs. 3.9 \( \pm \) 0.7 pg/ml). Catecholamines were not different between groups in the baseline period or during the intraduodenal glucose infusion. Hormone levels, in the presence of phloridzin, were not different between groups.

PVF during the baseline period was significantly higher in exercised dogs (25 \( \pm \) 3 vs. 18 \( \pm \) 2 ml.kg\(^{-1} \).min\(^{-1} \)). However, PVF was not different during the intraduodenal glucose infusion period in the presence (24 \( \pm \) 2 vs. 23 \( \pm \) 4 ml.kg\(^{-1} \).min\(^{-1} \)) or absence (27 \( \pm \) 2 vs. 21 \( \pm \) 3 ml.kg\(^{-1} \).min\(^{-1} \), exercised vs. sedentary dogs) of phloridzin.

NGGO, net transporter-mediated, and net passive glucose output. NGGO was negative in both rested and exercised dogs during the baseline period, reflecting net gut uptake of glucose from the blood (Fig. 3). During the first 60 min of the intraduodenal glucose load, NGGO rose in the sedentary group, averaging 4.02 \( \pm \) 0.53 mg.kg\(^{-1} \).min\(^{-1} \). Prior exercise caused a significant increase in NGGO in the presence of intraduodenal glucose (5.36 \( \pm \) 0.46 mg.kg\(^{-1} \).min\(^{-1} \)). This increase in NGGO was, in part, due to a \( \approx \)65% increase in the percent contribution of passive gut glucose absorption to total NGGO, which was \( \approx \)11% in sedentary dogs and 18% in exercised dogs (Fig. 4). This increase in the percent contribution of passive absorp-
tion was reflected by a doubling in the net rate of passive gut glucose absorption (0.93 ± 0.06 vs. 0.45 ± 0.07 mg·kg⁻¹·min⁻¹). The rate of transporter-mediated absorption increased ~20% with exercise but was not significantly different from that in sedentary dogs (4.41 ± 0.45 vs. 3.57 ± 0.48 mg·kg⁻¹·min⁻¹). After the administration of phloridzin, NGGO decreased in both sedentary and exercised dogs, so that rates in neither group were significantly different from zero (Fig. 3).

DISCUSSION

It was shown previously that absorption of intraduodenal glucose is accelerated after a bout of prolonged, moderate-intensity exercise (9). The increased gut glucose absorption facilitates the delivery of glucose to glycogen-depleted tissues (liver and muscle), accelerating replenishment of these stores. The method presented here is an extension of the method described by Uhing and Kimura (32) that we have previously adapted for use in the dog model (23). The experimental protocol takes advantage of arteriovenous and duodenal sampling techniques, as well as isotopic tracer methodology to determine the contributions of transporter-mediated and passive processes to the absorption of an intraduodenal glucose load in sedentary and exercised dogs. The components of gut glucose absorption have also been measured by the disappearance of glucose analogs from the gut (6, 17). Measuring passive absorption via this technique is difficult, because it is a relatively small component of total gut absorption and is reliant on the disappearance of a small fraction of the passive absorption marker from the gut. The appearance of tracers in the portal vein was used to calculate the contributions of passive and transporter-mediated processes to total gut glucose absorption. This method was first described by Uhing and Kimura (31) and adapted for use in the dog (23). The advantage of this for determination of passive transport is that, at the time of the first bolus, absorption of the passive marker, L-[¹⁴C]glucose, occurs on a background of zero and is relatively easy to detect. The appearance of tracers in the portal vein was assessed over a short interval after delivery of the bolus. This was done to minimize gradients in the ratio of tracers in the duodenal lumen. It should be noted that this technique gives the same results for the percent contribution of passive gut glucose absorption as previous work done by Lane et al. (17), in which isolated jejunal segments were perfused for 2 h.

The present studies and previous work (17, 23, 32) assessing passive gut glucose absorption have used L-glucose as a marker for the passive process. A considerable volume of work suggests that L-glucose does not interact with the SGLT-1 transporter (6, 13, 17, 32). For example, in basolateral membrane vesicles isolated from rat small intestine, the presence of 100 mM L-glucose did not inhibit radioactive D-glucose uptake, suggesting that L-glucose does not interact with the transporter (38). Work done by Ikeda et al. (13), using vesicles isolated from rabbit small intestine and Xenopus oocytes expressing a cloned version of SGLT-1, showed with competition experiments that L-glucose had no effect on D-glucose uptake. However, results of a study in the rat led to the conclusion that the present studies and previous work (17, 23, 32) assessing passive gut glucose absorption have used L-glucose as a marker for the passive process. A considerable volume of work suggests that L-glucose does not interact with the SGLT-1 transporter (6, 13, 17, 32). For example, in basolateral membrane vesicles isolated from rat small intestine, the presence of 100 mM L-glucose did not inhibit radioactive D-glucose uptake, suggesting that L-glucose does not interact with the transporter (38). Work done by Ikeda et al. (13), using vesicles isolated from rabbit small intestine and Xenopus oocytes expressing a cloned version of SGLT-1, showed with competition experiments that L-glucose had no effect on D-glucose uptake. However, results of a study in the rat led to the conclusion that the present studies and previous work (17, 23, 32) assessing passive gut glucose absorption have used L-glucose as a marker for the passive process. A considerable volume of work suggests that L-glucose does not interact with the SGLT-1 transporter (6, 13, 17, 32). For example, in basolateral membrane vesicles isolated from rat small intestine, the presence of 100 mM L-glucose did not inhibit radioactive D-glucose uptake, suggesting that L-glucose does not interact with the transporter (38). Work done by Ikeda et al. (13), using vesicles isolated from rabbit small intestine and Xenopus oocytes expressing a cloned version of SGLT-1, showed with competition experiments that L-glucose had no effect on D-glucose uptake. However, results of a study in the rat led to the conclusion that the present studies and previous work (17, 23, 32) assessing passive gut glucose absorption have used L-glucose as a marker for the passive process. A considerable volume of work suggests that L-glucose does not interact with the SGLT-1 transporter (6, 13, 17, 32). For example, in basolateral membrane vesicles isolated from rat small intestine, the presence of 100 mM L-glucose did not inhibit radioactive D-glucose uptake, suggesting that L-glucose does not interact with the transporter (38). Work done by Ikeda et al. (13), using vesicles isolated from rabbit small intestine and Xenopus oocytes expressing a cloned version of SGLT-1, showed with competition experiments that L-glucose had no effect on D-glucose uptake. However, results of a study in the rat led to the conclusion that the present studies and previous work (17, 23, 32) assessing passive gut glucose absorption have used L-glucose as a marker for the passive process. A considerable volume of work suggests that L-glucose does not interact with the SGLT-1 transporter (6, 13, 17, 32). For example, in basolateral membrane vesicles isolated from rat small intestine, the presence of 100 mM L-glucose did not inhibit radioactive D-glucose uptake, suggesting that L-glucose does not interact with the transporter (38). Work done by Ikeda et al. (13), using vesicles isolated from rabbit small intestine and Xenopus oocytes expressing a cloned version of SGLT-1, showed with competition experiments that L-glucose had no effect on D-glucose uptake. However, results of a study in the rat led to the conclusion that
L-glucose is not a valid marker for passive gut glucose absorption (26). It was suggested in this study that differences existed in the gut absorption of L-glucose compared with other nonmetabolized hexoses. It should be noted that gut absorption of the hexoses was determined by their subsequent urine collection. This is an indirect assessment of intestinal absorption and can be affected by differential renal handling (33). Additionally, if L-glucose had a significant, but minor, affinity for the SGLT-1 transporter and the changes in gut glucose absorption with exercise could be ascribed completely to transporter-mediated absorption, then the increase in what we describe as the passive component should be accompanied by a large and unambiguous increase in transport-mediated gut glucose absorption. Nevertheless, one cannot rule out from the present study that there is a fraction of L-glucose that is transported, and this possibility must be considered.

The work presented here shows that the increase in NNGO after exercise is accompanied by an increase in passive gut glucose absorption. Whereas the increase in transporter-mediated gut glucose absorption was not significant, it did tend to be higher as well. Despite this tendency for an increase in transporter-mediated absorption, its actual percent contribution to NNGO was decreased. We observed only a 24% nonsignificant increase in transporter-mediated absorption. A power analysis indicated that we had the power to detect a 50% change in transporter-mediated gut glucose absorption with a power of 0.95, with n = 7, assuming equal variance between groups. It should be noted, however, that, based on our subject number and the observed variance between groups, there is a ~18% chance that a type II statistical error occurred, which could have resulted in failure to detect a significant difference between groups. In both sedentary and exercised dogs, NNGO was less than the infusion rate of glucose into the duodenum. The differences between the infusion rate and NNGO can be attributed to glucose metabolism by the gut and delayed absorption of glucose over time (1). Previous work in the dog has shown that, when a glucose load is delivered to the gut, ~15–18% of that load is metabolized by the gut itself (1, 19). Additionally, previous work in the conscious dog model showed that, in the presence of an intraduodenal glucose infusion, there was a gradual increase in tracer-determined gut glucose absorption over time that approached the duodenal infusion rate (19).

There are several possible mechanisms for this increase in passive NNGO during an intraduodenal glucose load. Metabolic stresses such as exercise (9) and fasting (7) result in increased NNGO during an intraduodenal glucose load. These conditions are characterized by an increase in gut proteolysis, which serves to increase gluconeogenic substrate supply to the liver (8). This increased proteolysis could impair the gut’s ability to function as a barrier during feeding when it follows such a physiological stress.

Exercise is characterized by changes in circulating hormone levels, which result in increased production of glucose to meet the increasing energy demands of the body. There are several potential endocrine responses that are known to occur during exercise that, as a result of prolonged exposure during exercise, could potentially affect nutrient absorption in response to subsequent feeding. It has been reported that β-adrenergic stimulation of the small intestine in rats (14) and sheep (2) by epinephrine results in increased gut glucose absorption. The primary target of such stimulation has been postulated to be the SGLT-1 transporter. It is conceivable that this increase in catecholamines seen during prolonged exercise could enhance gut glucose absorption during feeding after exercise. Whereas a significant increase in transporter-mediated absorption was not observed, in the present study we do show that the passive component of gut glucose absorption under both sedentary and exercised conditions is indirectly dependent on SGLT-1 stimulation. In addition to the potential role of epinephrine in stimulating gut glucose absorption, the elevation in plasma glucocorticoid concentrations during exercise (27) could also conceivably lead to an enhancement in NNGO during an intraduodenal glucose load. Dexamethasone treatment in conscious rats increased the absorption of glucose by the gut after the delivery of an oral glucose load (29). Additionally, work done in rabbits has shown that the injection of dexamethasone can increase gut glucose absorption for extended periods of time after this treatment (12). During prolonged exercise, glucagon levels rise, whereas insulin decreases (35). Previous work has shown that elevated insulin levels increase gut glucose absorption (30), whereas increased levels of glucagon cause a delay in absorption (28). The intraduodenal glucose infusion still resulted in increased NNGO in exercised dogs, despite the prolonged exposure to reduced insulin, which persisted into the glucose infusion period, and elevated glucagon levels. In addition to the potential impact of these exercise-induced hormonal changes, the impact of exercise on splanchnic blood flow could potentially lead to alterations in gut absorption in the postexercise state. Previous work has shown that the changes in blood flow alter gut glucose absorption (34, 37). After the period of exercise or rest, PVF was significantly higher in exercised compared with sedentary dogs. During the intraduodenal glucose infusion, PVF was comparable in both groups. Even though blood flow was similar in both groups, potential changes in the microcirculation of the blood vessels perfusing the gut could facilitate the absorption of glucose from the gut.

In sedentary dogs, the delivery of a tracer bolus in the presence of phloridzin does not result in an increase in circulating radioactivity of either isotope, indicating an impairment of passive as well as transporter-mediated absorption. This finding is consistent with previous work that showed that a requisite amount of active transport is required for passive transport to occur (20, 21). In exercised dogs, where passive glucose absorption is enhanced, absorption of both glucose analogs is still inhibited by phloridzin administration, indicating that the enhanced passive glucose absorption after exercise is also dependent on
transport-mediated gut absorption. This suggests that the same fundamental processes are involved.

Transporter-mediated and passive gut glucose absorption have been calculated by using both direct and indirect estimates of intraduodenal glucose analog radioactivity because of inherent difficulties in duodenal sampling (23). In previous work that describes these calculations, there was no significant difference between the results obtained using different calculation methods (23). In this experiment, only data from the calculation of the passive fraction by using direct duodenal sampling are presented. It should be noted that the passive fraction was calculated by using equations both reliant on and independent of direct duodenal sampling and that there was no difference between results obtained with different calculation methods (data not shown).

After exercise, the delivery of an intraduodenal glucose load resulted in an increase in total NGGO. This was accompanied by a 65% increase in the percent contribution of the passive component of gut glucose absorption and an associated 100% increase in the mass of glucose absorbed by the passive process. Intraduodenal infusion of phloridzin, an inhibitor of the SGLT-1 transporter, completely abolishes NGGO during an intraduodenal glucose load in sedentary dogs. Here we show that NGGO during an equivalent glucose load is also not significantly different from zero in the presence of phloridzin in exercised dogs. Additionally, the absorption of L-[14C]glucose after the administration of the second tracer bolus was completely eliminated. These findings indicate that the added passive gut glucose absorption in the postexercise state is also dependent on a requisite rate of transporter-mediated gut glucose absorption.

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DISCLOSURES

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